

# Memorandum

**To:** Members of the Science Subcommittee of the ICOC  
**From:** Rosa Canet-Avilés, PhD, Chief Science Officer, Gil Sambrano, PhD., VP Review  
**Re:** March 19<sup>th</sup> Science Subcommittee Memo: Outstanding Issues and Proposed Clarifications  
**Date:** March 19<sup>th</sup>, 2026

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## Purpose of This Memo

The purpose of this memo is to clarify several topics that were discussed during the March 5<sup>th</sup> Science Subcommittee meeting and to provide additional context for the discussion scheduled for March 19<sup>th</sup>.

During the March 5<sup>th</sup> meeting, members of the Science Subcommittee raised important questions about two areas of the CIRM review and funding process. First, there were questions about how CIRM approaches what has historically been referred to as “Access and Affordability.” Second, there were questions about the proposed process used to manage application volume and how the proposed volume control process determines which applications advance to full GWG panel review.

Since that meeting, the CIRM team has reviewed the feedback from Subcommittee members and discussed possible clarifications. The goal of these clarifications is not to change CIRM’s underlying objectives, but to ensure that our expectations are clearly understood by applicants, reviewers, and the Board.

This memo therefore serves three purposes:

1. To summarize the key feedback received from the March 5<sup>th</sup> Science Subcommittee discussion.
2. To clarify CIRM’s approach to ensuring that therapies supported by the agency can ultimately reach patients.
3. To outline how these principles are being implemented in the PDEV and CLIN2 programs and how the CIRM team proposes to clarify aspects of the review process.

These clarifications are intended to support the Subcommittee’s discussion and to ensure alignment before materials are finalized for the March ICOC meeting.

## Feedback From the March 5<sup>th</sup> Science Subcommittee

During the March 5<sup>th</sup> Science Subcommittee meeting, several members raised questions and concerns about how CIRM’s expectations related to “Access and Affordability” are communicated and applied within the agency’s funding programs.

Several key themes emerged from the discussion.

First, Subcommittee members noted that access and affordability are conceptually different issues and expressed concern that the current terminology may unintentionally conflate the two. Members emphasized that investigators (particularly academic investigators) often have limited ability to determine the eventual price of a therapy or to control payer decisions.

Second, there was concern that the way affordability has sometimes been described could be interpreted as expecting applicants to demonstrate that a therapy will be affordable, which may not be realistic at early stages of development. Members noted that this type of expectation could unintentionally discourage innovative or transformative approaches that may initially appear costly but ultimately deliver significant clinical value.

Third, the Subcommittee highlighted the importance of clearly defining stage-appropriate expectations. Members emphasized that early development programs should focus on anticipating potential barriers to patient access, while later-stage programs may appropriately address implementation planning.

Finally, members asked for greater transparency about where access considerations influence the review process and where they instead inform post-award planning or programmatic oversight.

In addition to the discussion around Access and Affordability, Science Subcommittee members also raised questions about the proposed volume control process used to manage application volume and determine which applications advance to full Grants Working Group (GWG) panel review. In particular, they requested clarity about how reviewer selections and rankings are used to generate a composite score, how cut-off points are determined, and how the process ensures that applications advancing to full review reflect the strongest scientific proposals.

This was very helpful and constructive feedback. It highlighted areas where our intent may not have been clearly communicated and where terminology may have created unnecessary confusion.

In response, the team has reviewed how these expectations are described across program materials and is proposing several clarifications to ensure that CIRM's approach is clear and appropriately aligned with the stage of therapeutic development.

## Clarifying CIRM's Approach to Patient Access

CIRM's goal as a public funder is not only to support the development of promising therapies, but also to help ensure that those therapies can ultimately reach patients in California. Achieving this requires thinking about potential barriers to patient access during the development process.

CIRM does not determine the price of therapies and does not control reimbursement decisions. Those decisions are made by developers, healthcare systems, and payers. Instead, CIRM's role is to encourage development strategies that make it more likely that a successful therapy can realistically be delivered to patients.

In practice, this means asking applicants to consider issues that may affect whether patients can access a therapy if it succeeds. These considerations are incorporated into CIRM programs in ways that are appropriate to the stage of development.

Historically, these expectations were described using the term "Access and Affordability (A&A)". Based on feedback from the Science Subcommittee, we recognize that this terminology may create confusion by suggesting that applicants are expected to demonstrate that a therapy will be affordable.

To better reflect CIRM's intent, we are transitioning to the terms "Patient Access" or "Access Strategy". This language makes clear that the focus is on planning during development to support patient access, not on setting or predicting therapy pricing.

This clarification does not change CIRM's objective. It actually helps ensure that applicants, reviewers, and the Board share a clear understanding of how patient access considerations are incorporated into CIRM's development programs.

## Stage-Appropriate Expectations for Patient Access

### PDEV

The Preclinical Development (PDEV) program supports preclinical development of stem cell-based and genetic therapies that not only offer potential for transformative clinical impact but also meaningfully address current barriers to patient access for these types of therapies. The expectation is that the PDEV portfolio of projects incorporate learnings from the patient experience with first generations of stem cell-based and genetic therapies in the design, development and delivery strategies for the next generation of therapies. At the PDEV application stage, a PDEV applicant is currently instructed to describe whether the proposed therapy meaningfully addresses known barriers to patient access. The GWG review criteria currently incorporate as assessment of the therapy's potential to overcome barriers to access and affordability as one of several components of the value proposition of the proposed therapy.

Based on Board feedback and an assessment of the applicant descriptions and GWG review comments from the first PDEV cycle, the CIRM team is proposing a set of changes to facilitate a more comprehensive assessment of patient access strategy for the proposed therapy. The patient access strategy is a key component of the overall value proposition for the proposed therapy, and it also informs preclinical development activities, clinical trial design and clinical operations planning during the PDEV award. For example, design decisions that impact how the therapy is manufactured, tested and delivered to the patient have direct impact on how widely accessible the therapy will be to patients in clinical trials and after marketing approval. Aspects of the first-in-human clinical trial such as inclusion criteria, treatment regimen and follow-up regimen impact patient access in the clinical trial and they also influence pivotal trial designs and post-approval insurer coverage decisions.

The Board approved 12 new PDEV awards in last December, the batch of awards included several examples of patient access strategies intended to improve access to the proposed therapy for the intended patient population:

1. An AAV gene therapy for trigeminal neuralgia, a painful condition that affects disproportionately affects women (2:1): The one-time therapy is being developed as a local low-dose injection that can be performed in an outpatient clinic similarly to current pain relief injections thereby potentially reducing the burden on patients and the healthcare system.
2. An AAV gene therapy for limb girdle dystrophy: Anticipating that a new small molecule standard of care treatment by the time the proposed therapy enters clinical trials, the team is incorporating the small molecule in its IND-enabling studies to enable inclusive enrollment of patients already on the standard of care.

3. An autologous cell therapy for urinary incontinence: While the iPSC-derived cell therapy necessitates a complex manufacturing process, it is intentionally being designed for an elderly patient population with history of failed surgical treatment by utilizing a non-surgical delivery method similarly to existing bulking agents.

The CIRM team believes that the changes proposed below to PDEV Guiding Principles, GWG criteria and applicant instructions will allow for more consistent and comprehensive assessments of how each proposed therapy is being positioned to improve access for the intended patient population.

In addition, similarly to the CLIN2 program, the PDEV program incorporate stage appropriate patient access planning strategies that will ultimately better position the therapy for eventual market access. The PDEV application process has no entry criteria for stage-appropriate patient access planning but does instruct all applicants to incorporate market landscape and payer landscape research activities over the course of the PDEV award, which will be milestone in the PDEV award. No changes are proposed to the stage-appropriate patient access planning requirements for PDEV awardees.

## CLIN2

The ultimate goal of the CLIN2 program is to ensure that transformative cell and gene therapies entering late-stage clinical development have a viable path to patient access. To accomplish this, CIRM has worked with external experts to identify activities that directly impact patient access and have organized them according to the stage of clinical development. Each CLIN2 applicant is required to present a plan to achieve the indicated stage-specific goals as part of their application.

While the breadth and sophistication of the required activities increase as the product comes closer to pivotal trial stages and commercialization, projects at all stages benefit from accomplishing their own stage-appropriate tasks. These activities ensure that the applicant understands the market landscape (i.e., clinical demand, competition, barriers to patient entry), align their clinical endpoints with expectations of eventual payers and partners, assess the patient journey to make sure their drug development program is aligned with patient needs, and establish not only boards with relevant KOLs but also patient registries to collect long-term data to establish the impact and duration of their therapies.

The board approved 4 CLIN2s with patient access plans during the first cycle. Examples of applicants focusing on enhanced access include:

- A Phase 1 project developing an allogeneic iPSC-derived therapy for Parkinson's disease. The applicants intend to position their therapy in community hospitals where neurosurgeons are on staff, and to explore delivery methods that do not require MRI guidance.
- A Phase 2 project using AAV-based gene therapy to treat Dravet syndrome. In addition to gathering reimbursement insights from prescribers, clinical experts and payers, the applicants are developing an early access plan focused on manufacturing costs, conversion to commercial therapy, and equity considerations.

The tools provided to applicants and the process by which their plans are reviewed is further described in the **Proposed Program Clarifications** section.

## Proposed Program Clarifications

### PDEV

Below, we propose for the Board's consideration revised Guiding Principles for the PDEV program. We also provide for reference the changes to the GWG criteria and applicant instructions to reflect the revised patient access Guiding Principle.

The goal of the PDEV program is to advance a pipeline of innovative therapies for diseases affecting Californians to first-in-human clinical trials in order to contribute toward the CIRM Impact Goal of advancing 15-20 therapies to late-stage clinical trials. The PDEV program aims to achieve this goal by supporting preclinical development of stem cell-based and genetic therapies that not only offer potential for transformative clinical impact but also meaningfully address current barriers to patient access for these types of therapies.

### PDEV Guiding Principles

The Guiding Principles for the PDEV program encapsulate the overall goal of the program as well as its priorities for achieving the goal.

The PDEV Portfolio will:

- Have potential to delivery transformative improvements in patient outcomes by leveraging cutting-edge therapeutic technologies
- Advanced strategies to improve patient access to stem cell-based and genetic therapies
- Broadly address both prevalent and rare diseases affecting Californians

At the PDEV application stage, to facilitate a consistent and comprehensive applicant description of patient access therapies for the proposed therapy for the intended patient population and a corresponding consistent and comprehensive review, the CIRM team will incorporate the following updates to the application instructions and GWG criteria.

### Application Instructions – Value Proposition Section of the Application Proposal

**Current Instructions:** Describe the potential for the proposed therapy to be more accessible and affordable compared to available therapies or therapies currently in clinical development for the intended patient population and healthcare system.

**Revised Instructions:** Describe your overall strategy for patient access to the proposed therapy for the intended patient population.

- Highlight known challenges that limit eligible patients from receiving this type of therapy, indicate any characteristics of the modality and intended patient population.

- Describe how patient access priorities are informing the design, development and delivery of the proposed therapy including the following where applicable:
  - Therapeutic design and route of administration.
  - Current and future manufacturing and testing development.
  - Therapeutic administration and healthcare setting.
  - Clinical trial design and clinical trial operations.
  - Payer and reimbursement landscape research and market access planning

## GWG Review Criteria

In order to align with the PDEV Guiding Principle and to facilitate a comprehensive GWG assessment of the applicant's stage-appropriate patient access strategy, changes will be made to the sub-sections of the Value Proposition and Project Plan and Design GWG criteria. Deleted sections are indicated in strike out and inserted sections are shown as bolded text.

**Value Proposition** - *Evaluate the extent to which the therapy offers a compelling value proposition based on holistic consideration of the following.*

- Assess 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 (e.g., efficacy, safety, patient burden).
- Assess the expected impact of addressing the unmet medical need on patients, caregivers, and the healthcare system.
- ~~• Assess the therapy's potential to be more accessible and affordable compared to available treatments or therapeutics currently in clinical development for the intended patient population and healthcare system.~~
- **Assess whether the applicant has proposed a stage-appropriate strategy for enabling access to the proposed therapy for the intended patient population.**
- Evaluate the feasibility and practicality of the therapy's uptake by patients, caregivers, and the healthcare system.

**Project Plan & Design** - *Evaluate the project's plan and design to achieve an active IND.*

- Evaluate the extent to which the proposed activities are necessary and appropriate to efficiently and effectively progress the project to IND clearance. For example, consider proposed preclinical studies, IND-enabling studies, process and analytical development/testing, clinical protocol drafts and trial startup activities as stage-appropriate.
- Consider whether the PDEV objective will be achieved within the proposed budget and timeline.
- Assess the validity of the potential project risks identified along with the mitigation and contingency plans presented.
- ~~• Assess how well the project incorporates stage-appropriate access and affordability planning to support future market access.~~

The changes to the value proposition criteria are intended to facilitate a comprehensive assessment based on the applicant's incorporation of patient access priorities into the overall development strategy for the proposed therapy.

The changes to the project plan section are to remove the GWG review of adequacy of the Patient Access Planning checklist activities. The removal of this reviewer criteria focuses the GWG review on the patient access strategy as a component of the overall value proposition of the proposed therapy. All PDEV awardees are expected to make progress on stage-appropriate market landscape research and payer landscape research over the course of the PDEV award. They may use CIRM funding for these activities, which are incorporated into PDEV award operational milestones. The proposed change aligns the PDEV Patient Access Planning requirements with the Data Sharing and Management Plan requirements.

## CLIN2

The CLIN2 Guiding Principles are designed to accomplish the following:

- Offer transformative impact for patients, meaning therapies that provide significant benefits over existing therapies
- Address known barriers to access of stem cell-based and genetic therapies
- Broadly address both prevalent and rare diseases affecting Californians.

Of these principles, attempts to address access issues will require strategic planning that many early-stage applicants are unlikely to have fully considered. In order to assist applicants and awardees, particularly those who may have minimal experience with planning for patient access, CIRM provides:

- A checklist of required activities organized according to developmental stage (preclinical through Phase 1, 2 or 3 trials).
- A description of each activity and suggested ways to accomplish them (CIRM is also gathering information on the costs of each activity in order to help applicants with budgeting).
- Evaluation of applicant plans by access specialists during the GWG review.
- Awardee consultation with external experts to flesh out access planning.

The access plan review is performed by experts with whom CIRM has contracted. They evaluate each required activity (the number of activities reviewed depends on the clinical stage) and provide comments for each. Currently, the access specialists conduct their reviews prior to the GWG and present summaries during the GWG meeting. This approach is designed to allow GWG members to take into account the degree and thoroughness of access planning for each application under consideration; the extent to which this influences GWG scoring is left up to the individual GWG member. The benefit of this approach is that critical information (e.g., the adequacy or lack of preparation of an access plan for a pivotal trial) is available to the GWG. The downside is that there is no mechanism to ensure that GWG reviewers consider this information in a reproducible, quantifiable manner.

As an alternative, the access plan review results could be provided directly to the ARS (i.e., no longer presented during the GWG session) as part of a larger package including the GWG recommendation and the CIRM team recommendation. Here the advantage is that the information is put directly to the ultimate deciders. The downside is that the GWG no longer has access to this information during their deliberations.

The CIRM team is seeking Board guidance on the preferred approach.

## Issue for Science Subcommittee Input: Role of Patient

### Advocates in Review

CIRM staff is soliciting feedback from Patient Advocate members of the GWG and will continue to work with this group to fully develop the role. Given the goal of focusing volume control selection on scientific value, Patient Advocate members' role will be focused on the subsequent full GWG panel discussion (i.e., applications that advance to panel discussion).

To strengthen the Patient Advocate role at the full GWG panel discussion we are proposing:

- To define and include a Patient Perspective score

Patient advocate members have a very important role in the review process by providing a perspective that helps the GWG assess whether a proposed therapy has value that is ultimately meaningful to patients. We propose that this score, which is separate from the scientific score, will provide an additional dimension that the Application Review Subcommittee may consider in its programmatic review of PDEV and CLIN2 applications.

- Facilitate discussion between patient advocate members and the GWG chair prior to each GWG review.

Scientific and patient advocate members of the GWG have a good partnership on the GWG, but having additional opportunities to engage ahead of a review meeting can help highlight and strengthen the patient voice to benefit the review.

## Clarifications to the Review and Volume Control Process

### Background

Scientific review of CIRM applications by the Grants Working Group (GWG) is time and resource intensive, effectively limiting the number of applications that can be fully reviewed in a single cycle. It is often the case that the number of applications received in response to a funding opportunity exceed this limit and strategies to narrow the pool of applications are required. Over CIRM's history, different strategies have been tested and utilized such as setting limits on the number of applications that CIRM would accept from any given organization; implementing a preliminary application process; or filtering applications through a positive selection process. This challenge is not unique to CIRM, and many funding agencies utilize different strategies to narrow the pool of applications received including NIH, NSF, CPRIT, and others.

Over the last year, we tried a couple of new approaches, termed “presubmissions” (DISC4 & PDEV) and “qualification” (CLIN2) as methods to control volume that were dependent on the use of strict objective criteria we called “preferences”. Although these methods proved effective in narrowing the pool, the use of preferences, in particular, has limited advancement of applications based on a set of unrefined characteristics rather than on a scientific assessment of the proposals.

## What We Heard

Following the Science Subcommittee meeting of March 5, 2026, there were questions raised by board members related to this process that we are responding to by providing additional details or clarifying.

These are the key questions and concerns we heard.

- The proposed selection process is unclear:
  - Difficult to understand how reviewer selections affect outcomes.
  - How composite score is determined is unclear.
  - How cut-off is determined is unclear.
- What is the role of patient advocate members in the selection process

## GWG Selection Process Overview

The proposed approach which we term “GWG selection” is a modification of the existing positive selection process. The process can be adapted to each of the different funding opportunities, but with some differences related to the expected application volume as shown in the table below.

<b>Selection Process</b>	<b>Positive Selection (existing)</b>	<b>GWG Selection DISC4</b>	<b>GWG Selection PDEV</b>	<b>GWG Selection CLIN2</b>
<b>Submission</b>	Full App	Pre Sub Form	Full App	Full App
<b>Reviewer Scoring</b>	Advance or Not	Select & Rank	Select & Rank	Select & Rank
<b>Expected Reviewer Number</b>	15	15-30	15-20	15
<b>Assignments</b>	Optional	Required	Required	Required
<b>Number of Apps per Reviewer</b>	Open but must review minimum number	Fixed, must review same as all others	Fixed, must review same as all others	Fixed, must review same as all others

The GWG selection process will be applied to all programs requiring volume control (e.g., DISC4, DISC5, PDEV, CLIN2). A target number of applications to be reviewed by the full GWG panel will be established for each funding opportunity and cycle. The target number is based on preserving a high level of rigor in performing the evaluations by the 15 appointed scientific members of the working group along with the 7 patient advocate members (as prescribed in Prop 71 & 14). The number of available awards and expected success rate may also be considered in determining the number that advances to full review to ensure that the pool is sufficient while allowing for robust time and discussion during the GWG meeting phase.

GWG panels are tailored in their composition to the specific set of applications reviewed to ensure that the expertise is well matched. Recruitment of appropriate reviewers includes identifying specialists that can enhance the expertise of the panel. For CIRM, a complete evaluation may include elements not always present in other funding programs such as elements of population impact and patient access.

The target number and number of submissions (in a given funding cycle) determine the necessary parameters for setting up the GWG selection. If the number of submissions is at or below the target number then no selection is necessary. Otherwise, the number of reviewers, number of reviews per application, number of applications per batch, and total reviews required will be set to optimize the selection and ranking of the application pool.

The table below shows these parameters for different application pool sizes and different targets that approximate what we would expect across the four funding opportunities shown.

	<b>DISC5</b>	<b>DISC4</b>	<b>PDEV</b>	<b>CLIN2</b>
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

### **Illustrative Example of the Process**

To illustrate the process, we provide an example where we follow the fate of an application within a pool of 75 applications (such as PDEV). The goal is to narrow the pool to about 30 applications that advance to GWG panel review.

The illustrated process in brief:

- The pool of 75 applications is split into 20 overlapping batches of 15 applications each.
- Each batch is assigned to one of 20 total scientific reviewers.
- As shown by the sample application:
  - Each application will be contained within the batches of 4 different reviewers (out of the 20 total reviewers).
  - Each of the reviewers will select and rank the best 5 applications in their batch.
  - The sample application is selected by 3 out of the 4 reviewers that had the application in their batch.
  - Two reviewers ranked it as their favorite (#1 rank) and one ranked it as their second favorite (#2 rank). There is no rank for unselected applications.
  - A composite score is calculated for the sample application.

## How Is a Composite Score Calculated?

Applications are each given a composite score that combines two measurements from the scientific reviewers, selection and rank. The fraction of reviewers that selected the application measures the breadth of interest in the application, whereas the rank given by reviewers measures the intensity of interest by the reviewers. The two measurements are weighted 60% and 40% respectively to prioritize the breadth of interest over the intensity of interest. This, in part, mitigates ranking differences based on differences in quality within batches. Therefore the formula to calculate the composite score becomes the following:

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

For the sample application we can plug in values derived from the 4 reviewers' selections and rankings. Selections are converted into a binary value of 1 if selected and 0 if not selected. Rankings are converted into values that assigns 5 points to the top rank, 4 points to the second rank, 3 points to the third rank, etc. The two measures are normalized by dividing the total points by the total possible points.

	Selections	Selection Points	Rankings	Ranking Points
Reviewer 1	Yes	1	1	5
Reviewer 2	Yes	1	2	4
Reviewer 3	No	0	-	0
Reviewer 4	Yes	1	1	5

Plugging in the values:

$$60\% \times (3 \text{ selections} / 4 \text{ possible selections}) + 40\% \times (14 \text{ rank pts} / 20 \text{ possible rank pts})$$

$$= 60\% \times (0.75) + 40\% \times (0.70)$$

= 0.45 + 0.28

= 0.73

## How Might a Composite Score Affect Outcomes?

The range of composite scores is 0 to 1 with 1 being a perfect score. The purpose of the composite score is to combine two measurements but also to create a rank order of applications. Utilizing a composite of selection and ranking spreads the scores sufficiently to allow for a narrow range to establish a cut-off near the target number of applications. One measurement alone does not provide sufficient granularity.

Where the cut-off falls among the composite scores is dependent on several factors including target number, total pool size, and number of reviewers per application. For the example described here, the cut-off will typically fall between 0.30 and 0.35.

The table below shows how selections and rankings from 4 reviewers and the resulting composite score would affect outcomes.

Scenario	Picks	Rankings	Composite Score	Outcome
All pick, all rank #1	<b>4/4</b>	#1, #1, #1, #1	<b>1.000</b>	<b>Clear Advance</b>
All pick, mixed ranks	<b>4/4</b>	#1, #2, #3, #4	<b>0.880</b>	<b>Clear Advance</b>
3 of 4 pick	<b>3/4</b>	#1, #2, #1	<b>0.730</b>	<b>Advance</b>
2 of 4 pick	<b>2/4</b>	#1, #3	<b>0.460</b>	<b>Advance</b>
1 of 4 picks	<b>1/4</b>	#1	<b>0.250</b>	<b>Filtered</b>
Nobody picks	<b>0/4</b>	—	<b>0.000</b>	<b>Filtered</b>

## Establishing the 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. Defining the range by a percentage allows us to apply this rule across the variable target numbers for each funding opportunity.
- 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. Several funding agencies are now testing or utilizing

randomization as method to select among otherwise equally fundable proposals that cannot all be funded.

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

Applications that advance will be reviewed and scored against the full set of criteria by the GWG.

## The Final Step

- The CIRM President, with recommendation from CIRM scientific staff, will examine applications below the cut-off and may advance a limited number of additional applications.
- Advancement would be based on identifying an application that represents a unique opportunity aligned with the goals of the funding opportunity.
- Reviewers may provide brief comments or categorical assessments on the reviewed applications, but feedback to applicants is not guaranteed at this stage of review.

## Clarifications Regarding Information Provided to the Application Review Subcommittee

During the March 5 Science Subcommittee, the CIRM team presented information on how program guiding principles would be used to support funding decisions made by the Application Review Subcommittee (ARS). The goal of this step in the funding process is to provide ARS members with relevant information to support well-informed funding decisions.

For each funding cycle, the CIRM team intends to provide a memo summarizing relevant programmatic context and the CIRM team’s funding recommendations for the applications under consideration. CIRM team recommendations may consider:

- Available program budget
- Grants Working Group (GWG) scores and comments
- How applications address program Guiding Principles
- Prior awardee performance (if applicable)
- Relevant information that becomes available after GWG review

The Subcommittee asked the team to clarify whether and when the CIRM team may provide relevant information that becomes available after the GWG review.

## How information available to CIRM after GWG review would be communicated

In rare circumstances, CIRM staff may become aware of information concerning an applicant, institution, or relevant scientific or regulatory developments that might impact the success of an application *after GWG and before ARS funding decisions*. CIRM staff are not actively searching for such information. If (1) such information comes to staff's attention through ordinary duties (such as reviewing the literature and regenerative medicine industry news), public announcements, or direct confirmation with the applicant or institution, and (2) the information is relevant to the CIRM team funding recommendation to the ARS, CIRM would include the new information in a factual, non-identifying manner with citations in the public ARS memo. Importantly, the GWG scientific review and scores remain unchanged. Applications are **not returned to GWG for re-review**, preserving the separation between GWG scientific merit evaluation and CIRM staff programmatic context provided to ARS.

## Types of information that may be considered in CIRM team recommendations

Potential information may relate to the safety, efficacy, or probability of success for the therapy proposed in an application or the successful completion of the project as proposed. This information would come to CIRM's attention through press releases, peer-reviewed scientific publications, other public announcements, or direct communication with applicants or institutions. This may include:

- Regulatory or clinical developments concerning the candidate, or a closely related candidate in the same indication or using a similar therapeutic approach, where the development may impact the proposed project's probability of success. Specific examples: regulatory decisions or designations, adverse events, or trial read-outs.
- New information about an applicant or the applicant's institution. Specific examples: PI relocation to another institution (if verified by the PI and AOO), publicly announced changes concerning the institution's strategic priorities that may influence the application under consideration (for example, a company closing a business unit or out-licensing the candidate), or publicly announced legal proceedings involving the applicant or institution

## Summary and Next Steps

### Summary

The March 5 Science Subcommittee discussion highlighted the importance of clearly distinguishing between patient access considerations and therapy affordability, and of ensuring that expectations are appropriate to the stage of development. Members emphasized the need for clear guidance to applicants and reviewers on

what is expected, and for transparency in how these considerations are used in the review and funding process.

The discussion also underscored the need to clearly explain the volume control process, including how applications are evaluated and selected for advancement to full review.

Overall, the feedback reflects a shared goal: to ensure that CIRM's processes are clear, consistent, and aligned with the agency's mission of supporting therapies that can ultimately reach patients.

## Next Steps

In response to this feedback, the CIRM team will:

- **Clarify terminology** in program materials to focus on "Patient Access" and remove ambiguity related to affordability
- **Define stage-appropriate expectations** for PDEV and CLIN2, ensuring that access considerations are aligned with the level of development
- **Provide clearer guidance** to applicants and reviewers on how access considerations should be addressed and evaluated
- **Clarify the role of access considerations** in review versus programmatic decision-making
- **Refine and clearly describe the volume control process**, including how applications advance to full GWG review

These updates will be incorporated into program materials and presented to the Subcommittee and Board to ensure alignment prior to finalization.