DISC2 Quest Awards Informational Webinar

Scientific Programs and Education Team

April 7, 2023

CIRM
CALIFORNIA'S STEM CELL AGENCY

Scientific Programs and Education Team

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DISC2 Webinar: **Agenda**

Part 1: DISC2 Overview	**2:00 - 2:45 PM**

- CIRM Mission, Strategic Plan and Pillars of Funding
- DISC2 Quest Awards
    - Expected Outcomes and Eligible Candidate Types
    - Scope and Activities
    - Applicant Eligibility Requirements
    - Review Process and Criteria
    - Application Components
    - Resources for Applicants
    - Common Questions and Mistakes

Part 2: Q&A	**2:45 - 3:00 PM**

Mission Statement

OUR MISSION

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

Delivering on CIRM's Mission

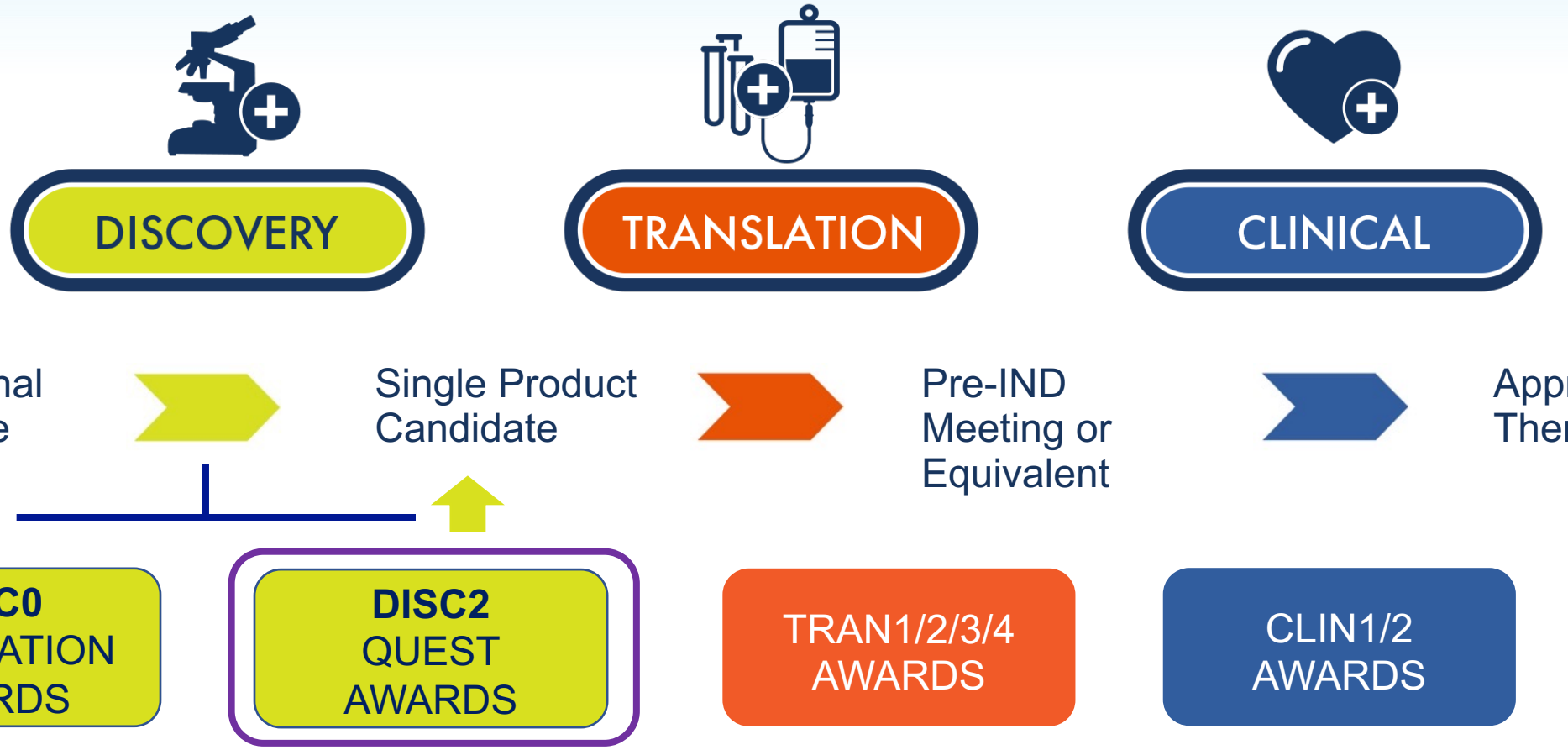
2006-2020 (Proposition 71)

- **Five Pillars of Investment**

2021 and Beyond (Proposition 14)

- CIRM's New Strategic Plan
  - align, enhance and interconnect existing pillars
  - develop next generation competency hubs
  - build knowledge networks

Core Funding Opportunities for Product Development



DISC Programs: **Expected Outcome** and **Support**

	Outcome	Funding	Duration	Progression
DISC2 QUEST AWARDS	Therapeutic Candidate	$1,500,000 (**Direct** Costs)	36 Months	TRAN1
	Technology Candidate	$500,000 (**Direct** Costs)	24 Months	TRAN2/3/4 or other
DISC0 FOUNDATION AWARDS	Basic Research	$1,000,000 (**Direct** Costs)	36 Months	DISC2 or N/A

Quest Awards: **Expected Outcome** (Deliverables)

Therapy Candidate

- **Single candidate** ready for translation (e.g. TRAN1)
- Demonstration of **reproducible disease/injury modifying activity** for candidate
- Measures of identity, activity and purity developed
- Target Product Profile

Technology Candidate

- **Prototype tool/technology** ready for translation (e.g. TRAN2/3/4)
- Demonstration of **performance** in test model(s) relevant to intended use
- Demonstration of **technical feasibility** to meet design requirements
- Target Product Profile

DISC2: Eligible Therapeutic Candidate Types

Cell Therapy (gene-modified or otherwise):

- where human stem/progenitor cells compose the therapy; or
- where human stem/progenitor cells are used to manufacture the cell therapy

Genetic Therapy (altering genome/manipulating nucleic acids in cells)

- that targets a human somatic cell for its therapeutic effect, **AND**
- intended to replace, regenerate, or repair the function of aged, diseased, damaged, or defective cells, tissues and/or organs

Other Therapy (small molecule, biologic, etc.)

- that acts on endogenous human stem cells for its therapeutic effect
- that is dependent on targeting human cancer stem cells for its therapeutic effect
- that modifies a stem cell therapy; **OR**
- where a human stem cell is necessary to manufacture the therapy (e.g. exosomes)
- where human stem cells are uniquely required for candidate identification and testing

DISC2: Eligible **Technology** Candidate Types

Diagnostics, Device or Tool Candidates:

- human **stem/progenitor cell-based** diagnostic test, device or tool/technology that can be used to discover, advance, monitor, or evaluate new therapies; **OR**

- a novel diagnostic test, device, or tool/technology that addresses a critical bottleneck to the discovery, development, or use of stem cell-based or genetic therapies; **AND**
  - where the proposed activities include and that propose proof of concept testing with human stem cells or relevant human somatic cells targeted by a gene therapy

IN SCOPE ACTIVITIES

What **activities** does DISC2 support?

Activities that contribute to the selection of a novel candidate that can immediately progress to translation to enable broad use, e.g.

- **Activities towards demonstrating Proof of Concept**
- Developing and implementing assays to **identify/test/characterize candidate**
- **Feasibility and reproducibility** assessment
- Developing a **Target Product Profile**
- Preparation for and conduct of stage-appropriate regulatory meetings, if applicable (e.g. INTERACT meeting)

What defines "Proof of Concept (POC)"?

Stem Cell Based Therapy Candidates (+/- other components)

For example, PSC-derived neuronal cells; gene-modified HSPCs, hNSC + biomaterials combination

Demonstration of reproducible disease/injury modifying activity (DMA), with the candidate* to be translated in a preclinical model relevant to the target indication

Allogeneic** candidate: demonstrated ***using product made** from the **same cells/line intended for translation;** line should be **clinically compatible

***Autologous** candidate: demonstrated ***using product made from 2 or more donor sources,** to establish reproducibility of process

What defines "Proof of Concept"?

Genetic Therapy Candidates *that are not also stem cell therapies*

For example, AAV delivered genes, ASOs, mRNA, oligonucleotides, or ex vivo gene-modified somatic cells, CAR T cells*

Demonstration of reproducible disease/injury modifying activity with the candidate* to be translated using a clinically relevant model AND

- ✓ establishing that the genetic therapy candidate targets or has activity on a clinically relevant human cell population

** Note: if a genetic therapy candidate is composed of cells, the allogeneic/autologous consideration for proof of concept applies, as described for stem cell therapy candidates*

What defines "Proof of Concept"?

Drug or Biologic Candidates

For example, small molecules, antibodies, peptides, exosomes, etc.

Demonstration of reproducible disease/injury modifying activity with the candidate to be translated

✓ on or with a clinically relevant human stem/progenitor or cancer stem cell population

- If a small molecule requires further optimization beyond the DISC2 project period (e.g. by medicinal chemistry to improve properties): the candidate will **not** be ready for translation
- If the candidate is itself manufactured from human stem/progenitor cells, DMA can be demonstrated without the strict requirement for testing on/with human stem/progenitor cells

What defines "Proof of Concept"?

Technology Candidates* (Diagnostic, Device, Tool)

For example, novel stem cell-based disease models for drug screening; diagnostics that incorporate stem cell components; tools for use with stem cell or genetic therapies; tools that address genetic therapy or stem cell bottlenecks

Demonstration that candidate (prototype) meets initial performance criteria in a test model relevant to intended use

For **NON- stem cell-based technology candidates,** POC includes testing with human cells to demonstrate utility as follows:

- using human stem cells (projects addressing stem cell bottlenecks)
- using human somatic cells (projects addressing gene therapy bottlenecks)

** Note: products containing allogeneic cells will need to be appropriately consented to be considered for translation*

What **activities** are **not** supported by DISC2?

Translational and Clinical Stage activities, for example:

- developing GMP, CLIA-compliant processes; GLP studies
- implementing Design Control, developing commercialization process
- Preparing for and conducting IND, IDE, 510(k) filings, etc.
- Preparation for and conduct of clinical trials

Exploratory activities that have not been justified as necessary for achieving the expected outcome (product) of the DISC2 program

Conditional**: Use of special supplemental funding to purchase, derive, or test hPSC lines that do not meet** FDA requirements for donor eligibility and/or have not been appropriately consented for clinical development and sale (allogeneic cell therapy candidates)

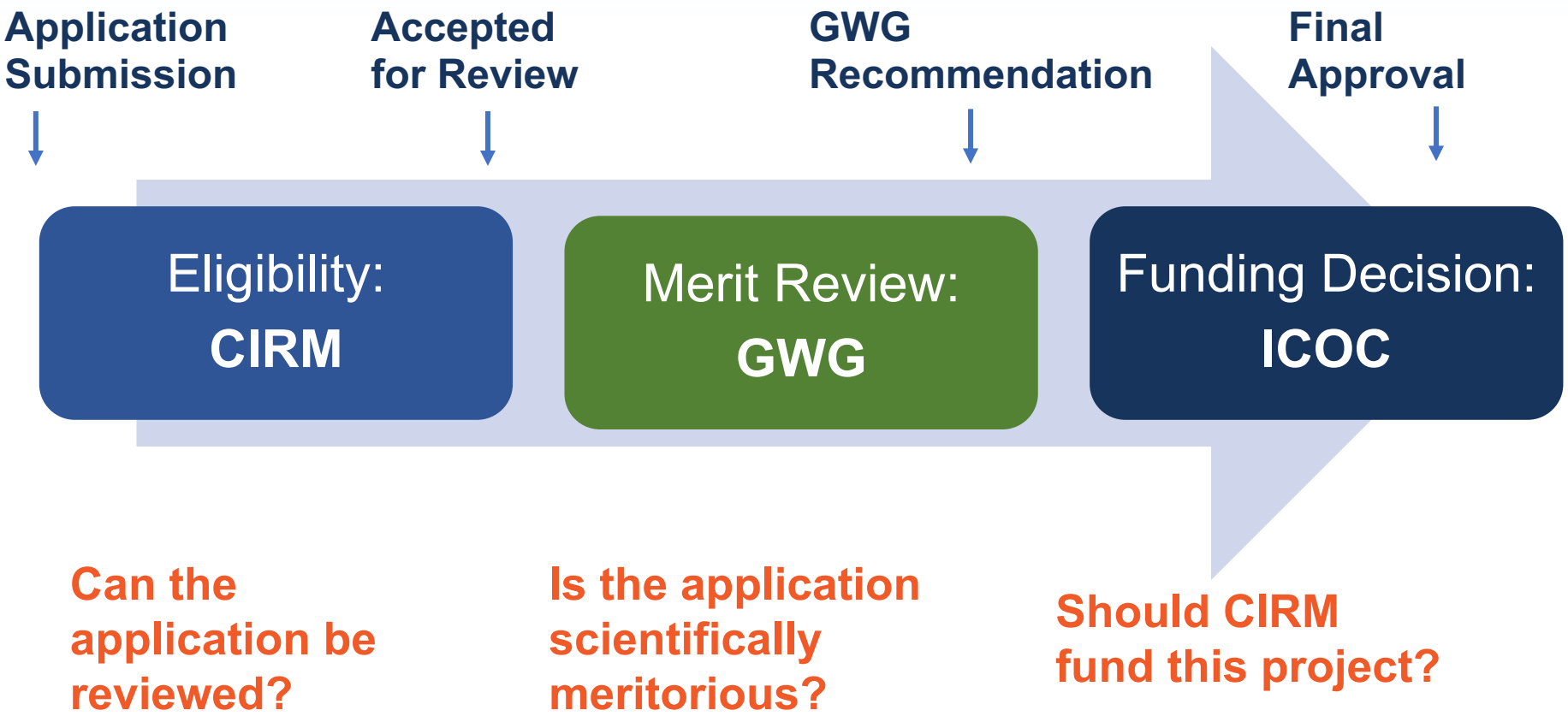
APPLICANT ELIGIBILITY

Applicant Eligibility: **Who Can Apply?**

- Only **CA institutions** can apply
- **PI** – Must commit least **20% effort**
- **PI** – limited to **one DISC2 application per review cycle**
- **PI** must **not have a substantially similar application** with overlapping activities pending review under **any** CIRM funding opportunity.
- Award must be able to start **within 90 days** of CIRM Board approval
- **For-profit** applicants must demonstrate **solvency**

REVIEW PROCESS and CRITERIA

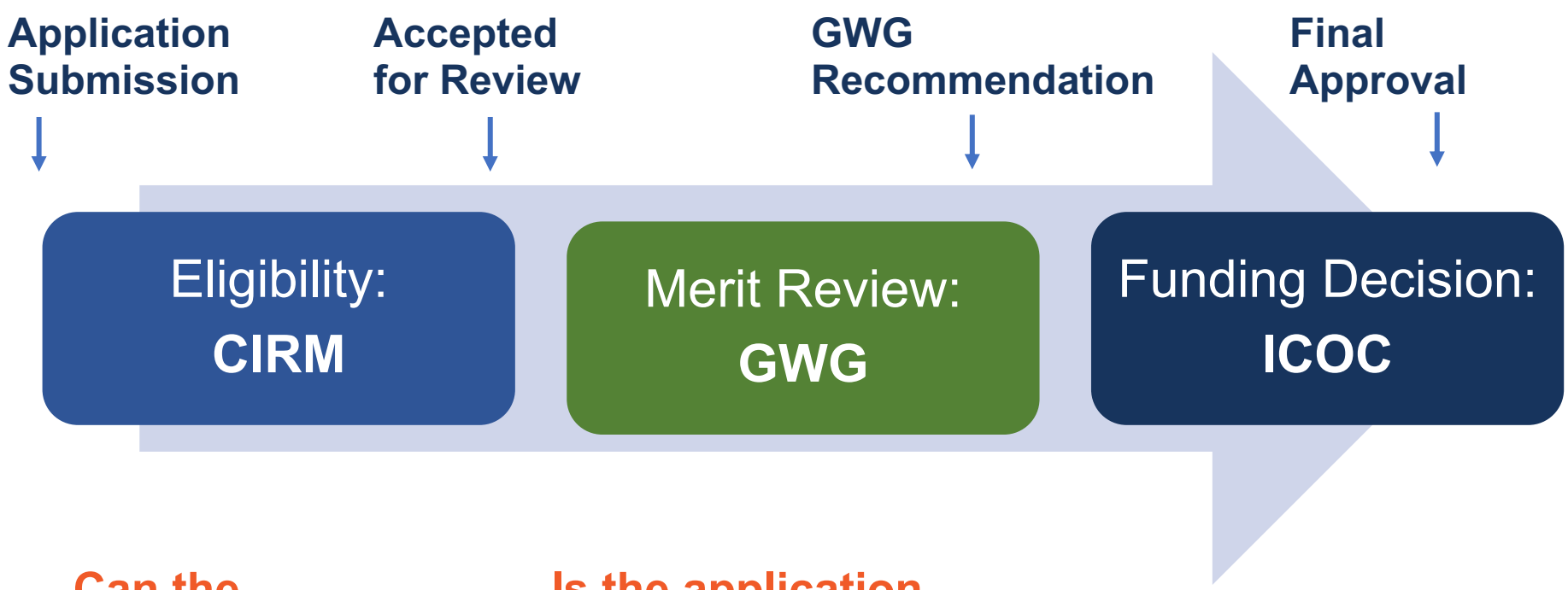
Application Review Process



Application Review Process

When application volume exceeds GWG capacity

➢ **POSITIVE SELECTION**



Positive Selection Overview

Review Process for **High Volume* Programs**

- **Stage 1: "Positive Selection"-** GWG members (Both Scientific and Patient Advocate Members from CIRM's Governing Board) conduct a pre-review of all applications to identify a subset that they believe are most impactful and responsive
- **Stage 2 : Applications selected** by any given GWG member in Stage 1 move to Stage 2, the CIRM Standard Review Process
- ***Unselected Applications:*** **do not advance to Stage 2 nor receive critiques,** but may consider reapplying

* When application volume exceeds GWG capacity

Scientific Review Criteria

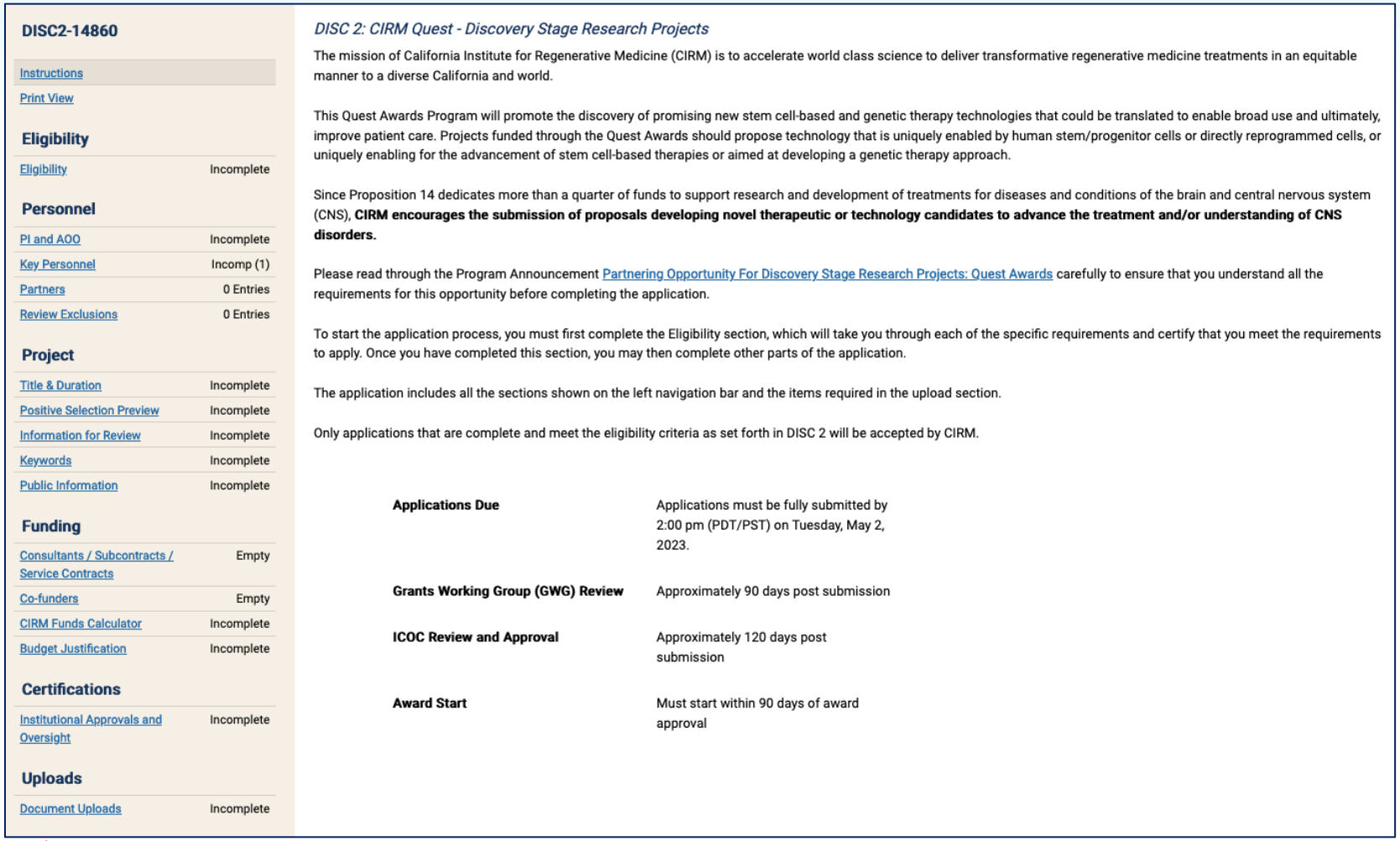
1) Does the project hold the necessary **significance and potential for impact**?
2) Is **the rationale sound**?
3) Is the project **well planned and designed**?
4) Is the project **feasible**?
5) Does the project **uphold principles of Diversity, Equity and Inclusion** (DEI)?

Application COMPONENTS and CONSIDERATIONS (I)

Application Components: Overview

Online Sections

Attachments, Templates



Application – 2 Major Components

1. Completed Online

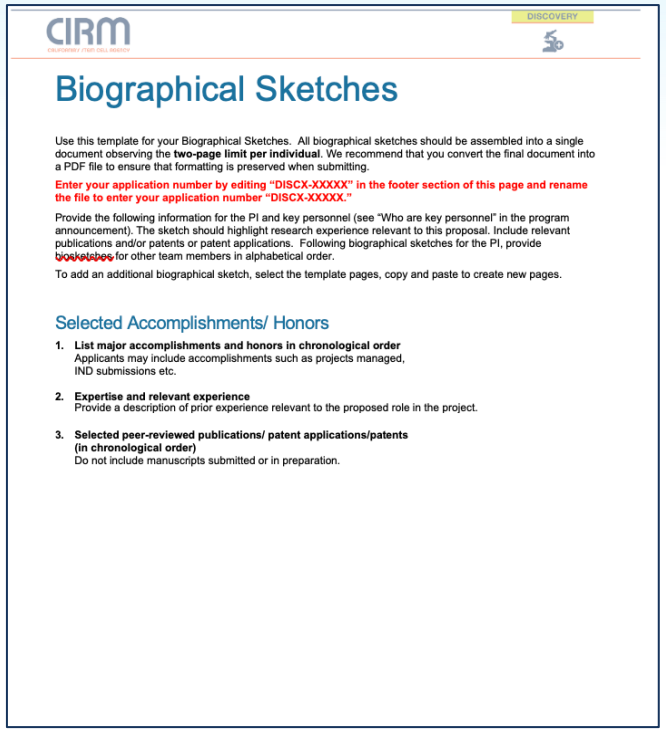
- ✓ **Applicant Details** (budget, key personnel, collaborators, etc.)
- ✓ **Positive Selection Preview Page-** a special summary used for first stage of high-volume review

2. Completed as Uploads (attached to online application)

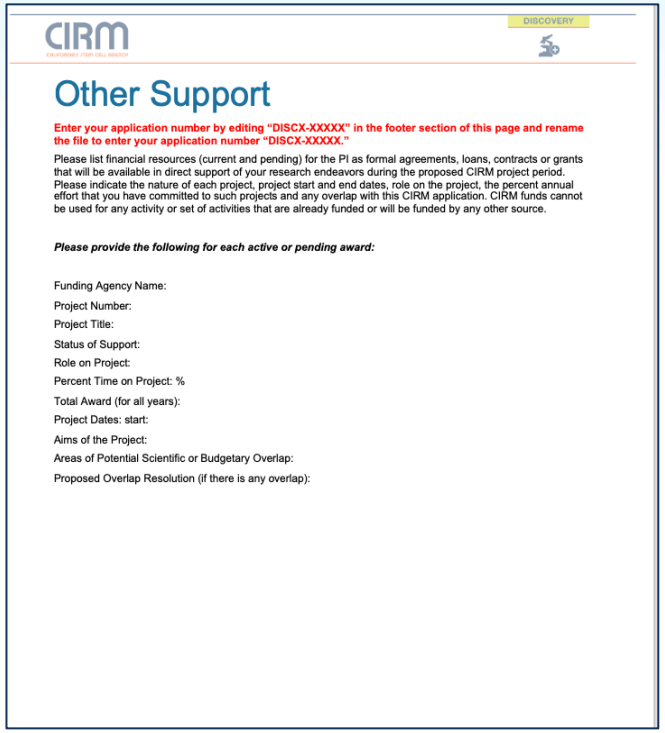
- ✓ **Required** - ***must use provided templates (found in Uploads Section)***
  - *Proposal*
  - *Other Support*
  - *Biological Sketches*
  - *Financial Feasibility, Solvency (For Profit Applicants Only)*
- ✓ **Optional**
  - *Letters of Support*
  - *IP Licenses and MTA*

Required Application Components: Uploads

Proposal



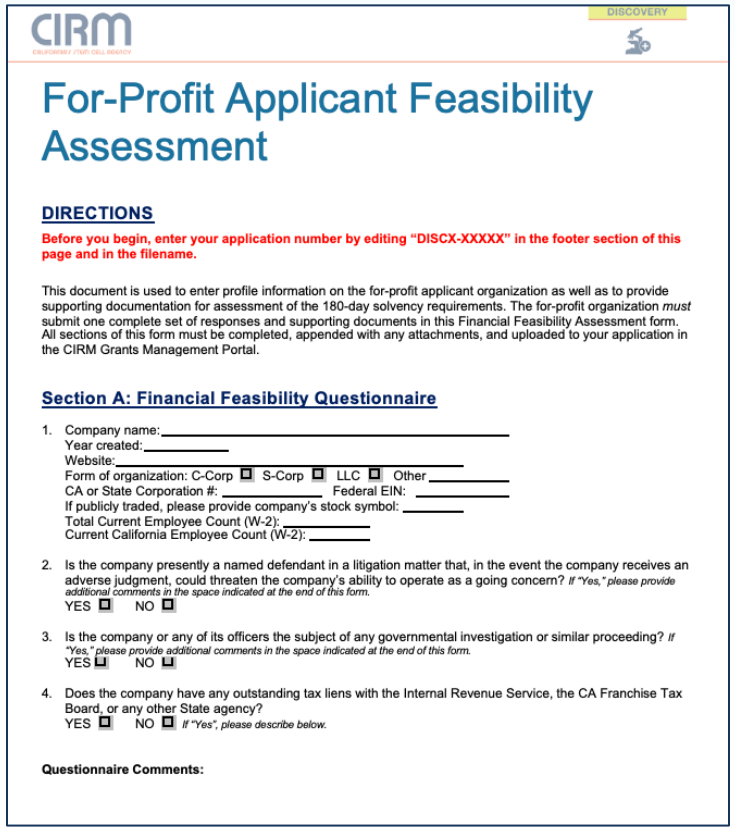
Biosketch



Other Support

Templates Found in Uploads Section

For Profit Applicants Only: **Required** Uploads



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): _____

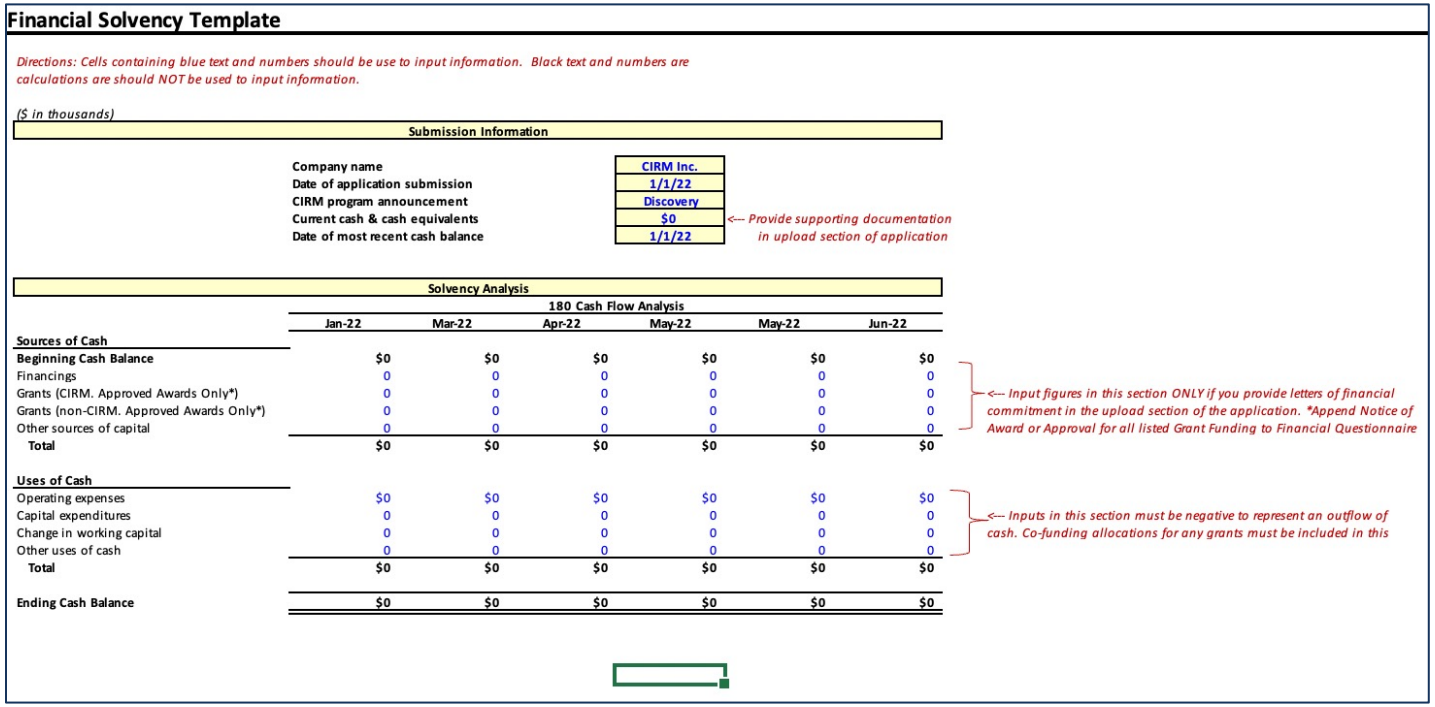
2. Is the company presently a named defendant in a litigation matter that, in the event the company receives an adverse judgment, could threaten the company's ability to operate as a going concern? *If "Yes," please provide additional comments in the space indicated at the end of this form.*
   YES ☐ 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 Feasibility Assessment Form



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*

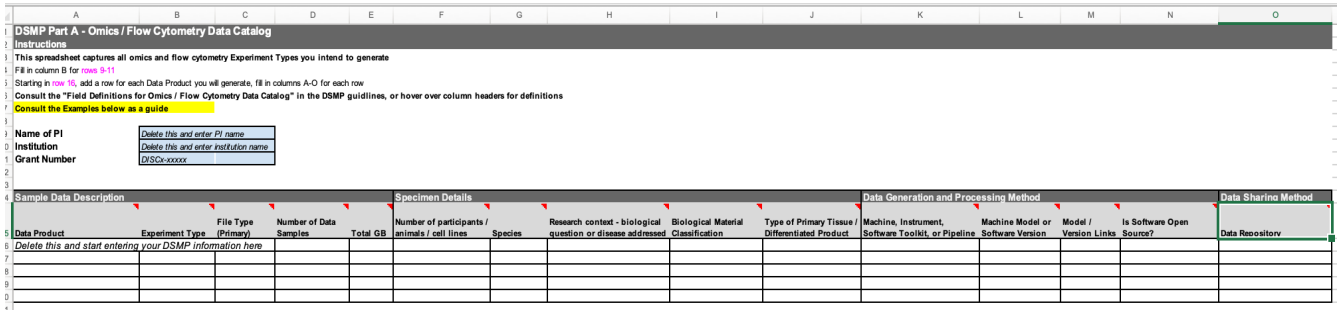
<--- *Inputs in this section must be negative to represent an outflow of cash. Co-funding allocations for any grants must be included in this*

Financial Solvency Spreadsheet

Data Sharing and Management Plan **(DSMP)**

Data Sharing Overview: Submitted with **Application**

DSMP: Submitted only **if/when Awarded**



DSMP Part A - Omics / Flow Cytometry Data Catalog

Instructions

This spreadsheet captures all omics and flow cytometry Experiment Types you intend to generate

Fill in column B for rows 9-11

Starting in row 16, add a row for each Data Product you will generate, fill in columns A-O for each row

Consult the "Field Definitions for Omics / Flow Cytometry Data Catalog" in the DSMP guidlines, or hover over column headers for definitions

Consult the Examples below as a guide

Name of PI	Delete this and enter PI name
Institution	Delete this and enter institution name
Grant Number	DISCx-xxxxx

Sample Data Description					Specimen Details					Data Generation and Processing Method				Data Sharing Method
Data Product	Experiment Type	File Type (Primary)	Number of Data Samples	Total GB	Number of participants / animals / cell lines	Species	Research context - biological question or disease addressed	Biological Material Classification	Type of Primary Tissue / Differentiated Product	Machine, Instrument, Software Toolkit, or Pipeline	Machine Model or Software Version	Model / Version Links	Is Software Open Source?	Data Repository
Delete this and start entering your DSMP information here														

Part A: Data Catalog

DSMP Guidelines and Templates at
www.cirm.ca.gov/information-for-applicants

Part B - Data Sharing and Management Plan (DSMP) for Omics/Flow Cytometry Data

Questionnaire

DO NOT SUBMIT DSMP with APPLICATION
If funded, submit DSMP as Just in Time (JIT) material during pre-funding administrative review (PFAR)

Table of Contents

1. Grant Number - required
2. Name of Applicant PI - required
3. Novel software in data processing or data reuse - if applicable
4. Proprietary software in data processing or data reuse - if applicable
5. Code availability - required
6. Additional Information for "Data Repository" - if applicable
7. Data Project Manager - required
8. Consent language related to data sharing - required for all human data
9. Data Use Limitation (DUL) records - required for all human data
10. Restrictions limiting extent of data sharing - required
11. Justification of omics or flow cytometry data that will not be shared - if applicable
12. Metadata and Data Standards - required
13. Feedback - optional

Questions 3, 4, 6 refer to entries in the DSMP Data Catalog

Part B: Questionnaire

Application Components: Proposal Template

- **Use the 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 Process: Resubmitting

- For resubmissions that did ***not pass Positive Selection***:
  - *Submit as a new application*

- For resubmissions that **received a merit score and GWG feedback** from a previous review:
  - Designate as a resubmission by selecting “yes” in the Information for Review Section
  - Complete a Resubmission Statement found in the Proposal Form (Uploads)

Substantially Similar Resubmission

Are you resubmitting a substantially similar proposal that addresses GWG reviewer comments?

◉ Yes ○ No

Table of Contents

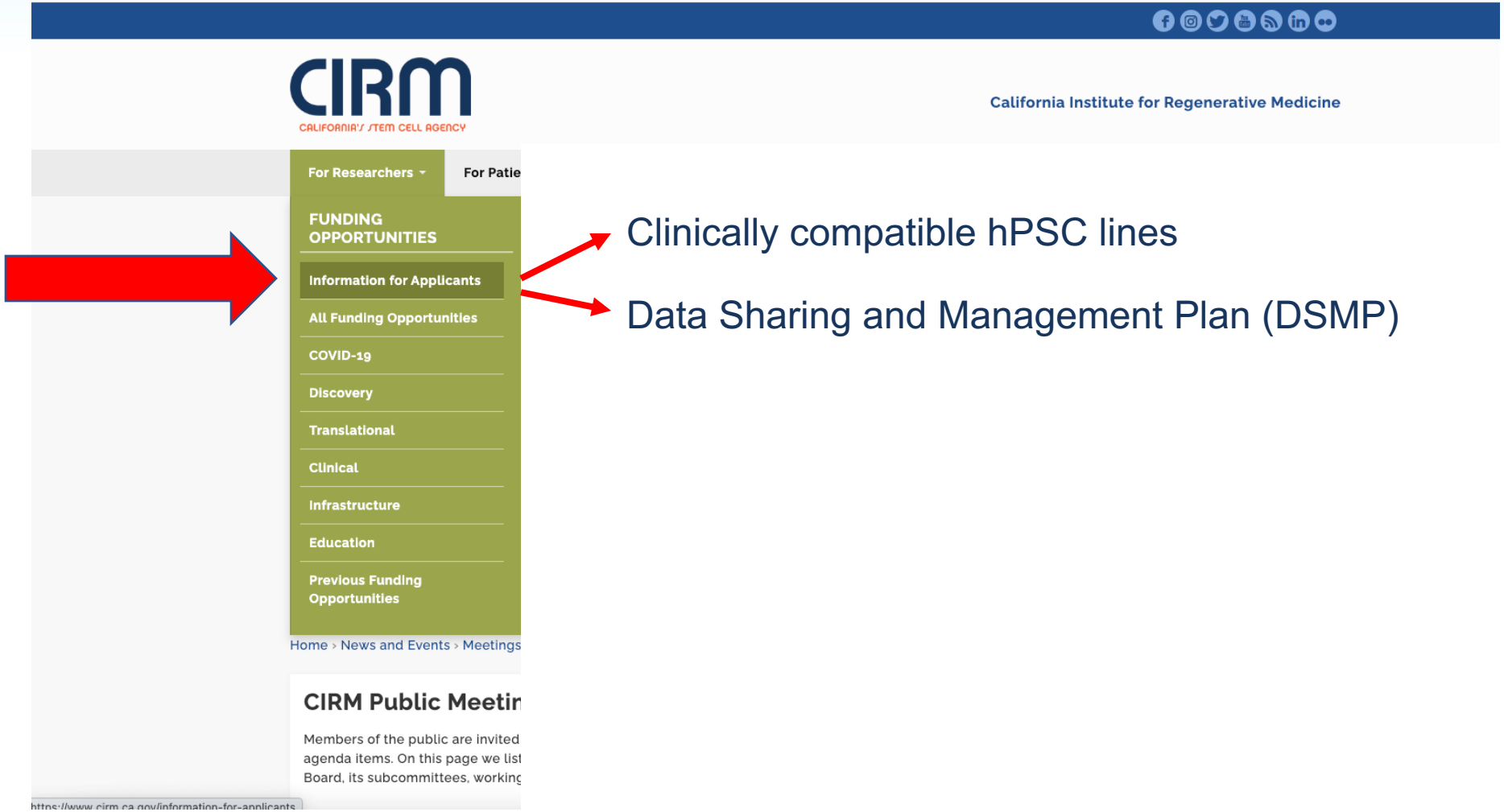
When you have finished the Proposal, please in the Table of Contents below.

Proposal Sections
Resubmission Statement (up to 1 page)
Statement of Significance and Impact (up to

RESOURCES for APPLICANTS

- Clinically Compatible hPSC lines
- Data Sharing and Management Plans
- Previous DISC2 Review Summaries

Information and Resources for Applicants



Clinically compatible hPSC lines

Data Sharing and Management Plan (DSMP)

Clinically Compatible Cell Lines

DISC2 grantees developing an **allogeneic cell-based therapeutic candidate** must employ a cell line that meets CIRM's definition of **Clinically Compatible**:

- ✓ Line can meet Good Tissue Practices (GTP) requirements for donor eligibility, or there is plan in place to address GTP
- ✓ Line has been appropriately consented by donor for intended use and for clinical development and sale.

hPSC lines from the CIRM iPSC Repository do not meet this definition

A special, optional budget can be requested for acquiring and evaluating clinically compatible hPSC lines *for the purpose of* candidate selection

Clinically Compatible hPSC Lines

www.cirm.ca.gov

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

www.youtube.com/CIRMTV

CIRM Information for Applicants: Clinically Compatible hPSC Lines

CIRM is providing a list of hPSC lines that, to the best of our knowledge, could potentially meet the definition of clinically compatible*. In addition, as part of the CIRM Industry Resource Partner (IRP) Program, the organizations indicated below as IRP Partners have worked with CIRM to provide CIRM researchers with access to their clinically compatible hPSC line(s) under a standard agreement. CIRM does not endorse nor require the use of CIRM Industry Resource Partners.

CIRM applicants and awardees may use the CIRM contact form below the table on this page to obtain more information about CIRM Industry Resource Partner offerings.

This table will be periodically updated as more CIRM Resource Partners are onboarded or as CIRM becomes aware of hPSC line providers. If you're a provider of clinically compatible hPSC lines or would like to obtain more information about participating in the IRP program, please email bd@cirm.ca.gov.

*To be considered **clinically compatible**, a therapeutic candidate that is to be composed of or manufactured from donor cells or tissues *must* meet the following requirements:

- Cells meet the Good Tissue Practices (GTP) requirements for donor eligibility, or there is plan in place to address GTP; and
- Cell source (tissue or cell line) has been appropriately consented by donor for intended use and for clinical development and sale.

CIRM List of Known Clinically Compatible hPSC Line Providers (hover over cell to see full text):

CIRM List of Known hPSC Line Providers

hPSC Resources

Item	Cell Type	Cell Lines Available	Cell Line…	IRP	IRP Offering	Cost (CIRM DISC2 Pr…
Novo Nordisk	hESC	NNGMP0161		Yes	Research grade vial…	Shipping cost only
ElevateBio	hiPSC	Multiple lines		Yes	Research grade vial…	CIRM pricing info upon requ…
I Peace	hiPSC	Multiple lines & medium	PBMC; Senda…	Yes	Research grade vial…	CIRM pricing info upon requ…
Reprocell	hiPSC	Multiple lines	Fibroblast; m…	Yes	GMP seed stock vial…	CIRM pricing info upon CDA…
AgeX	hESC	ESI-017, ESI-035, ESI-0…		No		
Allele Bio	hiPSC	Enquire with provider	mRNA	No		
Catalent	hiPSC	HLA-homozygous lines. …	Cord blood	No		
CiRA Foundation	hiPSC	Enquire with provider		No		
Fujifilm CDI	hiPSC	Enquire with provider		No		
Hadassah hSC RC	hESC	HAD-C 100, HAD-C 102,…		No		
Pluristyx	hiPSC	Enquire with provider		No		
Sampled	hiPSC	LiPSC-GR1.1	Cord blood; e…	No		
WiCELL	hESC	WA01, WA07, WA09, W…		No		

Data Sharing and Management

- DSMP Guidelines
- DSMP Templates for Awarded Projects
- Data Repositories Guidance

Data Sharing and Management

As articulated in CIRM's 2022-2027 strategic plan, CIRM is committed to building infrastructure that organizes and democratizes data through knowledge networks that foster a culture of open science and advance novel, discovery, translational and clinical research approaches. The CIRM knowledge networks will facilitate effective management, standardization, sharing and collaborative analysis of CIRM-funded data.

As an important step toward realizing this goal, CIRM requires that data generated using CIRM funds are shared using FAIR principles, as delineated in a **Data Sharing and Management Plan (DSMP)**. Please consult the DSMP Guidelines for CIRM data sharing requirements and guidance on how to prepare a DSMP.

Discovery Stage Programs (DISC0, DISC2)

Application Stage: Data Sharing Overview
A general overview of a plan for sharing data produced in the proposed project (Data Sharing Overview) must be included in the application. Instructions for completing a Data Sharing Overview are provided in the application.

Pre-Funding Administrative Review (PFAR) for awarded projects: DSMP
If a project is awarded and proposes to generate ***omics and /or flow cytometry data***, a DSMP must be submitted to CIRM as Just in Time (JIT) material during PFAR, using DSMP for Omics and Flow Cytometry Data templates.

DSMP Guidelines
DSMP for Omics and Flow Cytometry Data - Guidelines – Discovery Awards

DSMP templates (DSMP consists of 2 documents, Parts A & B)
Part A - DSMP for Omics and Flow Cytometry Data - Data Catalog
Part B - DSMP for Omics and Flow Cytometry Data - Questionnaire

Omics / Flow Cytometry Data

For ***data from other types of experiments*** (e.g., imaging, electrophysiology, etc.), CIRM may work with the awardee to develop a DSMP and establish data sharing milestones prior to CIRM issuing a Notice of Award.

Translational and Clinical Trial Stage Research

A DSMP must be submitted **as part of the application**. The template for the DSMP is provided as part of the online application in the Upload section.

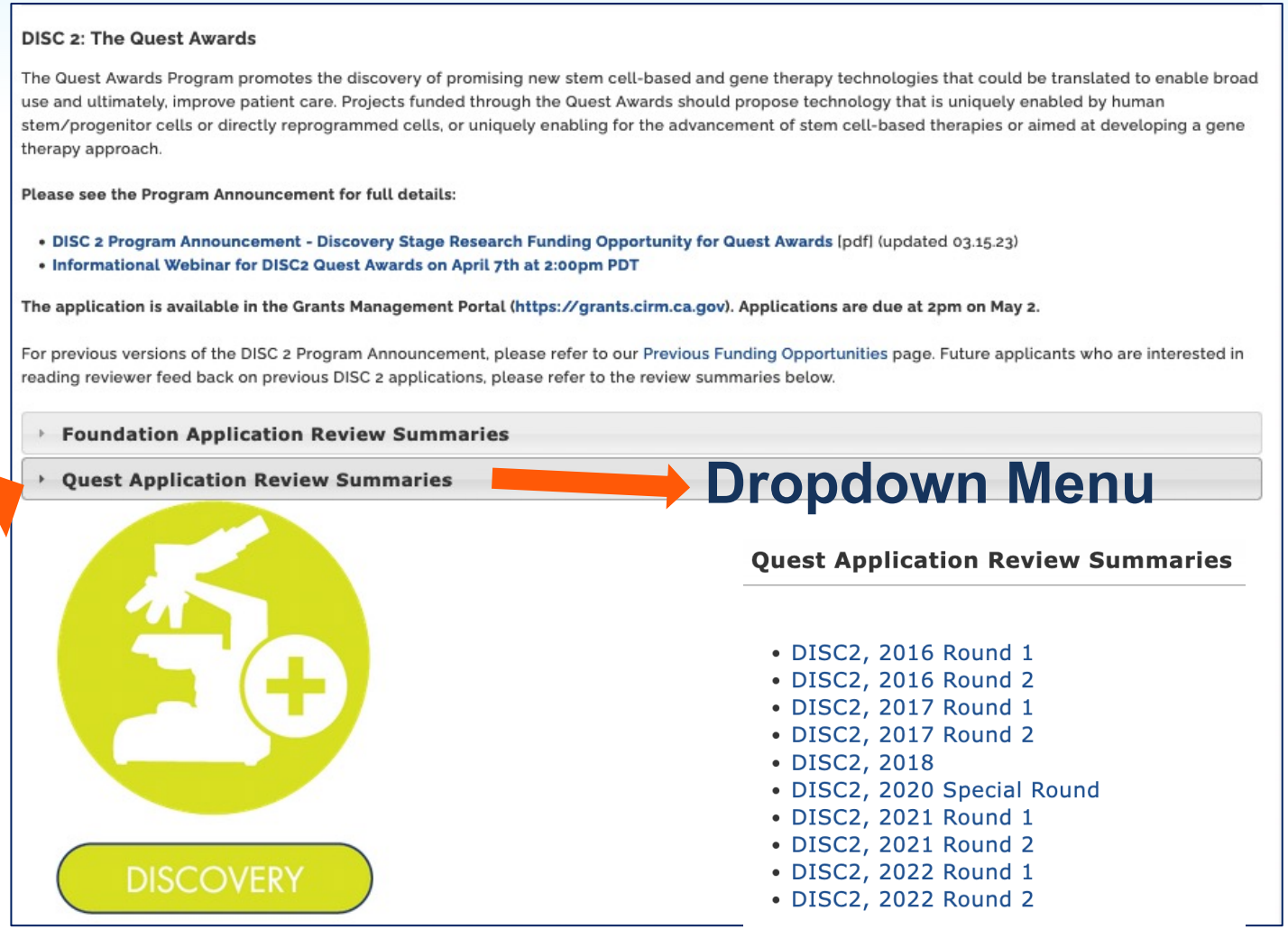
- DSMP - Guidelines – Translational and Clinical Awards

Data Repositories

CIRM expects that data will be deposited in established data repositories when possible. Please consult the **Data Repositories Guidance** for information about established data repositories.

- Data Repositories Guidance

Previous DISC2 Review Summaries



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

COMMON ISSUES – LESSONS LEARNED

Common **Issues** Affecting **Eligibility**

- **Missing key activities** needed to meet the Expected Outcome/Deliverable
- Selecting the **wrong candidate track** (technology vs. therapeutic)
- **Failure to include requisite** testing with human cells/stem cells
- Inclusion of **out-of-scope or stage-inappropriate** activities
- **Lacking a basis or rationale** for stem cells or genetic therapy
- **Not using the appropriate template**(s) for required Uploads
- **Incomplete** applications
- **< 20%** PI effort

Common **Issues** Affecting **Merit (Score)**

- **Unlikely to meet Expected Outcome** (too premature, too unfocused)
- **Preliminary data is insufficient or unconvincing**
- **Weak alignment with CIRM priorities** (superficial link to stem cells, genetic therapy or regenerative medicine)
- High **technical risk** (not acknowledging or addressing pitfalls)
- **Missing expertise** on team (Address in Key Personnel)
- **Grantsmanship** issues: poorly written, difficult to follow
- Failure to acknowledge relevant, existing literature
- **Poor DEI** Statement
- Missing letters of support from a critical collaborator

Contacts and Upcoming Deadlines

Programmatic Questions
discovery@cirm.ca.gov

Budgeting and Administrative Questions
grantsmanagement@cirm.ca.gov

Review Questions
review@cirm.ca.gov

Applications due May 2nd, 2023 @2PM PDT

Q & A

CIRM
CALIFORNIA'S STEM CELL AGENCY