

FY26/27 Program Guiding Principles & Review Process

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What We Heard

- Applications are being triaged without any scientific evaluation
- While CIRM cannot fund all projects, use of preferences may exclude classes of modalities and / or innovative projects
- Tailor guiding principles to each program
- Concerns around guiding principles & preferences for Discovery programs
- More transparency & stronger communication of preferences needed
- Requests for data to inform the discussion

Recap of Preferences

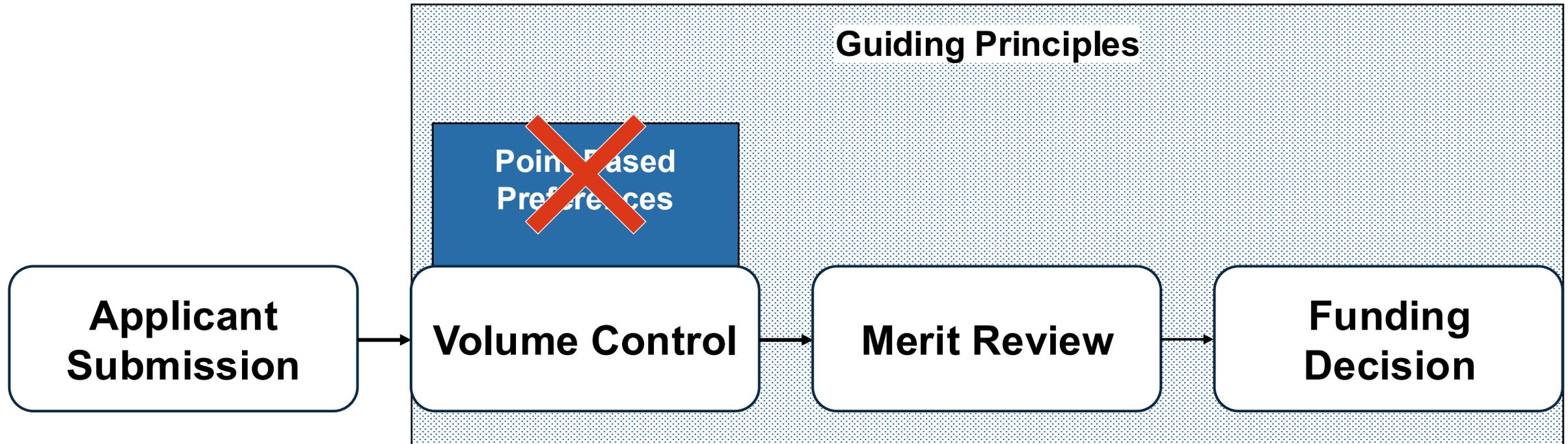
Point-based preferences combined **two separate objectives:**

- **Prioritizing** what we fund
- Application **volume control**

Limitations:

- Applied prior to scientific review
- Require iterative adjustments each cycle

We Propose Removing Point-Based Preferences



Today's Objectives

We are seeking Board feedback:

1 Agreement on what we should fund → Guiding Principles

2 Ensuring Guiding Principles are applied by the **right party** with the **right information** at the **right time**

Guiding Principles: PDEV & CLIN2

Guiding principles help CIRM shape its portfolio

PDEV

The PDEV portfolio will:

- Have potential to deliver transformative improvements in patient outcomes by leveraging cutting-edge therapeutic technologies
- Address known barriers to access and affordability of stem cell-based and genetic therapies
- Broadly address both prevalent and rare diseases affecting Californians

Guiding Principles: PDEV & CLIN2

Guiding principles help CIRM shape its portfolio

PDEV	CLIN2
<p>The PDEV portfolio will:</p> <ul style="list-style-type: none"> • Have potential to deliver transformative improvements in patient outcomes by leveraging cutting-edge therapeutic technologies • Address known barriers to access and affordability of stem cell-based and genetic therapies • Broadly address both prevalent and rare diseases affecting Californians 	<p>The CLIN2 portfolio will:</p> <ul style="list-style-type: none"> • Offer transformative impact for patients, meaning therapies that provide significant benefits over existing therapies • Address known barriers to access and affordability of stem cell-based and genetic therapies • Broadly address both prevalent and rare diseases affecting Californians

We request **Board feedback**

Guiding Principles: DISC4

Guiding principles help CIRM shape its portfolio

DISC4

The DISC4 portfolio will:

- Create multidisciplinary research approaches that integrate diverse sources of evidence
- Innovate through collaboration, network synergy, & data leverage
- Implement Neuro Task Force & other organizational priorities

We request **Board feedback**

Goals of This Meeting

1 Agreement on what we should fund → Guiding Principles

2 Ensuring Guiding Principles are applied by the **right party** with the **right information** at the **right time**

Guiding Principles Implementation

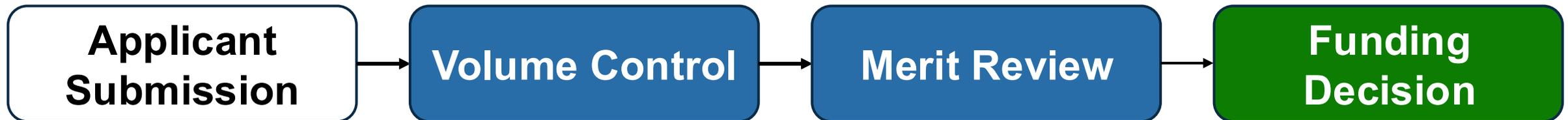
	Volume Control	Merit Review	Funding Decision
Responsible Party	GWG	GWG	ARS
How Guiding Principles Are Applied	Selection Criteria	Review Criteria	Programmatic Factors
How CIRM Team Supports	<ul style="list-style-type: none"> • Define Selection Criteria • GWG Composition • Selection Process (Assignments, Feedback) 	<ul style="list-style-type: none"> • Application • Define Review Criteria • GWG Review Process 	<ul style="list-style-type: none"> • GWG Recommendation • Guiding Principles Summary • CIRM Team Recommendation

Red text represents elements that are changing

Review Process for Volume Control

Purpose of Volume Control Step

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



Extent of Volume Control

	DISC5	DISC4	PDEV	CLIN2
Expected Demand (based on full app)	150-350	50-80	60-90	15-25
Target for Merit Review	50	24	30	10
Awards Available/Cycle	20-25	6	6-11	3-4
Cycles/Year	1	1	2	4

Goals of Proposed Process

- Refocus selection of applications on science rather than strict preferences.
- Align programs with a more consistent volume control process:
 - Applicants can use a unified procedure to apply across programs with minimal variability.
 - Leverage the long-standing learnings of positive selection process (since 2015) to continue making improvements.
- Increase efficiency and the opportunity to learn and implement improvements across programs.

Current Volume Control Processes

	DISC5	DISC4	PDEV	CLIN2
Current Process	Positive Selection	Pre-Submission	Pre-Submission	Qualification
Submission	Full Application	Pre-Sub Form	Pre-Sub Form	Full Application
Selection by	GWG	CIRM	CIRM	CIRM/GWG
Basis for selection	<ul style="list-style-type: none"> • Scientific value 	<ul style="list-style-type: none"> • Objective preferences 	<ul style="list-style-type: none"> • Objective preferences 	<ul style="list-style-type: none"> • Objective preferences • Scientific value

Proposed Volume Control Process

	DISC5	DISC4	PDEV	CLIN2
Proposed Process	GWG Selection	GWG Selection	GWG Selection	GWG Selection
Submission	Full Application	Pre-Sub Form	Full Application	Full Application
Selection by	GWG	GWG	GWG	GWG
Basis for selection	• Scientific value	• Scientific value	• Scientific value	• Scientific value

Red text indicates where changes from current process are proposed.

Unified GWG Selection Process

- Establishes the target number of applications for full panel discussion per program.
- Specifies the optimal (and fixed) number of reviews per application, number of applications reviewed by each reviewer, and total number of reviewers participating.
- GWG members evaluate applications based on scientific value described in respective Program Announcement and aligned with guiding principles.
- Applications receive a composite score that includes ranking.
- Advancement is determined by the composite score with cut-off made at natural break nearest to the target (additional round of selection can be performed if needed and President can select up to 3 additional).

Selection Model Parameters

	DISC5	DISC4	PDEV	CLIN2
Application Pool	200	100	75	20
Target for Advancement	50	24	30	10
Reviewers (Total number)	20	20	20	20
Applications/Reviewer	30	20	15	5
Reviews per Application	3	4	4	5
Total Reviews Needed	600	400	300	100

Composite Scores

- **Purpose:** Turn multiple GWG rankings into a numerical score that can be used to separate and select applications from the pool

Example PDEV Selection & Scoring:

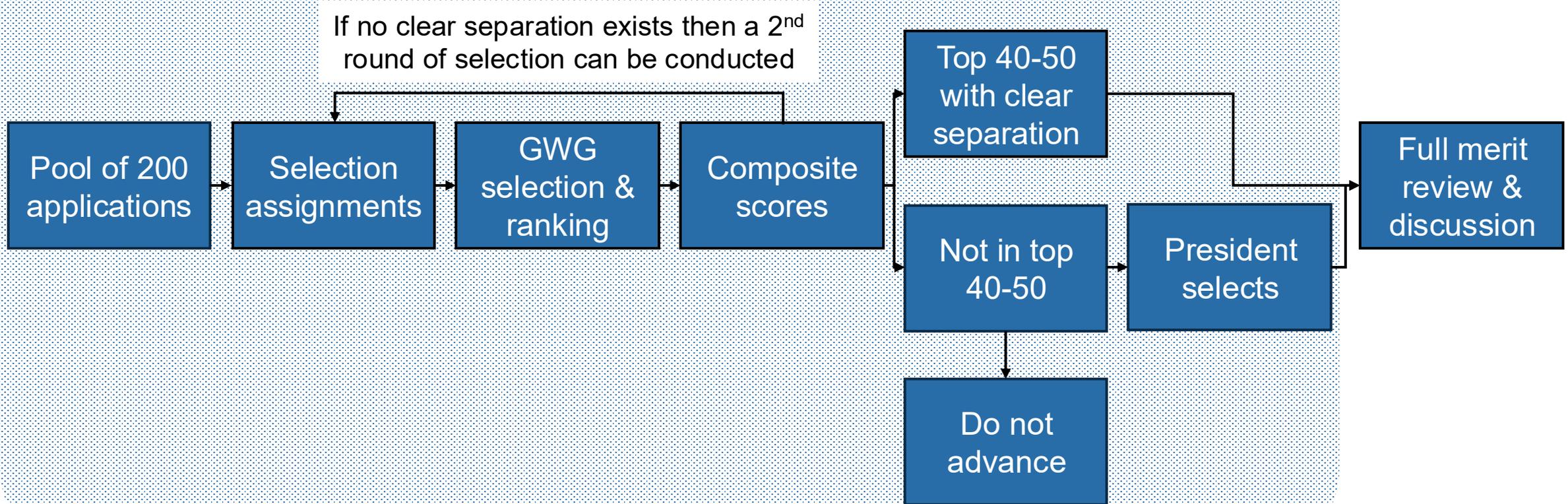
- Each application is assigned to 4 reviewers
- Each reviewer is assigned 15 applications, selects and ranks 5
- Selections & ranks are converted to composite scores

Application PDEV-12345		
GWG Reviewer	Selection	Rank
1	Yes (1 pt)	1 (5 pt)
2	Yes (1 pt)	2 (4 pt)
3	No	0
4	Yes (1 pt)	1 (5 pt)
Points/Max:	3/4	14/20
Weighting:	60% x (3/4)	40% x (14/20)

Composite Score = 0.73

Illustrative GWG Selection Process

GWG Selection



Selection Criteria and Guiding Principles

Guiding principles for CLIN2: *Desired CIRM Portfolio*

- Transformative impact for patients via significant benefits over existing therapies
- Address known barriers to A&A of stem cell-based and genetic therapies
- Broadly address both prevalent and rare diseases affecting Californians

Criteria for GWG selection of CLIN2 apps: *Scientific Value*

- Impact of the proposed treatment for patients if successfully developed
- Significance of the unmet need that is being addressed
- Practicality and feasibility of the proposed treatment to be adopted by patients and healthcare providers
- Readiness of project to advance and complete a successful clinical trial

Selection Criteria and Guiding Principles

Guiding principles for PDEV: *Desired CIRM Portfolio*

- Potential to deliver transformative improvements in patient outcomes by leveraging cutting-edge therapeutic technologies.
- Address unknown barriers to access and affordability of stem cell-based and genetic therapies.
- Broadly address both prevalent and rare diseases affecting Californians

Criteria for GWG selection of PDEV apps: *Scientific Value*

- The therapy's potential to provide a meaningful and substantial improvement in clinical outcomes for the intended population as compared to therapies currently available or in trials.
- Impact of addressing the unmet medical need on patients, caregivers, and the healthcare system
- The therapy's potential to be more accessible and affordable compared to available treatments or therapeutics currently in clinical development.
- Feasibility and practicality of the therapy's uptake by patients, caregivers, and healthcare system.

Selection Criteria and Guiding Principles

Guiding principles for DISC4: *Desired CIRM Portfolio*

- Multidisciplinary research approaches that integrate diverse sources of evidence
- Innovation through collaboration, network synergy, & data leverage
- Implement Neuro Task Force & other organizational priorities

Criteria for GWG selection of DISC4 apps: *Scientific Value*

- Impact of the proposed project in advancing understanding of a human disease, generating data/resources, or where outcomes rapidly advance a therapeutic or biomarker.
- Innovation relative to the current state of research such as applying novel frameworks to study of disease, cutting across silos, employs unique synergy of technologies, or utilizing innovative approaches.
- Responsiveness to DISC4 Focus Area.

Assessment of Selected Applications by GWG

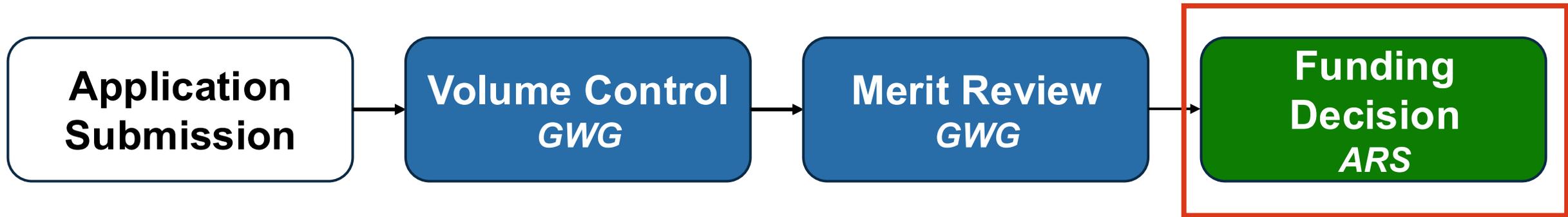
- Selected applications (narrowed pool) are evaluated and scored by a full GWG panel.
- Evaluations and scores are based on the full set of review criteria (detailed in memo), which include the following elements:
 - Value Proposition or Significance & Impact
 - Innovation (DISC4 only)
 - Rationale
 - Project Plan and Design
 - Project Team and Resources
 - Population Impact

Why Request a Full Application?

- Survey of GWG reviewers indicates that the majority (95%) use the full application to make final selections.
- Ensures that eligibility can be fully determined: unlikely that an ineligible application takes up a valuable slot.
- Ensures selected projects are at the appropriate stage of readiness with all regulatory, CMC, and product development elements in place (PDEV & CLIN2).
- The time from submission to award is significantly shorter and mitigates project changes and “staleness” over time.

How Guiding Principles Tie to Funding Decisions

Guiding Principles & Funding Decisions



Implementing Guiding Principles at Funding Decisions

CIRM Team Recommendations assist the Application Review Subcommittee in making well-informed funding decisions

In addition to GWG Summaries, the ARS may consider:

- Programmatic factors
- Recommendations from the CIRM Team
- Public comment

Subsequent slides describe how **guiding principles** are assessed and leveraged in **CIRM Team Recommendations**

Guiding Principles Summary for ARS: PDEV & CLIN2

*Information provided for all applications scoring 80+ and applications with a Minority Report**

PDEV/CLIN2 Guiding Principle Addressed	Information Provided to ARS
Transformative Clinical Impact	<ul style="list-style-type: none"> • Summary of GWG sentiment • Comparison to active awards & external landscape within the same indication
Access & Affordability	<ul style="list-style-type: none"> • Summary of GWG sentiment • Summary of A&A reviewer sentiment • CIRM knowledge of the modality / route of administration
Disease Representation	<ul style="list-style-type: none"> • Disease area representation of active CIRM portfolio

*A Minority Report is issued when 35% or more GWG members score an application 85 or above

Guiding Principles Summary for ARS: DISC4

*Information provided for all applications scoring 80+ and applications with a Minority Report**

DISC4 Guiding Principle Addressed	Information provided to ARS
Multidisciplinary research approach	<ul style="list-style-type: none"> • Summary of GWG sentiment
Collaboration, network synergy, & data leverage	<ul style="list-style-type: none"> • Summary of GWG sentiment • Comparison of research approaches and topic areas to active DISC portfolio • Potential to enhance DISC4 network
Neuro Task Force & other organizational priorities	<ul style="list-style-type: none"> • Fit within annual focus area • Additional considerations concerning evolving research landscape and funding needs

*A Minority Report is issued when 35% or more GWG members score an application 85 or above

CIRM Team Recommendation for ARS

Provided as a narrative memo for each funding cycle

CIRM team recommendations are based on:

- Available program budget
- GWG score & comments
- Guiding principles summary
- Prior awardee performance
- New information available to CIRM after GWG review

Sample ARS Memo (1/2): Overview

Memorandum

To: Members of the Application Review Subcommittee
From: [insert name or team authoring the memo]
Re: CIRM Team Recommendations: [Program Name]
Date: [ARS Meeting Date]

Introduction:

The CIRM team's role during Application Review Subcommittee (ARS) meetings is to assist the ARS in making well-informed funding decisions. The ARS is provided the funding recommendations of the GWG, which include the final scores, assessment against the review criteria, and summary of specific strengths and weaknesses. Beyond these recommendations, the ARS may also consider:

1. Programmatic factors
2. Recommendations from the CIRM Team
3. Public comment

This memo details the CIRM Team Recommendations for applications to CLIN2 which the ARS will consider on [DATE]. CIRM assessed all applications with a median GWG score of 80 or above based on available program budget, GWG score and comments, program guiding principles, prior awardee performance (if available), and any new information available to CIRM after the GWG review.

Summary of Program Budget Considerations:

Available Program Budget (Annual)	\$XXX M
Budget Utilization – GWG Recommended	\$XX M
Budget Utilization – CIRM Recommended	\$XXM
Remaining Program Budget	\$XX M (GWG Recommended) / \$XX M (CIRM Recommended)

Summary of CIRM Team Recommendations:

Application	Median GWG Score	CIRM Recommendation
CLIN2-12345	90	Fund
CLIN2-XXXXX	80	Fund
CLIN2-XXXXX	75	Not Fund

Summary of budget utilization

Summary of GWG scores and CIRM Team Recommendations for each application under consideration

Sample ARS Memo (2/2): Application Assessments

Application Assessments:

1. Application number: CLIN2-12345

Title: *Phase I/II Clinical Trial for [Indication]*

GWG Outcome:

Median	Mean	High	Low	Scores to fund	Scores not to fund
80	81	86	70	4	10

CIRM Team Recommendation:

CIRM **does** recommend that the ARS fund application CLIN2-12345. CLIN2-12345 represents the only CGT approach to treating [Indication], a disease which has no other treatments available. CLIN2-12345 is unique in its modality and target in the CIRM portfolio and the external landscape. The applicant has a successful track record in CNS-directed AAV therapies. The Access and Affordability activities can be further developed during PFAR using CIRM's A&A specialists.

Guiding Principles Summary:

Transformative Impact	<ul style="list-style-type: none"> - GWG note the lack of other therapies for [indication] and the high unmet need in this patient population. GWG sentiment indicates that the therapy proposed in this application has the potential for transformative impact. - CIRM's active PDEV portfolio contains 0 awards that address [indication] and the active CLIN2 portfolio contains 0 awards that address [indication] - Outside of CIRM (based on Globaldata), there are <ul style="list-style-type: none"> o 1 Phase 2 clinical program addressing a different subtype of this disease o 0 approved US treatments.
Access & Affordability	Based on A&A expert review, the application under consideration has not provided a sufficiently detailed plan to achieve A&A goals.
Disease Representation	The application under consideration addresses a rare disease (≈ 200,000 patients in the US) not represented in CIRM's portfolio

Complete GWG score outcomes

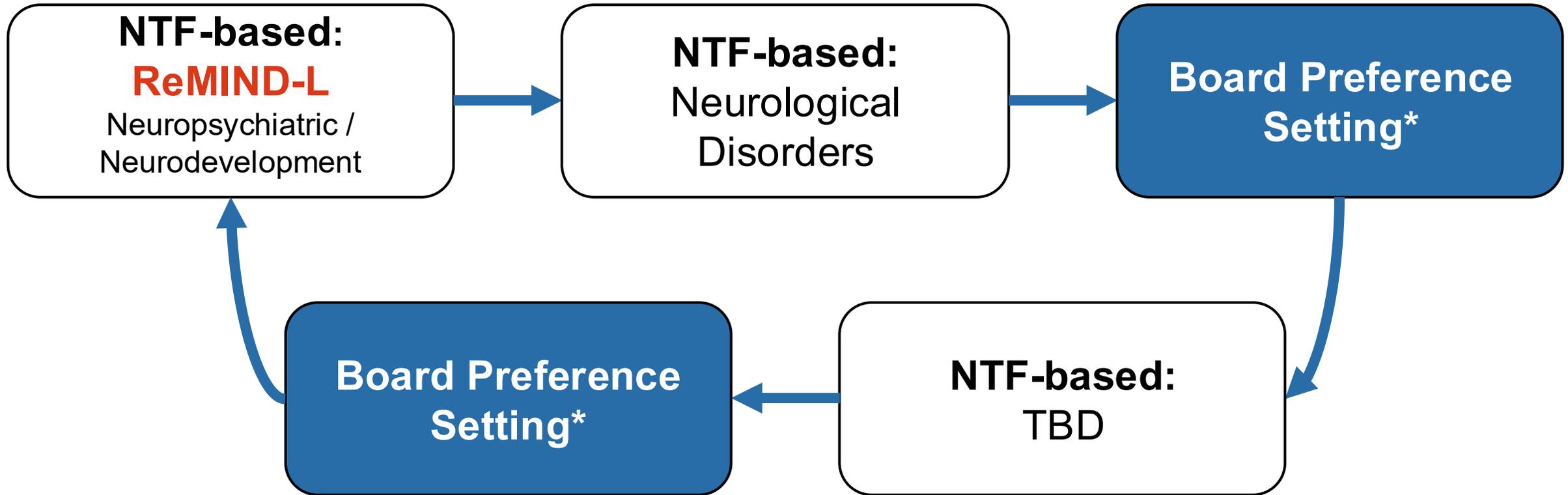
CIRM Team Recommendation and rationale

Guiding Principles Summary

DISC4 Annual Focus Area

DISC4 | Rotating Focus Areas: Alternating Neuro Cycles

Enabling NTF Prioritization while allowing other diseases to use this structure



*All cycles will be open to all-comers with alternating preferences determined by either NTF or by the Board each year based on portfolio analyses

DISC4 FY26/27: Focus Recommendation

Proposed Focus for FY26/27: Immune-Tissue Interactions in Disease and Repair

- Applicable to a broad spectrum of diseases affecting Californians
- Well-suited for multidisciplinary and omics-driven approaches, characteristic of DISC4
- Enables identification of novel targets and biomarkers distinguishing maladaptive vs. productive repair
- Supports development of improved human stem cell and organoid models
- Creates strong opportunities for network synergy across funded programs



We request **Board discussion**

PDEV Cycle Recurrence

We Propose Changing PDEV to One Cycle per Fiscal Year

- PDEV program currently specifies two application cycles per fiscal year
- Expected benefits of two cycles per year are not realized

Potential Benefit of Two Cycles per Fiscal Year	Applicability to PDEV Program
Alignment of program availability with project readiness	PDEV allows entry at any point across preclinical development lifecycle
Application resubmission with reduced delay between cycles	PDEV cycle overlap prevents resubmission in immediate next cycle
Batching of applications & awards over fiscal year	High chance of first fiscal year cycle exhausting majority of available program funds

Practical Implications of One PDEV Cycle per Fiscal Year

- All submitted applications compete for the full program budget
- Higher volume of applications reviewed to account for full program budget
- Unfunded applications may re-submit in the next fiscal year application cycle
- Timelines for program updates and application lifecycles are optimized

Request for Motion

We request a motion that the Science Subcommittee recommend the updated concept plans reflecting these changes to the ICOC.