CALIFORNIA'S STEM CELL AGENCY

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

To: Members of the Governing Board

From: Jonathan Y. Thomas, Chair

Date: March 11, 2013

Re: Policies to Implement Concept Proposal Adopted by the Board in Response to the IOM Report

At our meeting on January 23, 2013, the Board, after extensive debate and public comment, adopted a comprehensive response to the IOM's report on CIRM. The concept proposal approved by the Board addressed: (1) the perception of conflicts of interest arising from the participation by members of the Board appointed from research institutions in the Board's consideration of applications for research funding; (2) the grant review process, including programmatic review and the role of the Patient Advocates; (3) the Extraordinary Petition and Additional Analysis Option policies and the appeals process; (4) the division of responsibilities between the Chair and the President; (5) CIRM's Intellectual Property Policies; and (6) sustainability. We also identified three IOM recommendations within the President's jurisdiction: (1) increasing industry representation on CIRM's advisory panels; (2) the creation of a Scientific Advisory Board; and (3) funding for regulatory and ethics research. In its motion approving the concept proposal, the Board directed staff to draft the policy amendments necessary to implement the Board's action and to present them to the Board for its consideration at our March 19, 2013 meeting.

Following the Board's meeting, we established working groups composed of members of the Chair and President's staff to draft policies to implement the Board's concept proposals and to discuss staff's response to the IOM recommendations within the President's jurisdiction in a collaborative effort. These working groups addressed the following topics and included the following participants:

1. Perception of Conflict of Interest: Maria Bonneville, James Harrison, Paul Stein, Ian Sweedler, and Scott Tocher

2. Grant Review Process: Maria Bonneville, James Harrison, Pat Olson, Gil Sambrano, Paul Stein, and Scott Tocher

3. Extraordinary Petitions, Additional Analysis, and Appeals: Maria Bonneville, James Harrison, Pat Olson, Gil Sambrano, and Paul Stein

4. Division of Responsibility between the Chair and the President: Duane Roth, Jonathan Thomas, and Alan Trounson

5. Scientific Advisory Board: Ellen Feigal, James Harrison, Pat Olson, Duane Roth, Paul Stein, and Alan Trounson

6. Regulatory and Ethics: Ellen Feigal, Geoff Lomax, and Scott Tocher

This collaborative effort yielded the following proposals for the Board's consideration, and with respect to the items within the President's jurisdiction, the following action plans to implement the IOM's recommendations:

1. **Perception of Conflicts of Interest:** Pursuant to the concept proposal approved by the Board, members appointed from research institutions will abstain from participating in the Board's consideration of applications for research funding, even if they don't have a conflict of interest. To implement this proposal, staff proposes to amend the Board's bylaws to create an Application Review Subcommittee composed of the 10 Patient Advocates, the four industry members, and the Chair and Statutory Vice Chair. The 13 members appointed from research institutions would be ex officio members of the Subcommittee, meaning that they could participate in the Board's discussion of applications (absent any conflicts of interest) but could not vote. The Subcommittee's charge would include conducting programmatic review and acting on the Grants Working Group's recommendations relating to applications for research funding. The Subcommittee would meet concurrently with the Board whenever applications for research funding are presented for consideration. The proposed amendments to the Board's bylaws are attached as Attachment 1.

Recommendation: Approve amendments to the Board's bylaws to establish Application Review Subcommittee.

2. **Grant Review Process:** The concept proposal approved by the Board contemplated that programmatic review, which is currently conducted by the Grants Working Group (GWG), would now occur at the Board. To implement this proposal, staff proposes to amend the GWG bylaws to define Tiers I, II, and III and establish the range of scores in each tier: Tier I = 75 and above; Tier II = 65 – 74; Tier III = 64 and below. Tier II would be defined to include applications that were judged to be of moderate scientific quality or applications where consensus on scientific merit could not be reached, and may be suitable for programmatic consideration. CIRM staff would advise the members of the GWG of the new scoring system, and the scientific review would be conducted as it is currently. The scientific members of the GWG would score the applications and the Patient Advocates would participate in the review, but would not score or vote on individual applications.

Following the completion of scientific scoring and the consideration, under the guidance of the CIRM Review Office, of any motions for minority reports, the GWG, including the Patient Advocates, would vote on a motion to send the slate of applications (in rank order and in the respective tiers) to the Application Review Subcommittee for its

consideration. CIRM scientific staff would review the recommendations of the GWG, develop their own recommendations, provide a memorandum to the Subcommittee with the staff recommendations, and present those recommendations, along with the GWG recommendations, to the Subcommittee for its consideration.

As discussed above, the Application Review Subcommittee would consider the Grants Working Group recommendations, recommendations made by CIRM's scientific staff, and public comment, and would conduct programmatic review, moderated by the Vice Chairs of the GWG, before taking final action on the applications. Programmatic review would include consideration of factors such as portfolio balance, relevance to unmet health need, urgency of timeline, alignment with focus of Proposition 71, alignment with the goals and priorities of the Request for Applications, budget adjustments if necessary, and other stipulations. The proposed amendments to the GWG bylaws are attached as Attachment 2; the proposed amendments to the Board bylaws are reflected in Attachment 1.

Recommendation: Approve amendments to the GWG bylaws to: (a) establish and define tiers; (b) describe the process for considering minority reports and the slate of applications; and (c) transfer responsibility for programmatic review to the Application Review Subcommittee. Approve amendments to the Board bylaws regarding programmatic review.[1]

3. **Extraordinary Petitions, Additional Analysis, and Appeals:** The concept proposal adopted by the Board contemplated merging the Extraordinary Petition and Additional Analysis Option policies into the existing appeals process, which is administered by CIRM's scientific staff. To implement this proposal, staff proposes to repeal the Extraordinary Petition and Additional Analysis Option policies and to replace them with a new policy, modeled on the process for appeals based on conflicts of interest. Rather than being presented to the Board, appeals based on "material disputes of fact" and requests for reconsideration based on "material new information" would be presented to CIRM staff, who would determine whether the applicant had set forth clear grounds establishing the occurrence of a material dispute of fact or the existence of material new information, both as defined in the new policy. If staff determines that the applicant has made this showing, the President would determine whether additional scientific review is warranted. If so, a subset of the Grants Working Group consisting of at least three scientific members and one Patient Advocate would participate in the review and the scientific members would determine whether or not the resolution of the material dispute of fact or the new information, would have, in their view, changed the Grants Working Group's recommendation. This new recommendation would then be presented to the

[1] This policy would not apply to Requests for Applications (RFA) for which the initial peer review has already occurred, including the Genomics RFA, nor would it apply to the review of Research Leadership applications which will be presented to the Board in May.

Board for its consideration. The proposed Appeals and Requests for Reconsideration Policy is attached as Attachment 3.

Recommendation: Repeal Extraordinary Petition and Additional Analysis Option policies and adopt Appeals and Requests for Reconsideration Policy.

4. **Division of Responsibility between the Chair and the President:** Pursuant to the concept proposal approved by the Board, the Chair would be responsible for external, non-scientific matters including bond finance, sustainability, public communications, and government relations, while the President would be responsible for all scientific matters, including managing CIRM's scientific and administrative staff (other than staff reporting to the Chair) and the working groups, which report to the President.[2] The Chair and the President agreed to coordinate their actions to ensure that CIRM's employment policies are applied consistently to their respective staffs, but determined that no further changes to the Internal Governance Policy are required at this time. There is no attachment for this item.

Recommendation: No action required.

5. **Scientific Advisory Board:** The IOM recommended that CIRM establish a Scientific Advisory Board (SAB) comprising individuals with expertise in the scientific, clinical, ethical, industry, and regulatory aspects of stem cell biology and cell-based therapies. In response to this recommendation, the President plans to establish a single SAB that will provide counsel on such issues as RFAs, funding priorities, portfolio strategy, and other matters identified by senior management. The SAB will be separate and complementary to ad hoc panels and councils the Office of the President has the discretion to call upon and create. The SAB will engage with the President and key senior staff on critical and major strategic issues, including: the focus of CIRM's science and translational programs to ensure leadership and delivery within the current funding timelines; the development of CIRM partnerships that will align with future delivery of clinical outcomes; identification of new opportunities for CIRM in the field; identification of key areas that need funding and focus for CIRM; CIRM's international connections for amplifying CIRM's scientific and translational progress, and assessment of CIRM's funding model and how it can be fortified and transferred to other states and countries. Consistent with the IOM's recommendation to increase industry participation, the SAB will include industry members, and at least 50 percent of the members of the SAB will be from outside of California.[3] The SAB will exclude from consideration those

[2] To clarify that the Working Groups report to the President, we propose to amend Article VII, Section 1, of the Board's bylaws. See Attachment 1.

[3] CIRM's scientific staff are also committed to industry participation in other aspects of the agency's work, including participation by industry representatives on the Grants Working Group and the Clinical Development Advisory Panel.

individuals from institutions/companies that are CIRM grantees or loan recipients, and members of the SAB will abide by CIRM conflict of interest and confidentiality policies. For additional information about the SAB, please see Attachment 5.

Recommendation: No action is required because the creation of a Scientific Advisory Board is within the President's jurisdiction.

6. **Regulatory and Ethics:** CIRM management plans to establish initiatives on ethical and regulatory issues that relate to human subjects research. This may include a workshop and extramural research to explore topics such as the needs and expectations of different donor populations (patients, controls, disease groups) and a workshop to address priorities for the ethical conduct of human clinical trials research and to identify strategic focus areas. For additional information about CIRM's proposed response to the IOM's recommendations regarding ethics and regulatory issues, please see Attachment 6.

Recommendation: No action is required at this time.

IP Recommendations and Sustainability

In addition, the Intellectual Property and Industry Subcommittee met on February 27, 2013 to consider the IOM's recommendations regarding CIRM's intellectual property policies and will make recommendations to the Board at our meeting on March 19. Please see the materials associated with Agenda Item 7 for additional information about the Subcommittee's recommendations. Finally, as Chair, I continue to work on issues relating to CIRM's sustainability and plan to bring proposals to the Board for its consideration in the future, but it would be premature to present any sustainability proposals to the Board at this time.

One-Year Trial Period

In adopting the concept proposals in January, the Board recognized that responding to the IOM's recommendations is an iterative process and that adjustments to these proposals, or even a change in course, may be required based on experience. Consistent with that direction, I propose that the Board revisit these policies within one year to assess their effectiveness and to make adjustments, if necessary, and request that the President do the same with respect to the matters within his jurisdiction. Of course, if any one of these policies requires review at an earlier time, I will bring the matter to the Board at the earliest opportunity.

Conclusion

CIRM's staff, including members of the scientific staff, the President's Office, and the Chair's Office worked very hard on these proposals. In my view, this collaborative effort yielded very thoughtful, balanced, and responsive proposals, and reflects what we can accomplish when we work together. I look forward to discussing these proposals and action plans with you on March 19.

Attachments