Discovery Awards (DISC4)

Pre-submission Informational Webinar

April 28, 2025

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Quick Announcements

- Pre-submissions **due June 16, 2025.** Invitations expected ~60 days after due date
- Webinar recording and FAQ document will be posted in ~1-2 weeks
- Q&A will focus on general questions - specific programmatic questions may be directed to **discovery@cirm.ca.gov**

CIRM's Discovery & Education Team

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Webinar Panelists

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Linda Nevin
Senior Science Officer,
Portfolio Development & Review

Agenda

1 Part 1: Presentation — 3:00 - 3:30pm

- Program Overview
- Pre-submission Process
- Information and Resources

2 Part 2: Question & Answer — 3:30 - 4:00pm

Program Overview

Our Mission

Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world.

CIRM's Strategic Allocation Framework

The **Strategic Allocation Framework (SAF)** - Structured and data-driven approach to prioritize resource allocation and provide recommendations to the ICOC for continued implementation of CIRM's strategic plan

CIRM's Impact Goals

Accelerating Discovery & Translation

1. **Catalyze** the identification and validation of at least 4 novel targets and biomarkers, ensuring integration into preclinical or clinical research for diseases in California
2. **Accelerate** development and utilization of 5-8 technologies that have the potential to improve safety, efficacy, and/or quality of cell and gene therapies

Cell & Gene Therapy Approvals

3. **Advance** 4-7 rare disease projects to BLA
4. **Propel** 15-20 therapies targeting diseases affecting Californians to late-stage trials

Accessibility & Affordability of CIRM-Funded Cell & Gene Therapies

5. **Ensure** that every BLA-ready program has a strategy for access and affordability

Diverse Workforce Development

6. **Bolster** CIRM's workforce development programs to address gaps and meet evolving demands in regenerative medicine

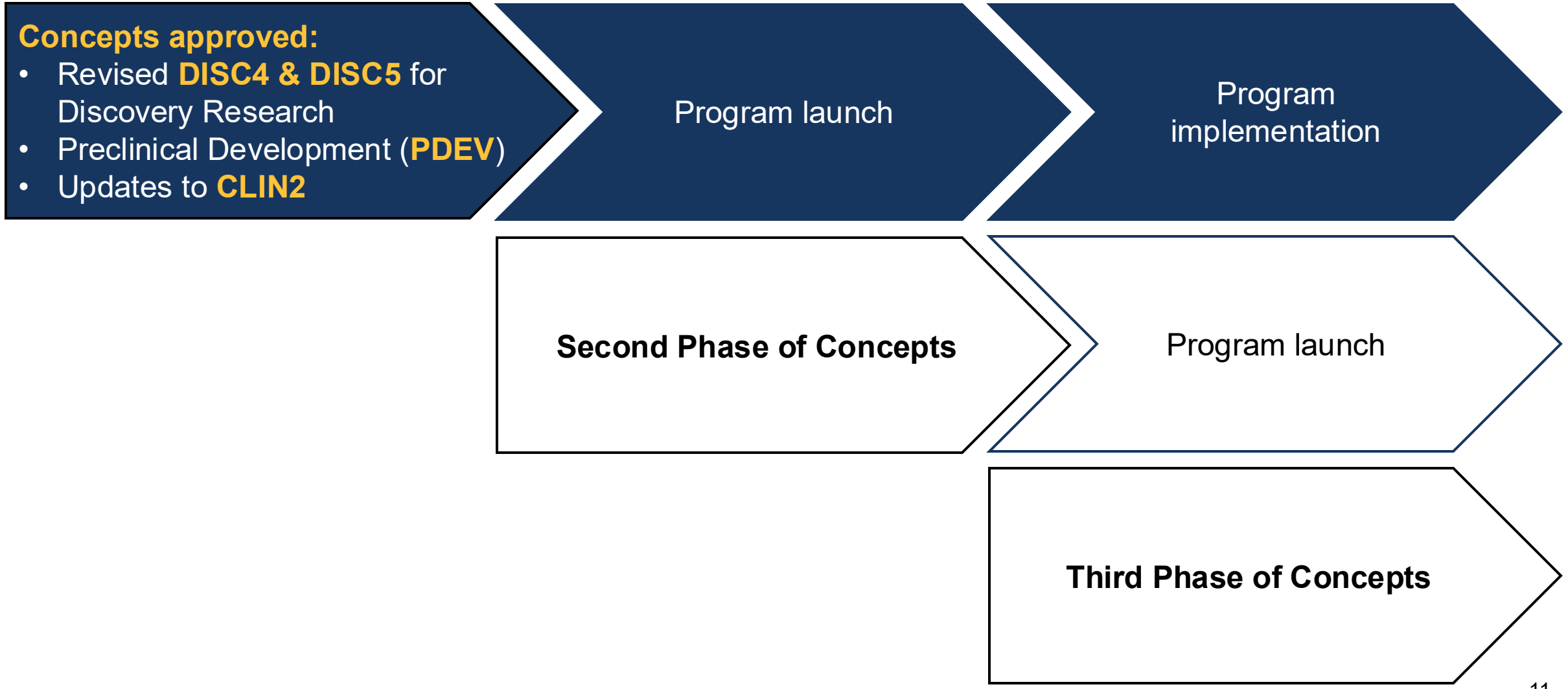
Goal 1 | Recommendations (1 of 2)

Goal 1 - Catalyze the identification and validation of at least 4 novel targets and biomarkers, ensuring integration into preclinical or clinical research for diseases in California

Support comprehensive discovery research through DISC4 & DISC5 funding structures

- Encourage collaborative, multidisciplinary innovation in stem cell and genetic research across diverse disciplines & disease indications with early engagement of industry to address reproducibility & scalability issues

SAF Implementation: 3 Phases



Discovery Programs

Objective of CIRM's Discovery programs is to support comprehensive discovery research across a diverse range of diseases and bottlenecks, to accelerate the development of potential therapeutics and biomarkers in regenerative medicine

Two complementary awards to support research at different scales and maturity

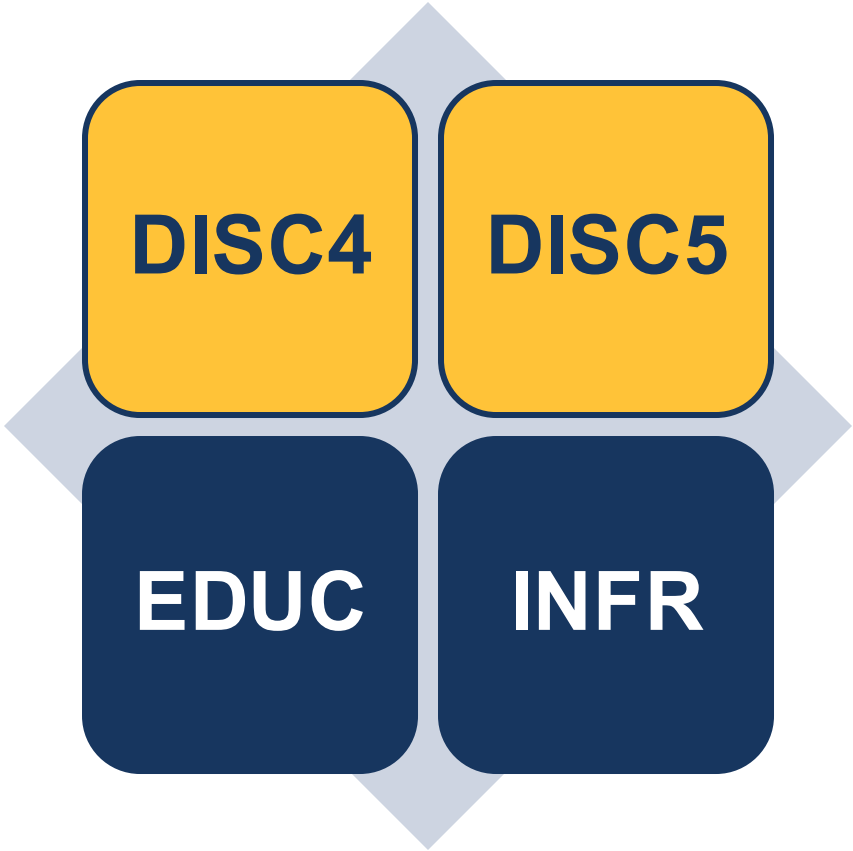
	DISC4	DISC5
Description	Large collaborative teams Integrating multiple disciplines & approaches	Small collaborative teams Innovative or exploratory research
Focus	Basic disease biology insights leading to novel targets and biomarkers	Stem cell biology and models, regenerative medicine bottlenecks

PA expected Summer 2025

Discovery Programs

Program Infrastructure to facilitate data and knowledge sharing within and beyond CIRM's network of grantees

- ✓ Program & Grantee Meetings
- ✓ Data Sharing Infrastructure
- ✓ External Partnerships
- ✓ Leveraging other CIRM funded resources including: training grants, research infrastructure, clinical infrastructure



Award Structure

	DISC4
Applicant	California non-profit or for-profit research institutions *Institutions may submit multiple applications per cycle*
Core Team	At least 5 California-based investigators* (1 PI + 4 Co-I)
Max Budget	$13M (Total Cost, inclusive of overhead) *Up to $14M (with matching funds)*
Max Duration	4 years

* Must be employed by California Organization at the time of application and throughout the project duration

Scope and Expected Outcomes

Approach

Expansive, cross-disciplinary and integrated studies led by large collaborative teams applying a range of technologies and approaches.

Projects should aim to achieve one or more of the following outcomes by the end of the award duration:

- Discovering novel mechanistic insights or advance our understanding of the pathobiology of human diseases
- Extending understanding of disease mechanisms to all affected populations
- Identification and validation of novel therapeutic strategies, targets, and/or biomarker(s)

Project Eligibility

To be eligible all projects must:

1. Address a key knowledge gap or research bottleneck in the study of human diseases
2. Include studies that employ human stem cells or genetic* research as part of the central approach or hypothesis
3. Provide strong justification for any proposed use of non-human models

* Research that alters genomic sequences of cells (edit, remove or add DNA sequences); or introduces or directly manipulates nucleic acids (e.g., coding and non-coding RNAs, antisense oligonucleotides) in human cells

Out of Scope Activities (DISC4 will NOT fund)

- ✗ Therapeutic or other commercial development activities including lead optimization, manufacturing, pre-clinical toxicology, and pharmacology studies and other activities targeted by CIRM's PDEV and CLIN programs
- ✗ Costs of activities performed by a separate out-of-state organization that retains intellectual property or independent publication rights in any intellectual property (e.g., invention, technology, data) arising out of the CIRM-funded project
- ✗ Costs incurred before the date of ICOC approval
- ✗ Activities already budgeted or paid for under a prior, existing or pending CIRM award, or which are already supported by another funder

What research activities are required and allowable?

- Activities associated with managing, preserving, and sharing data and knowledge from the study
- Any research activity contributing to achievement of the expected outcomes and aligns with eligibility requirements

Illustrative list only; Not exhaustive

- Study or use of stem cells and derivatives
- Genetic research/Genomics
- Reverse translation studies
- Bioengineering/Biomaterials
- Computational biology/Bioinformatics
- Study of primary human tissues
- Tool/tech development
- Target and biomarker discovery

What non-research activities will CIRM Fund?

- ✓ Partnering activities with patient-centered organizations or other project-relevant community groups
- ✓ Activities to support outreach or communication of research plans or outcomes with the wider public
- ✓ Travel and accommodation expenditures associated with attendance of CIRM organized meetings and conferences
- ✓ Engagement activities with trainees supported through CIRM's EDUC or INFR programs

Team Eligibility

	Eligibility Requirements
Applicant Org	• California non-profit or for-profit research institutions
Core Team	• All Core team members must be employed by a California organization at the time of application and throughout the project duration • 1 Principal Investigator (min 15% effort) • 4 or more Co-Investigators (min 10% effort) • Multi-Institutional (at least 1 Co-I employed by a different institution than PI)
Broader Team (including Key Personnel)	• Minimum 1 Key Personnel with relevant clinical expertise • Minimum 1 Key Personnel with relevant computational expertise • Minimum 1 Key Personnel with relevant industry/translational expertise • Minimum 1 Data Project Manager

Matching Fund Contributions

Maximum total project costs may be **increased up to an additional $1M per award** (maximum $14M per award) **IF** an equivalent (or larger) amount of eligible matching fund contributions is provided

The following contribution types (from any non-CIRM source) are eligible:

- **Unique resources** that will be leveraged by the project team (cell-lines, samples, computing resources, etc.)
- **Independently-funded activities** undertaken during the award period to generate data or resources that will be leveraged by the project team during the award period

Preference Topics

The following preference topic was approved for FY25/26 and will be prioritized at the pre-submission stage:

Neurological Diseases (including conditions and disorders of the brain, spinal cord, and peripheral nervous system)

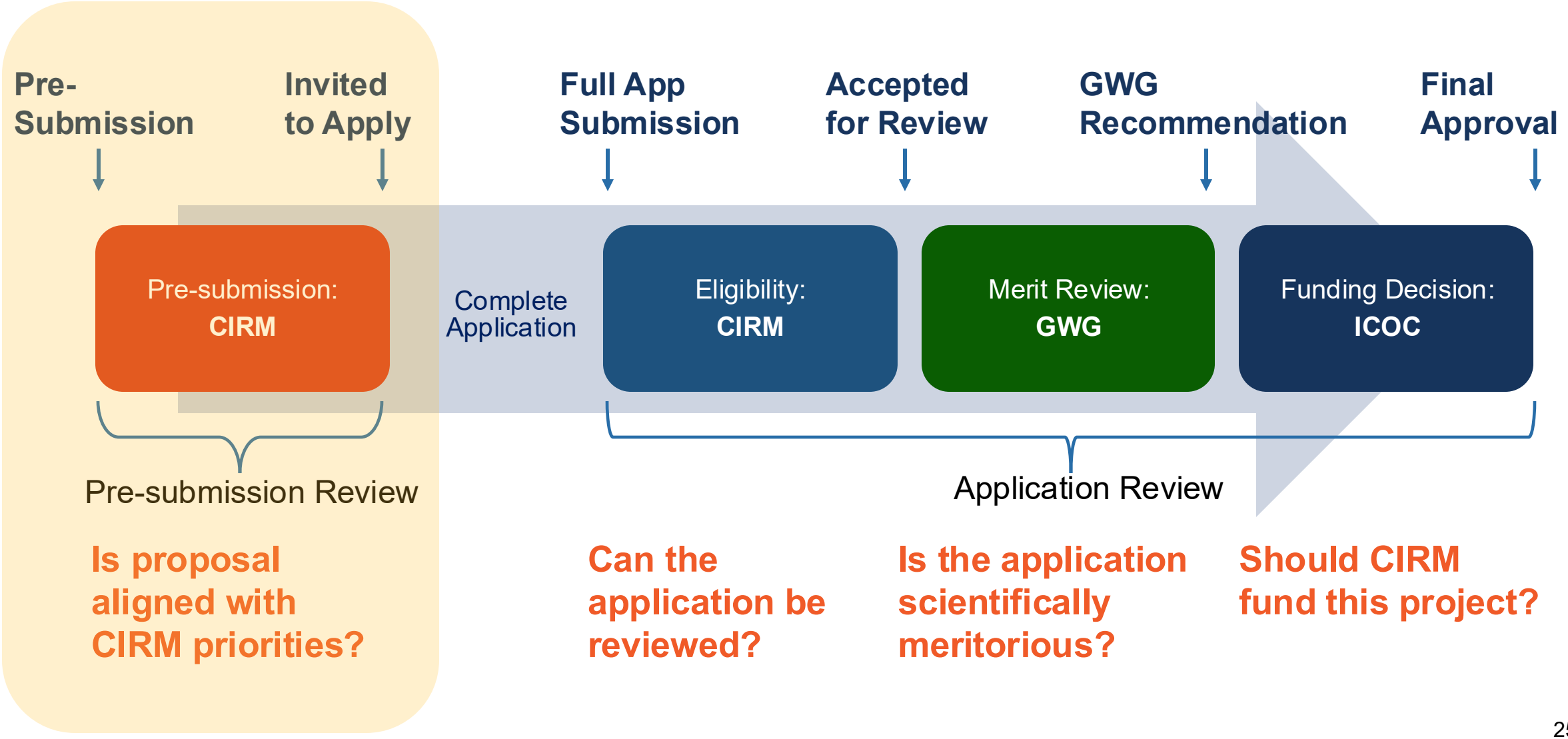
Pre-submissions that fall outside of these preference areas may still be considered if they represent a unique opportunity to advance the strategic goals of the DISC4 program

Scientific Review Criteria

1. **Significance**: Evaluate the project's significance and potential for impact
2. **Innovation**: Evaluate the project for innovation relative to the current state of research
3. **Rationale**: Evaluate the scientific rationale in the proposal
4. **Plan & Design**: Evaluate the project plan and design
5. **Population Impact**: Evaluate the extent to which the project considers the impact of successful outcomes across affected populations

Pre-Submission Process

Overview of DISC4 Pre-submission and Review Process



DISC4 Pre-submission Process

All Prospective Applicants must first complete a Pre-submission Form

1 Pre-submission

Applicant completes a short online form and proposal outline

2 CIRM Evaluation

CIRM ranks pre-submissions based on designated preference topics and program fit

3 Invitation to Apply

CIRM invites selected teams to submit a full application

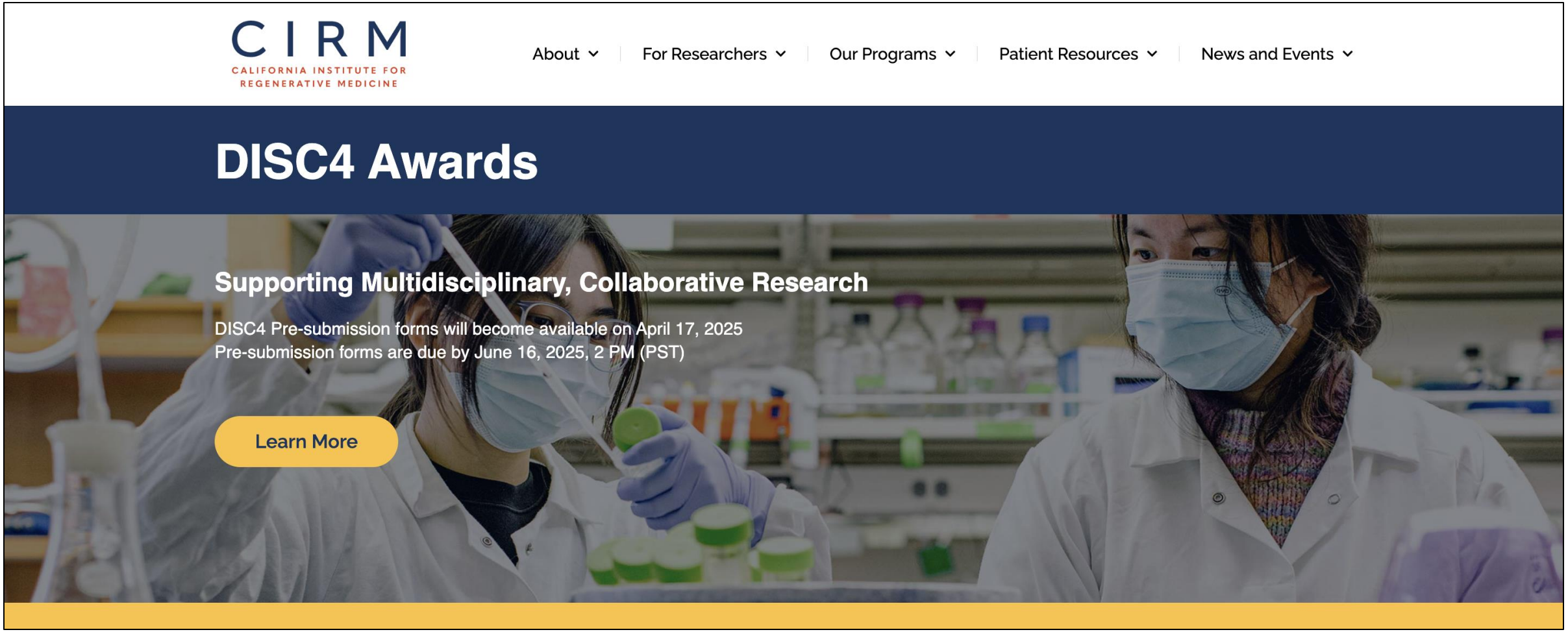
4 Full Application

Approx 90 days from invitation to due date

Pre-submission Evaluation Criteria

Pre-submissions will be evaluated and ranked according to the following criteria:
Does the project align with the cycle-specific Preference Topic? *Neurological Diseases (including conditions & disorders of the brain, spinal cord, & peripheral nervous system)*
Does the project hold strong relevance for understanding or addressing human diseases?
Does the project integrate cross-disciplinary approaches?
Does the project incorporate innovative approaches, particularly in stem-cell or genetic research?

DISC4 Landing Page



Visit cirm.ca.gov/disc4/ to learn more about our DISC4 funding opportunity

Pre-submission | Getting Started

- Log-in at http://grants.cirm.ca.gov/
- Click on “Open Programs”

Other Things You Could Do

- Browse current Open Programs to start a new application
- Review Your Applications to see all previously submitted, expired, abandoned, and withdrawn applications

- Select “Start a Pre-submission form for prospective DISC4 applicants”

RFAs and Programs Open For Applications	Actions
DISC 0 CIRM Foundation - Discovery Stage Research Projects: DISC0 Grant Application	Start a DISC0 Grant Application
DISC4 PSUB: Pre-submission form for prospective DISC4 applicants	Start a Pre-submission form for prospective DISC4 applicants

Pre-submission | Components

ONLINE SECTION

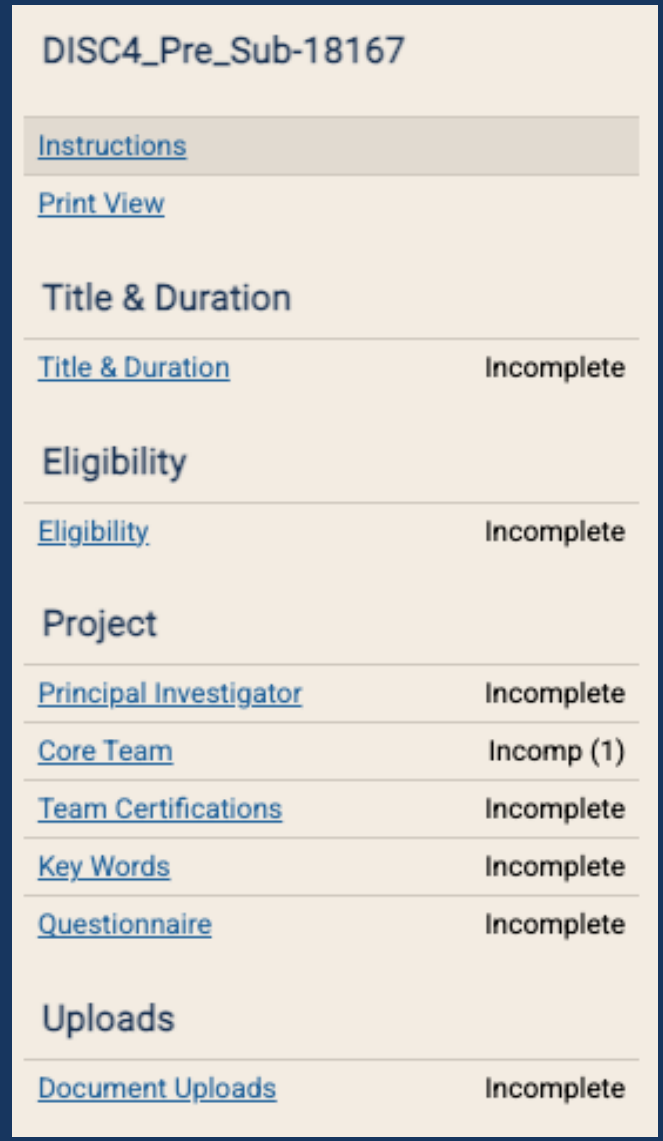
- Title & Duration
- Eligibility
- Principal Investigator
- Core Team (Co-investigators)
- Team Certifications
- Key Words
- Questionnaire

UPLOADS SECTION

- Proposal Outline – must use template provided

All sections are required

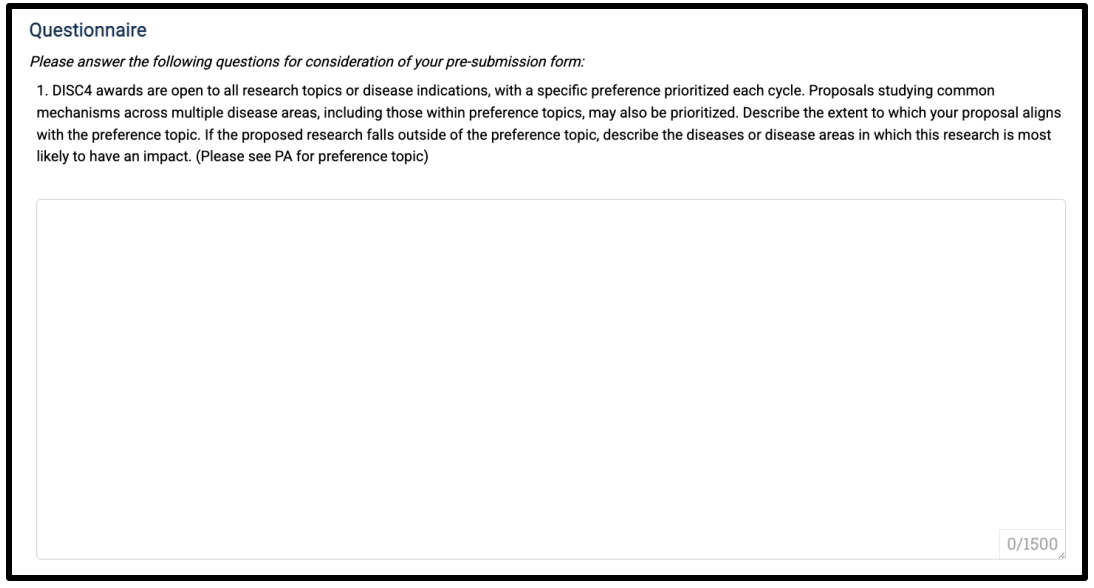
Required sections will change from "Incomplete" to "Complete"



Pre-submission | Questionnaire

4 short questions that highlight program fit
1500-character limit (~2 paragraphs) for each answer

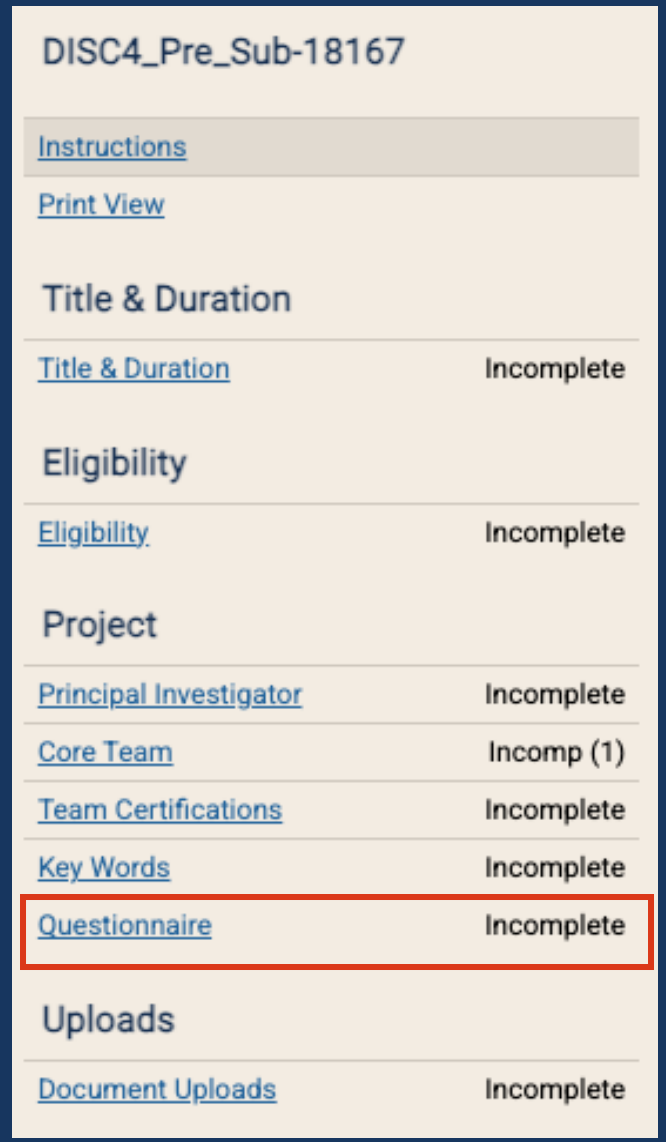
- Alignment with preference topic
- Cross-disciplinary integration
- Stem cell or genetic research approaches
- Vision for progression to preclinical development


Questionnaire

Please answer the following questions for consideration of your pre-submission form:

1. DISC4 awards are open to all research topics or disease indications, with a specific preference prioritized each cycle. Proposals studying common mechanisms across multiple disease areas, including those within preference topics, may also be prioritized. Describe the extent to which your proposal aligns with the preference topic. If the proposed research falls outside of the preference topic, describe the diseases or disease areas in which this research is most likely to have an impact. (Please see PA for preference topic)

0/1500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Instructions
Print View

Title & Duration

Title & Duration	Incomplete

Eligibility

Eligibility	Incomplete

Project

Principal Investigator	Incomplete
Core Team	Incomp (1)
Team Certifications	Incomplete
Key Words	Incomplete
Questionnaire	Incomplete

Uploads

Document Uploads	Incomplete

Pre-submission | Proposal Outline

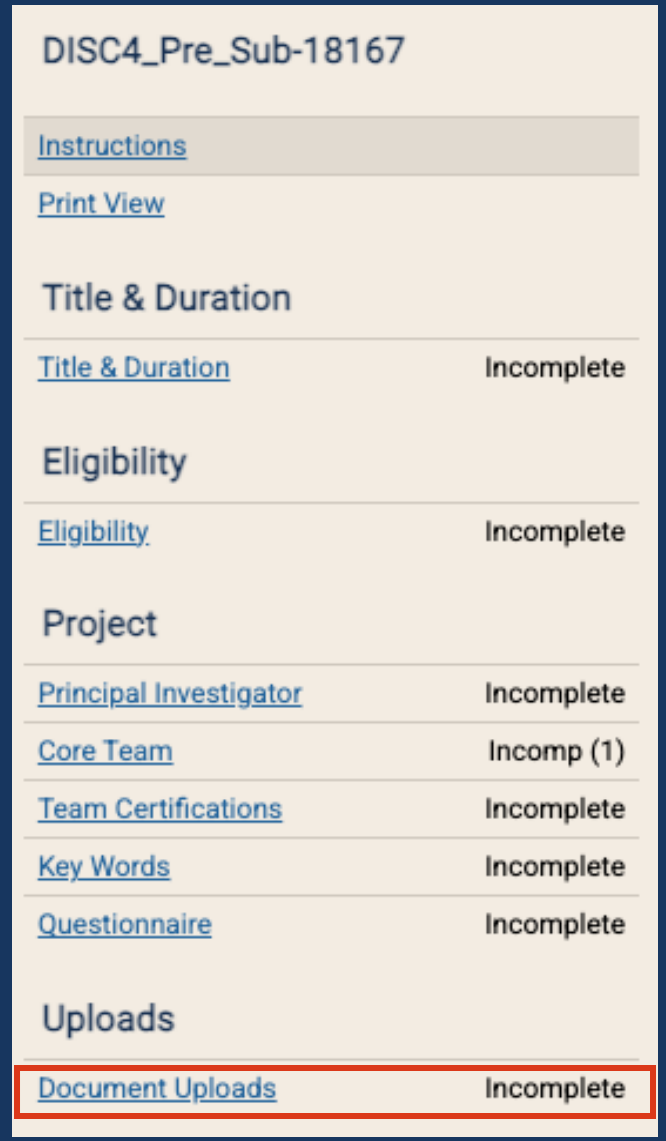
Part 1 Proposal Outline (Max 3 Pages including figures)

Open response format; Include the following elements:

- Overall objective and major aims
- Brief outline of research plan, key workflows and approaches
- Summary of scientific rationale and key supporting data

Part 2 Budget request and references (Max 1 Page)

- Outline of estimated budget request by core team member and year of funding; Recommend using table
- References for proposal outline can be listed here



Pre-submission | Proposal Outline Template

- **Use** the **current required Word Template**
- **Adhere** to prescribed page limits
- **Maintain formatting** (preset fonts, margins)
- **Follow instructions** for each section
- **Convert to PDF** when finished to upload
- **Do not alter** margins, font size, etc.
- **Do not exceed** page limits
- **Do not** leave sections **incomplete**
- **Do not** use a **“DIY”** template

Contacts and Deadlines

Pre-submissions due by June 16, 2025, 2pm PT

Programmatic Questions
discovery@cirm.ca.gov

Review Questions
review@cirm.ca.gov

Budget and Grants Admin Questions
grantsmanagement@cirm.ca.gov

Discovery

www.cirm.ca.gov/DISC4

Please reference documents on our website for guidance

Webinar and FAQ will be posted within 1-2 weeks

Information and Resources for Applicants

Information and Resources for Applicants

- Data Sharing
- Human Embryo & Embryo Model Research in California
- Shared Resources Labs for Stem Cell-Based Modeling

CIRM Data Sharing Requirement

1. **Develop a Data Sharing and Management Plan (DSMP)**
   - Metadata Catalog
   - Data Use Limitations (DUL) Institutional Certification
   - Questionnaire

2. **Deposit data in data repositories by end of award**
   - dbGaP
   - GEO
   - Pride
   - Flow Repo
   - NeMO
   - etc.

Human Embryo and Embryo Model Research in California

1. Regulations – Embryo Research

- CIRM regulations
- California Department of Public Health (CDPH) Guidelines for Human Stem Cell Research

"The following activities are not eligible for CIRM funding" / "Activities Not Permitted"

"(b) The culture in vitro of (i) any intact human embryo ..., after the appearance of the primitive streak or after **12 days** whichever is earlier."

2. CIRM Guidance for Oversight of Human Stem Cell-Based Embryo Models

"…human stem cell-derived embryo models that mimic peri- and post-implantation stages of development. CIRM recommends that:

(1) protocols involving such models be subject to annual SCRO review and approval…

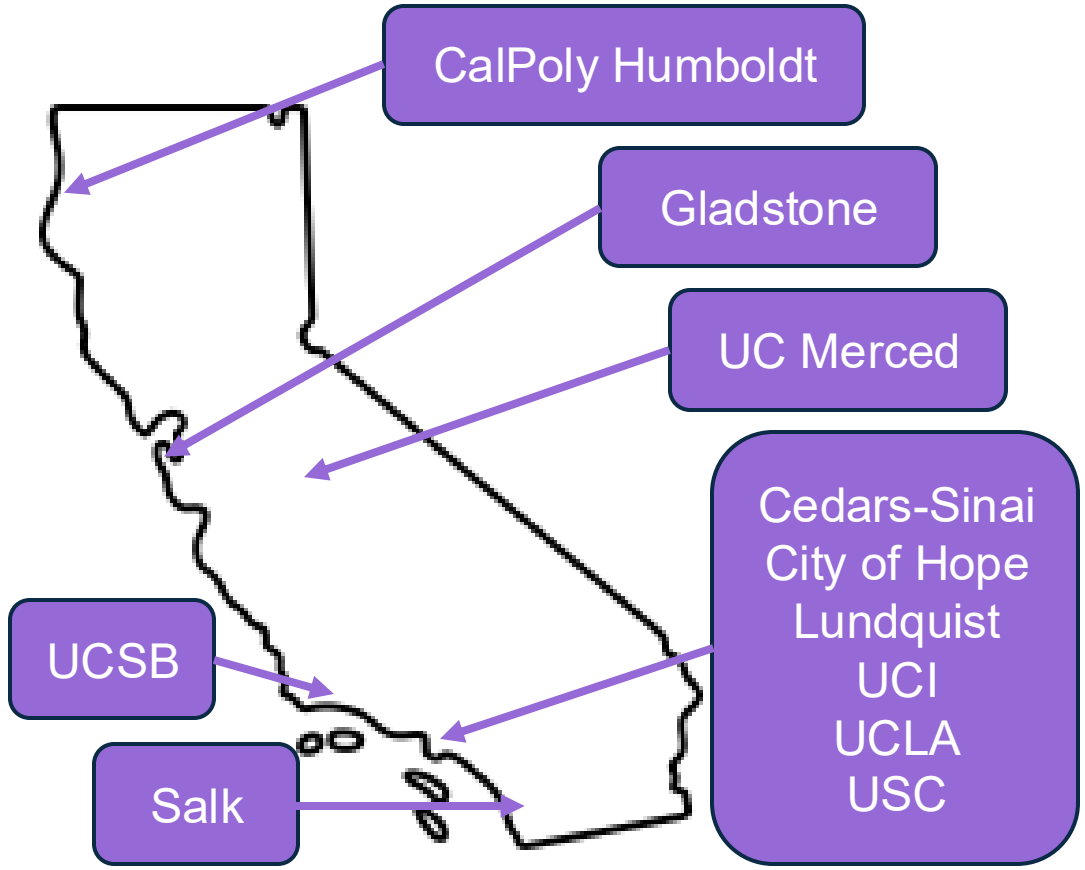
(2) the reason for the use of the … model shall be included in the scientific rationale

(3) the experimental stopping point should be defined ahead of time and not be open-ended."

Shared Resources Labs for Stem Cell-Based Modeling

CIRM-funded infrastructure program to support California researchers and educators by:

- Providing access to core facility, specialized services, and equipment
- Sharing models/expertise and resources for research **broadly across CA**
- Training researchers
- Providing educational resources / activities (including formal techniques courses)



General information: https://www.cirm.ca.gov/shared-labs/

Browse offerings: https://cirmhub.cirm.ca.gov/page/resource-center

Contact: ugrieshammer@cirm.ca.gov

Shared Resources Labs

Stem Cell-Based Modeling Expertise & Technologies

SRL	Organs / Tissues Modeled (2D, organoids)	Technologies / Services (Also available: omics, CRISPR, imaging, flow cytometry)
Cedars-Sinai	brain, heart, bone, blood, gut, lung, liver	automation, metabolism, **organ-on-chip**
COH	brain, heart, breast	single cell **proteomics**, electrophysiology, **bioprinting**, **hypoxic incubators**
Gladstone	brain, heart, immune	automated cell culture and imaging, **LNP delivery**, **HTP drug screening**
Humboldt	brain	
Lundquist	brain, heart, blood, lung, bone, cartilage, intestine, pancreas	metabolism
Salk	brain (aging)	metabolism, direct reprogramming
UCI		**imaging mass cytometry, 3D bioprinting**
UCLA	brain, skeletal muscle	automated cell culture and imaging, small molecule screening
UCM	vascular	small animal models for stem cell-based model characterization, microfluidic microvascular networks
UCSB	brain, retina, embryo (neuro dev)	**HTP drug screening, HTP lenti generation, HTP ELISAs**
USC	brain, kidney, intestine, cartilage	electrophysiology

Q&A

Common Questions

Can I schedule a consultation for my pre-submission?

Consultation calls will not be conducted during pre-submission stage. Applicants who are invited to submit a full application will have the opportunity to request in-depth consultations with CIRM Science Officers.

Can investigators be included in more than one DISC4 application?

An investigator cannot be listed as a Principal Investigator on more than one application. An investigator may be included in the core team (PI/Co-I) of up to two applications.

Can non-CA investigators be included in DISC4 applications?

Non-CA-based investigators are not eligible to serve as PI or Co-I on DISC4 awards.

DISC4 applicants are allowed to budget grant funds to support a non-CA-based collaborator through a grant subcontract, provided the out-of-state organization DOES NOT retain the intellectual property or independent publication rights of any intellectual property arising out of the CIRM-funded project.