

# Real Life™

**Gil Sambrano, PhD**

Vice President, Portfolio Development and Review

Flow Control Review Process

June 27, 2024

**CIRM**  
CALIFORNIA'S STEM CELL AGENCY

**TODAY**

	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep
ICOC / Sci. Sub. / NTF Meetings	▲ 2/22/24 ICOC	▲ 3/26/24 Sci. Sub.  ▲ 3/22/24 NTF ND	▲ 4/22/24 Sci. Sub.  ▲ 4/17/24 NTF ND	▲ 5/21/24 Sci. Sub.  ▲ 5/14/24 AAWG	▲ 6/27/24 ICOC  ▲ 06/04/24 Sci. Sub./NTF	▲ 07/11/24 Sci. Sub./NTF	▲ 8/7/24 AAWG  ▲ 08/16/24 Sci. Sub./NTF	▲ 9/26/24 ICOC  ▲ 09/13/24 Sci. Sub./NTF
Flow Control	CLIN1/2 Flow Control Starts				Flow Control Evaluation	Resume CLIN app submissions		
SAF Milestones					SAF Update Interim FY24/25 Research Budget Full FY24/25 Operations Budget		SAF Recommendations FY24/25 Research Budget	
SAF Analysis		<i>Collect data &amp; analyze</i>				<i>Provide recommendations</i>		
		Formation of SAF Analysis Group						

	Sep	Oct	Nov	Dec	Jan 25	...	May 25
ICOC / Sci. Sub. / NTF Meetings	<p>▲ 09/13/24 Sci. Sub./NTF</p> <p>▲ 9/26/24 ICOC</p>		<p>▲ TBD AAWG</p> <p>▲ TBD Sci. Sub./NTF</p>	<p>▲ 12/12/24 ICOC</p> <p>▲ TBD Sci. Sub./NTF</p>			
Flow Control			Earliest CLIN app approval from re-start				Earliest CLIN app approval from new opportunities
SAF Milestones	SAF Recommendations FY24/25 Research Budget						
SAF Follow Up	<p><i>Develop &amp; Amend Concepts</i></p>				Open new opportunities		

Define  
Problem

Develop Possible  
Solutions

Make  
necessary  
changes

**New CLIN  
Review  
Process**

**Clinical Flow  
Control Process**

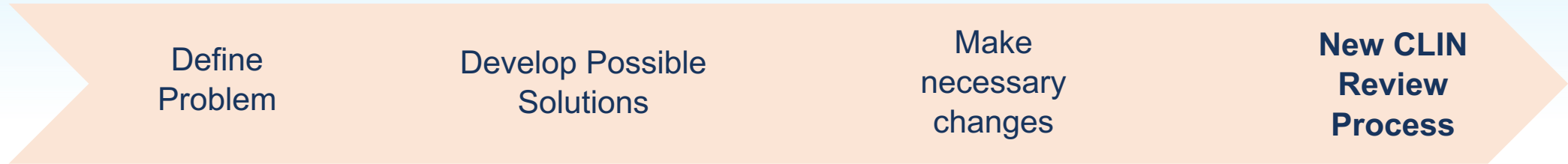
Gather Input

Identify Key  
Priorities

Stakeholder  
Alignment

**Updated  
Strategy  
& Goals**

**Strategic  
Allocation  
Framework**



## Clinical Flow Control Process

### Considerations:

- The flow control effort is focused on creating an updated CLIN review process to manage increasing numbers of applications.
- This effort will not address funding strategies.
- The process is intended to address the challenges under the existing CLIN program eligibility and structure.
- The effort intends to develop a process that will be adaptable and applicable beyond SAF.

## What led to the current CLIN review process?

- Over the 6 years prior to establishing this process (2014), CIRM had funded about 16 clinical trials.
- The field had not yet advanced many candidates to the clinical trial stage.
- CIRM was prepared to fund any meritorious project that had reached this stage.
- Each project was to be assessed independently of others since each cycle had only 1 or 2 proposals. Ranking did not make sense.

Program	Annual Awards*	Success Rate	Total Apps to Review	Cycles Held Per Year	Apps Per Cycle Needed
CLIN2	16	50-60%	28-32	11	3
CLIN1	11	50-60%	19-22	11	2

\*Based on annual budget comparable to 23-24.

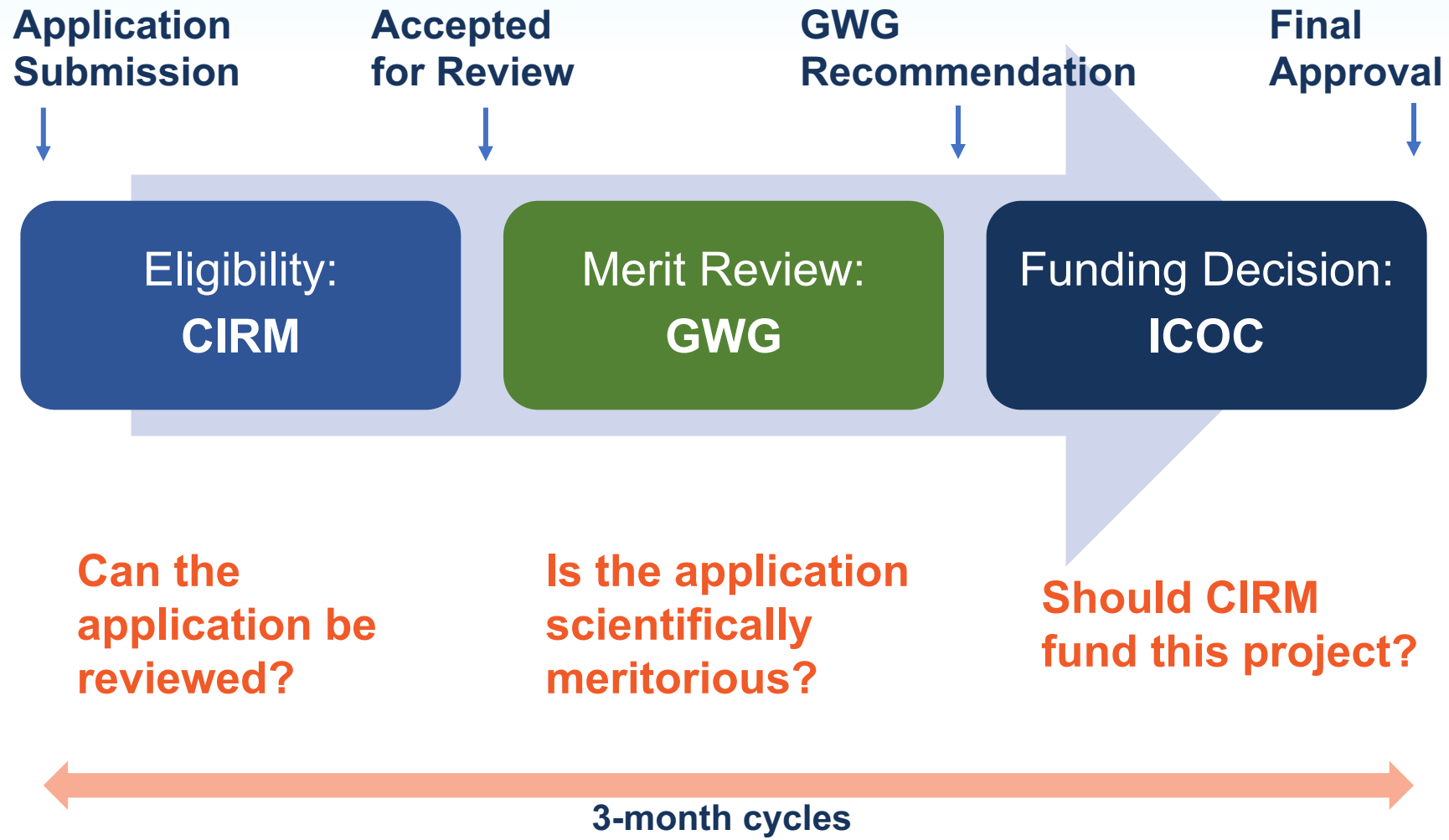
## The existing process is rigorous:

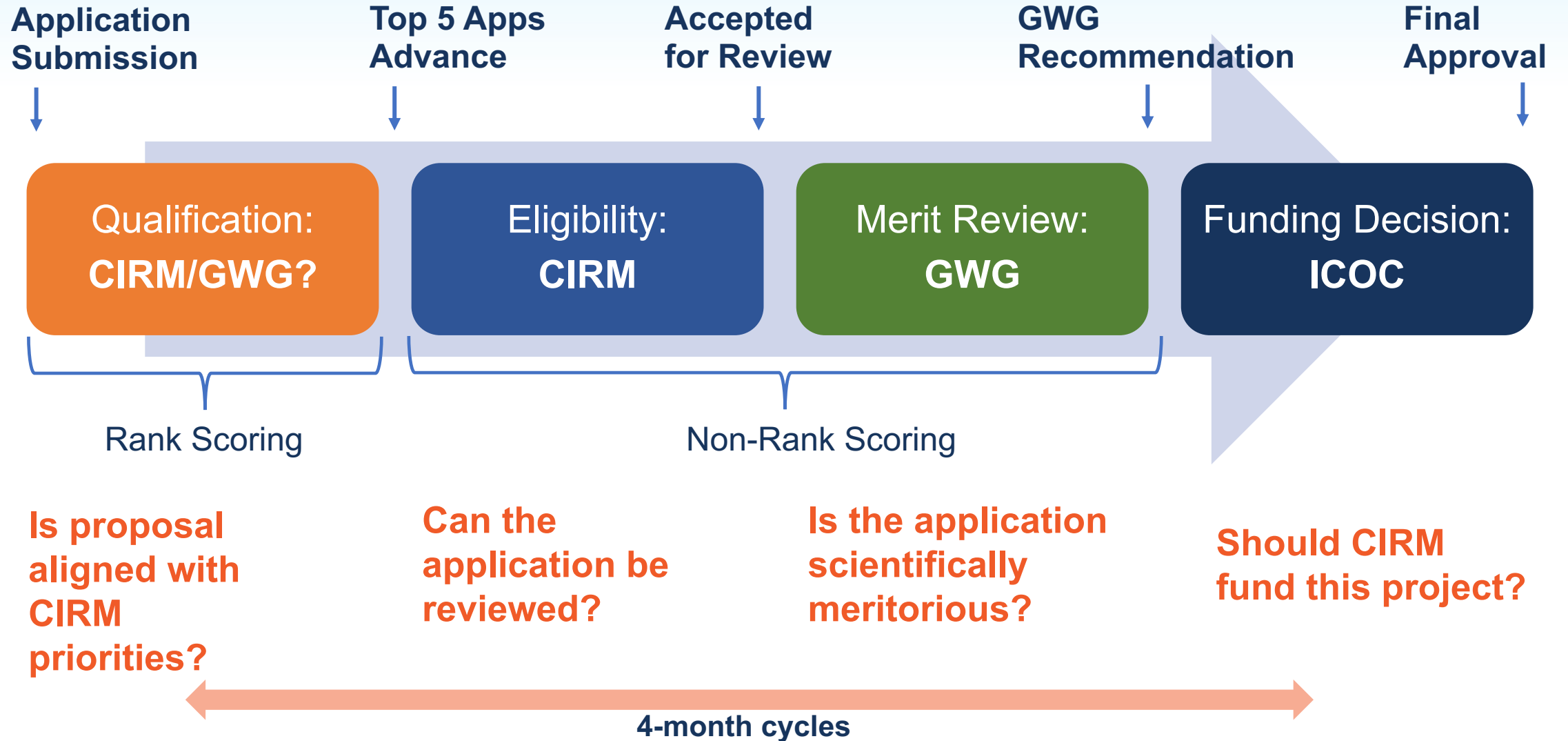
- Most applicants go through one application revision (sometimes more) before getting a recommendation to fund.
- With few applications per cycle, the full GWG panel can meaningfully contribute to each evaluation.
- Most successful applicants receive significant guidance from our Therapeutics Development team.
- GWG panels are tailored to the needs of each review cycle.

- Maximum contribution from full GWG panel on each application
- A tier 2 process that allows project improvement and prevents appeals
- Frequent, predictable and rapid process that allows applications to come in when ready
- Opportunities for clarification
- Participation of GWG patient advocates in evaluation of projects and DEI
- Alignment with the number of proposals CIRM will target for funding annually
- Rigorous review of the most promising applications



- Create a preliminary “filtering or qualifying” process that feeds into the existing CLIN review process
  - Allows for continued level of rigor and attention but limits the number that benefit from it
  - Is generally aligned with number of projects we have historically targeted but allows us to address large influx when it occurs
- Develop a completely new process for CLIN or adopt DISC/TRAN approach
  - May allow for greater number of apps to be reviewed but with less rigor/attention
  - Frequency would need to be less to accommodate changes
  - Would likely require more extensive policy changes and changes to applications/programs





- Applies only to CLIN1 and CLIN2, not CLIN4
- Create a qualifying score based on objective (and subjective) criteria
- Rank submissions and advance top 5 to next cycle. Retain submissions in competitive pool for 2 cycles with multiple opportunities to advance.
- If pool has 5 applications or less, all advance.

## STEP 1: Objective criteria are scored by CIRM team

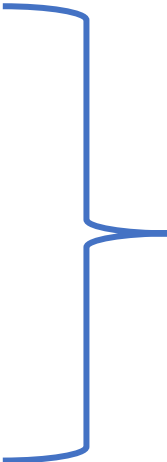
- Points are awarded for each criterion met.
- Apps are then ranked by their scores. Top 5 qualify for review.
- If there are ties, those applications move to step 2.

## STEP 2: Subjective criteria are scored by GWG experts

- GWG experts score applications based on 4-5 key elements.
- Apps are ranked by their scores to break ties.

An app that does not qualify can (i) be withdrawn by the applicant or (ii) be re-ranked for up to two additional cycles, after which it cannot be resubmitted for 6 months.

- Example objective criteria scored by CIRM
  - CA organization
  - Pipeline project (progression event)
  - Therapeutic type (cell therapy, etc.)
- Example subjective criteria scored by GWG experts
  - How well does it address an unmet need?
  - Impact on patients if successful
  - Improvement over SOC
  - Adequate DEI plan?



Applied if objective criteria are not sufficient to select top apps.

Although we are choosing criteria that are generally supported by Prop 14 or the CLIN program concept/announcement, they do have programmatic value.

If comparing otherwise eligible applications, what should be advantaged? We recommend supporting (but invite additional suggestions):

- California-based organizations over non-California organizations
- Cell therapy and gene therapy over small molecules and traditional biologics
- Project advancements (e.g., advancing from CLIN1 to CLIN2) over new projects
- Later stage of development (phase 3/pivotal or CLIN2 over CLIN1) compared to others
- Projects targeting a disease/condition of the brain or central nervous system

Subjective criteria are derived from the main Review Criteria that are already used by the GWG in their full evaluation of applications and specifically focused on the significance and impact criterion and DEI criterion.

- 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?



- Limit Tier 2 resubmissions to one time (resubmissions scored 1 or 3)
- Tighten internal deadlines for resolving eligibility issues
  - Single eligibility notice, one chance to resolve
  - Moves out of cycle, if cannot fix by deadline

- Update GWG bylaws to restrict tier 2 process for CLIN reviews
- Update Concept and PA to define qualification step and selection criteria