Report on CIRM's Trial Pre-Application (PreApp) Process

EXECUTIVE SUMMARY

In December 2008, the ICOC approved the trial of a pre-application (PreApp) process to provide an open competition for grant funding that removed institutional limits on the number of applicants and which did not exceed CIRM's capacity to process applications and conduct reviews in timely and effective manner. The trial PreApp process was applied to 3 RFA competitions over the last year including RFA 08-07 Basic Biology Research Awards I (BBI), RFA 09-01 Disease Team Research Awards (DT), and RFA 09-02 Basic Biology Research Awards II (BBII). During the course of this trial we sought feedback via surveys of applicants who submitted a PreApp to each of the RFAs, external reviewers who evaluated PreApps, and also Grants Working Group (GWG) reviewers who evaluated the full applications from invited applicants. This report provides a summary of how the PreApp process was implemented as well as results compiled to date from the surveys.

The PreApp process used in this trial is based on similar procedures to those employed by other funding agencies including the National Science Foundation, Susan G. Koman Foundation, Michael J. Fox Foundation, The Bill and Melinda Gates Foundation, US Department of Defense, and in some cases the NIH. The overall process was coordinated and managed by CIRM Review Officers who do not participate in the scientific evaluation or selection of the PreApps. The PreApps were evaluated by both external scientific experts (3 per PreApp) as well as internal CIRM Science Officers (2-3 per PreApp). CIRM Science Officers used the same criteria as the external scientific reviewers but focused their evaluation on the responsiveness of the PreApp to the RFA objectives. For each competition, CIRM invited the best 30 to 60 PreApp proposals to submit a full application.

We have observed that the PreApp process has encouraged many new successful applicants – more than 50% of applicants had never previously applied for a CIRM grant. In response to a survey of applicants:
1. When given a choice between a process of review that requires limiting the number of applications submitted per institution versus an open submission of PreApps for consideration to apply, 87% preferred the PreApp process.
2. The majority (69%) of respondents also seemed satisfied with the length and content of the PreApp. Some (21%) preferred a lengthier PreApp and a few (4%) preferred a shorter PreApp.
3. New PI applicants did well under this process as 33% of BBI applications and 52% of DT applications approved for funding by the ICOC had not previously applied to CIRM. Funding approval for BBII applicants will be determined in April 2010.

For the BBI and BBII PreApps, the name of the PI and applicant institution were not made available to reviewers in an attempt to conduct a relatively blind review focused on the merits of the proposal. Basic Biology applicants were asked their preference for anonymity in the review and 54% of respondents were in favor and 41% were against. Many of those in favor of anonymity felt that the review may be unfairly biased by the reputation of investigators or institutions, or in some cases whether the applicant was at a for-profit company or academic institution. PreApp reviewers for BBI and BBII were also asked to comment on anonymity and opinions were similarly divided. However, it was clear from both applicants and reviewers of the

DT RFA that anonymity is not appropriate for competitions like Disease Teams where the track record of investigators was viewed as more critical.

PreApp reviewers and GWG meeting reviewers were also supportive of the PreApp process. PreApp reviewers were asked if they believed the information solicited from the applicants was sufficient to evaluate the PreApps and most respondents (81%) thought this was the case. All reviewers responding to the survey indicated that the online PreApp process was easy to use and that the scoring system was generally adequate, but some would have liked to provide further comments on a few PreApps. GWG reviewers recognize that consideration of significantly more than 60 standard research proposals at a review meeting becomes intractable and when surveyed most (81%) preferred the PreApp process over institutional limits as mechanism to pare down applications. Several GWG reviewers who have participated in previous CIRM reviews indicated that the overall quality of applications reviewed after the PreApp process was better than without PreApp. In support of these comments, we found correspondingly fewer BBI or DT applications scored in the bottom quartile by the GWG than in previous competitions.

When considering the overall costs of implementing the PreApp review process we find that it is relatively economical and is significantly less (about half the total cost) than reviewing an equivalent number of full applications with conventional review. Cost is less not only in dollars but also in time and effort on the part of applicants, GWG reviewers, and CIRM science staff. Given that the PreApp process provides an opportunity for more applicants to compete, is generally supported by both applicants and reviewers, is cost-effective, and can be adequately managed under allowable CIRM staff limits, we recommend that the PreApp system be adopted on an ongoing basis for recurring RFAs where the number of applications expected is likely to exceed the number that can be reasonably reviewed at a single GWG review meeting.

Overview

The goal of the PreApp review is to provide a greater opportunity to California scientists and organizations to compete in CIRM Requests for Applications (RFA). A larger pool of applicants provides a more diverse and more robust wealth of ideas from which to draw and achieve our mission. Identifying the best scientific ideas, however, requires the conduct of a rigorous scientific peer review. The conventional peer review of applications is resource intensive and limits the number of applications that can be reasonably and adequately reviewed. It is unfeasible to review more than 60 applications (40 if more complex like Disease Teams) at a GWG review meeting. To solve this issue, CIRM has previously set limits on the number of applications that it will accept from any given organization. It has relied on the applicant institutions to select those proposals that it believes are the most competitive to submit to CIRM. Although these institutional limits have worked to limit the sheer number of applications received by CIRM, such limits have in some cases also prevented often less senior or less influential scientists from bringing their ideas forward. We feel this works against our interest of fostering new ideas and the building of an integrated scientific community for stem cell research. We have therefore proposed and tested the PreApp process described below as a possible solution. Similar PreApp procedures have been implemented by other funding agencies including the National Science Foundation, Susan G. Koman Foundation, Michael J. Fox Foundation, The Bill and Melinda Gates Foundation, US Department of Defense (Breast Cancer Research Program, Autism Research Program), Damon Runyon Cancer Research Foundation, The Dana Foundation, and in some cases the NIH (e.g., Interdisciplinary Research Consortium Awards).

To be successful, the PreApp process must be capable of processing several hundred applications if necessary but must also be efficient and expeditious in identifying proposals that are most closely aligned with the RFA objectives and likely to be most competitive in a full application review. The PreApp process must balance acquiring the most pertinent information about a scientific proposal for proper review and minimizing the effort by applicants in conveying and submitting their idea. Another critical factor is that appropriate scientific expertise is sought to review the PreApps. Although the PreApp process can achieve all of the above, there are some consequences to utilizing this method. For example, toward maintaining efficiency and expediency we cannot practically request or collect written critiques for each PreApp reviewed and therefore cannot always provide specific details to the applicants about why they did or did not succeed at this stage. In addition, the PreApp process will add about 2 months to the timeline between the release of an RFA and the final approval of awards by the ICOC. Still, the overall timeframe from PreApp due date to issuance of the Notice of Grant Award (NGA) is about 2 to 3 months shorter than the average NIH cycle of 11 months from application due date to NGA.

CONDUCT OF THE TRIAL PREAPP PROCESS

The PreApp process was applied to 3 RFA competitions over the last year including RFA 08-07 Basic Biology Research Awards I (BBI), RFA 09-01 Disease Team Research Awards (DT), and RFA 09-02 Basic Biology Research Awards II (BBII). This provided an opportunity to test the process on two similar competitions (BBI, BBII) and on one competition that was relatively complex (DT).

The PreApp process tested utilizes a system of ranking that is similar to that used by other funding agencies to handle large volumes of pre-applications. The process described below was applied in the same way to all PreApps including those that involved a collaborative funding partner. Review criteria for the PreApps were clearly described in RFA. Those projects deemed to be most responsive and meritorious based on the review criteria were invited to submit full applications, which then underwent a full review by the Grants Working Group.

The PreApp process was coordinated and managed by CIRM Review Officers who do not participate in the scientific evaluation or selection of the PreApps.

PreApp Forms

PreApp forms were created in an interactive PDF format and were available to applicants on the CIRM web site approximately 5 weeks prior to the submission deadline. The forms were tailored to each RFA to collect information necessary for review of the proposals. All PreApps were submitted, processed, and reviewed electronically.

Basic Biology PreApp forms collected information about the PI and applicant institution on one page and project information on 2 pages. Project information included: Title of Project, Specific Aims, Preliminary Results, Experimental Design and Approach, and Significance of the Proposed Research. In addition, applicants were asked to select key words related to the project including Cell Category (e.g., embryonic, adult), Cell Behavior/Molecular Features (e.g., microRNA, epigenetics), and Cell Tissue Type (e.g., cardiac, liver). These keywords are considered in conjunction with the content of the research proposal itself to direct the PreApp to the appropriate reviewers.

The Disease Team PreApp forms collected information about the PI, co-PIs, Partner PI, team membership and applicant institution on 3 pages and project information on 3 pages. Project information included a description of the Title of Project, Project Objective, Project Status, Preclinical Research and Development Plan and Milestones, and Research Team Leadership. In addition, applicants were asked to select key words related to the project including Disease Category, Therapeutic Approach (e.g., cell therapy, small molecule), Cell Category, and Specialized Methods. Here too, the keywords are considered in conjunction with the content of the research proposal itself to direct the PreApp to the appropriate reviewers.

Processing and Review

PreApps were submitted, processed and reviewed electronically. CIRM staff and scientific reviewers were required to declare conflicts against a comprehensive list of applicant individuals and organizations compiled from PreApps for each RFA. Scientific reviewers and CIRM staff reviewers in conflict with a PreApp could not be assigned as reviewer of the PreApp, and were recused from discussion, scoring and voting on the merits of the PreApp.

External Review

Each PreApp was assigned, based on relevant expertise, to three external scientific reviewers. Each scientific reviewer evaluated approximately 10 to 25 proposals depending on type of RFA and content of the PreApp.

For BBI, CIRM received 135 PreApps and we recruited the assistance of 16 external reviewers who on average evaluated 25 PreApps each. For BBII, CIRM received 154 PreApps and we recruited the assistance of 19 external reviewers who on average evaluated 24 PreApps each. For DT, CIRM received 73 PreApps and we recruited the assistance of 20 external reviewers who on average evaluated 10 PreApps each.

Up to 40 external scientific experts were initially sought for each RFA in anticipation of a large number of applications and/or varied expertise needs. Once PreApps were received, CIRM staff pared down the number of external reviewers to that necessary to conduct the review.

For their evaluation, reviewers are asked to carefully consider the RFA objectives and evaluate scientific merit against the criteria specified in the RFA. They were each provided a copy of the RFA and specific guidelines that focused on the review criteria. Reviewers were asked to place each assigned PreApp in one of 4 categories: 1) yes invite, 2) maybe invite, 3) do not invite, or 4) top application (optional, for the best 2 or 3 PreApps in their assignment list).

All reviewers accessed the PreApps and submitted evaluations via a secure CIRM Review System web site. No written critiques were collected or requested. Reviews were done independently and scientific reviewers did not see other reviewers' evaluation or have access to PreApps that were not specifically assigned to them. Reviewers were allowed approximately 3 weeks to complete their evaluation.

Internal CIRM Review

Following the evaluation by external reviewers, CIRM Science Officers then evaluated the PreApps. For their evaluation, CIRM Science Officers used the same criteria as the external scientific reviewers. However, CIRM Science Officers focused their evaluation on the responsiveness of the PreApp to the RFA objectives and considered the recommendations made by the external scientific reviewers. Reviewers placed each assigned PreApp in one of 4 categories described above.

Internal reviewers were not assigned to any PreApp with which the reviewer had a conflict. Approximately 7-10 CIRM Science Officers participated in each PreApp review and each evaluated 15 to 40 proposals depending on type of RFA and content of the PreApp.

Once all evaluations were completed, CIRM conducted a formal internal review meeting that was led by CIRM Review Officers who do not participate in the evaluation of PreApps.

Attendance at the internal review meeting was limited to those necessary to conduct the review including CIRM Science Officers, CIRM Review Officers, CIRM Legal Staff, and the CIRM President. All attendees declared conflicts against the full list of applicant individuals and institutions and certified their review of this list. Rules of confidentiality and non-disclosure were applied to this meeting.

During the closed session, the CIRM Review Officer presented the rules of confidentiality, non-disclosure, conflicts of interest and the process of review. The Review Officer also presented an overview of the RFA objectives and review criteria. The recommendations from both external

scientific reviewers and Science Officers on all PreApps were presented and discussed to identify the top 40- to 60 PreApps. The PreApps were ordered according to the level of enthusiasm across all reviewers with those having a unanimous recommendation to invite on top and a unanimous recommendation not to invite at the bottom.

The PreApps were considered and discussed taking into account any discrepancies among reviewers. For each application, the science officers took a majority vote to invite or not invite the applicant to submit a full application. The CIRM President and CIRM CSO do not participate in the vote unless the Science Officers are at a tie.

Following this internal review, invited and deferred applicants were notified of their status by email. Invited applicants were reminded that their research proposal described in the full application must be the same as that described in the PreApp.

EVALUATION OF THE PREAPP PROCESS

It was our expectation that the PreApp process would provide a necessary and beneficial tool to expand CIRM's capacity to accept research proposals from a broader and more diverse pool of applicants. This process would provide rigor in review and would introduce an important perspective from the CIRM Science Office in judging the appropriateness of proposals to CIRM's strategic objectives and mission. Finally, it was our expectation that much could be learned to improve the process of review by conducting this trial and collecting feedback from participating reviewers and applicants. During the course of this trial we surveyed applicants who submitted a PreApp to each of the RFAs, external reviewers who evaluated PreApps, and also GWG reviewers who evaluated the full applications from invited applicants.

Survey of Applicants

Applicants who submitted a PreApp to the Basic Biology I RFA 08-07, Disease Team Research Awards RFA 09-01, and Basic Biology II RFA 09-02 were surveyed to gage whether the trial PreApp process is achieving our intended objectives. The survey was conducted anonymously via a secured web site. Applicants were informed that responding to the questionnaire is anonymous, voluntary, and has no effect on the outcome of their PreApp. CIRM received a total of 117 responses from all 3 competitions.

When given a choice between a review process that requires limiting the number of applications submitted per institution versus an open submission of PreApps for consideration to apply, 87% (102) preferred the PreApp process. 69% (81) of the respondents were also satisfied with the length and content of the PreApp, while 21% (25) preferred a lengthier PreApp and 4% (5) preferred a shorter PreApp.

For the BBI and BBII PreApps, the name of the PI and applicant institution were not made available to reviewers in an attempt to conduct a relatively blind review focused on the merits of the proposal. Applicants were asked their preference for anonymity in the review. The results were split with 54% in favor and 41% against anonymity. Many of the respondents in favor of anonymity felt that young investigators may be unfairly regarded since they may not have yet achieved the credentials and reputation of more senior investigators. In addition, some felt that

reviewers might favor more prestigious institutions simply by reputation or give less credence to less familiar institutions. Additionally, knowledge that an applicant is a for-profit institution might in some cases unfairly influence the review. Many reiterated that it is the scientific merit and responsiveness of the proposal that should be the focus of review and not the identity of the applicant. Those against anonymity felt that the accomplishments (such as publication record) and institutional environment are very important in assessing the likelihood of success of a project. Additionally, some indicated that anonymity is difficult to maintain and reviewers are likely to recognize the applicant through the description of their research.

Additional comments included several requests for more time between RFA posting and application deadlines as well as more time between PreApp deadline and full application deadlines. One respondent cited the Gates Foundation as a good model for anonymous review of brief applications similar to CIRM PreApps. Several respondents noted that they felt this was overall a fair and appropriate process and appreciated the opportunity to provide feedback.

Performance of Applicants

In addition to the online survey, the PreApp form requested information about the applicant's previous participation on CIRM initiatives. The PI applicants were asked to indicate whether they had previously submitted an application to CIRM and whether they had pending or active awards from CIRM. For each RFA, the percentage of PI applicants who had not previously applied to a CIRM initiative ranged from 54% to 64%. The percentage of PI applicants who did not already have an active or pending CIRM award ranged from 69% to 81%.

PI applicants were permitted to apply to only one of the Basic Biology competitions and therefore there is no overlap between PI applicants for BBI and BBII. It was the choice of the PI as to which competition they preferred to enter. A slightly larger number of PreApps were received for BBII than BBI: 154 versus 135 PreApps. Interestingly, BBII received more PreApps from new PI applicants who have not previously submitted an application to CIRM (64%) than were received for BBI (54%). In addition, the percentage of new PI applicants among those invited to apply was greater for BBII (56%) than BBI (39%). For BBI, new PI applicants represent 33% of applications approved for funding by the ICOC. Funding for BBII applicants will be determined in April 2010.

The Disease Team RFA received 73 PreApps and 31 full applications were reviewed by the GWG. The percentage of those invited to apply who were not previous PI applicants to CIRM is 52% and of the percentage of new PI applicants among those approved for funding by the ICOC is 50%.

GWG Reviewer Survey

GWG reviewers who participated in the review of full applications for each of the RFAs were surveyed regarding the PreApp process. Results are available for BBI and Disease Teams competitions, with 21 out of 30 GWG members responding to the survey. The BBII applications will be reviewed in February and reviewers will be surveyed following that review.

In order to keep the number of applications to be reviewed at a given RFA's review meeting manageable, GWG members were asked which process he/she thought is best suited to advance CIRM's goals. Choices included 1) limits on number of applicants per institution, 2) the PreApp process, or 3) other process.

Although a few reviewers felt that institutional limits were a good idea, most were concerned that institutional limits would impose unfair restrictions and might encourage preferences based on the seniority of investigators or politics within institutions rather than quality of the proposed research. Thus, most (81%) preferred the PreApp process or in some cases suggested implementation of a triage system. Several reviewers felt it was important that the PreApp process allow adequate review of proposals so that potentially high-risk, high-gain ideas are not missed. Reviewers also stressed the importance of having clearly focused review criteria and a process that explicitly solicits applicants to address the criteria in their application. In agreement with these comments, each CIRM RFA specifically detailed the review criteria for the PreApp process and distinguished these from the review criteria for the full application. In addition, the information requested in both the PreApp and full application specifically addressed each criterion. One reviewer suggested that the need for limits or a PreApp process could be overcome by having RFAs that are much more restrictive in scope such as one targeted solely to neurological diseases or cell therapy approaches. It was recognized by the reviewer, of course, that this approach would then require issuing many more varied RFAs and holding many more review meetings to capture the breath of research funded by CIRM.

Reviewers were also asked if they thought the PreApp process would remove the least competitive applications for review by the GWG. Three reviewers did not provide a response to this question but 94% of those that did respond, agreed that PreApp process would remove the least competitive applications and many expressed great confidence in CIRM scientific staff and external scientific reviewers to identify the most competitive proposals using the PreApp process.

Several GWG reviewers who have participated in previous CIRM reviews indicated that the overall quality of applications reviewed after the PreApp process was better than without PreApp. In support of these comments, we found correspondingly fewer BBI or DT applications scored in the bottom quartile by the GWG than in previous competitions.

Survey of PreApp External Reviewers

Following the completion of each PreApp review, external GWG reviewers where surveyed regarding the experience with this new process. A total of 17 reviewers of the 55 that participated provided responses to the survey. Reviewers were asked about the adequacy of the PreApp forms for review, anonymity, ease and effectiveness of the process, and the method of scoring.

Reviewers were asked if they believed the information solicited from the applicants was sufficient to evaluate the PreApps, based on the RFA review criteria, and what additional information might have been helpful to review. Generally, most reviewers (81%) thought the PreApps solicited sufficient information from applicants. Those that did not, felt that a few additional paragraphs might have helped. One reviewer of DT PreApps thought that many applicants did not present sufficient substantive information. The reviewer felt that either the

applicants needed to focus projects on fewer aims or CIRM needed to consider a longer application form.

All reviewers responding to the survey indicated that the online PreApp process was easy to use and that the scoring system was generally adequate. However, several reviewers felt it was important to have an optional comment box in which they might be able to better explain their selections for some of the PreApps. For example, reviewers would have liked the opportunity to explain that a particular PreApp was placed in the "do not invite" category due to lack of responsiveness rather than the experimental design or preliminary data. One reviewer cautioned that such comments should be optional and to be used only as needed, since requiring comments would make the process much more complicated.

PreApp reviewers were also asked their opinion about the anonymity of applicants. As previously indicated, the Basic Biology PreApp proposals were presented to reviewers without the PI or applicant institution information and it was made clear to reviewers that the qualifications of the PI were not a review criterion at this stage of review. On the other hand, Disease Team PreApps very clearly identified the PI, institution, and team of investigators to reviewers and the team leadership was considered an important criterion for the PreApp review.

Interestingly, the opinion of the PreApp reviewers for Basic Biology competitions was similar to that of the applicants. Four reviewers thought the process should be anonymous, 3 were uncertain and 3 thought it should not be anonymous. Those that opposed anonymity felt that knowing the background and qualifications of the PI were important determinants in their evaluation as to whether the proposal was credible and could be accomplished as proposed. Others felt that anonymity was not absolute since some applicants cited their own work in the proposal and in some cases their identity could be uncovered. For Disease Team reviewers, it was clear that anonymity was not favored, as most (86%) thought the identity and composition of the team were critical for evaluation of these PreApps.

Costs of PreApp Review

The implementation of the PreApp review process is relatively economical and is significantly less than reviewing an equivalent number of full applications with conventional review. Cost is less not only in dollars but also in time and effort on the part of applicants, GWG reviewers, and CIRM science staff.

On average CIRM spent for each PreApp review about $12,500, which reflects largely the honoraria for specialist reviewers plus preparation for the internal review meeting. To this we add the cost of the review of the full invited applications. For example, the review of 31 full applications by the GWG, which included the cost of a 2.5-day review meeting and the participation of 17 specialists, is estimated at about $140,000. This includes lodging, travel, honoraria, meals, and venue for the review. Thus, the total cost for review of Disease Team applications with PreApp review is about $152,500. If all 73 applicants had submitted full applications, the review would have required 2 consecutive GWG meetings and the total cost using conventional review could have been up to $280,000. The approximate cost of the BBI review of 41 full applications by the GWG is on the order of about $80,000 plus the cost of

PreApp review. Had all 135 PreApps received required a full GWG review, the cost could have been about $180,000 using two extended GWG review meetings.

Conclusions and Follow-Up

Although the full set of outcomes of this trial still awaits the completion of the Basic Biology II GWG review, the results suggest that applicants, PreApp reviewers and GWG reviewers favor this process. The process has created an opportunity for many applicants to compete that have not previously applied to CIRM and a significant number of these have succeeded in acquiring a grant. The process allowed us to consider more proposals within a single review cycle than would have been possible using conventional review.

Of course, improvements and streamlining are necessary to ensure that the process continues to provide an effective system of review. It is clear, for example, that external PreApp reviewers need the option to include clarifying comments on their evaluations. Some simply provided this information by email but we propose to provide a clear place in the online review system for PreApp reviewers to provide comments as needed. In some instances, it is appropriate to allow additional space for applicants to include information about their research proposal and we intend to make adjustments were applicable.

Another item, which was not captured in the surveys but is reflected in multiple queries from applicants, is the desire to receive some general feedback on why an application was not invited for review. Most queries were generally sufficiently addressed by discussing them with the CIRM review officer. However, we are considering mechanisms that would allow us to provide applicants with a sense of the evaluation without imposing on PreApp reviewers the need to submit a written critique. We are proposing, for example, to have PreApp reviewers indicate a score for each review criterion that can be shared with the applicant. Applicants would then know, for example, whether their idea was well regarded but perhaps not considered responsive to the RFA, or whether their preliminary data was not convincing despite a good experimental design.

The issue of anonymity appears to be the most divided and is clearly not appropriate for some competitions such as Disease Teams. We will consider maintaining anonymity were appropriate, while also taking steps to ensure that reviewers are indeed focused on the review criteria and give adequate consideration to new investigators.

Finally, should a PreApp process be fully adopted by CIRM, continued feedback from applicants and reviewers will be an important contributor to maintaining a robust and effective process.