Review Process for Proposed Concepts

Overview

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CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Agenda

1. GWG and Application Review
2. Introduction of Two-Stage Review
3. Method for Proposed Concepts:
    a. DISC5 – Positive Selection
    b. CLIN2 – Qualification
    c. PDEV & DISC4 - Pre-Submission
4. Scoring Method
5. Programmatic Review and Team Recommendations

CIRM Grants Working Group

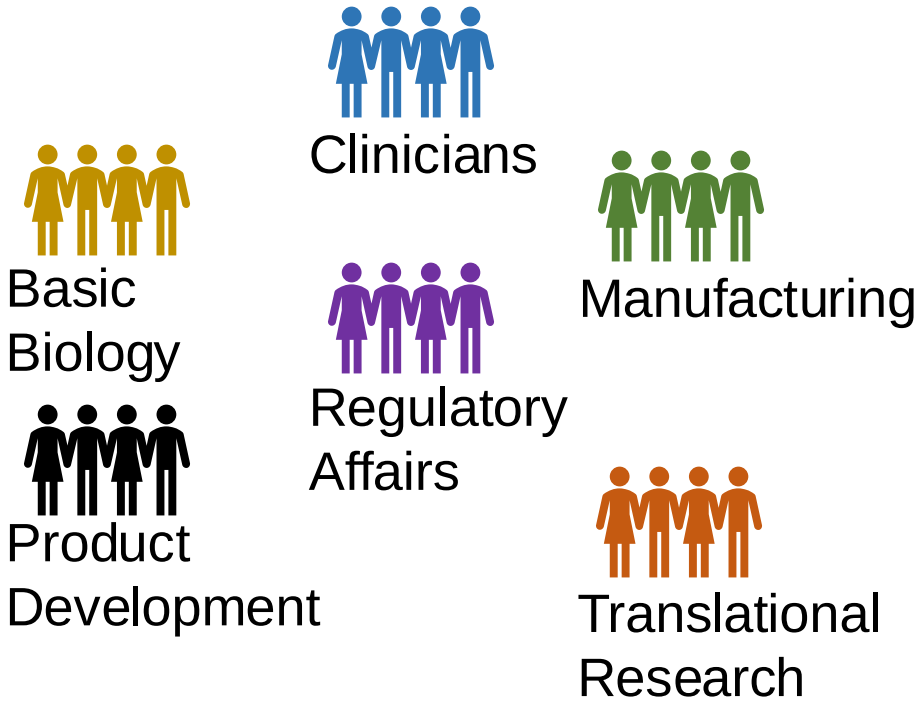
- The CIRM Grants Working Group* (GWG) is responsible for evaluating the scientific merit of all applications submitted to CIRM and to provide funding recommendations to the ICOC.
- GWG Panel Composition:
  - Up to 15 scientist members from outside of California
  - 7 patient advocate or nurse members of the ICOC
  - Chair of the ICOC, ex-officio member

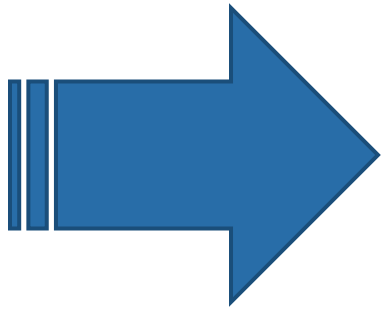
**Formally defined as the "Scientific and Medical Research Funding Working Group" within Prop 71 and Prop 14.*

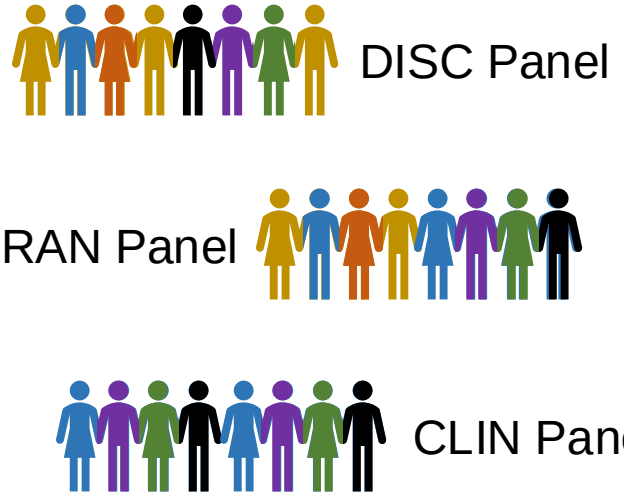
CIRM Grants Working Group

- All members must be appointed by the ICOC and serve for variable terms.
- The GWG functions as a singular group with rotating scientific members and patient advocates / nurse members of the ICOC.
  - CIRM does not have standing study sections for review like NIH or others.
  - All applications for a review cycle go to the same panel.
- Expert GWG panels are assembled to meet the needs of each review type and each cycle of review.

How GWG Panels Provide the Necessary Expertise







Expertise pool

250 to 300 appointed members

GWG Panels

15 scientific members that create a diverse panel with varied perspectives and relevant expertise for each review

CIRM Grants Working Group Member Roles

GWG Scientists
15 Members

→ Scientific evaluation (expertise aligned with review cycle)
Provides scientific score on all applications

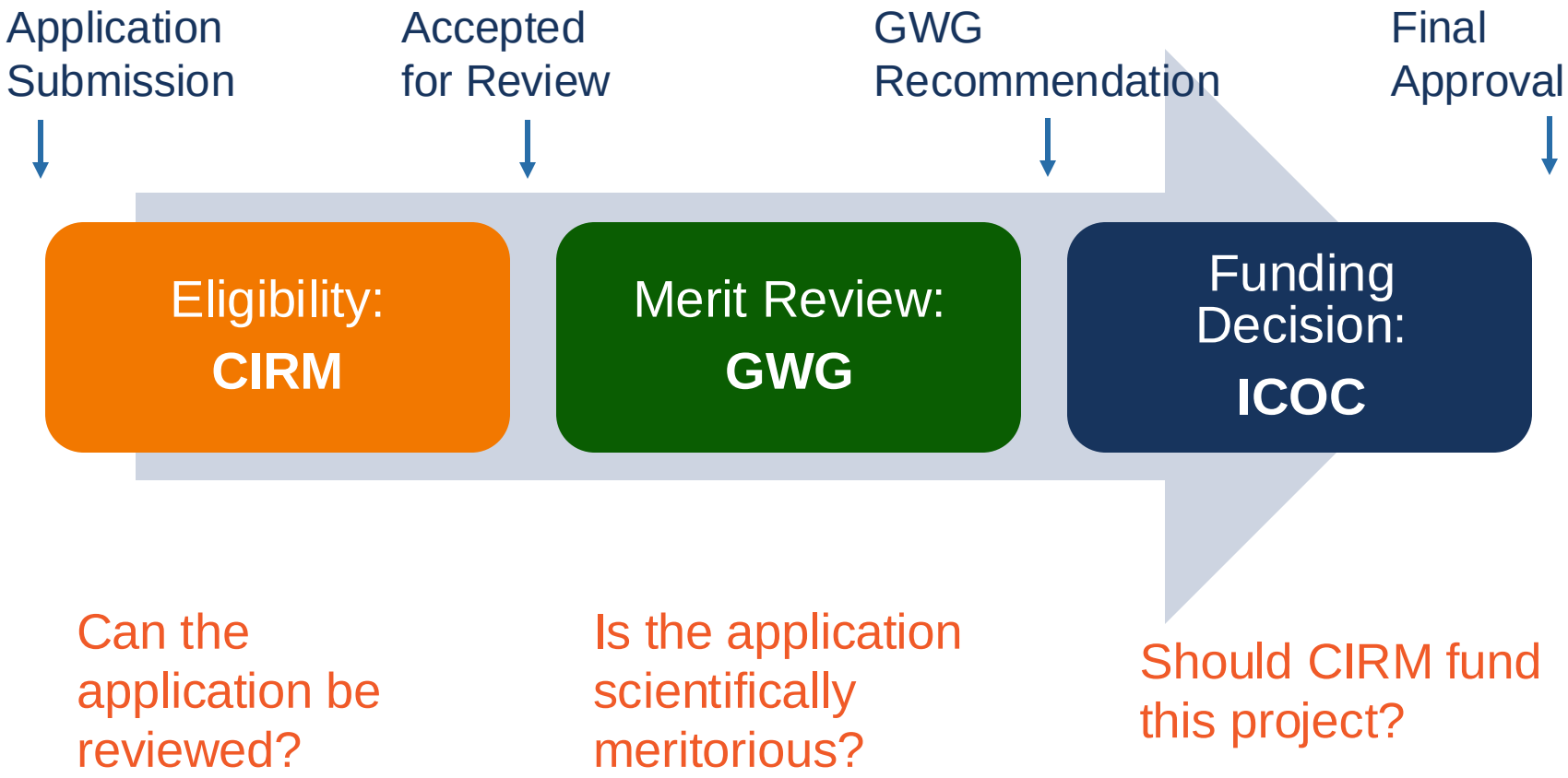
GWG Board Members
7 Members

→ Patient perspective on significance and potential impact, oversight on process
Provides DEI score on CLIN applications
May provide a suggested scientific score

Scientific Specialist
(non-voting)

→ Scientific evaluation (specialized expertise as needed)
Provides initial but not final scientific score

Conventional One-stage Review Process



Considerations for Effective GWG Review

- Allow **adequate time for reviewers** to discuss each application: the more applications in a review cycle, the less time available for each one.
- **Minimize the application assignment burden** per reviewer: the more applications each reviewer is assigned to, the less effort that is expended on each one. (NIH average is 6-8, CIRM varies from 6 to 10)
- **Maximize expertise**: a greater level of expertise is available with more focused set of applications; broader scope limits available expertise.
- Alignment of review with **targeted number of awards**: based on expected or known success rate, applications reviewed should align with target number.

Two-Stage Review

Purpose of Two-Stage Review

1. The number of applications received for many funding opportunities often exceed the capacity of the GWG to appropriately review in a single cycle.

2. In the past, CIRM has used different mechanisms such as a pre-application process or limited the total number of applications that could be submitted by an institution.

Today, we will discuss the proposed two-stage review process for each of the funding opportunity concepts of **DISC4, DISC5, PDEV, and CLIN2**.

How was the process chosen for each program?

- Processes were chosen using a decision tree, based on the following goals:
  - Manage large numbers of applications
  - Implement strategic priorities
  - Limit applicant burden

- Key questions for choosing each process:
  - Can the GWG appropriately and effectively review all eligible applications?
  - Must preferences/priorities be determined discretely or comparatively?
  - Is a complete application necessary to assess the priorities?

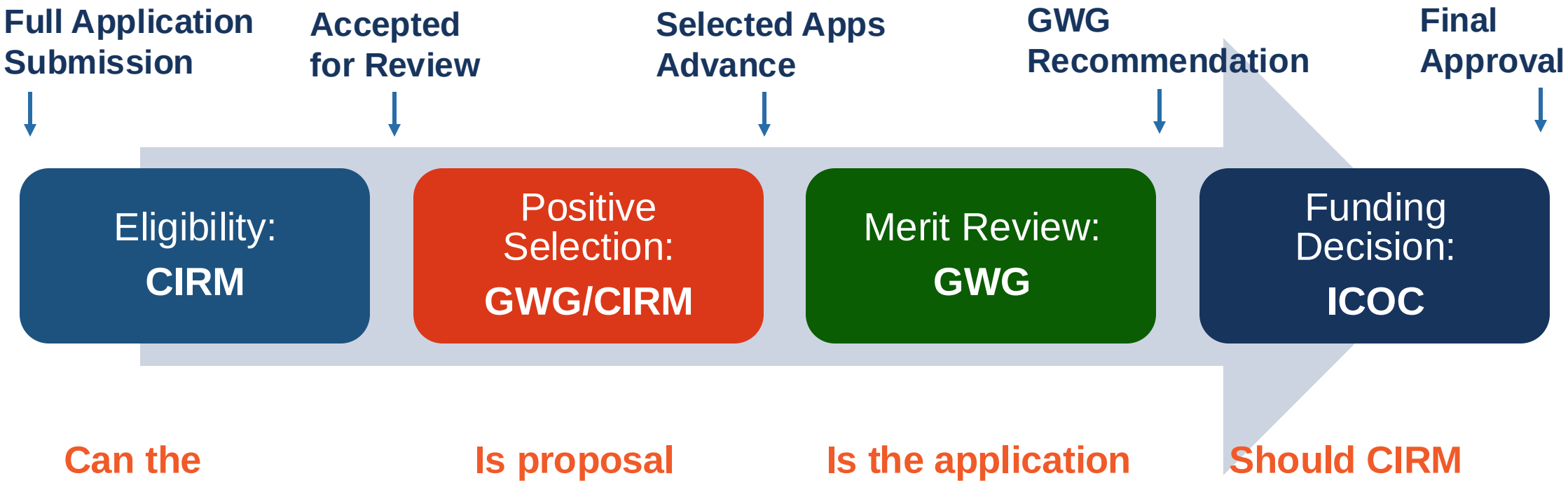
Two-stage Methods in New and Amended Concepts

Program	Two-Stage Method	Submission Content	Adoption	Cycles Per Year
DISC5	Positive Selection	Full Application	Established 2015	1
CLIN2	Qualification	Full Application	Established 2024	4
PDEV	Pre-Submission	Pre-submission form	New	2
DISC4	Pre-Submission	Pre-submission form	New	1

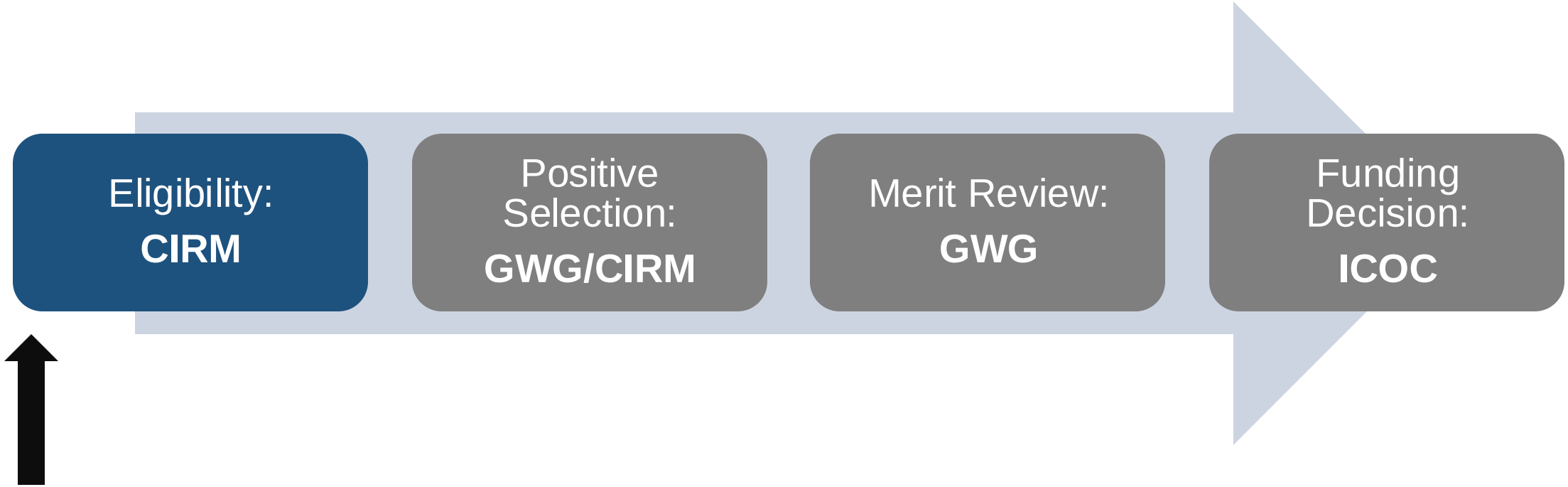
All approaches described are based on established methods at CIRM and other funding agencies such as NSF, CPRIT, and NIH.

DISC5

Positive Selection Process for DISC5

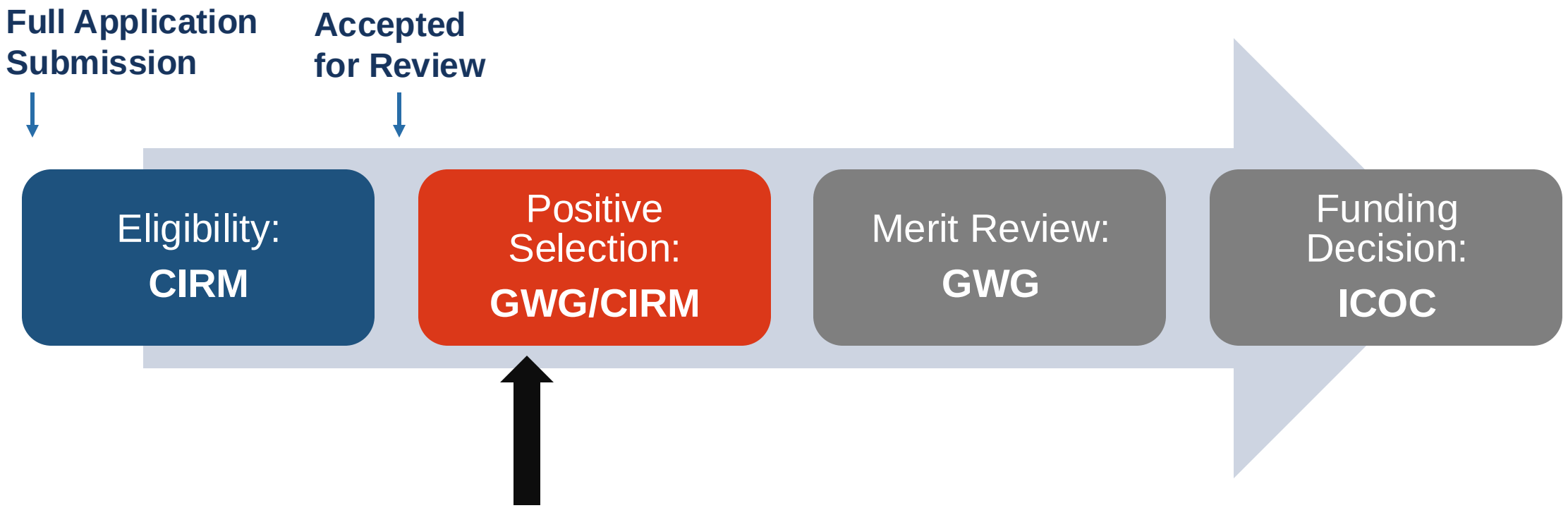


Positive Selection Process for DISC5



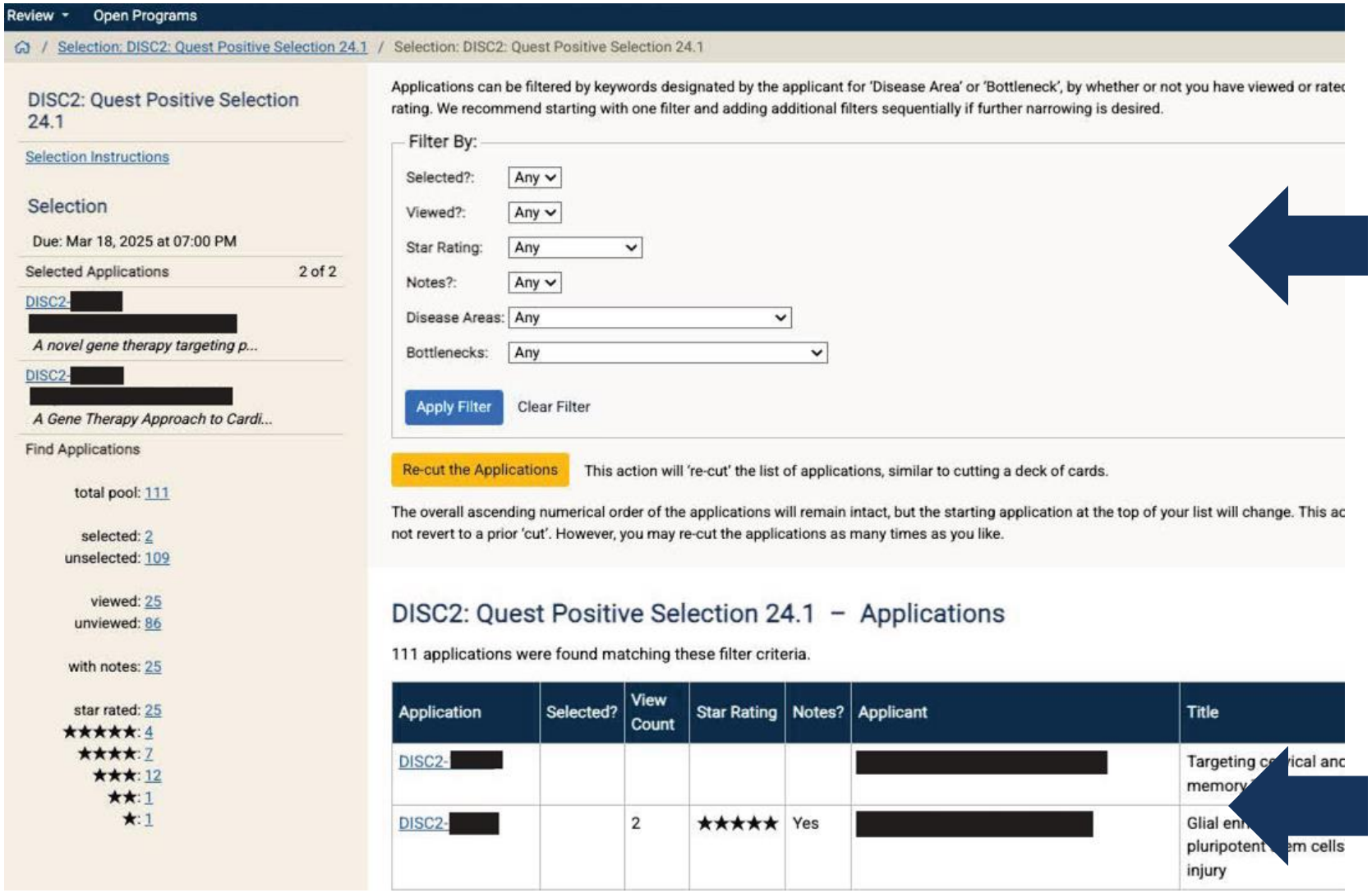
Full application is submitted and an initial eligibility review is made by the CIRM Team

Positive Selection Process for DISC5



GWG members conduct a pre-review of applications focused on potential for impact (reviewers use the criterion defined in PA) and select which ones to advance to a full review

Positive Selection Process for DISC5

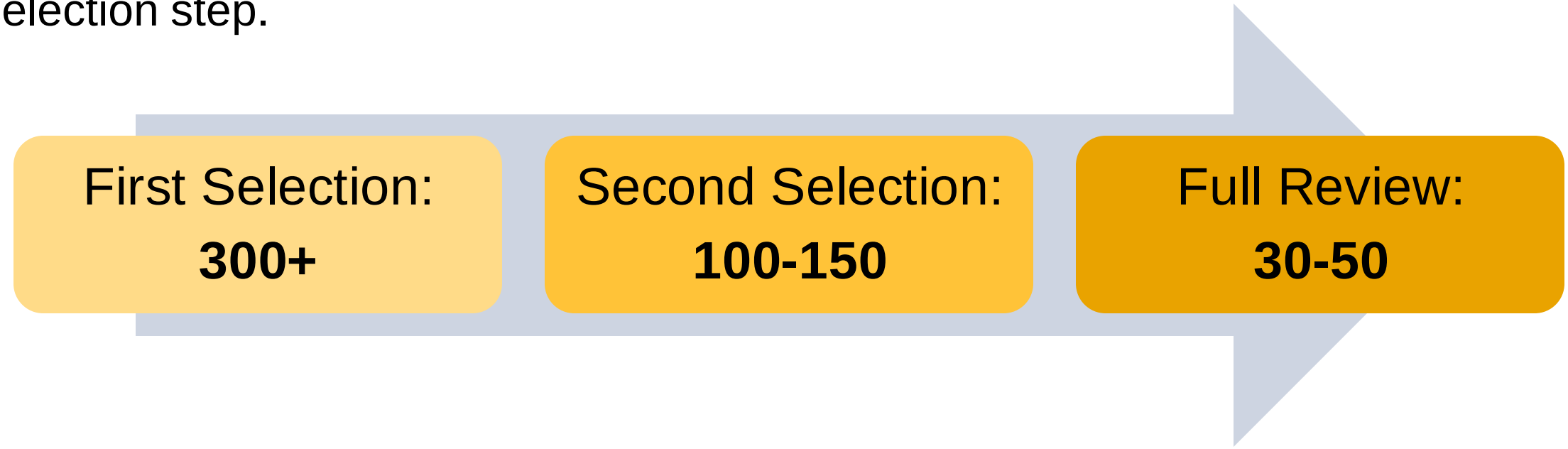


Reviewers have multiple ways to sort and filter applications.

Reviewers can view all applications in a table format and examine each via a summary page or full application as needed.

Positive Selection Process for DISC5

- Positive Selection can scale to large number of applications by iterating the selection step.



- Process is conducted online and can be completed in 2-3 weeks.

Positive Selection Process for DISC5

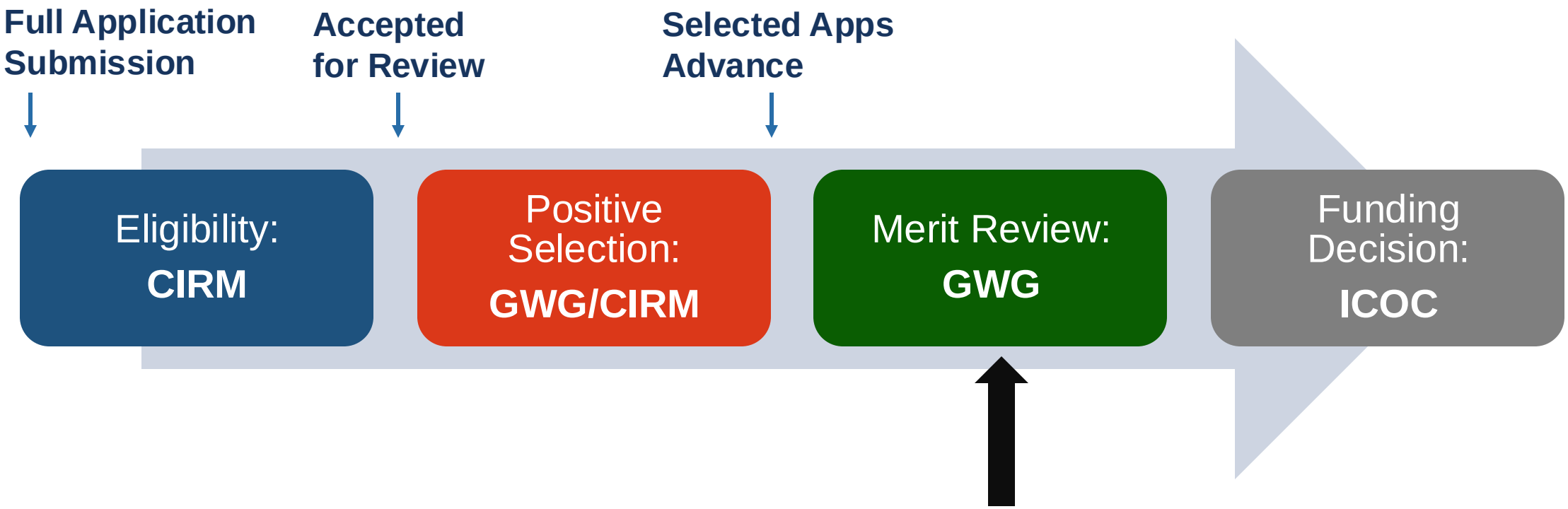
Full Application Submission

Accepted for Review

Eligibility: **CIRM**	Positive Selection: **GWG/CIRM**	Merit Review: **GWG**	Funding Decision: **ICOC**

The CIRM President and CIRM Programs Team examine non-selected applications to determine if any merit a full review based on responsiveness and unique opportunity. The remainder are not considered further

Positive Selection Process for DISC5



Selected applications advance to GWG evaluation and panel discussion. GWG panel scores apps and makes funding recommendation to ICOC.

Positive Selection Process for DISC5

Full Application Submission

Accepted for Review

Selected Apps Advance

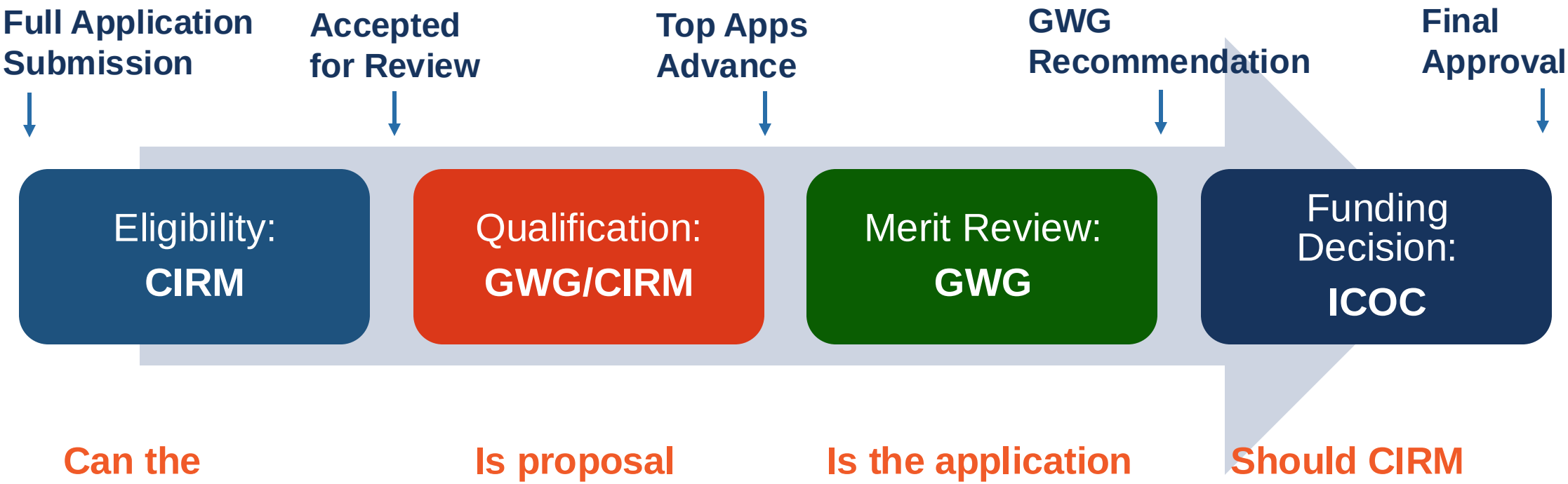
GWG Recommendation

Eligibility: **CIRM**	Positive Selection: **GWG/CIRM**	Merit Review: **GWG**	Funding Decision: **ICOC**

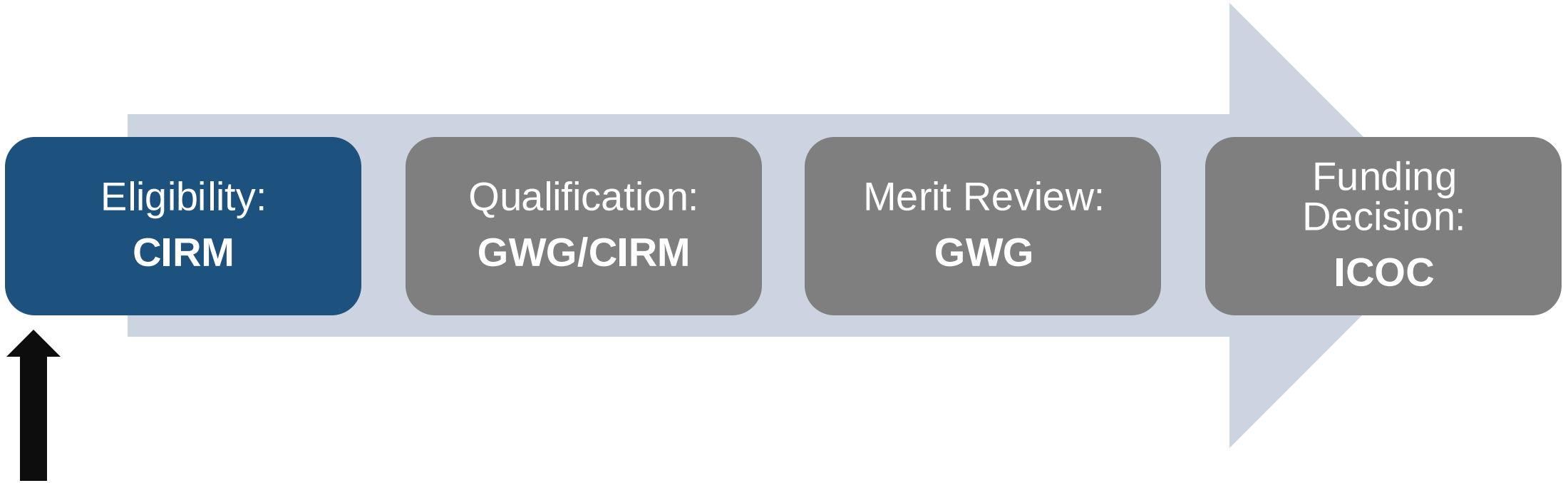
ICOC considers GWG recommendations and makes final decision to fund or not fund applications.

CLIN2

Qualification Process for CLIN2

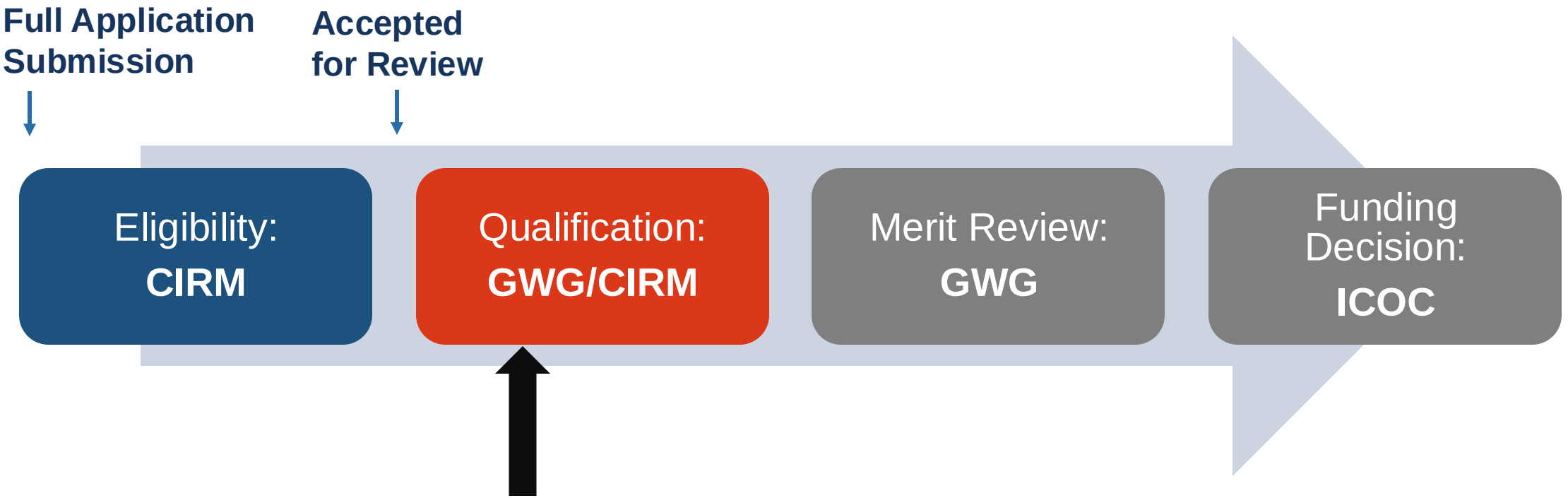


Qualification Process for CLIN2



Full application is submitted and an initial eligibility review is made by the CIRM Team.

Qualification Process for CLIN2



The CIRM Review Team examines key information in the applications to score them against objective criteria defined in the PA. Goal is to advance up to 7 applications per cycle.

CLIN2 | Preferences for FY25/26

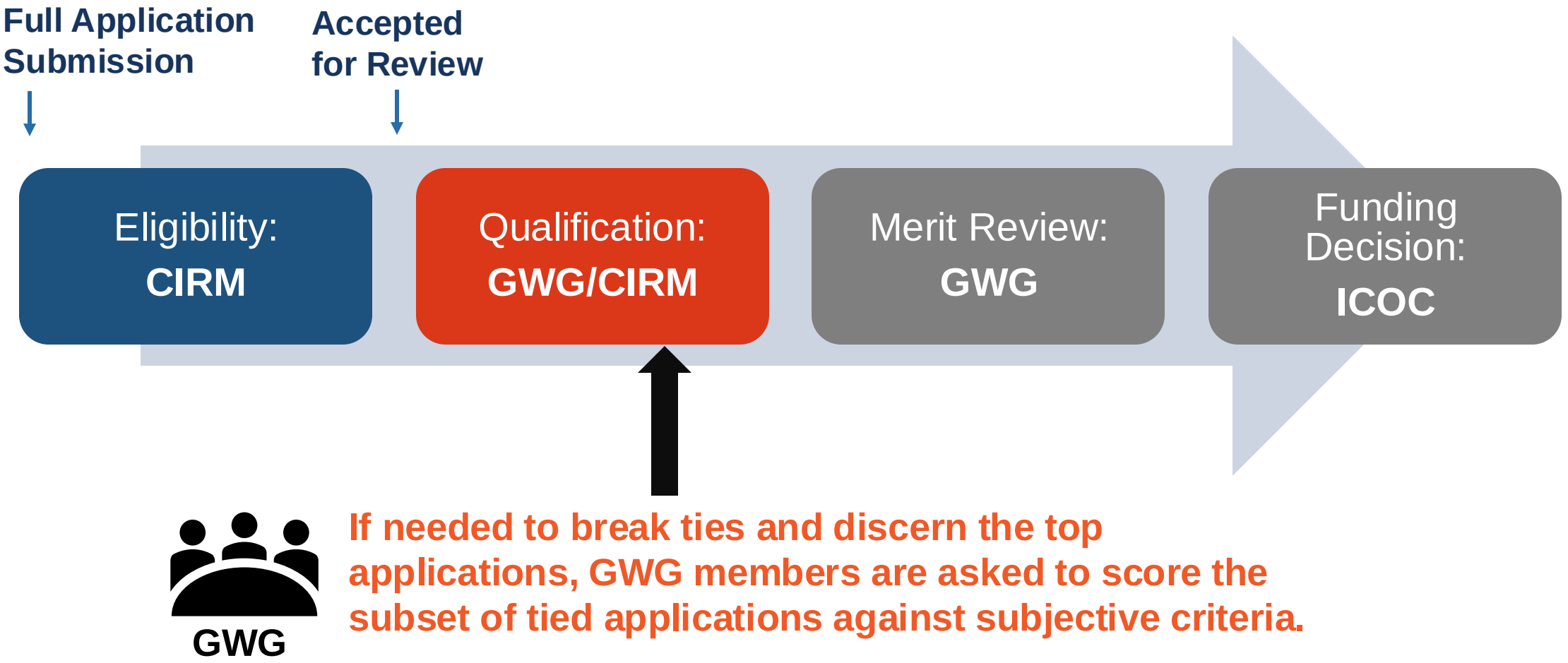
Preferences will be factored in during Qualification and ARS review

Concept Preferences	Rationale
Pluripotent stem cell-derived therapies	• Propositions 71 and 14 • Potential to address patient access & affordability barriers
In vivo genetic therapies	• Potential to address patient access & affordability barriers
Non-viral nucleic acid delivery	• Potential to address patient access & affordability barriers
Diseases of the brain and CNS (Prop 14)	• Proposition 14 priority
CA organizations	• CA taxpayer-funded initiative
Progressions from IND-enabling or pipeline trial awards	• Advance CIRM-funded therapies
Fast Track, RMAT, or breakthrough designations	• Leverage greater FDA access
Pivotal trials	• Fastest route to BLA

CLIN2 | Qualification Rubric

Criteria		Key Considerations
1	**Prop 14 Preferences**	• PSC-derived therapies, in vivo gene therapies, diseases of the brain and CNS
2	**Other Preferences**	• Non-Viral Nucleic Acid Delivery • Progression from Pipeline Program • CA organization • Fast Track, RMAT, or Breakthrough Designation • Pivotal Trial
3	**Novelty of therapeutic approach**	• Differentiation compared to CIRM active awards portfolio
4	**Under-represented therapeutic/disease area**	• Targeting a therapeutic/disease area under-represented in CIRM active awards portfolio

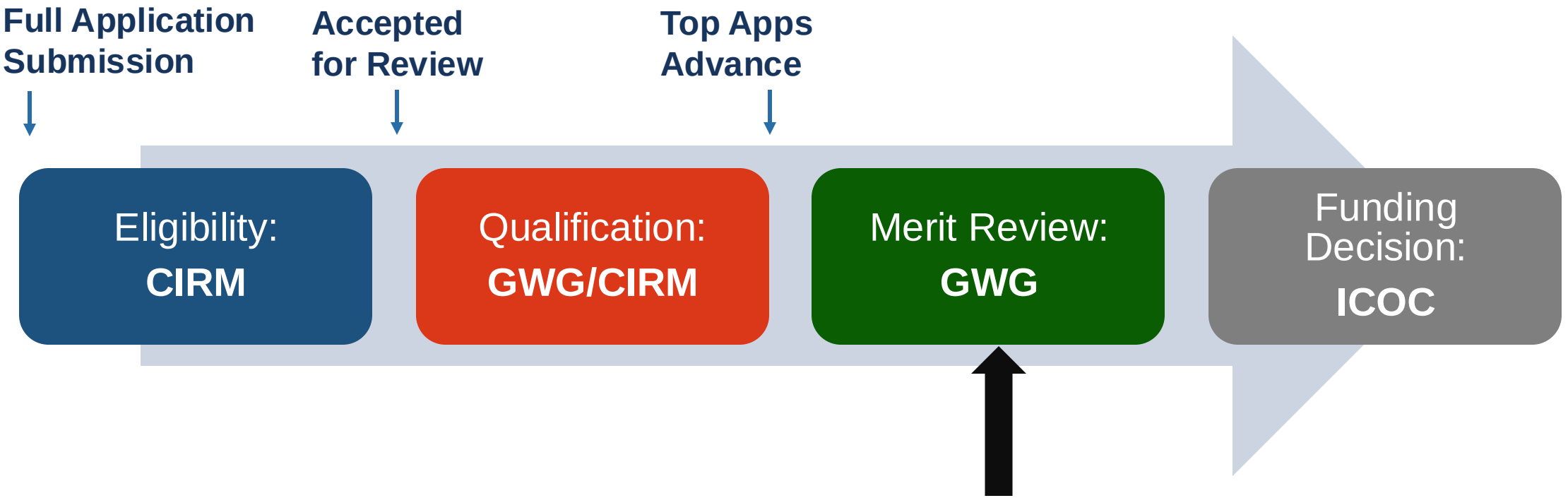
Qualification Process for CLIN2



Qualification Process for CLIN2

- Subjective Criteria (assessed and scored by GWG members)
  - How significant is the unmet need that is being addressed?
  - How impactful could the proposed treatment be for patients if successfully developed?
  - How practical and feasible is the proposed treatment for it to be adopted by patients and healthcare providers?
  - How responsive is the proposal in providing a DEI plan?
  - Does the application include all necessary components for proper evaluation?

Qualification Process for CLIN2



Selected applications advance to GWG evaluation and panel discussion. GWG panel scores apps and makes funding recommendation to ICOC.

Qualification Process for CLIN2

Full Application Submission

Accepted for Review

Top Apps Advance

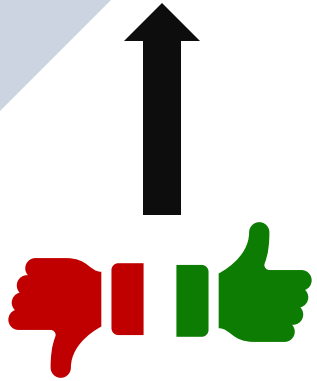
GWG Recommendation

Eligibility: **CIRM**

Qualification: **GWG/CIRM**

Merit Review: **GWG**

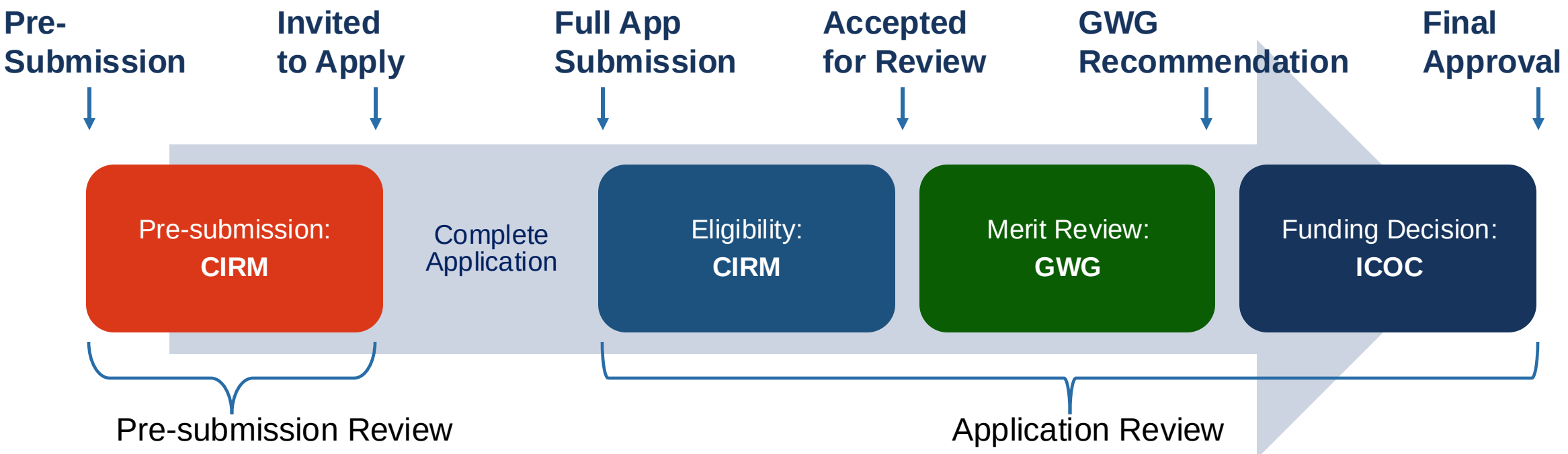
Funding Decision: **ICOC**



ICOC considers GWG recommendations and makes final decision to fund or not fund applications.

PDEV/DISC4

Pre-submission Process for DISC4 & PDEV



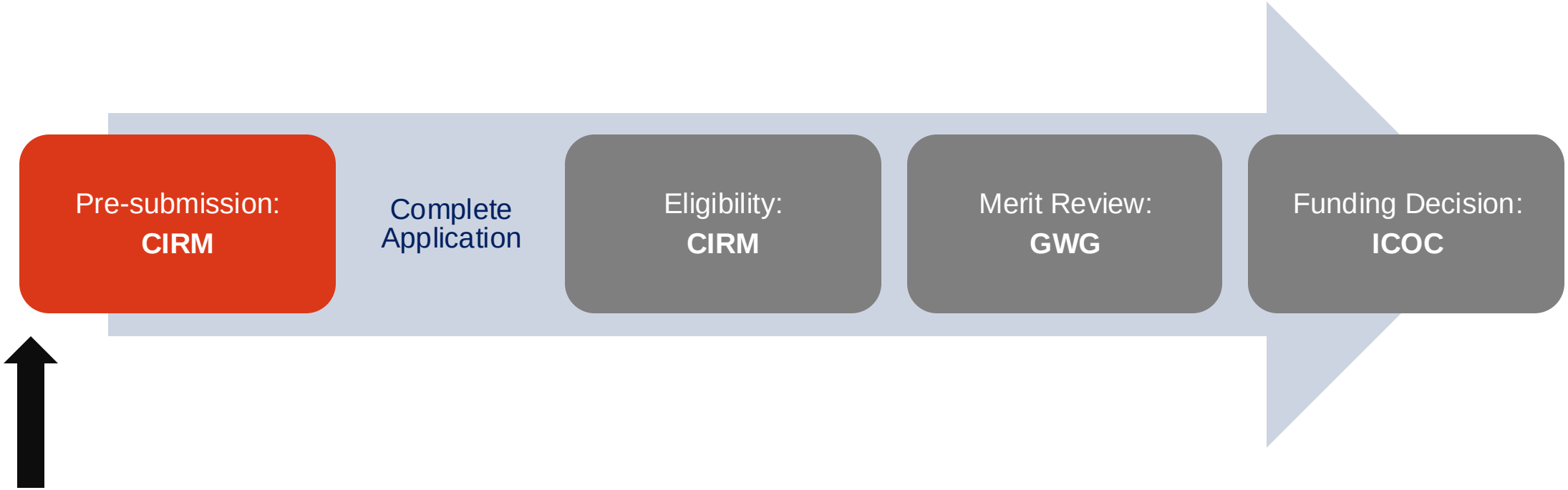
Is proposal aligned with CIRM priorities?

Can the application be reviewed?

Is the application scientifically meritorious?

Should CIRM fund this project?

Pre-submission Process for DISC4 & PDEV



Applicants submit an online form that collects key information.

Pre-submission Process for DISC4 & PDEV

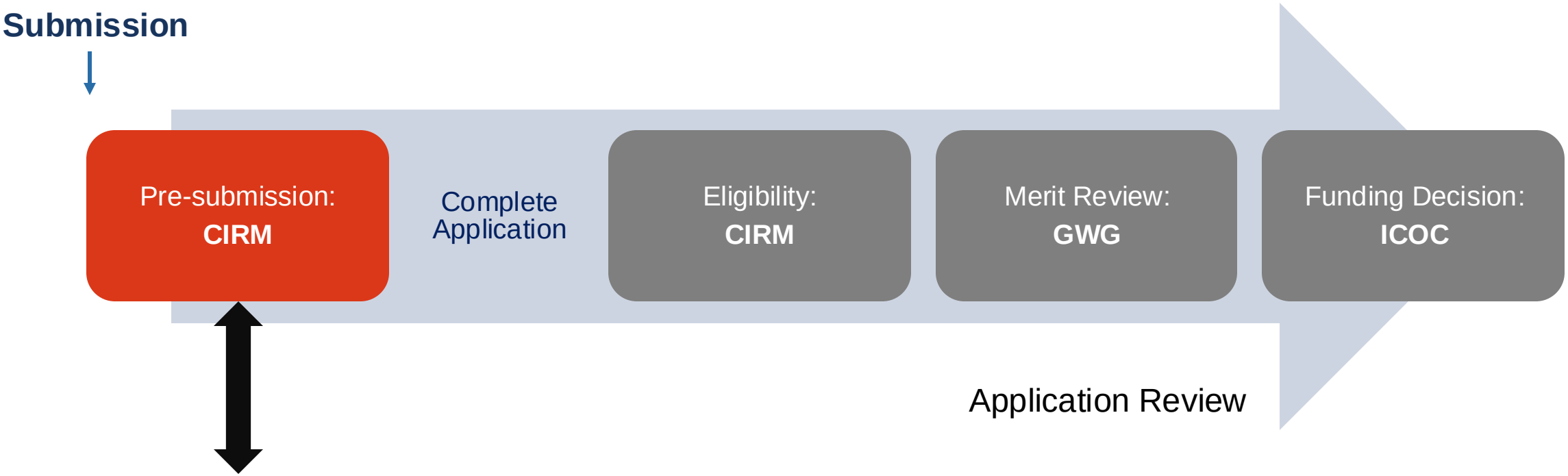
Pre-submission Forms

- Online pre-submission forms will be available to prospective applicants in the CIRM Grants Management System.
- Forms will collect sufficient information to perform initial eligibility and evaluate for program fit including:
  - Eligibility
  - Team Personnel
  - Project Title & Keywords
  - Project Information
  - Proposed Activities

Outline of proposed forms provided to illustrate content.

Pre-submission Process for DISC4 & PDEV

Pre-Submission

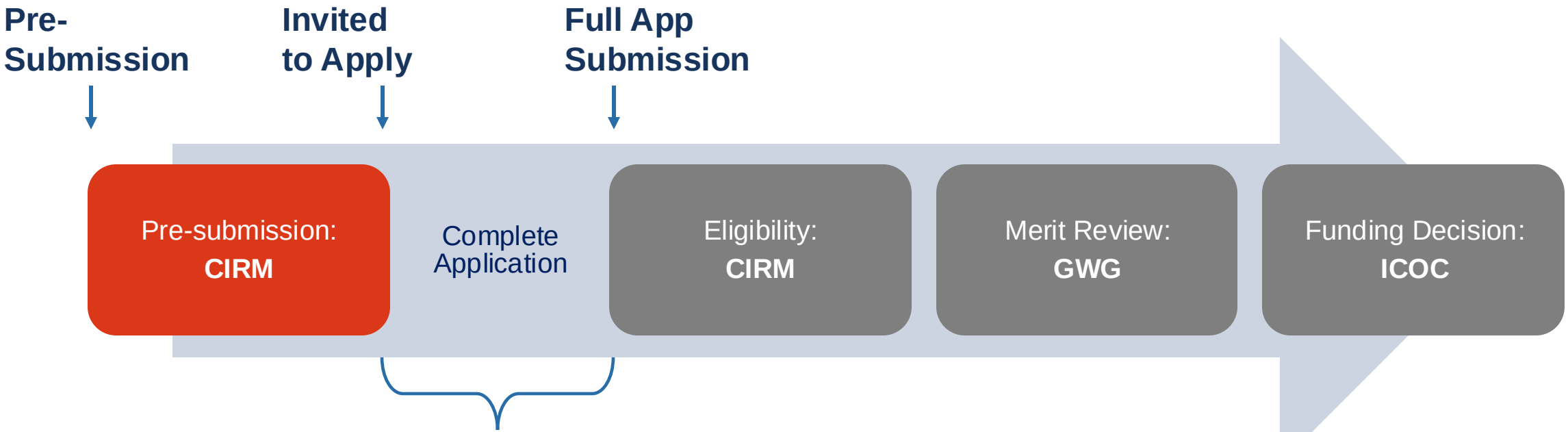


CIRM Program Team members examine the pre-submissions to score and rank them based on defined strategic priorities and criteria.

Pre-submission Process for DISC4 & PDEV

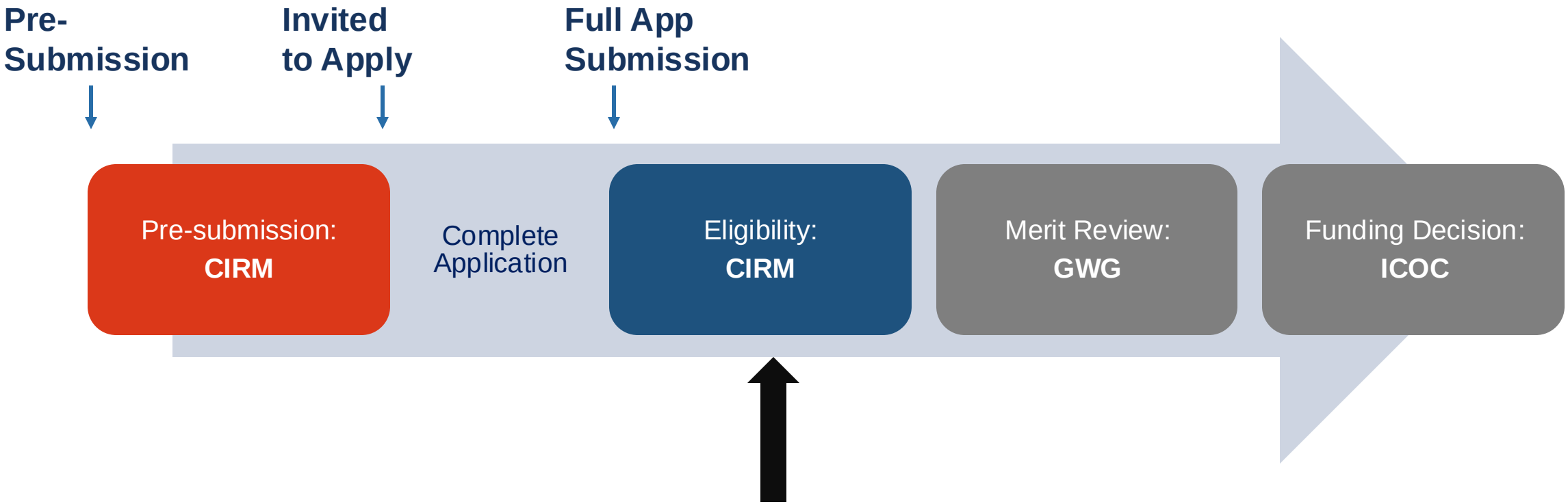
Pre-submissions that most align with the priorities are invited to apply, not exceeding the number that can be appropriately reviewed by the GWG

Pre-submission Process for DISC4 & PDEV



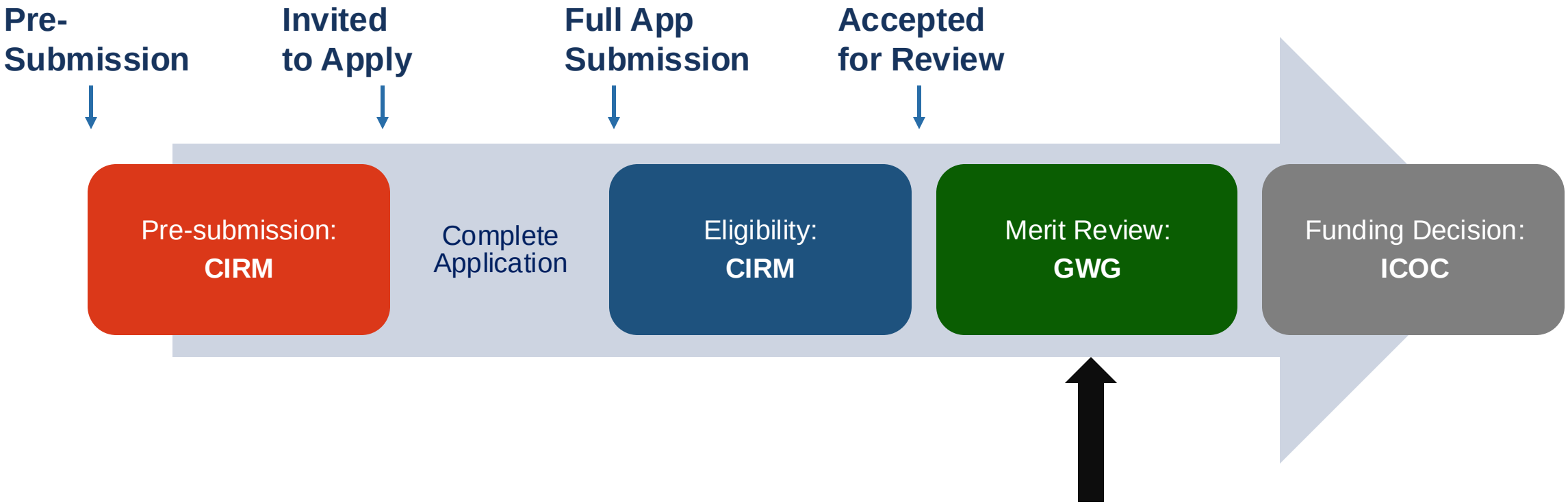
Invited applicants have several weeks to complete the full application and submit.

Pre-submission Process for DISC4 & PDEV



Full applications go through a final eligibility step to ensure alignment with pre-submission.

Pre-submission Process for DISC4 & PDEV



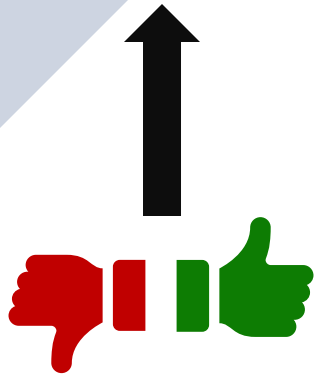
GWG

Accepted applications advance to GWG evaluation and panel discussion. GWG panel scores apps and makes funding recommendation to ICOC.

Pre-submission Process for DISC4 & PDEV

Pre-Submission → **Invited to Apply** → **Full App Submission** → **Accepted for Review** → **GWG Recommendation**

Pre-submission: **CIRM**	Complete Application	Eligibility: **CIRM**	Merit Review: **GWG**	Funding Decision: **ICOC**



ICOC considers GWG recommendations and makes final decision to fund or not fund applications.

DISC4 | Pre-Submission Selection Criteria

Criteria	Key Considerations
Preference topics (by FY)	• Neurodegenerative Diseases (FY 25/26)
Relevance to human disease biology	• Relevant to prevalent diseases or diseases of high unmet need • Includes significant target validation or early translational plan
Cross-disciplinary and systems biology	• Includes of major clinical, or computational workflows • Applies cross-disease or cross-organ systems biology approach
Stem cell or genetic research innovations	• Includes Strong/Innovative stem cell-based approaches • Includes Strong/Innovative genetic research in approaches

PDEV | Preferences for FY25/26

Preferences will be factored in during pre-submission and ARS review

Concept Preferences	Rationale
Pluripotent stem cell-derived therapies	• Propositions 71 and 14 • Potential to address patient access & affordability barriers
In vivo genetic therapies	• Potential to address patient access & affordability barriers
Non-viral nucleic acid delivery	• Potential to address patient access & affordability barriers
Diseases of the brain and CNS (Prop 14)	• Proposition 14 priority
Progression from DISC2 & TRAN1 Awards	• Advance CIRM-funded therapies
Pre-IND or INTERACT meeting conducted	• Accelerate to IND clearance

PDEV | Pre-Submission Selection Criteria

Criteria	Key Considerations
Prop 14 Preferences	• PSC-derived therapies, In vivo Gene Therapies, Diseases of the brain and CNS
Other Preferences	• Non-Viral Nucleic Acid Delivery • Pre-IND Meeting Conducted • Progression from DISC2 or TRAN1
Under-represented therapeutic/disease area	• Targeting a therapeutic/disease area under-represented in CIRM active awards portfolio
Novelty of therapeutic approach	• Differentiation compared to CIRM active awards portfolio

Scoring Method

GWG Scientific Scoring

Non-Graded Approach

Scores:

1 Warrants funding

2 Needs improvement

3 Do not fund

Each application is assessed **independently**

A score of “2” allows applicants to respond to reviewer concerns and resubmit a corrected application without starting over.

Graded Approach

Scores:

85+ Warrants funding

<85 Do not fund

Applications are **ranked by score**

Applicants with a score below 85 are encouraged to apply for the next cycle with guidance from CIRM on revisions.

GWG Scientific Scoring

- With more meritorious applications coming to CIRM than we can fund, our process is adopting the graded scoring of 1-100 across programs.
- Recommendation from peer review literature suggest using larger number of grades as it generally increases the “correctness” of a panel’s choices although it has diminishing returns.*
- CIRM’s scoring method is different from others because it is **both binary** (fund or don’t fund line) and **graded** (multiple levels of enthusiasm above and below the fund line).
- Scores alone do not provide a full picture to discern differences among applications and additional data is necessary (e.g., reviewer comments, votes)

*Feliciani, T., *Research Policy*, 51;4 (May 2022)

Programmatic Review & Team Recommendations

Programmatic Review at ARS

- The Application Review Subcommittee (ARS) of the ICOC makes the final funding decisions on all applications.
- Decision-making is informed by GWG recommendations, CIRM Team recommendations, and public comments.
- The ARS may also consider:
  - Fit or alignment of an application with CIRM mission and strategic plan
  - Potential impact of a project on patients (risk/benefit ratio)
  - CIRM portfolio of funded projects (underrepresented or overrepresented approaches)
  - DEI elements of an application
  - Availability of funds

CIRM Team Recommendations

- Generally, the CIRM Team will default to the GWG recommendation in the absence of a reason to do otherwise.
- In the context of having more applications recommended than the budget can support, the CIRM Team will offer recommendations to the ARS based on factors such as:
  - A unique opportunity to advance an urgent goal or priority of an RFA/PA
  - Perspective on a Minority Report or differing GWG assessments
  - Optimizing CIRM's portfolio of projects
  - Optimizing the use of available funds
  - Likelihood of success based on experience managing similar CIRM projects
  - New information that comes to CIRM's attention impacting on potential success/failure of the proposed project

Thank you!