



Science Subcommittee, Governing Board/Independent Citizens' Oversight Committee (ICOC)

Proposed process for addressing critical questions and issues raised by peer review of Clinical Trial and Disease Team Research Awards

Introduction – The Opportunity and the Challenge

The California Institute for Regenerative Medicine (CIRM) is charged with supporting the development of cures and therapies based on stem cell science. Moving an innovative technology into the clinic involves years of development, intensive resource investment, and navigating an evolving regulatory landscape. In CIRM's commitment to move promising studies towards and into the clinic, CIRM has developed and funded initiatives aimed at research of product candidates moving towards an FDA investigational new drug or biologics filing, and for research of investigational products in exploratory, first-in-human through early phase clinical trials. These are complex grants requiring multidisciplinary expertise for execution, and a multidisciplinary group of external experts to review the applications. In an effort to conduct a robust peer review process that is timely, our overarching principle is to ensure a complete package of information so that a well-informed set of recommendations and decisions can be made.

The Proposed Process

We suggest the proposed process for addressing critical questions and issues that could impact on peer review of an application.

- Proactive approach – prior to major disease team or clinical trial research award submissions, CIRM will hold a Questions and Answers Session with investigators. This may be a telecon or webinar with investigators. The session would not just focus on the logistics of the submissions process, but would address what would be considered key categories of information for the application, and would address applicant questions
- CIRM will ask the Grant Working Group reviewers to provide their reviews of applications 14 days in advance of a review meeting, along with a list of key questions/issues – e.g., critical gaps

in information or ambiguities in how the information was provided

- This list of questions/issues from the reviewers, plus any additional questions/issues from CIRM's scientific officers, will be provided to the applicant approximately 10 days in advance of a review meeting, and the applicant(s) will be asked to provide written responses, limited to the specific questions posed, that can be shared with the peer review in advance of the scheduled session
- Questions that arise during the peer review may be of two kinds
 - 1) pivotal questions for which there may be a concise answer not requiring the submission of additional supplemental information
 - 2) pivotal questions that require a more complex explanation and the submission of additional supplemental information responsive to the questions posed:
 - In advance of the review session, CIRM staff will ask each applicant to identify the key contact person that should be available during a defined time period on the day of review to address pivotal questions that may arise during the peer review. The key contact may assemble additional experts from their team to help address pivotal questions.

Pivotal Questions for which there may be a concise answer not requiring the submission of additional supplement information:

On the recommendation of the Chair of the Grants Working Group, if the questions or issues are primarily clarifying in nature and could potentially be answered concisely without requiring the submission and review of additional information, the scientific team, in collaboration with the assigned reviewers, would consolidate these key questions and CIRM would telephone the identified application contact. The contact, and other experts from their team they would like to provide input, would be given an opportunity to respond within a defined time frame to allow the response to be considered by the peer review during its regular meeting. Given time restrictions, this could only apply to pivotal questions that can be answered concisely without the need for submission of additional materials. There would be no direct interaction between the reviewers and the applicant during this process. A telephone call, and a response in real time during the grant review of that particular application, would be the optimal process. As a back up - if contact and answer cannot be achieved within the duration of the Grants Working Group review session, the Grants Working Group reviewers could provide a conditional funding recommendation, pending the receipt of the desired response from the applicant within a defined and rapid time frame. This response could be documented by email and provided to the Grants Working Group reviewers but not require further discussion. The questions and response would subsequently be shared with ICOC, to provide them with a better understanding of the application.

Pivotal Questions requiring a more detailed explanation and submission of supplemental information:

On the recommendation of the Chair of the Grants Working Group, if questions or issues arise during peer review that require a more detailed explanation and the submission of additional information before the Grants Working Group reviewers can recommend whether or not to fund an application, the peer review may recommend that the consideration of the application be deferred pending receipt of the information. The Grants Working Group reviewers would work with CIRM's scientific staff to formulate the questions and permissible format of answers, and the applicant would be given an opportunity to respond, limited to the specific questions and issues posed, within a set period of time (e.g., as soon as possible – maximum of one month – and prior to the ICOC meeting for consideration of the project) and these responses will be circulated to the Grants Working Group reviewers for a telephonic conference to arrive at a scientific score and funding recommendation.

- An option to consider is that the responses be circulated to the entire Grants Working Group, but that the telephonic review can be held with a quorum of 15 members, which would need to include among them the initial primary and secondary peer reviewers, any key specialist, the chair of the GWG, the patient advocate co-chairs of the Grants Working Group, and if one is represented on the GWG, the patient advocate for that specific disease.
- Funding recommendations would be presented to the ICOC for final decisions.

This modification of the process, that emphasizes a proactive and expedited approach, should facilitate a robust yet timely review of awards that are so critical to CIRM's mission.

Given the importance and complexity of CIRM's Clinical Trials and Disease Team Awards, it is critical that reviewers have the answers to pivotal questions that could affect their funding recommendations. The proposed process would provide the reviewers with an additional level of certainty and a stronger foundation for making fully informed recommendations regarding the funding of these clinically applicable studies. The additional steps proposed would not unduly delay the peer review process, would be feasible to implement if there were a limited number of applications in which pivotal questions would arise, and would enhance the peer reviewers' ability to thoughtfully evaluate applications.