DISC2 Quest Awards

Informational Webinar

April 15, 2024

CIRM
CALIFORNIA'S STEM CELL AGENCY

Mission Statement

OUR MISSION

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

Scientific Programs and Education Team

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Vice President

Kelly Shepard, PhD
Associate Director

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Sr. Science Officer

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Science Officer

Daisy Xin, PhD
Science Officer

Sara Taylor, PhD
Project Manager

Webinar Panelists

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Vice President,
Scientific Programs & Education

Chan Lek Tan, PhD
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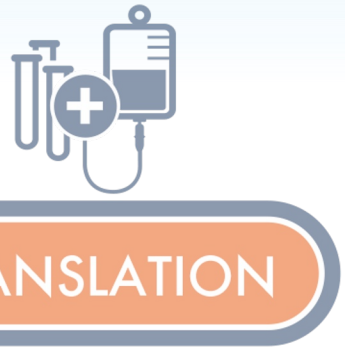
Associate Director,
Scientific Programs & Education

Hayley Lam, PhD
Associate Director,
Portfolio Development & Review

Apryl Rhinehart
Grants Management Officer,
Grants Management

DISCOVERY Pillar Programs

DISCOVERY



TRANSLATION

CLINICAL

Foundational Knowledge → Single Product Candidate → Pre-IND Meeting or Equivalent → Approved Therapy

DISC0 FOUNDATION AWARDS

ReMIND (DISC4 and DISC5) AWARDS

DISC2 QUEST AWARDS

TRAN1/2/3/4 AWARDS

CLIN1/2 AWARDS

DISC Funding Opportunities

Program	Outcome	Team Size	Max Budget*	Duration	Progression
DISC0 Foundation Awards	Basic Research	Single PI	$1.5M	3 years	DISC2 or N/A
	Multidisciplinary Basic Research	PI + 1-2 Co-I	$3M		
DISC2 Quest Awards	Therapeutic Candidate	Single PI	$1.75M	3 years	TRAN
	Biomarker Candidate	Single PI	$1.5M		
ReMIND-L (DISC4)	Neuro Mechanistic Insights	PI + 4+ Co-I	$10M	4 years	DISC2 or TRAN or N/A
ReMIND-X	Neuro Proof-of-Concept	PI + 1+ Co-I	$1M	2 years	ReMIND-L or DISC2 or N/A

*Direct project costs

DISC2 Webinar Agenda

Part 1: Presentation	**3:15-3:55 PM**

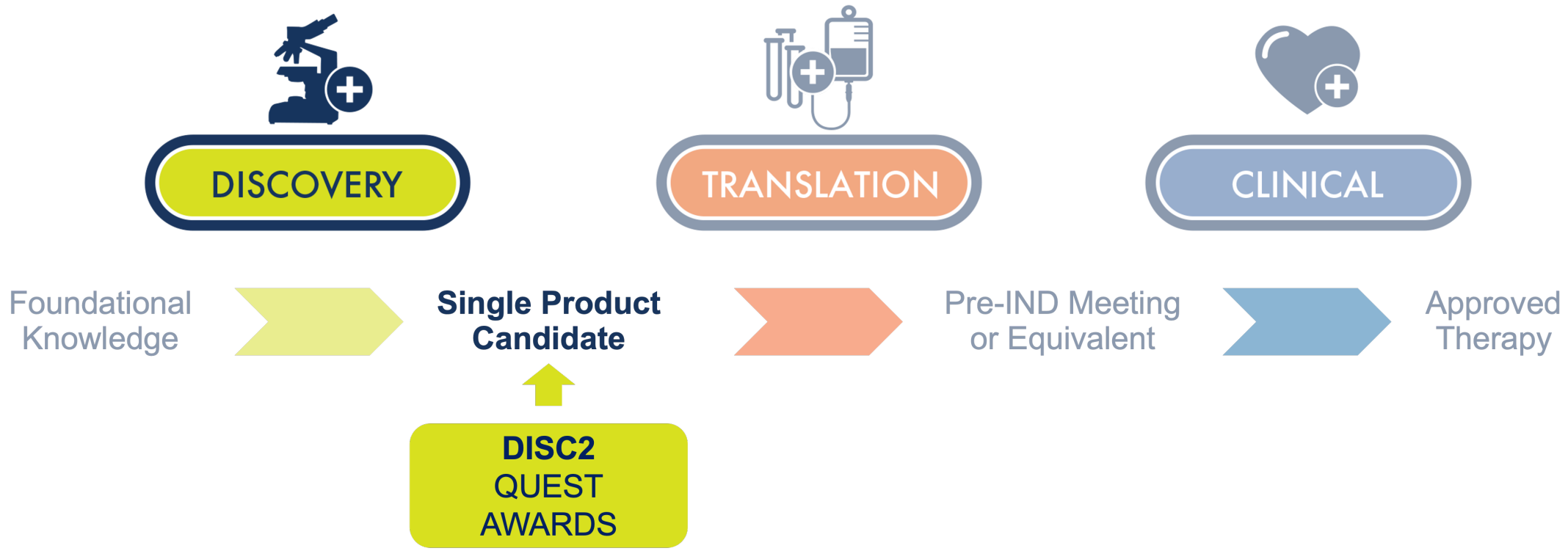
- Program Overview and Updates
    - Therapeutics Track
    - Biomarker Track
- Application Process
- Review Overview
- Resources and Contacts
- Common Issues

Part 2: Question & Answer	**3:55-4:30 PM**

DISC2 | Program Overview

DISC2 | What are we looking for?

DISC2 Quest Supports Selection of Candidates for Translational Progression



DISC2 | What are we looking for?

All Proposals MUST propose

1. Eligible* Candidate Type (Therapeutic or Biomarker)
2. Studies to achieve Expected Outcomes

*Uniquely enabled by human stem cells or uniquely enabling for the advancement of human stem cell-based or genetic therapies

DISC2 | Two Candidate Tracks

	Therapeutic	Biomarker
Expected Outcome	**Therapeutic candidate**	**Biomarker candidate**
Duration	3 years	3 years
Max budget **Direct Project Costs**	$1.75M	$1.5M
CA eligibility	California non-profit or for-profit research institutions	
Applicant	Single Principal Investigator	
Min PI effort	20%	
Progression	TRAN1	TRAN2

Therapeutic Track | Eligible Candidate Types

Candidate Type	Criteria
A Cell Therapy	• Human stem cell or progenitor cells compose the therapy **or** • Human stem cells or progenitor cells are used to manufacture the therapy
B Genetic Therapy	• Alters genomic sequence, or introduce or directly manipulate nucleic acids in cells **and** • Targets a human somatic cell for therapeutic effect **and** • Is intended to replace, regenerate or repair the function of aged, diseased, damaged, or defective cells, tissues, and/or organs
C Other Modality	• Acts on endogenous human stem cells for its therapeutic effect **or** • Targets human cancer stem cells for its therapeutic effect **or** • Modifies a stem cell therapy **or** • Requires human stem cells to manufacture the therapy
D Other Modality	• *Uniquely requires* human stem cells for candidate identification and testing

Therapeutic Track | Expected Outcome

Expected Outcome: A candidate that is ready for translation

Therapeutic Candidate	✓ Selection of a single therapeutic candidate ✓ Draft Target Product Profile (TPP) developed ✓ Measures of identity, activity, and purity developed ✓ Demonstration of reproducible disease/injury modifying activity with candidate (DMA)

ALL therapeutic candidate proposals must aim to select a single candidate for further translation by the end of the award **AND** demonstrate reproducible disease/injury modifying activity (DMA) with *the selected candidate* in a preclinical model relevant to the target indication

Therapeutic Track | Disease Modifying Activity

Additional requirements for demonstrating DMA for each therapeutic type:

Candidate Type	Additional Requirements
Cell Therapy	• **Allogeneic**: DMA demonstrated using product made from a clinically compatible* cell line that meets GTP requirements for donor eligibility and has been appropriately consented for intended use and for clinical development and sale • **Autologous**: DMA demonstrated with candidates **derived from 2 or more donors** to establish reproducibility
Genetic Therapy	• Evidence demonstrating that the selected candidate targets or has activity in a clinically relevant human cell population
Other Modalities Acting on Stem Cells	• DMA demonstrated with clinically relevant human stem/progenitor or cancer stem cell population

* See Resources section for a list of CIRM's clinically compatible cell line resource

Therapeutic Track | Eligible Activities

CIRM will fund the following activities:

- ✓ Studies to identify/test/characterize a candidate
  - Assessments to inform critical quality attributes
  - Assessments of safety or biodistribution necessary for candidate selection
- ✓ Therapeutic feasibility and initial reproducibility assessment
- ✓ Optimization of candidate
  - Testing cell lines, vectors
  - Identifying structure-function relationships
- ✓ Proof of concept studies and demonstration of disease modifying activity
- ✓ Developing target product profile
- ✓ Preparation for and conduct of appropriate regulatory meetings

Biomarker Track | Eligible Candidate Types

Candidate Type	Criteria
Supports Therapeutics Development or Clinical Use	Biomarker that supports the development or clinical use of any therapeutic of the following modalities: • **Cell therapy**: Human stem and progenitor cells compose or are used to manufacture the therapy • **Genetic therapy**: Alters genomic sequence, or introduces or directly manipulates nucleic acids • **Other modality**: Acts on or targets human stem cells or cancer stem cells, modifies a stem cell therapy, or requires human stem cell for manufacture
Uniquely Enabled by Stem/Progenitor Cells	Biomarker for which human stem/progenitor cells are *uniquely enabling* for identification, testing, validation or, assessment

Biomarker Track | Expected Outcome

Expected Outcome: A candidate that is ready for translation

Biomarker Candidate	✓ Selection of a single biomarker candidate and specify context-of-use (COU) ✓ Development of a draft Biomarker Candidate Profile ✓ Selection of analytical method with basic measures of performance and reproducibility ✓ Demonstration that biomarker can be reproducibly measured at relevant levels ✓ Initial proof-of-concept using relevant clinical data/samples supporting relevance of biomarker

Biomarker Track | Eligible Activities

CIRM will fund the following activities:

- ✓ Studies to identify/specify/characterize a candidate
  - Profiling or unbiased screening studies
  - Studies to understand the relationship between biomarker and biology relevant to proposed context-of-use
- ✓ Studies necessary to refine or specify proposed context-of-use
- ✓ Testing and characterization of analytical methods
  - Compare methods or develop custom assays
  - Performance assessments including specificity, sensitivity, accuracy, and precision
  - Development of indices, scoring matrices, or algorithms
- ✓ Initial proof-of-concept using appropriate clinical data/samples
- ✓ Preparation and completion of appropriate regulatory meeting or submission

Both Tracks | Eligible Activities

CIRM will also fund the following activities:

- ✓ Activities intended to promote and uphold principles of Diversity, Equity, and Inclusion (DEI) in the conduct of the study
- ✓ Activities associated with sharing data and knowledge from the study

Both Tracks | Ineligible Activities

CIRM generally cannot support the following activities under DISC2:

- ✕ Activities covered by CIRM's TRAN program including but not limited to:
  - Development of GMP/CLIA compliant process
  - Implementation Design Control including initiation and maintenance of Design History File
  - Preparation for filing of an IND, 510(k) or IDE with the FDA, or validation testing under CLIA
  - Planning or preparation for commercialization
- ✕ Preparation for and conduct of clinical trials
- ✕ Clinical validation studies of candidate biomarker necessary for final regulatory acceptance

DISC2 | Application Process

Application | Getting Started

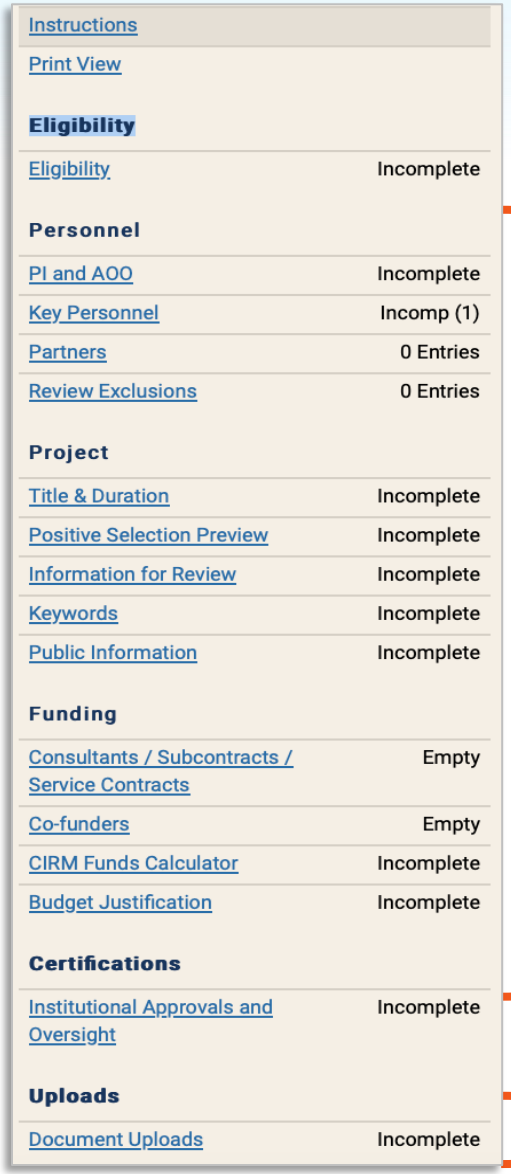
Visit https://grants.cirm.ca.gov/ and choose intended application:

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

RFAs and Programs Open For Applications	Actions
DISC 2 CIRM Quest - Discovery Stage Research Projects: DISC2 Grant Application	Start a DISC2 Grant Application
DISC 4 ReMIND-L - A discovery stage funding opportunity under the ReMIND program: DISC4 Grant Application	Start a DISC4 Grant Application
EDUC 1 CIRM Conference Awards II: EDUC1 Grant Application	Start a EDUC1 Grant Application
EDUC 1.10: CIRM Conference - The 2023 Alpha Stem Cell Clinic Annual Symposium Grant Application	Start a CIRM Conference - The 2023 Alpha Stem Cell Clinic Annual Symposium Grant Application
The PI/PD of all applications/pre-applications/LOIs created here will be the person whose name is listed at the top of this page. *You cannot use these links to create applications for any other PI/PD.*	

Application | Components



Online section

- Eligibility
- Personnel
- Project information, including **Positive Selection Preview Page**
- Funding/Budget Information, including Subcontracts
- Certifications

Uploads section

Required – *must use templates provided*

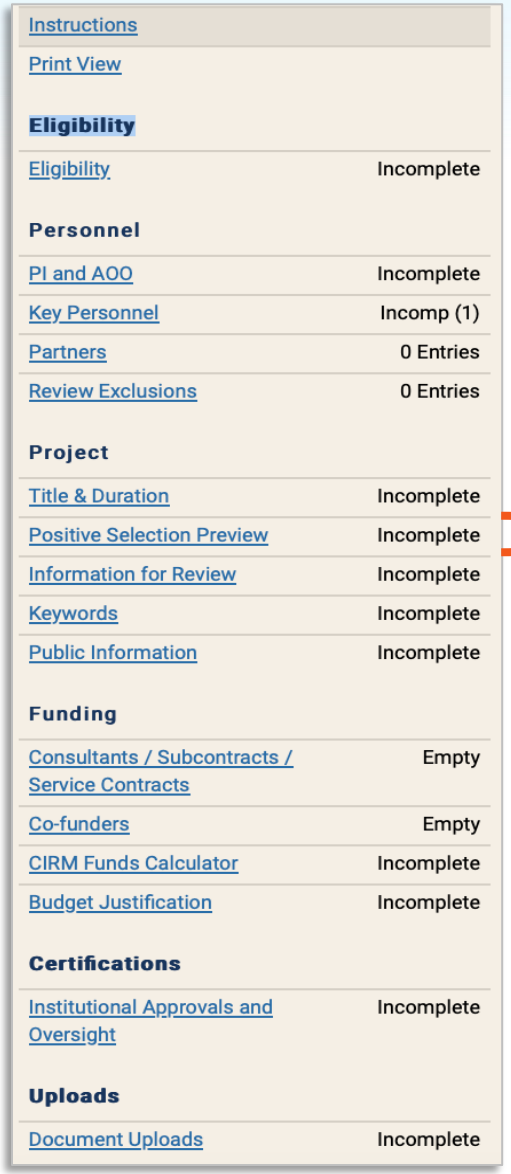
- Proposal
- Biographical Sketches for Key Personnel
- PI Other Support
- Financial Solvency Questionnaire & Worksheet *(for-profit applicants only)*

Optional

- *Letters of Support*
- *Quotes and Other Budget Data*
- *IP, Licenses, and MTA*

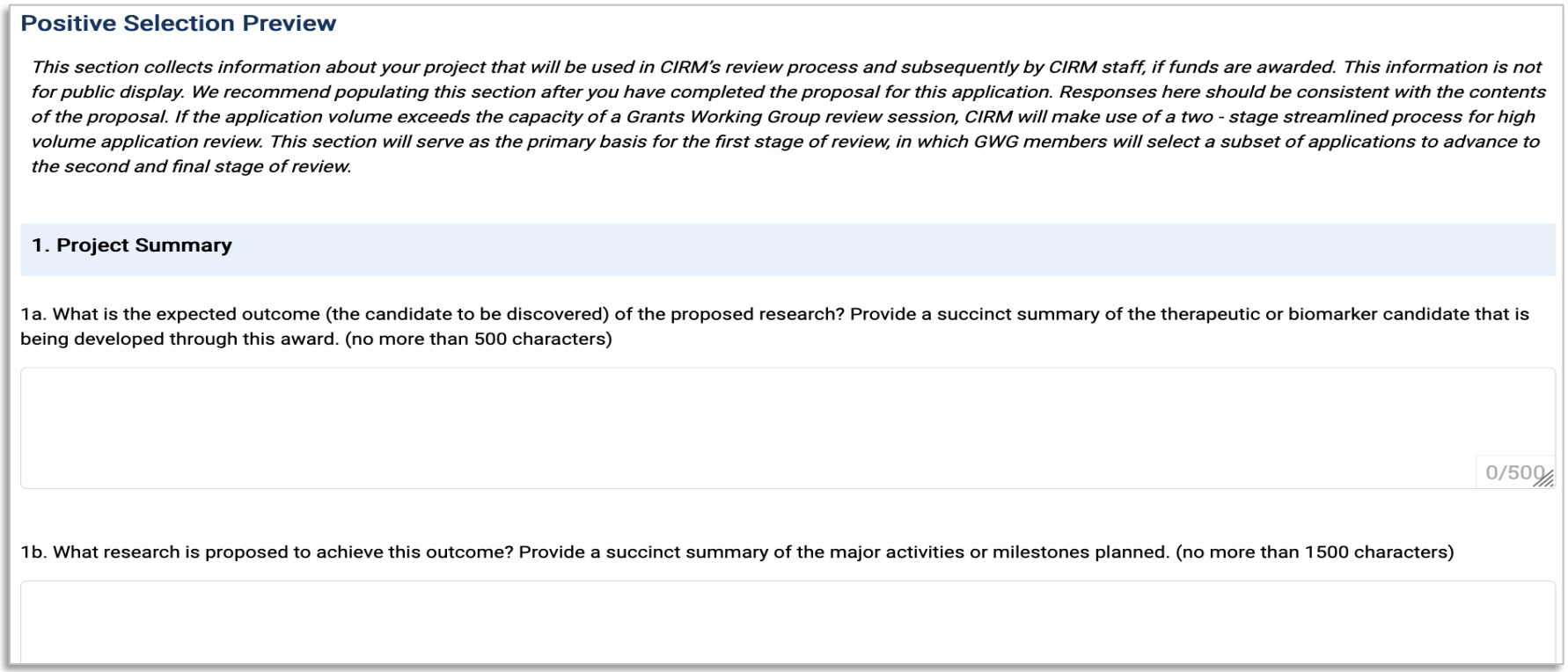
Required sections will change from "Incomplete" to "Complete"

Application | Positive Selection Preview Page

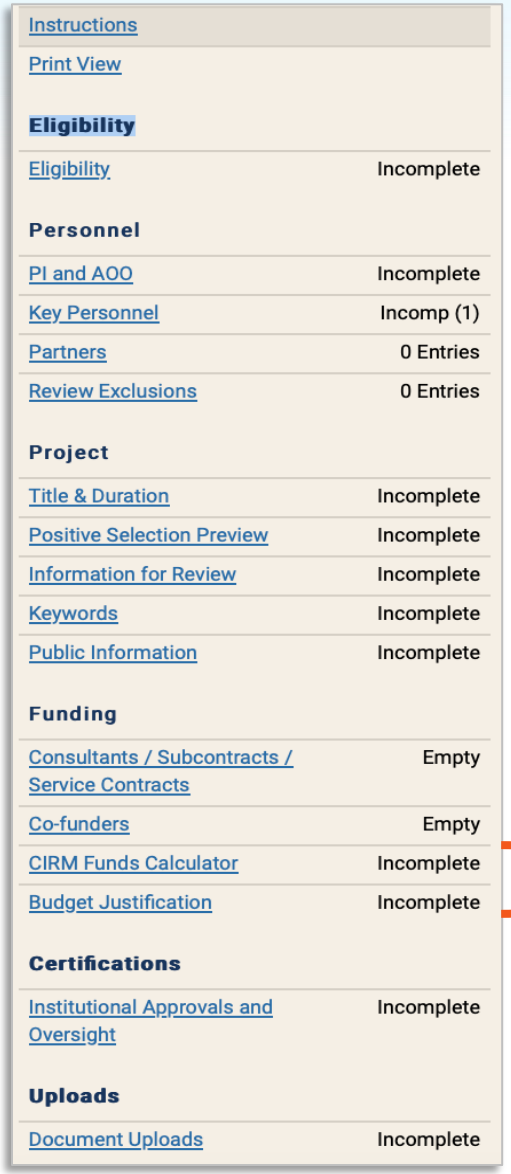


Positive selection preview provides the primary description of the application available to reviewers in the first phase of the review process

Applicants are encouraged to devote significant attention to the completion of this page



Application | Budget: Funds Calculator, Justification



- Direct and Indirect Project Costs entered by year in Funds Calculator
- Subcontracts, co-funding entered in separate section, pulled into Funds Calculator
- All costs/year justified in narrative Budget Justification section

CIRM Funds Calculator

The following budget section allows the applicant to calculate the CIRM-funded overhead (Facilities and Indirect Costs) to arrive at the Total Funds Requested from CIRM.

CIRM-funded Facilities Costs are limited to the current applicable, federally negotiated rates for the organization as defined by the Office of Management and Budget (OMB) Circular A-21 or A-122 for Non-Profit applicant organizations. Facilities Costs for For-Profit applicant organizations are limited to 35%. These rates are applied to the Adjusted Direct Project Costs.

CIRM-funded Indirect Costs (i.e. administrative overhead) are limited to no more than 20% for non-profits and are applied to the Adjusted Direct Project Costs plus the Facilities Costs. For-profit organizations cannot claim indirect costs.

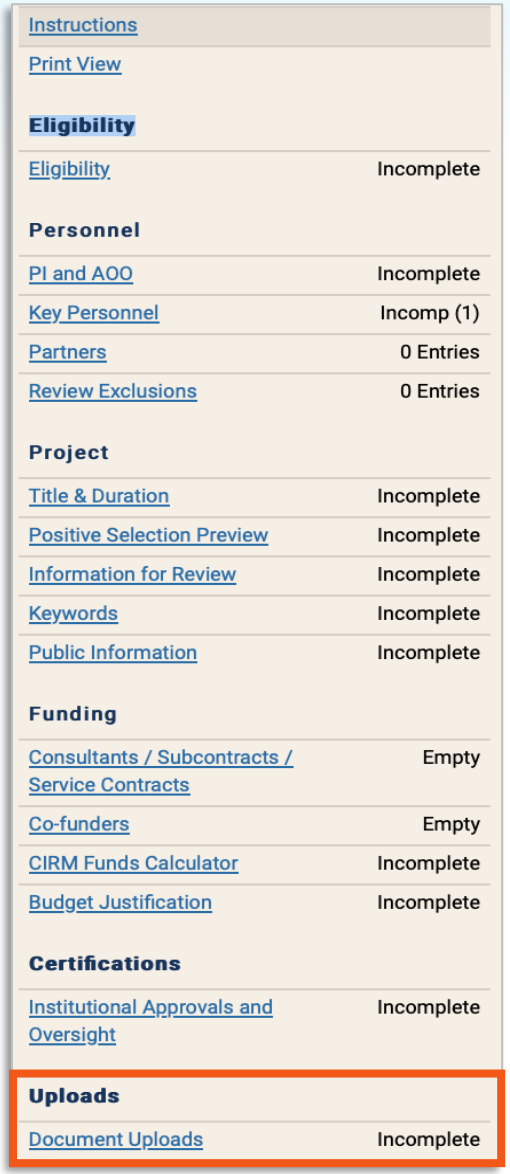
CIRM will fund direct project costs of up to $1,500,000 per award to achieve a biomarker candidate. Award duration is up to three years.

CIRM will fund direct project costs of up to $1,750,000 per award to achieve a therapeutic candidate. Award duration is up to three years.

Please provide values for all editable fields. If a given budget category is not applicable, enter "0" (zero).

Total CIRM Funded Direct Project Costs	Year 1	Year 2	Year 3	Total
Personnel				0
Supplies				0
Equipment				0
Travel				0
Data Sharing				0
Other				0
Subcontracts	0	0	0	0
Total CIRM Funded Direct Project Costs	0	0	0	0

Application | Upload Section



Name Status Templates Uploaded Files Upload Button

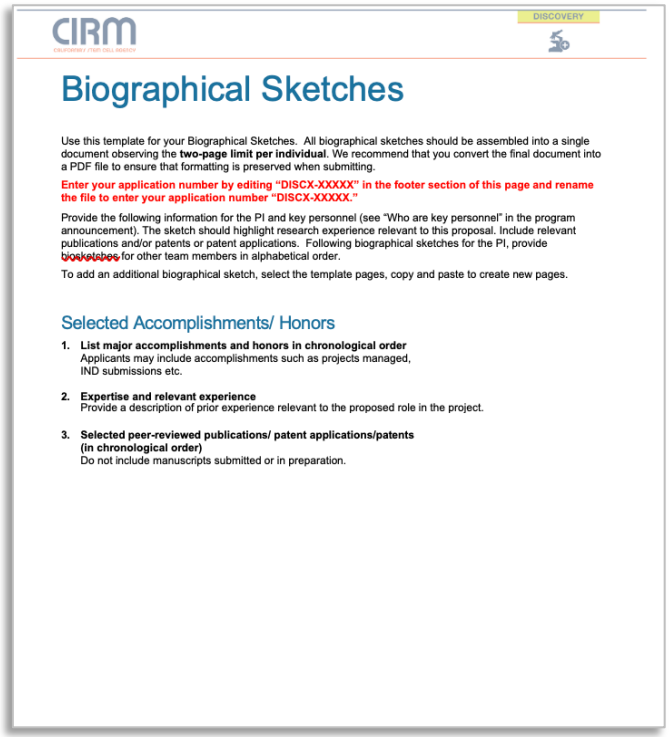
Document Name	Status	Template	Uploaded Files	Acceptable File Types	Upload
Proposal	Incomplete	MSWord	*none*	pdf	Choose File *
Biographical Sketches for Key Personnel	Incomplete	MSWord	*none*	pdf	Choose File *
Letters of Support **If Applicable** In a single PDF, provide any signed letters of collaboration, institutional support, or commitment and availability of co-funding.	Complete	*none*	*none*	pdf	Choose File
PI Other Support	Incomplete	MSWord	*none*	pdf	Choose File *
IP, Licenses and Material Transfer Agreements **If Applicable** Please provide a description of any relevant intellectual property or licensing/material transfer agreements.	Complete	*none*	*none*	pdf	Choose File

* REQUIRED

Required Uploads | All Applicants

Proposal

Biosketch



CIRM DISCOVERY

Biographical Sketches

Use this template for your Biographical Sketches. All biographical sketches should be assembled into a single document observing the **two-page limit per individual**. We recommend that you convert the final document into a PDF file to ensure that formatting is preserved when submitting.

Enter your application number by editing "DISCX-XXXXX" in the footer section of this page and rename the file to enter your application number "DISCX-XXXXX."

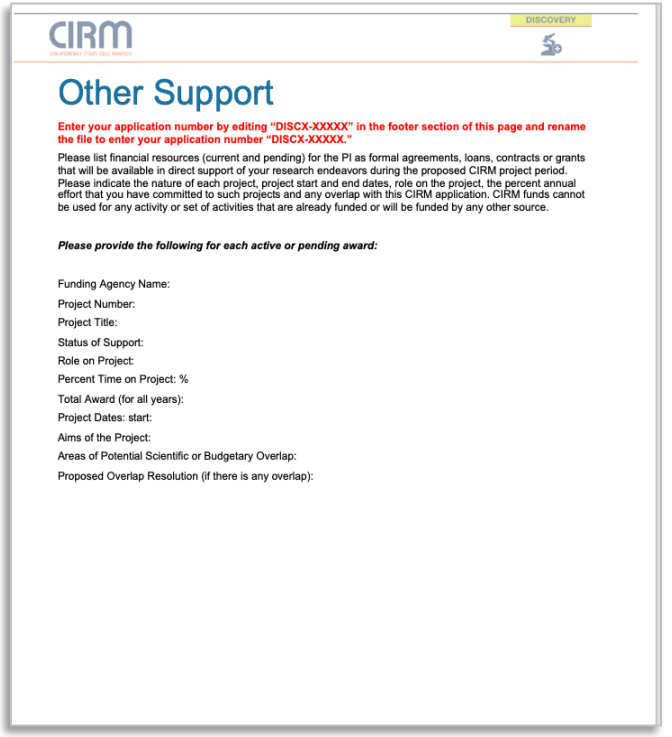
Provide the following information for the PI and key personnel (see "Who are key personnel" in the program announcement). The sketch should highlight research experience relevant to this proposal. Include relevant publications and/or patents or patent applications. Following biographical sketches for the PI, provide ~~bios/sketches~~ for other team members in alphabetical order.

To add an additional biographical sketch, select the template pages, copy and paste to create new pages.

Selected Accomplishments/ Honors

1. **List major accomplishments and honors in chronological order**
   Applicants may include accomplishments such as projects managed, IND submissions etc.
2. **Expertise and relevant experience**
   Provide a description of prior experience relevant to the proposed role in the project.
3. **Selected peer-reviewed publications/ patent applications/patents (in chronological order)**
   Do not include manuscripts submitted or in preparation.

Other Support



CIRM DISCOVERY

Other Support

Enter your application number by editing "DISCX-XXXXX" in the footer section of this page and rename the file to enter your application number "DISCX-XXXXX."

Please list financial resources (current and pending) for the PI as formal agreements, loans, contracts or grants that will be available in direct support of your research endeavors during the proposed CIRM project period. Please indicate the nature of each project, project start and end dates, role on the project, the percent annual effort that you have committed to such projects and any overlap with this CIRM application. CIRM funds cannot be used for any activity or set of activities that are already funded or will be funded by any other source.

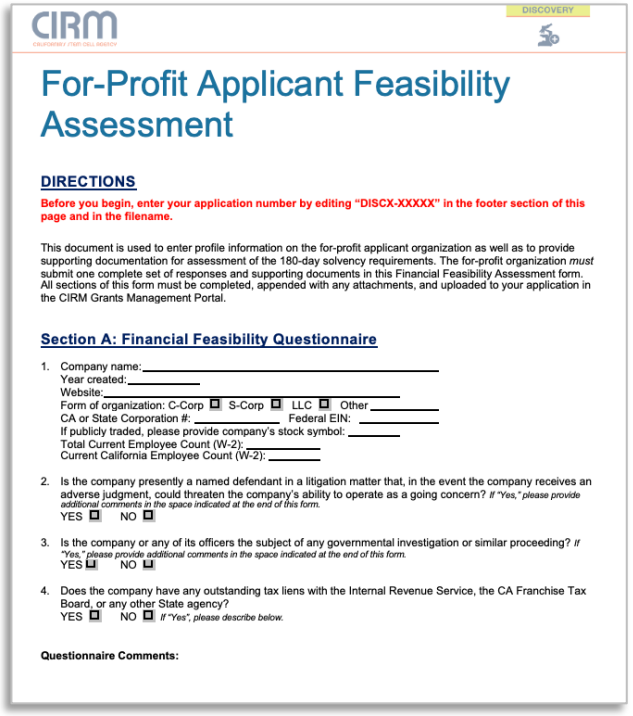
Please provide the following for each active or pending award:

Funding Agency Name:
Project Number:
Project Title:
Status of Support:
Role on Project:
Percent Time on Project: %
Total Award (for all years):
Project Dates: start:
Aims of the Project:
Areas of Potential Scientific or Budgetary Overlap:
Proposed Overlap Resolution (if there is any overlap):

You must use provided Templates Found in Uploads Section

Required Uploads | For-Profit Applicants Only

Financial Feasibility Assessment and Solvency Form



CIRM

DISCOVERY

For-Profit Applicant Feasibility Assessment

DIRECTIONS

Before you begin, enter your application number by editing "DISCX-XXXXX" in the footer section of this page and in the filename.

This document is used to enter profile information on the for-profit applicant organization as well as to provide supporting documentation for assessment of the 180-day solvency requirements. The for-profit organization *must* submit one complete set of responses and supporting documents in this Financial Feasibility Assessment form. All sections of this form must be completed, appended with any attachments, and uploaded to your application in the CIRM Grants Management Portal.

Section A: Financial Feasibility Questionnaire

1. Company name: _____
   Year created: _____
   Website: _____
   Form of organization: C-Corp ☐ S-Corp ☐ LLC ☐ Other _____
   CA or State Corporation #: _____ Federal EIN: _____
   If publicly traded, please provide company's stock symbol: _____
   Total Current Employee Count (W-2): _____
   Current California Employee Count (W-2): _____

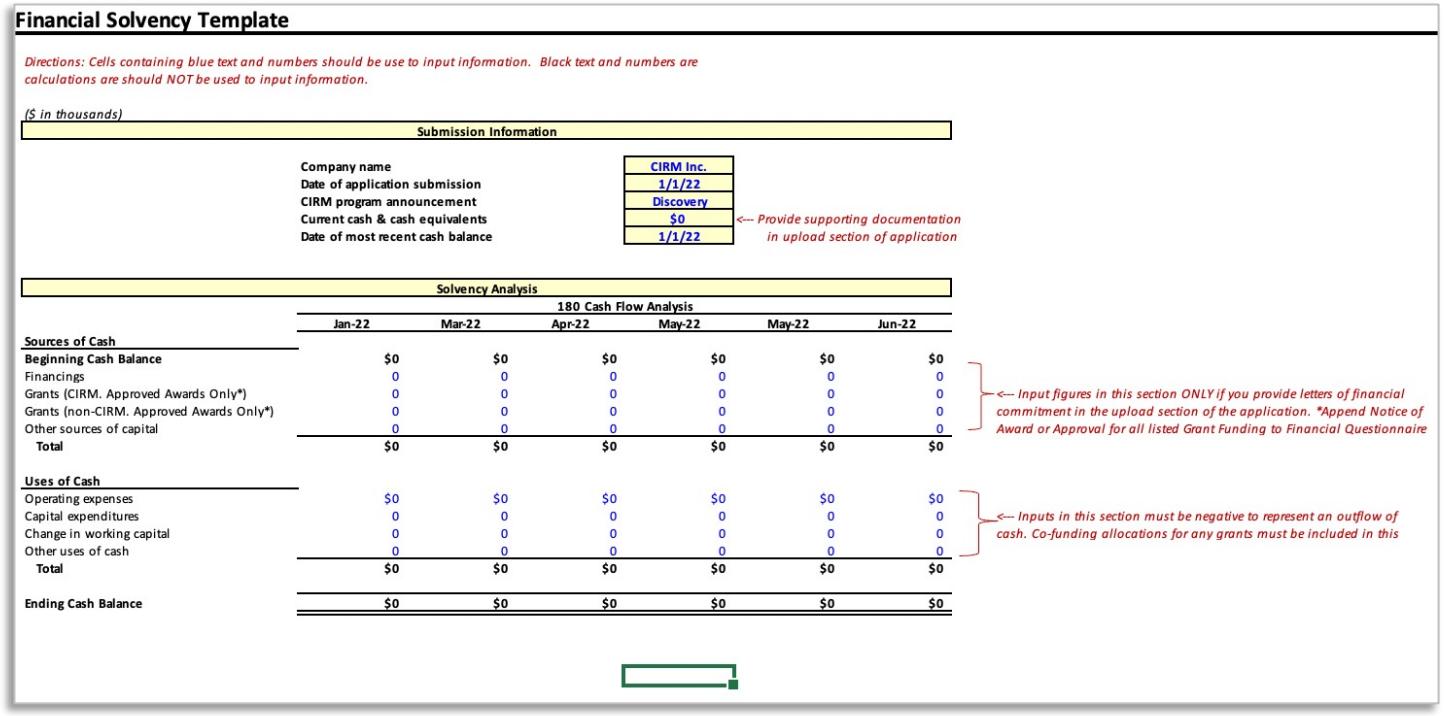
2. Is the company presently a named defendant in a litigation matter that, in the event the company receives an adverse judgment, could threaten the company's ability to operate as a going concern? *If "Yes," please provide additional comments in the space indicated at the end of this form.*
   YES ☐ NO ☐

3. Is the company or any of its officers the subject of any governmental investigation or similar proceeding? *If "Yes," please provide additional comments in the space indicated at the end of this form.*
   YES ☐ NO ☐

4. Does the company have any outstanding tax liens with the Internal Revenue Service, the CA Franchise Tax Board, or any other State agency?
   YES ☐ NO ☐ *If "Yes", please describe below.*

Questionnaire Comments:

Financial Solvency Template



Financial Solvency Template

Directions: Cells containing blue text and numbers should be use to input information. Black text and numbers are calculations are should NOT be used to input information.

($ in thousands)

Submission Information

Company name	CIRM Inc.
Date of application submission	1/1/22
CIRM program announcement	Discovery
Current cash & cash equivalents	$0
Date of most recent cash balance	1/1/22

<-- *Provide supporting documentation in upload section of application*

Solvency Analysis

180 Cash Flow Analysis

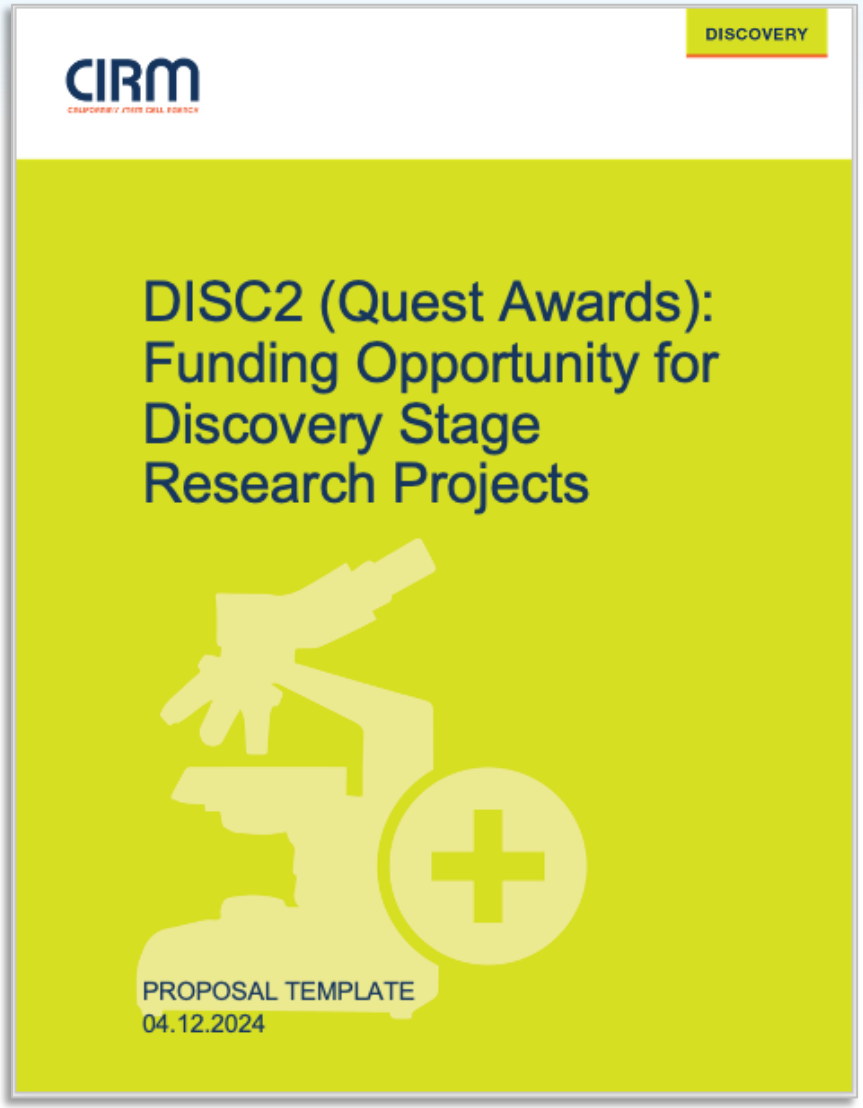
	Jan-22	Mar-22	Apr-22	May-22	May-22	Jun-22
Sources of Cash						
Beginning Cash Balance	$0	$0	$0	$0	$0	$0
Financings	0	0	0	0	0	0
Grants (CIRM. Approved Awards Only*)	0	0	0	0	0	0
Grants (non-CIRM. Approved Awards Only*)	0	0	0	0	0	0
Other sources of capital	0	0	0	0	0	0
Total	$0	$0	$0	$0	$0	$0
Uses of Cash						
Operating expenses	$0	$0	$0	$0	$0	$0
Capital expenditures	0	0	0	0	0	0
Change in working capital	0	0	0	0	0	0
Other uses of cash	0	0	0	0	0	0
Total	$0	$0	$0	$0	$0	$0
Ending Cash Balance	$0	$0	$0	$0	$0	$0

<-- *Input figures in this section ONLY if you provide letters of financial commitment in the upload section of the application. *Append Notice of Award or Approval for all listed Grant Funding to Financial Questionnaire*

<-- *Inputs in this section must be negative to represent an outflow of cash. Co-funding allocations for any grants must be included in this*

You must use provided Templates Found in Uploads Section

Required Uploads | Proposal 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

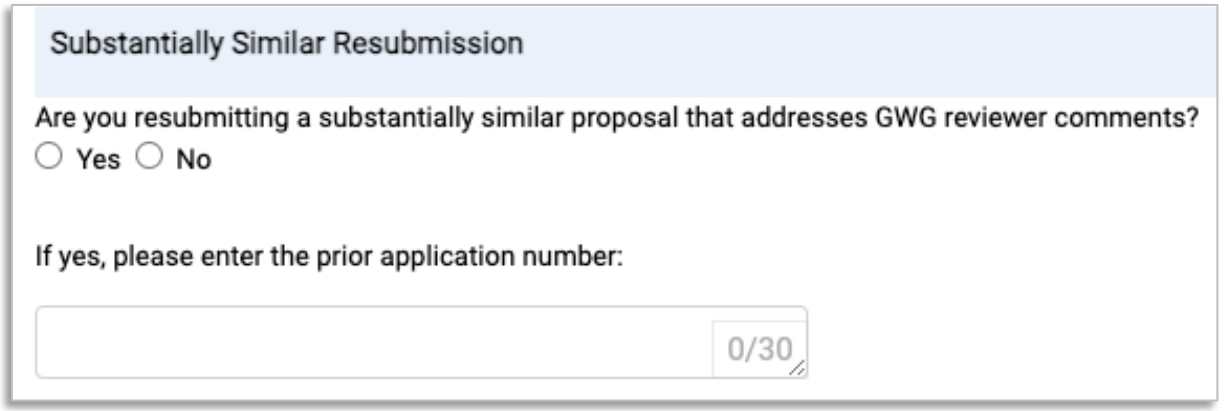
Application | Resubmissions

DID NOT previously pass Positive Selection:

- Submit as a new application

DID previously pass Positive Selection and received a merit score and GWG comments:

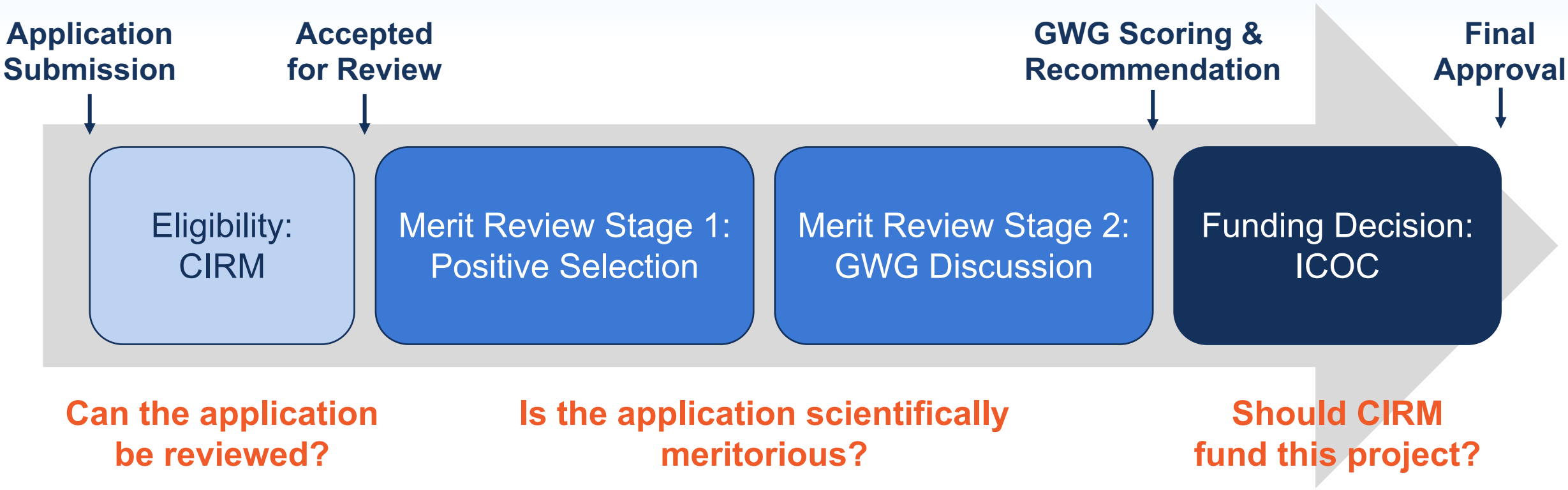
- Designate as a resubmission by selecting “yes” in the Information for Review Section



- Complete a Resubmission Statement found in the Proposal Template (Uploads)

DISC2 | Review Overview

Application Review Process



Merit Review Stage 1: Positive Selection

- Performed when the total number of applications exceeds the capacity of the GWG to review in a single cycle.
- GWG members (including scientific experts and patient advocate/nurse Board Members) conduct a pre-review of applications and select which ones to advance to a full review
  - Applications selected by any given GWG member in Stage 1 move to Stage 2 (GWG Discussion)
  - The CIRM President and CIRM scientific team will examine non-selected applications to determine if any merit moving to Stage 2
  - Unselected Applications do not advance to Stage 2 nor receive critiques

Merit Review Stage 2: GWG Scoring Method

1 to 100 Scoring

- Score of **85 to 100**: Application has exceptional merit and warrants funding
- Score of **1 to 84**: Application is not recommended for funding
  - Score of **80 to 84:** Application has merit but not ready to be funded at this time – if resubmitted in a future DISC competition, this application can *bypass* positive selection and automatically undergo full scientific review

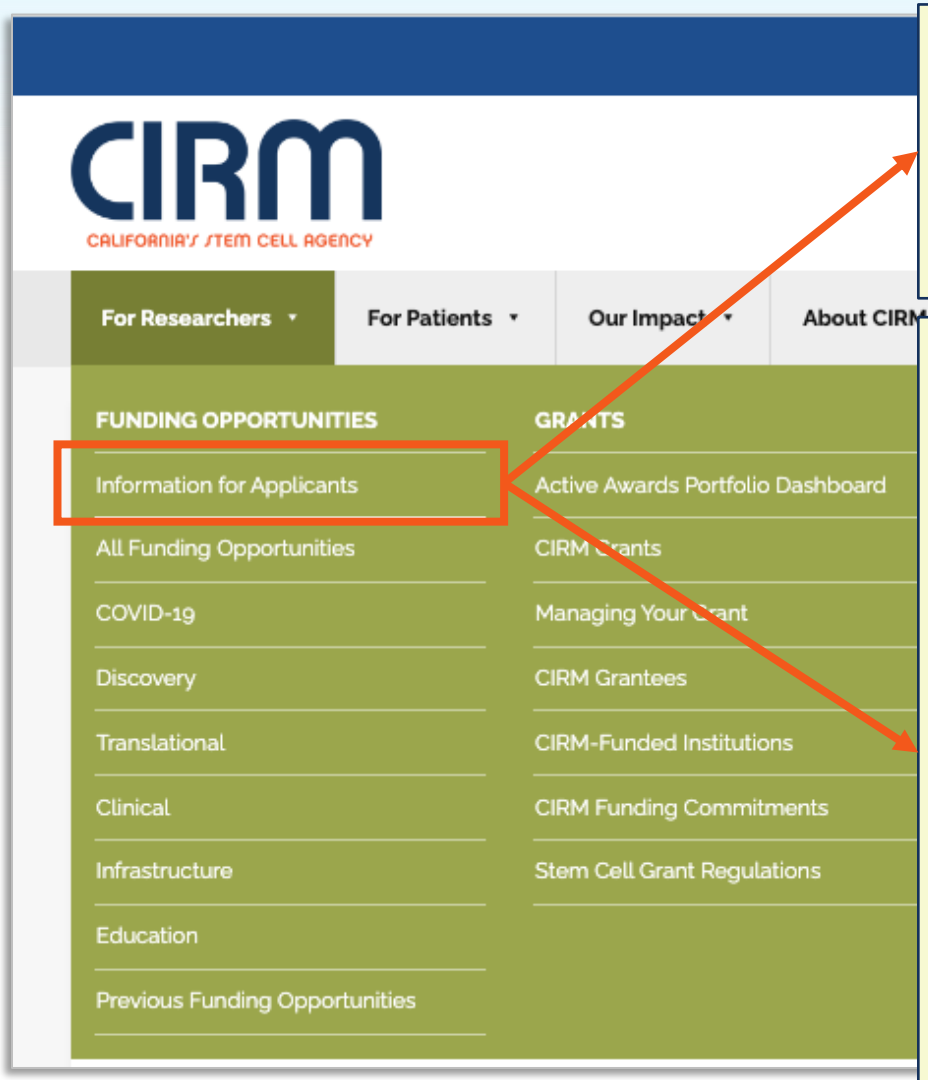
Applications receiving *any* score can revise and resubmit in future DISC competitions

Scientific Review Criteria

1. Does the project hold the necessary **significance and potential for impact**?
2. Is **the rationale sound**?
3. Is the project **well planned and designed**?
4. Is the project **feasible**?
5. Does the project **uphold principles of Diversity, Equity and Inclusion** (DEI)?

DISC2 | Resources and Contacts

Information and Resources for Applicants

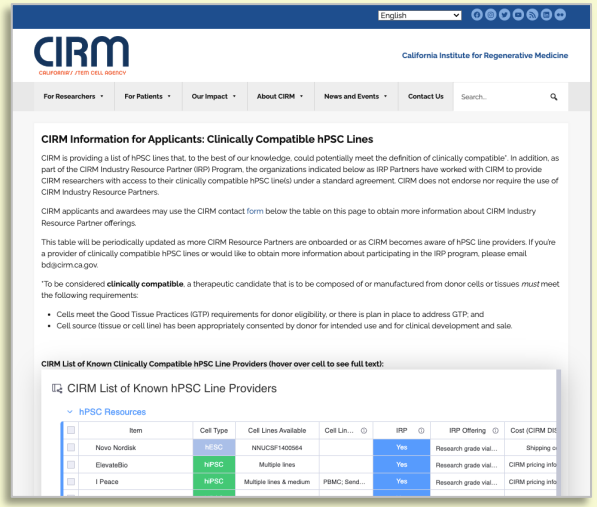


Data Sharing and Management

- Data Sharing Guidelines
- DSMP Templates for Funded Awards
- Data Repository Guidance

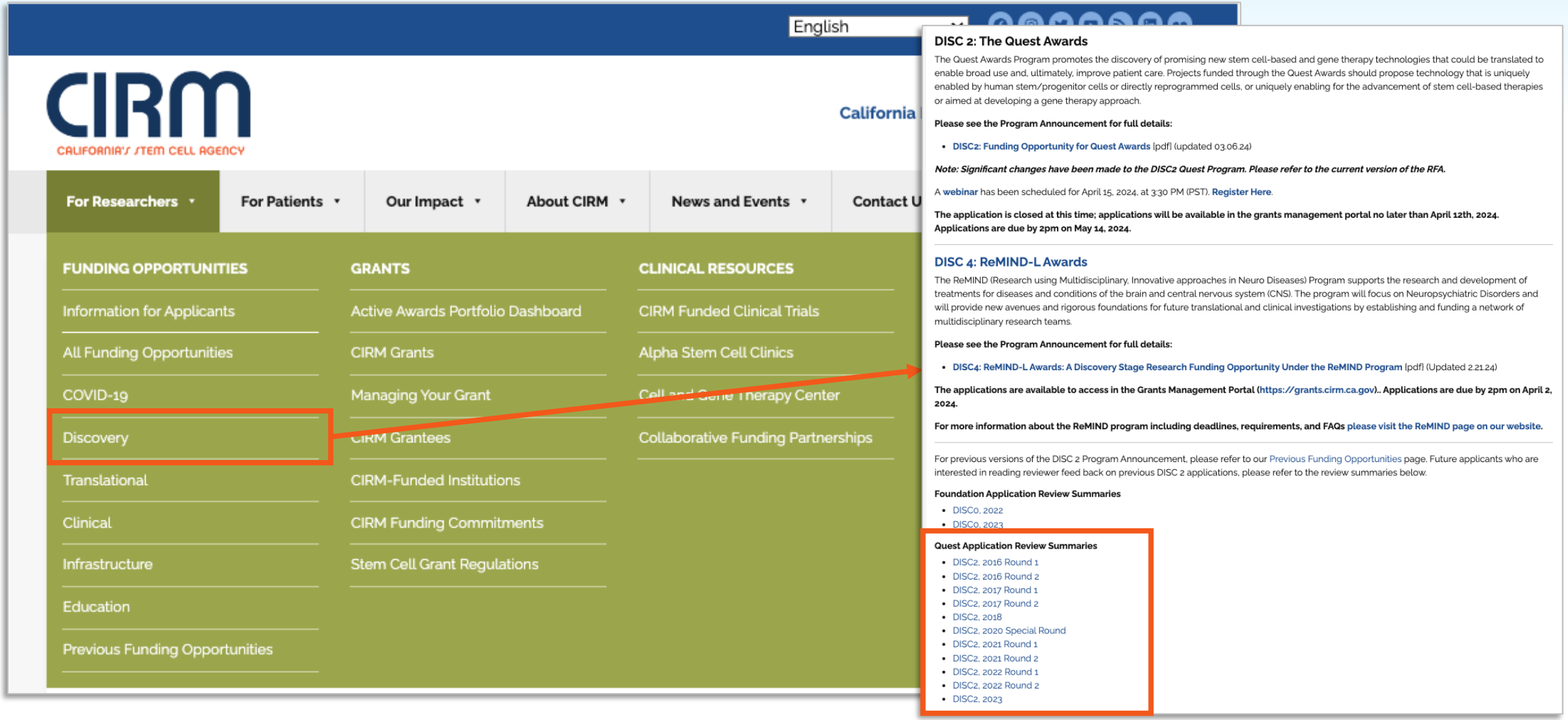
Clinically Compatible hPSC lines

- Information about clinical compatibility
- List of clinically compatible lines and vendors
- Informational webinar: https://youtu.be/HPnUFp5LJNQ?si=OV5KINs5FCQCw-Zl



PSC-Derived Regenerative Medicine Therapies: Selecting the Optimal Cell Line – Webinar (June 2022)

Previous DISC2 Review Summaries



https://www.cirm.ca.gov/about-cirm/funding-opportunities-discovery-stage-research

Contacts and Deadlines

Programmatic Questions
discovery@cirm.ca.gov

Budgeting and Administrative Questions
grantsmanagement@cirm.ca.gov

Review Questions
review@cirm.ca.gov

https://www.cirm.ca.gov/about-cirm/funding-opportunities-discovery-stage-research/

Recordings of this webinar and slide deck will be posted in ~1 week

Applications due May 14, 2024 at 2pm PT

DISC2 | Common Issues

DISC2 | Common Issues

- Ineligible Candidate Type
- Does Not Achieve Expected Outcomes
- Out-of-Scope or Stage-Inappropriate Activities
- Serious Application Submission Issues

DISC2 | Common Issues

Ineligible Candidate Type | Does Not Achieve Expected Outcomes | Out-of-Scope or Stage-Inappropriate Activities | Serious Application Submission Issues

Examples:

- Proposes non-cell/genetic therapeutic that acts on a stem/progenitor cell (Category C) **but** target population is not commonly understood to be a stem/progenitor cell type
- Proposes non-cell/genetic therapeutic that has unique requirement for stem cells for candidate identification and testing **but** fails to adequately support this contention (e.g., superficial use of stem cell models)

DISC2 | Common Issues

Ineligible Candidate Type	**Does Not Achieve Expected Outcomes**	Out-of-Scope or Stage-Inappropriate Activities	Serious Application Submission Issues

Proposal does not lead to a development candidate

Examples:

- "… after the award period, we plan to continue optimizing the candidate…"
- "… after selecting the candidate, we plan to demonstrate DMA of candidates in XYZ model in a future award…"

DISC2 | Common Issues

Ineligible Candidate Type	Does Not Achieve Expected Outcomes	**Out-of-Scope or Stage-Inappropriate Activities**	Serious Application Submission Issues

Examples:

- Proposal includes plans to conduct a clinical trial
- Proposal includes process development (e.g., GMP production, scale up) before establishing compelling evidence of disease modifying activity

DISC2 | Common Issues

Ineligible Candidate Type	Does Not Achieve Expected Outcomes	Out-of-Scope or Stage-Inappropriate Activities	**Serious Application Submission Issues**

Examples:

- Not using the provided template(s) for required uploads
- Incomplete applications

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Q&A