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Flow Control Review Process
Science Subcommittee
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Timeline (slide 1/2)

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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.*
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		Formation of SAF Analysis Group	***Collect data & analyze***				***Provide recommendations***	

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Timeline (slide 2/2)

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	Sep	Oct	Nov	Dec	Jan 25	…	May 25
ICOC / Sci. Sub. / NTF Meetings	9/26/24 ICOC *09/13/24 Sci. Sub./NTF*		*TBD AAWG* *TBD Sci. Sub./NTF*	12/12/24 ICOC *TBD Sci. Sub./NTF*			
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			***Develop & Amend Concepts***		Open new opportunities		

Two Parallel Efforts

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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

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Two Parallel Efforts

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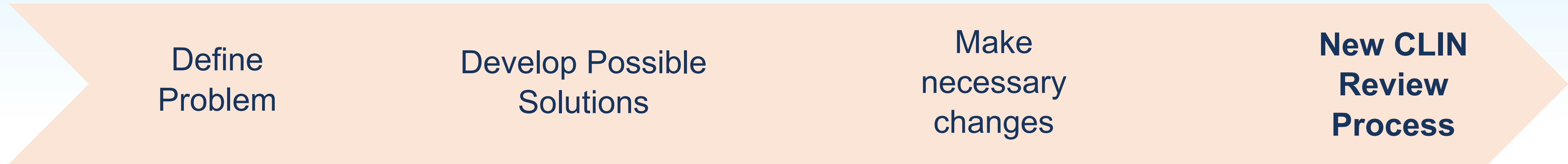

Clinical Flow Control Process

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.

Creation of the Current CLIN Review Process

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.

Alignment of the process with award targets

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.

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What would we like to keep?

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- 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

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Possible Approaches

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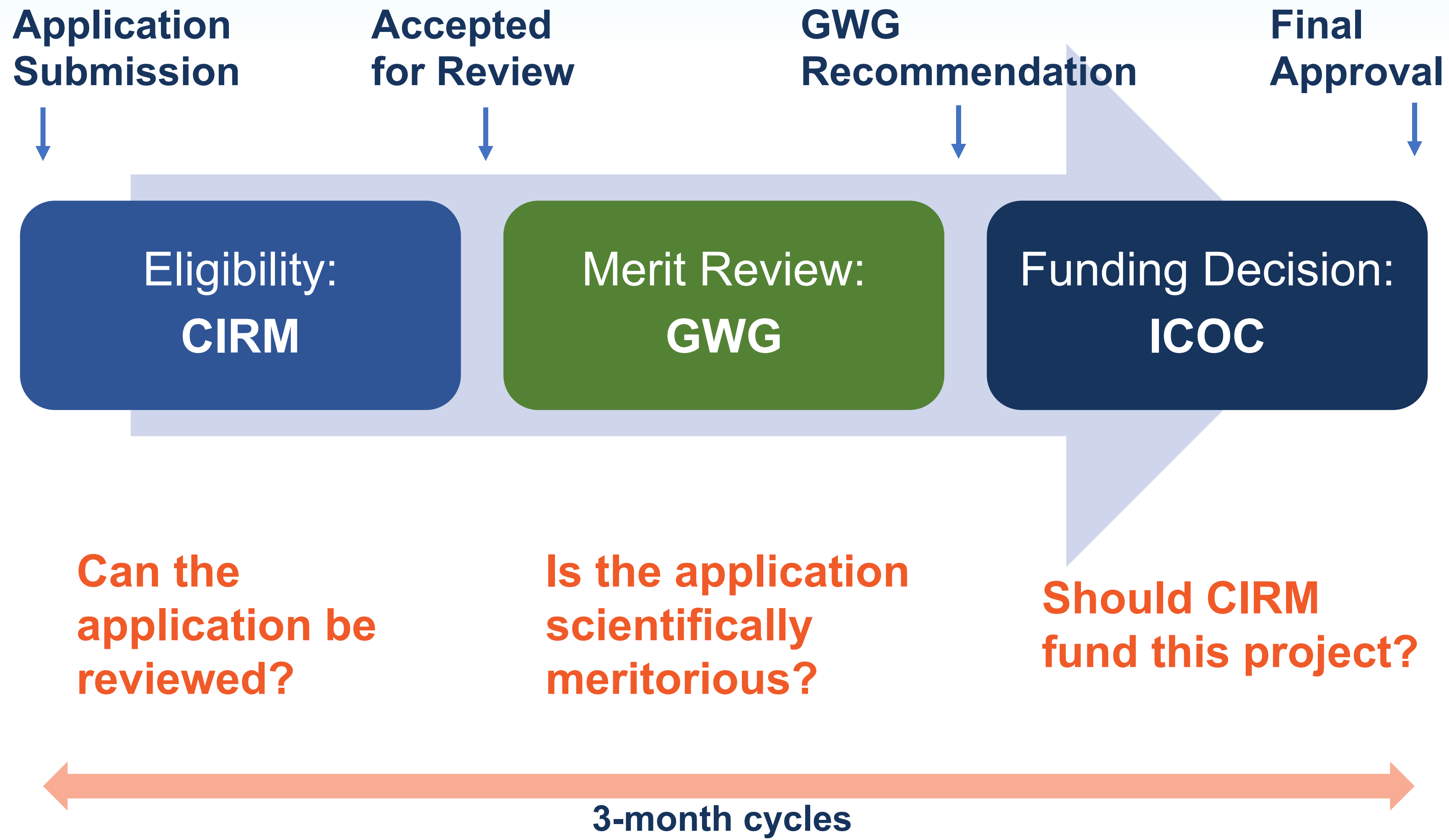
- Create a preliminary "filtering or qualifying" process that feeds into the existing CLIN review process
  - Allows for continued level of rigor and attention but limits the number that benefit from it
  - Is generally aligned with number of projects we have historically targeted but allows us to address 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

Current CLIN Application and Review Process



Proposed CLIN Application and Review Process

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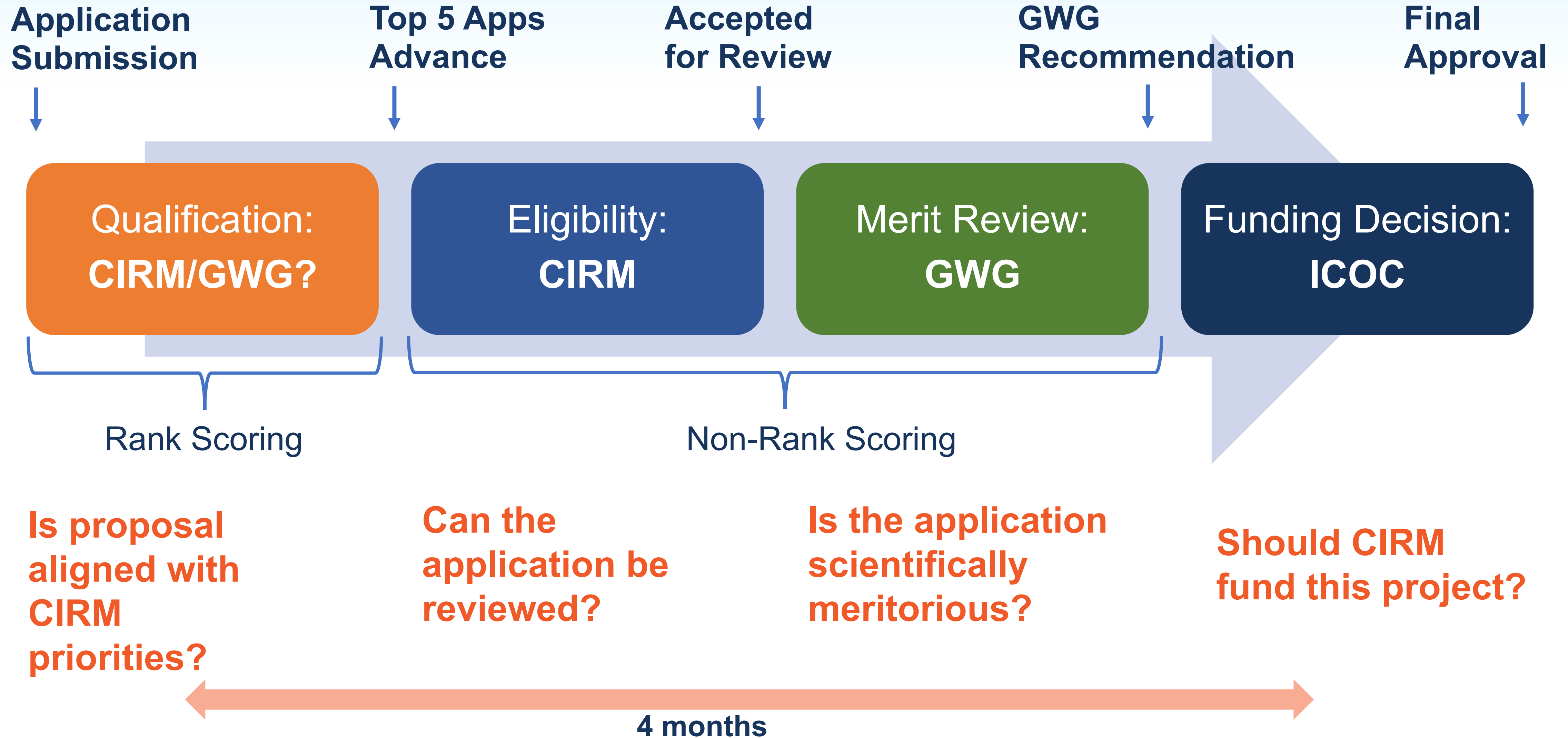

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Qualification Process

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- 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.

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Qualification Process

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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.

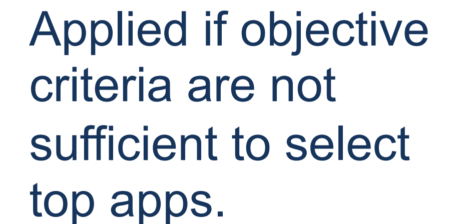
STEP 2: Subjective criteria are scored by GWG experts

- 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.

Qualification Process

- Example objective criteria scored by CIRM
  - CA organization
  - Percent spend in CA
  - 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
  - Sound rationale?



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Recommended Objective Criteria

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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
- Advanced trials (phase 3/pivotal or CLIN2 over CLIN1) more than early-stage trials
- Projects less likely to receive funding from other sources or not adequately funded by NIH

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Changes to Non-Ranked Process

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- 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

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What policies or regulations need to change?

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- Update GWG bylaws to restrict tier 2 process for CLIN reviews
  - Requires ICOC approval
- Update Concept and PA to
  - Define qualification step and selection criteria
  - Create clearer eligibility criteria (if needed)
  - Refine review criteria (if needed)