

FY26/27 Program Guiding Principles & Review Process

Rosa Canet-Avilés, Ph.D., CSO
Gil Sambrano, Ph.D., VP, Review
ICOC/ARS Meeting
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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
 - Focus PDEV & CLIN2 on access rather than affordability with clear expectations of applicants
- Concerns around guiding principles & preferences for Discovery programs
- More transparency & stronger communication of preferences is needed
- Requests for data to inform the discussion

Recap of Preferences

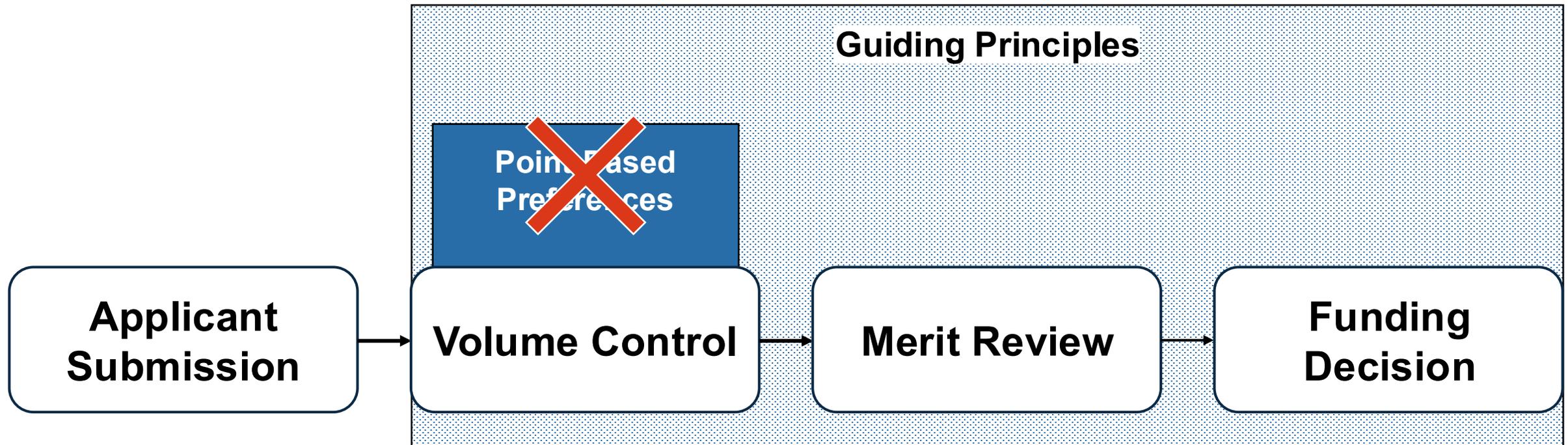
Point-based preferences combined **two separate objectives:**

- **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

- 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**
- 3 Other updates to funding programs

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 • Advance strategies to improve patient access to 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 and those in clinical trials • Address known barriers to access of stem cell-based and genetic therapies • Broadly address both prevalent and rare diseases affecting Californians

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

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**

3 Other updates to funding programs

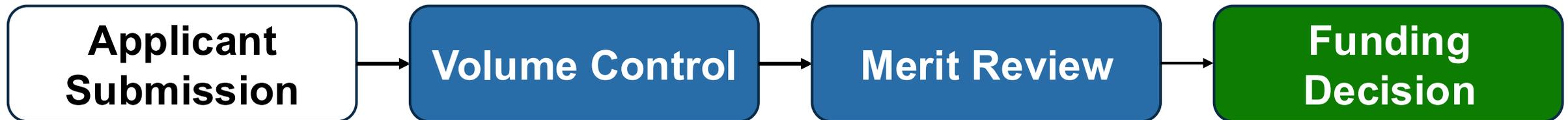
How CIRM Applies Guiding Principles

	Volume Control	Merit Review	Funding Decision
Responsible Party	GWG	GWG	ARS
How Guiding Principles Are Applied	Selection Criteria	Review Criteria	Programmatic Factors
What Happens	<ul style="list-style-type: none"> • Applications are assigned to GWG members • GWG selects and ranks applications 	<ul style="list-style-type: none"> • GWG assesses merit based on review criteria 	<ul style="list-style-type: none"> • GWG provides recommendation • CIRM Team provides recommendation based on Programmatic Factors • ARS decides what to fund

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.



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.

Process Overview

1. Applied to all programs requiring volume control (e.g., DISC4, DISC5, PDEV, CLIN2)
2. A target number of applications for full GWG panel discussion is established (number that provides for a full discussion and rigorous review).
3. The target number and number of submissions (in a given funding cycle) determine the necessary parameters for setting up the GWG selection.
4. In the process, scientific reviewers will select and rank applications based on assessment of scientific value.

Select & Rank 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

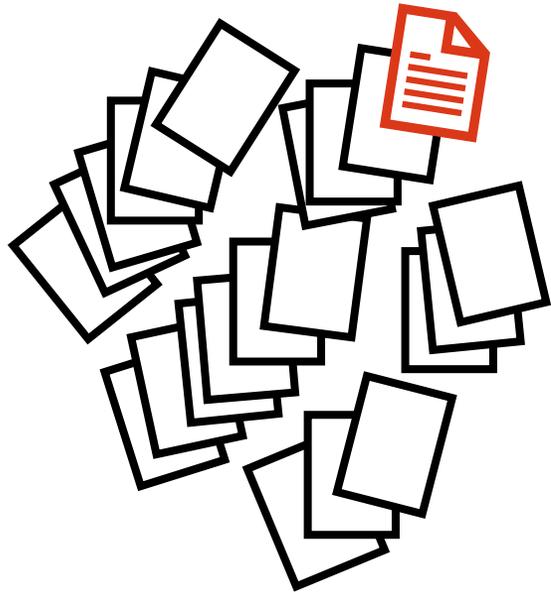
Select & Rank Model Parameters

PROCESS
EXAMPLE

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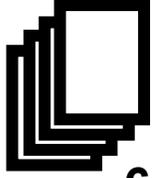
Illustrative GWG Selection Process

Total Application Pool of 75

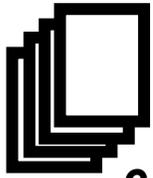


Reviewer 1

Select and rank 5 of 15 assigned applications

					
1	2	3	4	5	6-15

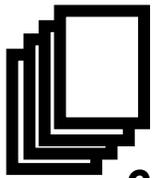
Reviewer 2

					
1	2	3	4	5	6-15

Reviewer 3

					
1	2	3	4	5	6-15

Reviewer 4

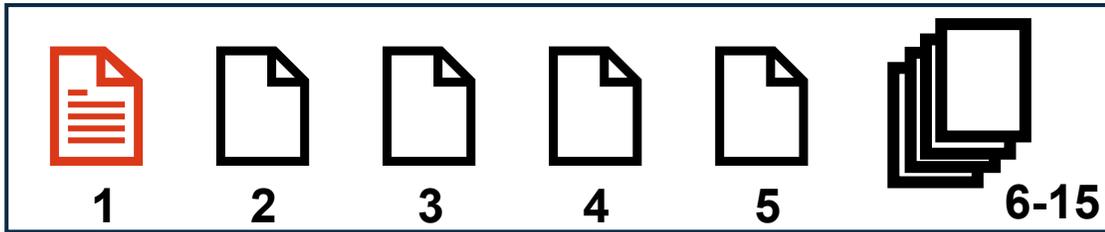
					
1	2	3	4	5	6-15

Pool is split into overlapping batches of 15 and each batch assigned to a reviewer.
(20 reviewers total)

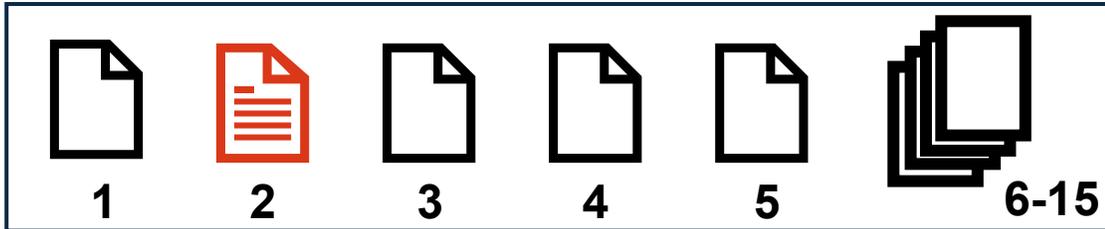
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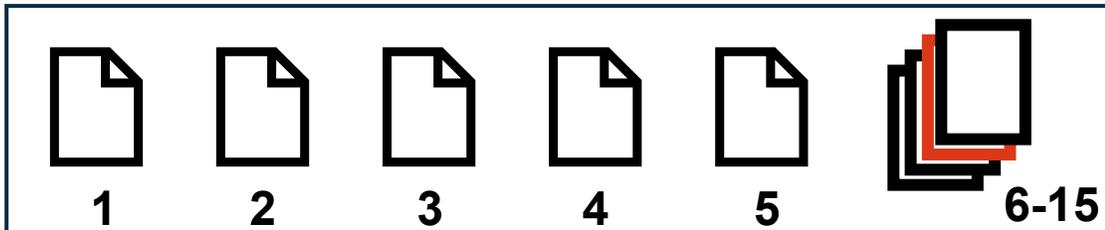
Reviewer 1



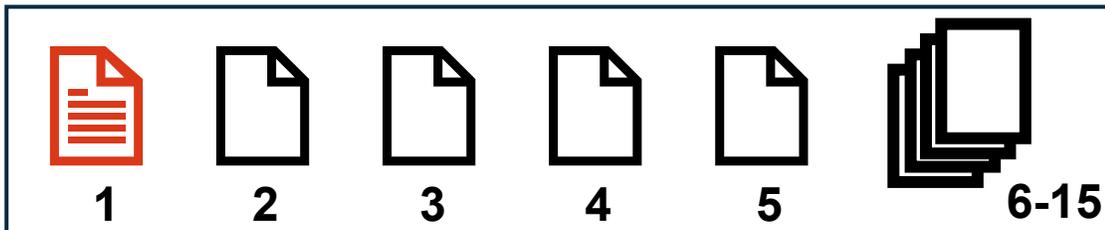
Reviewer 2



Reviewer 3



Reviewer 4



**Composite
Score**

Composite Score

Applications are given a composite score that combines two measurements, selection and rank.

$$60\% \times \text{Selection} + 40\% \times \text{Rank}$$

Selection (60% weight)

What fraction of assigned reviewers picked the application?

Measures consensus: do multiple independent reviewers agree this app deserves full review?

Rank (40% weight)

How highly did reviewers rank this app among their picks?

Measures intensity: how much did they like this app compared to their other selections?

How an Application Gets its Score



Example Application PDEV-XXXXX

Assigned to 4 reviewers that each select 5 out of 15

GWG Reviewer	Selected?	Rank
Reviewer 1	Yes (1 pt)	#1 (5 pts)
Reviewer 2	Yes (1 pt)	#2 (4 pts)
Reviewer 3	No (0 pts)	—
Reviewer 4	Yes (1 pt)	#1 (5 pts)

Calculation

Selection

3 out of 4 reviewers picked = $3/4 = 75\%$

Rank

$(5 + 4 + 0 + 5) / (5 \times 4) = 14/20 = 70\%$

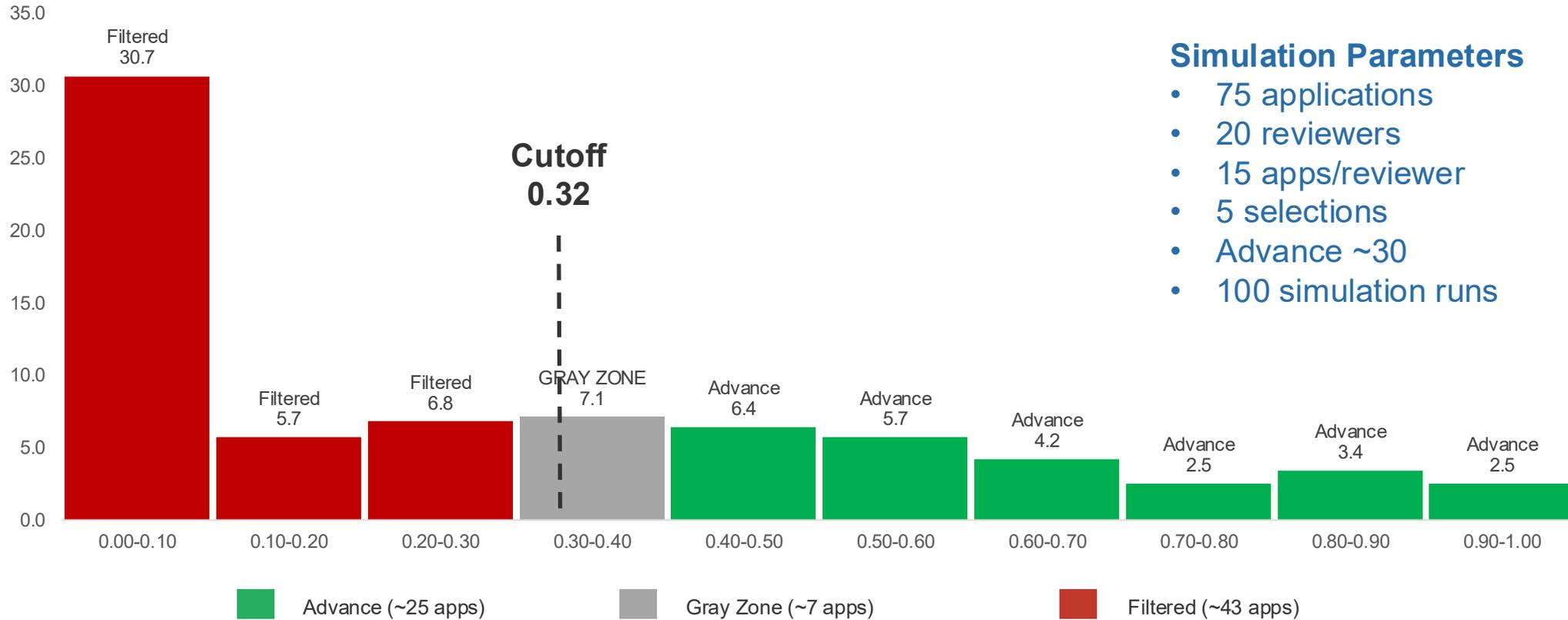
Composite Score

$60\% \times 0.75 + 40\% \times 0.70$

= 0.73

What the Distribution Looks Like

75 PDEV applications scored by composite formula



Based on simulations using historical GWG scores. Actual outcomes will vary depending on application quality, reviewer assignments, and program-specific conditions

Establishing Cut-Off

- Cut-off will be set at the closest numerical break (i.e., no ties) to the target number of applications, not to exceed 10% more or fewer than target.
- If a clear break does not exist in this range, the range of applications will be randomized to select up to the target number and avoid any bias selection.

	Rank	Composite Score	Outcome
	28	0.3400	Advances
	29	0.3200	Tied - Advances
Target →	30	0.3200	Tied - Advances
	31	0.3200	Tied - Advances
Cut-off →	32	0.3067	Does Not Advance

Roles of CIRM President and Patient Advocates

CIRM President

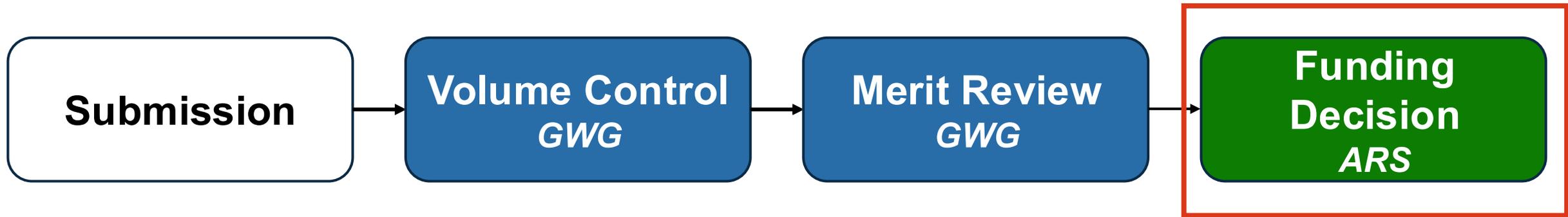
- May examine applications below the cut-off (with recommendation from CIRM staff)
- May advance a limited number of applications that represent a unique opportunity aligned with the goals of the funding opportunity

Patient Advocates

- Patient Advocates will have a strengthened role during GWG panel discussion:
 - Define and include a Patient Perspective score
 - Pre-discussion orientation including Patient Advocates and GWG Chair

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

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

CIRM Team Recommendation for ARS

CIRM team recommendations are based on:

- Available program budget
- GWG score & comments
- Programmatic factors
- Prior awardee performance
- New information available to CIRM after GWG review

Programmatic Factors: PDEV & CLIN2

PDEV/CLIN2 Guiding Principle	How the Guiding Principle is Assessed
Transformative Clinical Impact	<ul style="list-style-type: none"> • Comparison to active awards & external landscape within the same indication
Patient Access (CLIN2 only)	<ul style="list-style-type: none"> • Summary of Access Specialist Reviewer comments • CIRM knowledge of the modality / route of administration
Disease Representation	<ul style="list-style-type: none"> • Comparison to CIRM's active award portfolio by disease area

Programmatic Factors: DISC4

DISC4 Guiding Principle	How the Guiding Principle is Assessed
Multidisciplinary research approach	<ul style="list-style-type: none"> • N/A - assessment provided in GWG review summary
Collaboration, network synergy, & data leverage	<ul style="list-style-type: none"> • Consideration of research approaches and topic area compared to active DISC4 portfolio & pending awards
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

CIRM Team Recommendation Memo

Provided at each ARS meeting

The CIRM Team recommendation memo will include:

- Summary table and rationale for all recommendations
- Analysis of programmatic factors for:
 - Minority reports
 - Applications where the CIRM recommendation differs from GWG
 - Any application with a GWG score higher than or tied with the lowest scoring CIRM-recommended application

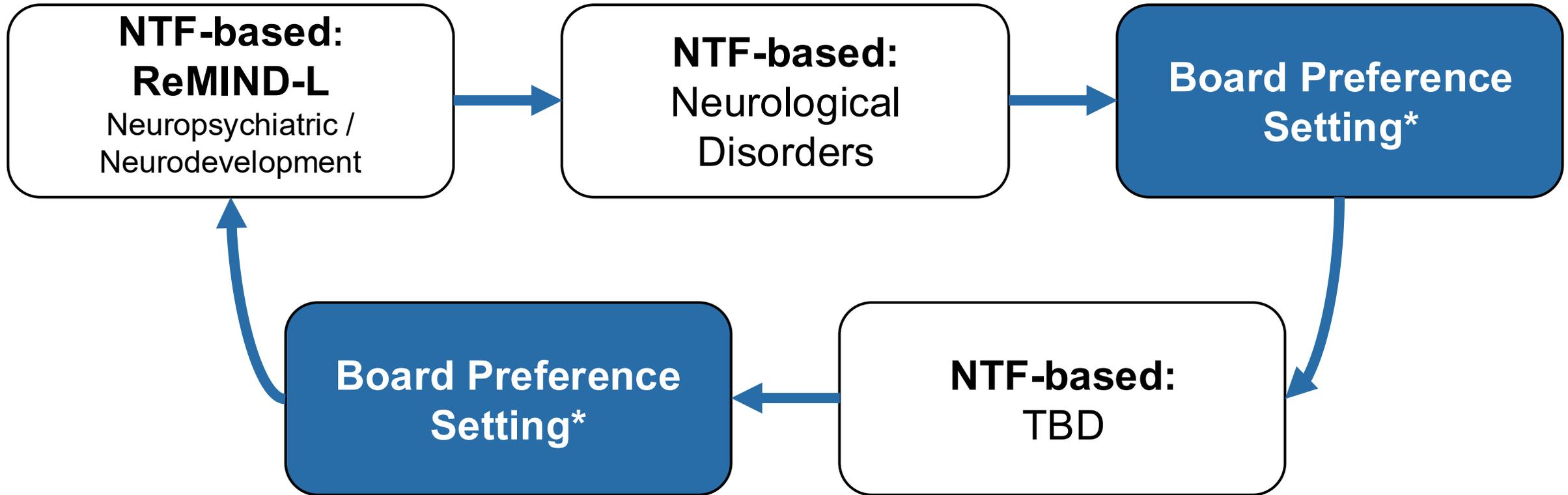
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DISC4 Annual Focus Area

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



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

CIRM requests ICOC approval of the following:

- Amendments to the DISC4, PDEV, and CLIN2 concept plans
- Implementation of the proposed GWG selection process in all programs requiring volume control
- The DISC4 program focus area for the FY 26/27 funding cycle
- A once per year PDEV funding cycle