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MEMORANDUM

To: Members, Governing Board
California Institute for Regenerative Medicine

From: James C. Harrison

Date: March 3, 2014

Re: Review of Board Actions in Response to IOM Recommendations
(Our File No.: 2297-0)

INTRODUCTION

On December 12, 2013, the Institute of Medicine (the "IOM") presented a report to CIRM's Governing Board regarding the IOM's review of the agency's funding model, strategic plan, operations, and governance. Following that meeting, the Board held two additional public meetings to consider the IOM report and recommendations. At the second of these meetings, on March 19, 2013, the Board adopted a comprehensive response to the IOM's recommendations, including extensive amendments to existing policies and new policies to address the IOM's concerns. The actions approved by the Board involved: (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. In addition, CIRM's scientific staff reported to the Board regarding their plans to address two IOM recommendations within the President's jurisdiction: (7) increasing industry representation on CIRM's advisory panels and establishing a single Scientific Advisory Board and (8) funding for regulatory and ethics research.

In amending CIRM policies, the Board recognized that the policies may need to be adjusted in the future to ensure that they are effective in addressing the IOM's recommendations. The Board therefore adopted these changes on a trial basis and agreed to

revisit the policies within one year to assess their effectiveness and to make adjustments, if necessary.

Below, we describe the policy changes approved by the Board and describe CIRM's experience operating under these policies.

SUMMARY OF POLICIES ADOPTED IN RESPONSE TO IOM REPORT

I. Amendments to Board Bylaws

A. Policy Change: Create Application Review Subcommittee

- Members appointed from academic and research institutions that are eligible for CIRM funding are precluded from voting on *any* applications for funding.
- All funding decisions are made by the Application Review Subcommittee, which is composed of the 10 Patient Advocates, the four industry members, and the Chair and Statutory Vice Chair.
- 13 members appointed from academic and research institutions are ex officio members of the Subcommittee, meaning that they may participate in the Board's discussion of applications (absent any conflicts of interest) but are prohibited from voting.
- The Subcommittee's charge includes conducting programmatic review (described below) and acting on the Grants Working Group's recommendations relating to applications for research funding.
- The Subcommittee meets concurrently with the Board whenever applications for research funding are presented for consideration.

B. Experience with Policy Change

The IOM's description of the perception of conflicts of interest on CIRM's Board generated substantial media interest, consistent with long-running criticism of the structure of CIRM's Board. Following the Board's decision to create the Application Review Subcommittee and to preclude members appointed from academic and research institutions from voting on research awards, the Chairman, the Vice Chair, the Senior Director for Communications, and others participated in meetings with editorial boards across the state. The Board's action received very favorable editorial coverage and appears to have largely addressed the perception of conflict of interest. A collection of the editorials that followed these meetings is attached to this memorandum as Attachment A.

The Board's decision to preclude members appointed from academic and research institutions from voting on *all* applications for research funding was difficult because it involved depriving these members of their right to vote on applications in which they have *no financial interest* in order to address the perception of a conflict of interest. However, the policy ensures that the Board may continue to benefit from the participation of these members in the discussion of applications in which they have no financial interest. Furthermore, it reflects a compromise and was a central component of the Board's response to the IOM recommendations.

C. Policy Change: Transfer Responsibility for Programmatic Review to Application Review Subcommittee

- Programmatic review, which was conducted by the GWG under the leadership of a Patient Advocate, is now conducted by the Application Review Subcommittee.

- Programmatic review by the GWG involved the consideration of nonscientific factors, such as portfolio balance. By transferring programmatic review to the Application Review Subcommittee, the Board effectively limited the GWG's role to making scientific recommendations, under the leadership of a scientific member of the GWG, to the Application Review Subcommittee.

- Programmatic review at the Subcommittee includes 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.

D. Experience with Policy Change

CIRM has now conducted six Grants Working Group meetings under the new policy. Initially, some members of the GWG expressed concerns about the policy and the GWG's role, but with some additional adjustments made by staff[1], the policy seems to be working well. In addition, as discussed below, programmatic review by the Application Review Subcommittee has functioned well.

[1] Members of the GWG may now make motions, before scoring an application, to impose a condition or conditions on the application (e.g., removal of an aim). If the motion is successful, the application is scored as modified by the condition.

II. Amendments to GWG Bylaws

A. Establish Fixed Funding Tiers

- Defined Tiers I, II, and III and established the range of scores in each tier: Tier I = 75 and above; Tier II = 65 – 74; Tier III = 64 and below.

- Tier II 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.

B. Transfer Responsibility for Programmatic Review to Application Review Subcommittee

- Programmatic review is now conducted by the Application Review Subcommittee.

- Following the completion of scientific scoring (incorporating any conditions recommended by the GWG) and the consideration of any motions for minority reports, the GWG, including the Patient Advocates, 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.

C. Responsibility of CIRM Staff to Review GWG Recommendations

- To provide assistance to the Application Review Subcommittee, particularly with respect to its consideration of applications in Tier II, the Board directed CIRM scientific staff to review the recommendations of the GWG and make any additional recommendations.

- CIRM's scientific staff provides a memorandum to the Subcommittee with the staff recommendations and presents those recommendations, along with the GWG recommendations, to the Subcommittee for its consideration.

D. Experience with Policy Change

As with the transfer of programmatic review from the Application Review Subcommittee to the Board, the decision to established fixed funding tiers required adjustments by members of the GWG. After six GWG meetings, GWG members have become accustomed to the new scoring methodology, which appears to be working well.

The Application Review Subcommittee has conducted five reviews under the new policies. The Application Review Subcommittee has considered the GWG's recommendations,

staff recommendations, and public comment, and has considered motions to move applications from Tier II into Tier I. For each review, CIRM's scientific staff has made a series of recommendations regarding applications. To date, CIRM staff has made recommendations with respect to 13 applications, and the Board has followed all but one of these recommendations. Programmatic review by the Application Review Subcommittee has functioned effectively and efficiently.

III. Adoption of Appeal and Request for Reconsideration Policy

A. Policy Change

- The Board repealed the Extraordinary Petition Policy, which governed appeals submitted directly to the Board.
- In its place, the Board adopted the Appeal and Request for Reconsideration Policy.
- Under this policy, appeals based on "material disputes of fact" and requests for reconsideration based on "material new information" are presented to CIRM staff, who determine whether the applicant has 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 determines 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 participates in the review and the scientific members 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 is then presented to the Board for its consideration.

B. Experience with Policy Change

Since the new appeals policy has been in place, CIRM staff have received 17 appeals/requests for reconsideration, all of which have been denied. Of course, applicants have continued to submit letters and make public comments at Board meetings pursuant to the Bagley-Keene Open Meeting Act, but to date, the Application Review Subcommittee has not acted on any verbal appeals.

IV. Other Recommendations

A. Allocation of Duties Between Chair and President

The IOM expressed concern about overlapping responsibilities between the Chair of CIRM's Governing Board and the President. In response, the Board agreed that the Chair should have responsibility for external, non-scientific matters including bond finance, sustainability, public communications, and government relations, while the President should 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, rather than the Board. In addition, the Chair and the President agreed to coordinate their actions to ensure that CIRM's employment policies are applied consistently to their respective staffs. No policy amendments were required to implement this decision.

B. Scientific Advisory Board

The IOM recommended that the President establish a single Scientific Advisory Board 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 appointed a Scientific Advisory Board which met in August of 2013. CIRM's scientific staff presented the Scientific Advisory Board's report to the Board in October and December 2013.

C. Ethical and Regulatory Research

The IOM urged CIRM to explore additional funding to address regulatory and ethical issues. In response, CIRM: (1) developed educational materials, including a donor education brochure, to support the iPSC Bank, (2) is considering a proposal for a supplemental award to evaluate the effectiveness of the informed consent for the iPSC Bank, and (3) incorporated the IOM's recommendations relating to clinical trial safety into the Alpha Clinic RFA.

D. Intellectual Property Policies

The IOM recommended that CIRM consider conforming its intellectual property policies more closely to federal law, which does not provide for a return to the government for its investment in scientific and medical research, and that CIRM plan for the oversight of its awardees' intellectual property obligations after the agency shuts its doors. In response, the Board adopted the recommendations of the Intellectual Property and Industry Subcommittee, which met on February 27, 2013 to consider the IOM's recommendations regarding CIRM's intellectual property policies. Specifically, the Board declined to take action to conform CIRM's policies more closely with federal law because Proposition 71 requires that the State have an opportunity to share in any revenues generated by CIRM-funded research. In addition, the Board

directed staff to explore appropriate oversight of awardees' intellectual property policies following the agency's termination. Staff has had several discussions with officials in various state agencies to discuss responsibility for enforcement of grantees' obligations to CIRM if CIRM is no longer in existence and is continuing to explore this issue.

JCH:NL
Attachment
(00215627-3)

ATTACHMENT A

Stem-cell agency reforms shift focus to its good work

By U-T San Diego Editorial Board 12:47 p.m. March 10, 2013

In 2004, California voters established a unique state stem-cell research agency when they approved Proposition 71 and gave it $3 billion in bond funding.

The California Institute for Regenerative Medicine quickly established itself as a leader in stem-cell research. But CIRM has also been its own worst enemy, facing repeated and appropriate criticism over conflicts of interest. The agency's governing board, which has the final say on grant applications, includes scientists and executives from institutions seeking grants. Even though members never had the right to vote on grants involving their employers, the potential for you-scratch-my-back-I'll-scratch-yours voting was obvious.

In 2009, the Little Hoover Commission, a state watchdog agency, recommended the Legislature make several changes in CIRM's structure to address this issue. Incredibly, the agency responded with a dismissive press release that depicted its critics as ignorant.

Four years later, CIRM, under new leadership, is finally taking the criticism seriously. In January, members who represent grant-seeking institutions were stripped of their right to vote on any grants. The board also voted to have grant applications be reviewed in a much more public process, and to give CIRM's staff more authority to evaluate grant appeals before they are brought to the board.

These actions followed key recommendations from a report the agency commissioned from the Institute of Medicine, an arm of the National Academy of Sciences.

In a meeting with the U-T Editorial Board, CIRM board chairman Jonathan Thomas and Dr. Larry Goldstein, director of the UC San Diego Stem Cell program, made the case that these changes should quell the long criticism of the agency and put the focus on where it belongs: what CIRM-funded research has achieved.

An independently produced economic impact study shows the agency's first $1.5 billion in grants have generated $286 million in new tax revenue in California and created thousands of jobs. But the potential for transformative medical breakthroughs is the even bigger headline. CIRM has funded promising projects in treatment of cancer, Alzheimer's, heart disease, stroke, HIV/AIDS, autism, ALS (Lou Gehrig's Disease), epilepsy, blood disease, bone deterioration, diabetes, eye diseases, muscular dystrophy, multiple sclerosis, incontinence and more. The state agency's grants arguably have made California the world leader in medical research, attracting talented scientists and doctors from other states and nations.

There remains a residue of cynicism about CIRM. Critics say the agency board did the minimum necessary to avoid an intervention by the Legislature – and also acted to buff the agency's image should it seek more bond funding from California voters before its present funding runs out in 2017, as is now projected.

These views may have some merit. But on balance, we think the California Institute for Regenerative Medicine has – at long last – responded properly to the fair criticism it faced. Instead of being exasperated by CIRM, more people should be excited about the great work it is doing.

Sacramento Bee

Editorial: Stem cell agency finally addresses potential for conflicts

By the Editorial Board
Published: Sunday, Apr. 7, 2013 - 12:00 am | Page 6E

Politics is the art of the possible. Jonathan Thomas, who chairs the oversight committee for California's stem cell institute, has taken important steps in reducing the potential for conflicts within this agency.

He hasn't gone as far as we would like, or that independent outside reviewers have recommended, in reforming governance of the California Institute for Regenerative Medicine. But he's persuaded CIRM's oversight board to make some changes it has long resisted. He's achieved what's possible, at least for now, and the board may empower him to go further.

Since voters agreed to create the institute in 2004 through Proposition 71, CIRM has become the most influential funder of stem cell research in the world. To date, it has issued more than 520 grants and committed more than $1.5 billion – money that has attracted hundreds of scientists to California so they can seek research funding. The goal is to make California an international epicenter for developing new therapies to treat a wide range of diseases.

Yet because of the way Prop. 71 was crafted by Robert Klein – the bond financier who wrote the initiative and chaired the institute until 2011 – CIRM has always held serious potential for insider dealings. By law, 13 of its 29-member oversight board must be representatives of UC campuses and other institutions who are eligible for funding. Ten other members represent disease advocacy organizations, who clearly have a stake on how CIRM spends $3 billion in state bond funds.

The potential for conflicts became real in 2007, when the CEO of a research institute in San Diego, a member of the CIRM oversight board, intervened to endorse a grant application for his institution. That led to the disqualification of grant applications from 10 institutions that were the focus of improper lobbying by oversight board members.

Two years ago, in response to that incident and others, CIRM asked the Institute of Medicine, a blue-ribbon committee of the National Academy of Sciences, to examine the institute's internal workings. The Institute of Medicine report found that CIRM's oversight board was encumbered by "almost unavoidable conflicts of interest." It recommended that CIRM eliminate positions on the oversight board reserved for institutions vying for stem cell grants. It also recommended that the oversight board remove itself entirely from the role of approving or rejecting grant applications, and leave that job to CIRM's scientific reviewers.

Aware that his board was unlikely to go along with such sweeping changes, Thomas, an investment banker with a Yale law degree and scholarship in the sciences, brokered a compromise. At a meeting last month, he persuaded the institute's oversight board to adopt changes that will prevent board members of funding-eligible institutions from voting on grants. They will still be allowed to discuss individual grants, but not vote on them.

We think Thomas and the oversight board should go further and adopt the Institute of Medicine recommendations. But that is politically unlikely. As is now obvious, it will be up to the Legislature to fully remove representatives of funding-eligible institutions from being involved in decisions about grants that could come back to them.

Thomas, to his credit, recognizes that his compromise may not be the perfect solution. He wants to test out the new policy for a year, and see how it works. There's a lot riding on the outcome. CIRM is expected to run out of funds in 2017, and while philanthropy and foundation money could extend that for a few years, supporters of California stem cell research clearly want to go back to the ballot to seek additional funding. To make that case, CIRM supporters can't afford any more scandals about insider dealing. The next year will reveal whether it is on the right track.

Read more here: http://www.sacbee.com/2013/04/07/5320481/editorial-stem-cell-agency-finallyaddresses.html#storylink=cpy

Modesto Bee

Previous Story
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Stem cell agency takes steps to reduce potential conflicts

April 9, 2013

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He hasn't gone as far as we would like, or that independent outside reviewers have recommended, in reforming governance of the California Institute for Regenerative Medicine. But he's persuaded CIRM's oversight board to make some changes it long has resisted. He's achieved what's possible, at least for now, and the board may empower him to go further.

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Join The Conversation

Modesto Bee is pleased to provide this opportunity to share information, experiences and observations about what's in the news. Some of the comments may be reprinted elsewhere in the site or in the newspaper. We encourage lively, open debate on the issues of the day, and ask that you refrain from profanity, hate speech, personal comments and remarks that are off point. Thank you for taking the time to offer your thoughts.

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Mercury News editorial: State stem cell agency is taking Institutes of Medicine advice

San Jose Mercury News
Posted:
MercuryNews.com

Jonathan Thomas is a very different chairman of California's stem cell agency than his predecessor, Robert Klein.

Klein pioneered California's move to become "the stem cell state." His vision secured an incredible $3 billion in funding for stem cell research through Proposition 71 in 2004, bringing thousands of cutting-edge scientists to Golden State research centers. But he built a protective shield around the board, and results of that were mixed. It prevented political influence from the Legislature on board appointments and funding decisions, which was wise, but it also prevented oversight to deal with conflicts of interest among board members that critics identified from the start.

Thomas recognizes that the California Institute for Regenerative Medicine has to mature. He is improving transparency and public accountability, which will enable the institute to look beyond Proposition 71 funding toward its next phase.

A critical evaluation by the prestigious Institutes of Medicine, the health arm of the National Academy of Sciences, found the agency beset by conflicts of interest that compromised its integrity in awarding research grants. Of the 29-member governing board, 13 were from institutions that competed for grants. Under Thomas' reforms, those members will not vote on the remaining $1.2 billion in grants to be distributed.

The critical report also said the agency should involve private industry to a greater extent. To advance stem cell research to the point of cures for diseases such as diabetes and Alzheimer's, private donors, partners and investors will need to be convinced of a financial return.

Researchers at Stanford, UCSF and other California institutions are making breakthroughs. If the stem cell agency can establish a record as a good steward of public dollars to finance brilliant science, it can continue to play a useful role in stimulating and guiding research to bring the potential cures from stem cell research to fruition.

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

The state stem cell agency

Item #13: Consideration of final adoption of policy amendments approved in response to the Institute of Medicine recommendations

Thursday, March 13, 2014

ICOC Board Meeting

Amendments to Board Bylaws

Create Application Review Subcommittee:

- Members appointed from institutions that are eligible for CIRM funding are precluded from voting on *any* applications for funding, but may participate in discussion absent conflict of interest.

- The Subcommittee's charge includes conducting programmatic review (described below) and acting on the Grants Working Group's recommendations relating to applications for research funding.

- The Subcommittee meets concurrently with the Board whenever applications for research funding are presented for consideration.

Amendments to Board Bylaws (Continued)

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Transfer Responsibility for Programmatic Review to Application Review Subcommittee:

- Programmatic review, which was conducted by the GWG under the leadership of a Patient Advocate, is now conducted by the Application Review Subcommittee.

- Programmatic review at the Subcommittee includes 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.

Recommendation: Approve Board Bylaws as amended.

Amendments to GWG Bylaws

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Establish Fixed Funding Tiers:

- Defined Tiers I, II, and III and established the range of scores in each tier: Tier I = 75 and above; Tier II = 65 – 74; Tier III = 64 and below.

Transfer Responsibility for Programmatic Review to Application Review Subcommittee:

- Programmatic review is now conducted by the Application Review Subcommittee.

Amendments to GWG Bylaws (Continued)

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Responsibility of CIRM Staff to Review GWG Recommendations:

- To provide assistance to the Application Review Subcommittee, particularly with respect to its consideration of applications in Tier II, the Board directed CIRM scientific staff to review the recommendations of the GWG and make any additional recommendations.

Recommendation: Approve GWG Bylaws as amended.

Adoption of Appeal and Request for Reconsideration Policy

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

- The Board repealed the Extraordinary Petition Policy, which governed appeals submitted directly to the Board.

- In its place, the Board adopted the Appeal and Request for Reconsideration Policy.

- Under this policy, appeals based on "material disputes of fact" and requests for reconsideration based on "material new information" are presented to CIRM staff, who determine whether the applicant has 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.

Adoption of Appeal and Request for Reconsideration Policy (Continued)

- If staff determines that the applicant has made this showing, the President determines 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 participates in the review and the scientific members 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.

Recommendation: Approve Appeal and Request for Reconsideration Policy.