INFRASTRUCTURE

INFR8: CIRM Community Care Centers of Excellence

REQUEST FOR APPLICATIONS

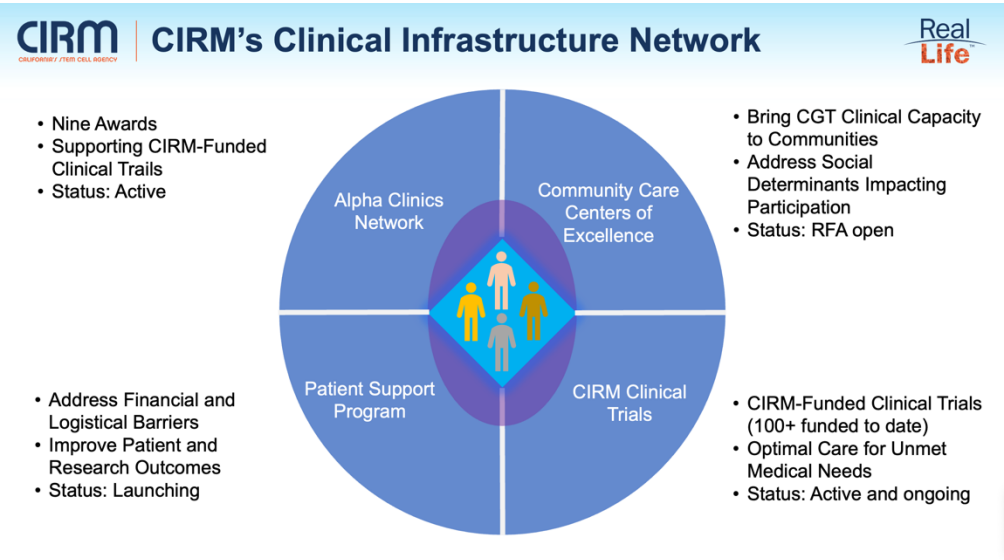
04.03.24

INFR8: CIRM Community Care Centers of Excellence

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. Proposition 14 promotes the accessibility of regenerative medicine treatments by expanding the number and geographic reach of centers where specialized treatments can be accessed. The proposition directs CIRM to administer three programs aimed at expanding access to treatments arising from institute-funded research: (1) the Alpha Clinics, (2) the Patient Support Fund, and (3) the Community Care Centers of Excellence[1].

In October 2022, the ICOC approved nine Alpha Clinics awards which are now supporting CIRM's Clinical Stage Programs (CIRM-funded clinical trials).[2,3] The ICOC have also approved funding for the Patient Support Program in March 2024 to administer the Patient Support Fund.[4] The Patient Support Program will provide informational, logistical, and financial support to patients seeking specialized treatments. This request for applications (RFA) is intended for the Community Care Centers of Excellence program. Collectively, these three programs will be referred to in this RFA as CIRM's "Clinical Infrastructure Network."



Achieving broad population representation in clinical research is vital to CIRM's scientific mission, in part, because such representation is necessary for a complete

[1] https://www.cirm.ca.gov/wp-content/uploads/archive/files/about_cirm/Prop-14-full-text.pdf
[2] https://www.cirm.ca.gov/wp-content/uploads/archive/files/agenda/INFR4%202022%20Alpha%20Clinics%20Summaries.pdf
[3] https://www.cirm.ca.gov/clinical-trials/
[4] https://www.cirm.ca.gov/wp-content/uploads/2023/08/INFR7-PSP-08_11_23-rev.pdf

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and comprehensive evaluation of new treatments. To support an inclusive population representation, all CIRM-funded clinical trials include a diversity, equity, and inclusion (DEI) plan, which is evaluated for merit at the application stage and progress on the plan is monitored during the award period. Further, the state of California has identified "vulnerable populations" to be considered in health planning and reporting with ultimate the aim of reducing health disparities.[5,6]

CIRM has performed a needs assessment and recognizes that social and economic determinants (varying both geographically and within defined sub-populations) contribute to disparities in research participation. 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. The CCCEs will work in partnership with the Clinical Infrastructure Network and other CIRM programs to expand equitable access to communities and populations that would otherwise have more limited opportunities in the absence of these centers.

Contact

For information about this program announcement, send email correspondence to:

ccce@cirm.ca.gov

[5] https://leginfo.legislature.ca.gov/faces/billTextClient.xhtml?bill_id=202120220AB1204
[6] https://www.gov.ca.gov/wp-content/uploads/2022/09/9.13.22-EO-N-16-22-Equity.pdf

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Award Information

How is the program structured?

Core Activities

Applicants must propose performance of the following core program activities under this award:

- **Clinical Trial Support**: Applicants must be able to provide patients access (referrals) to FDA regulated regenerative medicine clinical trials or approved products available within CIRM's Clinical Infrastructure Network. Applicants must be a licensed and certified healthcare facility[7] with a demonstrated capacity to support human subjects' protocols[8] consistent with FDA guidelines[9] in a health research context. CIRM funding may be used to develop the capacity to support clinical research protocols involving cell, gene or regenerative medicine treatments. Applicants may propose to operate (1) a Support Site or (2) a Support and Delivery Site.

  1. **Support Site Only**: A Support Site will facilitate patient access to FDA regulated regenerative medicine clinical trials or approved products available within CIRM's Clinical Infrastructure Network.

     Support Sites must have the infrastructure to perform clinical activities necessary for facilitating patient access to regenerative medicine clinical trials or approved products. These activities include:

     - Clinical trial cohort identification, outreach, and engagement
     - Patient navigation including referrals to CIRM's Clinical Infrastructure Network.
     - Clinical research support including screening, enrollment, pretreatment evaluation or work up, or post-intervention follow-up and monitoring, and evaluation of outcomes (Real World Evidence).

     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.

  2. **Support and Delivery Site**: Support and Delivery Sites should (a) perform the clinical support activities described above in addition to (b) delivering investigational or approved regenerative medicine products. These additional activities include:

     - Working with sponsors to initiate clinical trial agreements or contracts for the delivery of approved products.
     - Developing operations and management systems to address the unique technical needs of performing regenerative medicine clinical trials or delivering approved products including manufacturing, processing, and delivery.
     - Enrolling and providing coordinated care to patients in clinical trials or the delivery of approved products.

[7] https://data.chhs.ca.gov/dataset/healthcare-facility-locations
[8] https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html

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- **Career Development:** Applicants must propose career development programs to advance the knowledge or experience of physicians, nurses, research coordinators, community health workers or other health care professionals that are integral to the education, navigation or delivery of regenerative medicine clinical trials or 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 programs for the placement of trainees participating in CIRM-funded education programs. Applicants should apply the MRCT Workforce Development Logic Model[10] to describe their career development program.

  Programs may include educational seminars intended to provide health care providers with information related to the delivery of regenerative medicine clinical trials and treatments. Applicants should consider how health education or delivery occurs among underserved populations in their catchment area and propose activities that facilitate or otherwise support sustainable workforce education, training or certification. Examples include the development of training or certification programs designed to qualify patient navigators or community health worker for providing services eligible for reimbursement.[11]

- **Outreach and Engagement**: Applicants must develop outreach and engagement programs to enable awareness and informed access to clinical trials, regenerative medicine treatments and career development opportunities. Programs should be adapted to the needs of different populations and serve to support the successful attainment of DEI objectives. Programs may seek to address a range of barriers or conditions that contribute to disparate access to treatments**.** Programs should include the capacity to inform patients about clinical trials being conducted in CIRM's Clinical Infrastructure Network. Applicants should apply the MRCT Participant and Community Engagement Logic Model[12] to describe their outreach and engagement program.

  Applicants should consider opportunities to facilitate referral and access to care authorized under the California Cancer Care Equity Act[13] with specific emphasis on referring patients to clinical trials being conducted at Alpha Clinic or CCCE sites. Applicants may propose engagement, education, or navigation of families participating in newborn genetic screening programs where participants may benefit from regenerative medicine treatments offered in the Clinical Infrastructure Network.

- **Community-Based Partnerships**: Applicants must allocate a minimum of $625,000 in the award budget for community-based partnerships. Applicants should propose at least one partnership with a community-based organization or organizations to support clinical research, career development and/or outreach and engagement. Emphasis should be placed on supporting activities that

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

[10] MRCT Center Diversity Toolkit Version 1.0 July 2020 https://mrctcenter.org/diversity-in-clinical-research/wp-content/uploads/sites/8/2021/03/5-Fillable-Logic-Model-Workforce-Development.pdf

[11] https://www.cms.gov/newsroom/press-releases/cms-finalizes-physician-payment-rule-advances-health-equity

[12] MRCT Center Diversity Toolkit Version 1.0 July 2020 https://mrctcenter.org/diversity-in-clinical-research/wp-content/uploads/sites/8/2021/03/4-Fillable-Logic-Model-Participant-Community-Engagement.pdf

[13] https://leginfo.legislature.ca.gov/faces/billTextClient.xhtml?bill_id=202120220SB987

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reduce disparities and support broad representation in clinical research. Examples include:

- Targeted interventions aimed at reducing disparities in referrals to clinical trials with the overall aim of increasing the referral or participation rates of medically underserved patients and vulnerable populations. Interventions may include engagement or partnerships with patients/communities, primary care providers, provider networks and professional associations.
- Partnerships with sovereign groups including American Indian tribes where established norms and policies govern the conduct of research, management/ownership of data and reporting of results. Such partnerships should seek to bring visibility to opportunities for regenerative medicine treatments to address unmet medical needs in accordance with prevailing norms and policies.
- Engagement of military veterans to support access to regenerative medicine opportunities. Veterans have an elevated prevalence of neurological conditions that may be ameliorated through CIRM programs focused on research and development of treatments for diseases of the brain and central nervous system (CNS). The CIRM program needs assessment suggested veterans are particularly interested in regenerative medicine approaches, but informational and access barriers exist.

Applicants should discuss how community-based partnerships can address informational, economic, or social determinants impacting access to regenerative medicine treatments. Creating community-based partnerships is expected to make research more relevant to participants and communities and speed the translation of discoveries into practice.[14] Efficacious partnerships will serve to produce the following outcomes:

- **Trust**: Trust and trustworthiness of the profession (professionals, researchers, healthcare systems) by the individual and the community are important considerations during communications and collaborations between researchers and participants/community groups.
- **Respect**: Patients, participants, and communities should be seen and treated as important partners in research and should know what they deserve and should expect from the partnership and research. Each other's expertise is recognized in a bidirectional co-learning process.
- **Capacity-building (benefit)**: Partnerships should serve to build the capacities or field strength of all partners. In the context of this program, one important outcome is developing sustainable capacity to address barriers or conditions that contribute to disparate access to treatments.

Applicants should consider whether partner activities require research ethics, compliance and safety training and set aside funds for this purpose.

CIRM recognizes that community-based partnership opportunities may evolve over the award period in relation to factors such as the completion of additional needs assessment, new clinical trial opportunities, the emergence of partners as the CCCE program gains visibility, or new opportunities provided by CIRM's clinical infrastructure network. Applicants may discuss a process or framework for developing partnerships in the context of their program without committing to

[14] https://allofus.nih.gov/sites/default/files/elsi_engagement_and_retention.pdf

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specific partnerships at the time of application. New partnership agreements may be developed over the life of the award.

- **Network Collaboration and Development**: The Community Care Centers of Excellence should work in collaboration with the Alpha Clinics and Patient Support Program to assist patients in accessing clinical trials and approved treatments. Each awardee will be required to contribute to a steering committee and working groups designed to advance the objective and strategic aims of this program. Steering committee functions include: supporting consistent and coordinated program implementation, facilitating collaborative opportunities between Clinical Infrastructure Network members, and proposing new capacities consistent with the program's objectives.
- **New Capacities:** Applicants 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, Centers may propose new capacities, consistent with CCCE program objectives, to improve overall performance.

Applicants are encouraged to propose holistic and integrated approaches for satisfying the objective of this program. Specifically, consider how your clinical, career development, community-based partnership and network development initiatives can work in tandem or synergistically to enhance the capacity of CIRM's Clinical Infrastructure Network to treat patients and address barriers or conditions that contribute to disparate access.

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 clinical, career development or engagement and outreach programs.
- ✓ Partnerships with community-based organizations.

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

- ✘ Direct cost of providing an investigational product or approved product to patients.
- ✘ Activities and costs already supported under another CIRM award.

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What is the award amount and duration?

The CIRM Governing Board has allocated $60.2 million for funding of the CCCE program to support the (1) core operations, (2) community-based partnerships, (3) building renovation, and equipping facilities for a five-year duration. This opportunity provides two categories of award based on whether the proposed site will offer clinical trial support only or both support and deliver as shown below.

- A Clinical Trial Support Site may request a total award amount of up to $7.5 million per award.
- A Clinical Trial Support and Delivery Site may request a total award amount of up to $10.054 million per award.

Community-Based Partnership Funds

All applicants must allocate $625,000 ($125,000 per year average) from the total award amount to community-based partnerships. This amount reflects a minimum commitment and applicants may commit additional funds for community-based partnerships in their proposed budget. Funds will be released by CIRM on receipt of a partnership agreement between the applicant organization and the community-based partner(s) and/or their fiscal agent. These funds can be distributed at the discretion of the applicant organization over the life of the award, and specific partnership agreement do not need to be in place at the time of application.

Facilities Funding

Applicants may allocate funds from the total award amount to support facilities renovation and/or equipment. Funds may be utilized for renovating existing facilities or acquiring equipment 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 are not be limited to:

- Renovation of facilities necessary for the delivery of investigational or approved products to patients
- Purchasing or leasing equipment for the manufacturing or processing of products, including but not limited to mobile manufacturing facilities
- Renovation of facilities necessary to navigate, screen or follow up with patients who are participating in clinical trials or receiving approved treatments

Pursuant to Proposition 14, CIRM shall prioritize applications for 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. Funds will be disbursed pursuant to a CIRM Notice of Award. The first payment will be issued upon initiation of an award, and subsequent payments will be disbursed on a regular interval at CIRM's option. Continued funding is contingent upon timely progress, as outlined in the project milestones and timeline established under the Notice of Award.

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** involve additional funding from CIRM (see "Plans for Risk Mitigation & Financial Contingency" under application components).

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 120 days of approval

Given the urgency of CIRM's mission, the approved awardee 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) Must be a non-profit organization located in California

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 hospital/clinics and facilities accreditations and operational medical facilities in California.

(3) Must have demonstrated ability to perform human subjects research in a health research context

Applicants must have a licensed and certified healthcare facility[15] with a demonstrated capacity to support human subjects protocols[16] consistent with FDA guidelines[17] 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 collaboration with established training or accreditation programs. Proposed collaborations should be described in a letter of support or memorandum of understanding.

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

(5) Patient Protections

The licensed and certified healthcare facility associated with the application must not provide direct to consumer fee for service interventions involving "stem cell therapies"[18] 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"

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

- The applicant' Chief Executive Officer, Chief Financial Officer, or Chief Operational Officer 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 applicant 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.

Who can apply?

Organizations Eligible to Apply for this Opportunity

Only California organizations can 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 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 objectives and not less than 30% on average over the project period. (Note: "project" includes both the CIRM-funded and applicant co-funded components.) Any effort for which salary from CIRM is claimed must be expended in California.
- Must be authorized by the applicant organization to conduct the work and assume the responsibilities of the PD.

[18] "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 ***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 Community Care Center of Excellence program will be required to provide a statement describing:

- 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.
- How the assembled site team and collaborators will bring diverse and inclusive perspectives and experience to the implementation of proposed activities.
- How the research team demonstrates a successful track record for promoting and valuing diversity, equity, and inclusion (DEI).

Evaluation and Knowledge Sharing Plan

Knowledge sharing contributes 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 center's (1) core competencies, (2) training programs and (3) outreach and engagement efforts. Applicants should propose how this information can be made available to CIRM collaborators and the broader community.

All CIRM Clinical Infrastructure Programs are required to capture and report general metrics associated with the recruitment and accrual of patients in clinical trials. Applicants should describe their capacities to capture and report data related to patient recruitment and accrual.

This program represents a unique CIRM funding opportunity to develop individual, programmatic, organizational and systems-level knowledge to expand access to regenerative medicine treatments. Knowledge gained from this program should inform CIRM's broader commitment to polices aimed at increasing access to regenerative medicine treatments. Applicants should describe their methodologies for ensuring robust evaluation, synthesis and reporting of knowledge gained from program implementation. Include considerations for returning results to participants, community partners, policy makers and the public. Responsive proposals should include qualitative and quantitative methodologies and culturally appropriate dissemination methods.

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Application Review Information

Schedule and Deadlines

Applications Due	2:00 pm (PDT/PST) on August 15, 2024
Grants Working Group (GWG) and Facilities Working Group (FWG) Review	Approximately 90 days post submission
Application Review Subcommittee of the ICOC Review and Approval	Approximately 120 days post submission
Award Start	Must start within 120 days of award approval

What is the process for evaluating an application?

Pre-submission Consultation

Prospective applicants are encouraged to contact CIRM before applying with questions or to discuss their project's eligibility or budget considerations.

Eligibility Review

CIRM will assess whether the proposed project meets eligibility requirements. 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 if CIRM deems it appropriate, allow an opportunity to remedy. If CIRM deems it inappropriate, or if the applicant does not remedy the deficiency in a timely manner, CIRM will terminate all further action on the application.

CIRM may exercise its authority to make eligibility determinations at any time before an award is executed.

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 https://www.cirm.ca.gov/board-and-meetings/board/.

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.

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

Facilities Review

The merit of renovation and capital equipment plans described in the application will be assessed by the Facilities Working Group (FWG), which is composed of six patient advocates from the CIRM Governing Board (ICOC), four real estate specialists, and the Chair of the ICOC. The FWG makes recommendations regarding funding for buildings and capital equipment to the Application Review Subcommittee.

The eleven members of the FWG will evaluate the renovation and capital equipment sections of the applications and score them applying the review criteria described below for facilities components. The FWG 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 FWG's review; or 3) do not fund the project and do not allow resubmission.

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?

Members of the GWG will evaluate and score applications based on the following four review criteria:

1. Does the proposed CCCE offer a significant value proposition that would enhance the ability of CIRM's Clinical Infrastructure Network to expand equitable access to regenerative medicine treatments?

Would the proposed CCCE accelerate and/or expand access to regenerative medicine treatments?

Would the proposed center expand the value of CIRM's Clinical Infrastructure Network; for example, broadening the Network's reach, providing new expertise, offering new or unique career development opportunities, or contributing to trust building, respect and new capacities / benefits to proposed partners?

Does the proposed center offer a sufficient, impactful, and practical value proposition for patients, trial sponsors and/or health care providers?

2. Is the project well planned and designed?

Are the clinical operations appropriately planned and designed to provide meaningful, accelerating, and impactful resources that will expand the accessibility of regenerative medicine treatments?

Do the proposed career development activities serve to develop the workforce integral to the delivery of regenerative medicine treatments?

Do the proposed outreach and engagement activities meaningfully address the referral gap experienced by vulnerable and underrepresented populations?

Do proposed community-based partnerships hold the potential to address informational, economic, or social determinants impacting access to regenerative medicine treatments?

Does the proposal include meaningful collaboration with the Alpha Clinics to assist patients in accessing clinical trials and approved treatments?

Will the evaluation plan contribute to robust evaluation, synthesis and sharing of knowledge gained from program implementation?

3. Is the project feasible?

Is the plan feasible and likely to be implemented within the proposed timeline?

Does the applicant have appropriate experience conducting human subjects research?

Is the proposed team appropriately qualified and staffed and have access to all the necessary resources to support patients, career development, outreach and engagement programs and community-based partnerships?

For Support and Deliver sites, does the applicant have appropriate experience conducting clinical research and, do they possess the ability to manage investigational or approved regenerative medicine products within the project timeline?

4. Will the proposed center effectively serve the needs of underserved, disproportionately affected communities or vulnerable populations?

Do the proposed activities hold the potential to increase referrals or access (e.g. enrollment) of underserved and disproportionately affected communities or vulnerable populations to clinical trials or approved treatments?

Does or will the applicant team offer effective tools and resources to engage and recruit demographically diverse patient cohorts?

Does or will the project team bring diverse and inclusive perspectives and experience to the implementation of proposed activities?

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How will the merit of the facilities components be evaluated?

Members of the FWG will evaluate and score applications based on the following key questions:

1. Does the proposed renovation/facilities improvement project support the applicant's proposed CCCE activities?

Does the scope of work, as defined by the facilities narrative, plans, and other relevant information, describe a facility that best supports the goals of the proposed CCCE?

Is the proposed location of the facility appropriate for its goals?

2. Are the renovations/facility improvements feasible as proposed?

Is the proposed construction timeline, including key milestones and activity timelines, feasible and appropriate for the project?

Is the project staffed with appropriate levels of renovation/construction expertise?

3. Does the proposal include the appropriate equipment and clinical facilities to support the proposed CCCE activities?

Do the plans include appropriate physical infrastructure to support the proposed use?

Is the space layout appropriately designed for the intended use?

4. Are the renovation/facility improvement costs appropriate?

Do the proposed costs adequately account for design, construction, equipment, contingencies, and any other anticipated costs?

5. Does the applicant ensure diversity, equity and inclusion goals for design and construction?

Is the project appropriately budgeted to adhere to the prevailing wage requirements of Prop 14?

Is the applicant committed to diversity, equity and inclusion for design and construction contracts?

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 applicant must create a login in the system to access application materials and apply. Applications are available in the system only to the PD and their designee. A PD may submit only a single application.

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What components does an application include?

The Grants Management Portal provides instructions for completing all the necessary components and submitting a final application. The application is designed to collect information necessary to appropriately evaluate the proposal and for CIRM to rapidly initiate an award if approved for funding. Applicants are required to indicate key personnel, collaborators and partners involved in the project, describe how the proposal addresses the objectives of the funding opportunity, provide a detailed plan of proposed activities, complete a detailed budget, and provide reference materials that confirms the status of the project.

The main body of the Scientific Proposal contains the following sections:

1. **Program Summary:**

Provide a brief description of the overall structure and objectives of the proposed Community Care Center of Excellence.

2. **Value Proposition/Strategic Aims:**

   a. Discuss how your proposed center represents a holistic and integrated approach for satisfying the objective and strategic aims of this program.

   b. How will clinical, career development, community-based partnership and network development initiatives work in tandem or synergistically to enhance the capacity of CIRM's Clinical Infrastructure Network to address barriers or conditions that contribute to disparate access to treatments.

3. **Plan and Rationale for Performing Required Activities:**

   a. Describe how the proposed center will support and expand access to clinical trials or regenerative medicine treatments. Describe the level of clinical support you aim to provide and develop over the award period (e.g. cohort identification, patient screening, enrollment, pretreatment evaluation or work up, post-intervention follow-up and monitoring, and evaluation of outcomes). Discuss how the center will be responsive to any unique needs of the populations being served.

      For support and delivery sites, describe how you plan to deliver investigational products or approved regenerative medicine treatments. Describe how you will ensure the clinical team will satisfy certification or accreditation requirements for the delivery of cell or gene therapies.

   b. Describe how the proposed center will support 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. How will the center collaborate with the Alpha Clinics or CIRM Education programs to adapt, expand, or otherwise utilize established training opportunities.

   c. Describe how your outreach and engagement programs will enable awareness and informed access to clinical trials and regenerative medicine treatments. Discuss how broader awareness among the audiences contemplated for this program will serve to expand equitable access to regenerative medicine treatment opportunities. Explain how will the program

address barriers or conditions that contribute to disparate access to treatments.

d. Describe how the centers community-based partnerships will support clinical research, career development and/or outreach and engagement. Discuss how the partnership(s) will build trust, respect, and benefit. Explain what existing gaps are intended to be filled by the community-based partnership. Explain how will these partnership(s) address informational, economic, or social determinants impacting access to or participation in research. Address how you propose to manage partnership agreements to ensure successful outcomes. Describe steps to be taken to ensure community partners have appropriate field competency and research ethics, compliance and safety training?

4. **Add value to CIRM's Clinical Infrastructure Network:**

   a. Describe how the proposed center would expand the value of the CIRM's Clinical Infrastructure Network.

   b. Describe how the clinic will coordinate with the Network partners (Alpha Clinics and Patient Support Program) to expand referrals to and enrollment in clinical trials.

5. **Network Integration Plan:**

   a. Describe any proposed collaborations with Alpha Clinic sites or other CCCE applicants.

   b. Discuss how these collaborations will (i) increase access to treatments to those patients most likely to benefit, (ii) integrate cell and gene therapy expertise into other collaborators, and (iii) ensure broad access to treatments for all Californians.

6. **Timeline**:

Provide an activities-based timeline for clinic set-up, establishment of training program(s) and development of lead offerings in Gantt chart-like format.

7. **Project Team**.

   a. Describe the qualifications and staffing of the team and proposed collaborators that support its ability to establish, operate, and maintain the center according to the proposed project plan and timelines.

   b. Describe the team structure, leadership, and communications plan.

8. **Organizational Experience, Capacity, and Resources.**

   a. Describe organizational experience, capacity, and resources that demonstrate the capacity to support or deliver clinical trials.

   b. Explain how the proposed center will overcome existing gaps that currently limit patient access to regenerative medicine clinical trials or approved products.

   c. Identify your organizational experience conducting human subjects research and implementing a human subjects protection programs.

      For support and delivery sites, describe how you proposed to perform IRB review of clinical protocols, perform safety monitoring or other required oversight activities.

   d. Describe the proposed service area of your clinic (include a map if available) and populations served including any satellite or affiliated sites that can be

utilized to achieve the objectives of this program. Discuss how your proposed configuration of sites and service providers increases the likelihood of patients enrolling in clinical trials or accessing approved products.

e. Describe available organizational capacities and resources that will enable the team to successfully implement the proposed project plan.

9. Addressing Underserved Communities.

Provide a statement describing:

a. How the center will support and facilitate outreach and study participation by underserved and disproportionately affected populations in the clinical trials they serve.

b. How the assembled center team and community-based partners will bring diverse and inclusive perspectives and experience to the implementation of proposed activities.

c. How well the center's team demonstrates a successful track record for promoting and valuing diversity, equity and inclusion (DEI).

10. Evaluation and Knowledge Sharing Plan:

Describe plans intended to capture operational information vital to evaluating or replicating the (1) center's core clinical competencies, (2) training programs and (3) outreach and engagement efforts. Describe capacities to capture and report data related to patient recruitment and accrual. Propose metrics to measure the success of interventions aimed at reducing disparities in referrals to clinical trials or participation rates of medically underserved patients and vulnerable populations. Include considerations for returning results to participants, community-based partners, policy makers and the public. Include qualitative and quantitative methodologies and socially and culturally appropriate dissemination methods.

11. Contingency Plan:

Summarize potential risks, costs associated with those risks, and mitigation strategies, together with a financial contingency plan outlining viable funding sources in the event that costs exceed the amount of funding disbursement. Discuss how you would adapt outreach and engagement programs or community-based partnerships in light of rapid advances and changes in the field of regenerative medicine.

12. References:

List all references used in the body of the proposal.

The main body of the <u>Facilities Proposal</u> contains the following sections (if renovation or major equipment costs are requested):

1. Renovation/Facility Improvements Project - Executive Summary:

High-level summary describing how the proposed CCCE renovations/facility improvements support the proposed CCCE core activities, including expanding access to clinical trials or regenerative medicine treatments. Describe how the proposed renovation or facility improvement will leverage existing capacity or infrastructure.

2. Basic Project Information:

Site address and location, square footage, and occupancy classification of the proposed facility. Description of existing building occupancy and construction type, building age, any known historic significance or other pertinent site details.

Description of adjacent uses, regulatory jurisdiction (Authority Having Jurisdiction or AHJ), and storage/use of any proposed chemical/hazardous materials. Description of the proposed scope of construction, equipment, and design layout. Description of any potential risks and associated mitigation measures.

3. Facilities Project Team:

Description of organization and qualifications of the team that will be responsible for executing the proposed renovation/facility improvement project, such as the design personnel (e.g., Architect of Record (AOR), Engineer of Record), construction personnel (e.g., General Contractor), and any other pertinent team members.

4. Design Narrative:

Description of the proposed scope of construction, equipment, and design layout of the CCCE. Outline of the laboratory plan and workflow discussing how the spaces support the research. Description of key process and equipment. Discussion of how the design addressed key project drivers. Description of any potential risks and associated mitigation measures.

5. Commitment to Diversity, Equity and Inclusion (DEI):

Description of DEI outreach for design and construction contracts, such as opportunities for small business enterprises, minority-owned businesses, disabled veteran-owned businesses, women-owned businesses, and LGBTQ-owned businesses.

6. Plans and/or Graphics:

Existing and proposed floor plans to scale of CCCE and any other diagrams that describe the proposed improvements. The information provided should include adequate information to describe the scope of work.

7. Construction Cost:

List of items and their cost. High level description of cost drivers, such as adherence to prevailing wage laws (see Other Requirements below).

8. Facility Project Schedule:

Gantt-like schedule consistent with overall timeline. Include milestones and tasks, such as design, permitting, construction, equipment and commissioning, necessary to complete the proposed renovation/facilities improvement project and activate the proposed facility.

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, 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 their 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).

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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.

Who are Key Collaborators and Community-Based Partners?

Key Collaborators include any proposed collaborator or collaborating organization conducting activities integral to the program plan. Key Collaborators may be paid or unpaid with award funds, but such funding should **not** be allocated from the $625,000 Community-Based Partnerships budget.

Community-based organizations designated to be recipients of Community Based Partnership funding should be designated as "Community-Based Partners." A "community-based organization" means a public or private nonprofit organization of demonstrated effectiveness that— (A) is representative of a community or significant segments of a community; and (B) provides educational or related services to individuals in the community. A community-based organization provider must be a public or private non-profit organization with a 501(c)(3) status or a fiscally sponsored entity of a 501(c)(3) non-profit organization.

What should one know before preparing the budget?

A specific and well-justified activities-based 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 applicable sections of the Grants Administration Policy for Facilities and Equipment Grants and for research and training funds are detailed in the Grants Administration Policy for Clinical Stage Projects. Generally, project costs for personnel, supplies, travel, equipment, and subcontracts may be claimed. Limits for specific cost categories must be observed.

What are Direct Facilities Costs and how much can an applicant claim?

Direct Facilities Costs are general operating costs of the Awardee's facilities attributable to housing all elements of the CIRM-funded project or activity. Eligible costs are operation and maintenance costs such as utilities, janitorial services, routine maintenance, repairs and library expenses. Facilities costs related to depreciation or capital debt are unallowable. 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 A21 or A-122. Facilities rates are applied to direct costs exclusive of the costs of renovation/construction, 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.

What are indirect costs and how much can an applicant claim?

Indirect Costs will not be funded under this RFA.

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Award Administration

Issuance of Award

A CIRM award is issued via a Notice of Award 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 Notice of Award 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 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 the project timeline and budget risks and will provide details for covering such costs, including the source of funding. CIRM reserves the right to make adjustments to the timeline for inclusion in the 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

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

CIRM Regulations

Awards made through this program announcement will be subject to all applicable CIRM regulations. These regulations can be found on CIRM's website at https://www.cirm.ca.gov/our-funding/cirm-stem-cell-grant-regulations.

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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 no longer qualifies as a California Organization, etc.

A list of frequently asked questions regarding managing a CIRM award can be found at https://www.cirm.ca.gov/researchers/managing-your-grant.

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RFA 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 that directs and controls the award activities from the California location.

"**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".

"**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.

"**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 $25,000 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.