CIRM
CALIFORNIA'S STEM CELL AGENCY

MEMORANDUM

To: Members, Science Subcommittee, Governing Board
California Institute for Regenerative Medicine

From: James C. Harrison, General Counsel

Date: November 23, 2015

Re: Proposed Amendments to Grants Working Group Bylaws

INTRODUCTION

Consistent with our efforts to refine and improve the CIRM 2.0 machine, we have reviewed the bylaws of the Grants Working Group and propose a number of amendments. These amendments are intended to improve upon the conduct of peer review and to reconcile the bylaws with the adoption of the CIRM 2.0 Translation and Discovery Programs. The proposed amendments are summarized below.

PROPOSED AMENDMENTS

Terms of GWG Member (Art. IV, § 3): Under Proposition 71, a member of the GWG may not serve more than two *consecutive* terms. (Health & Saf. Code, § 125290.50(b).) Thus, a member who has served two consecutive terms may be re-appointed after skipping a term. Proposition 71 also specifies that the terms of the members of the GWG shall be staggered so that one-third of the members serve two-year terms, one-third serve four-year terms, and one-third serve six year terms. (*Id.*) However, Proposition 71 does not address the length of time a member who has served two consecutive terms must be a non-member before he or she is eligible for re-appointment.

To address this gap, we propose to amend the bylaws to specify that a member who has served two consecutive terms is eligible for re-appointment after two years have passed since the member's previous term expired.

Review of Non-Clinical Program Applications (Art. VII, § 3): For CIRM's Clinical Program, the Board approved a scoring system that is consistent with both the volume of applications per review cycle (generally fewer than five) and the regularity of the review cycle (monthly). Under this system, applications receive a score of 1 (exceptional merit, recommended for funding), 2 (improvement needed but could be resubmitted), and 3 (sufficiently flawed that same project may not be resubmitted). While this system has been effective for the review of applications for Clinical awards, we do not think it would be appropriate for the review of non-Clinical Programs, including the Discovery and Translation Programs, for which we expect a higher volume of applications and a less frequent review cycle (approximately every 6 months), or for programs for which we expect to make only a small number of awards on a one-time basis.

For non-Clinical Program applications, therefore, we propose to revert to our former scoring system (1 to 100) with two tiers: (1) average score of 85 or above, recommended for funding, and (2) average score of 84 or below, not recommended for funding. In addition, for those programs for which only one application is expected to be funded, we propose to specify that the application that receives the highest average scientific score shall be deemed to be the GWG's recommendation for funding.

Motions regarding GWG's Recommendations (Art. V, § 2; Art. VII, § 6): Under Proposition 71, only the Patient Advocate members of the Board are eligible to serve on the Grants Working Group. (Health & Saf. Code, §§ 125290.55(a), 125290.60(a), 125290.65(a).) As a result, the non-Patient Advocate members of the Board rely upon their colleagues to act as a bridge between the GWG and the Board and to provide oversight of the GWG. Frequently, during the course of a meeting of the Application Review Subcommittee, the Patient Advocate members of the Board will describe the rigor and fairness of the GWG's review of an application. We would like to formalize this practice by incorporating such a finding into the motion considered by the GWG at the end of each review. We would also like to ensure that, before a review is completed, all members of the GWG feel that the review has been scientifically rigorous and that there has been sufficient time for all viewpoints to be heard.

Currently, at the end of each review, the members of the GWG consider a motion to forward the recommendations to the Board. The purpose of this motion is to attest to the fact that the scores accurately reflect the recommendations of the GWG. We propose to add two parts to this motion: (1) the full GWG will consider whether there was sufficient time for all viewpoints to be heard, the review was scientifically rigorous, and the scores reflect the recommendations of the GWG, and (2) the Patient Advocate members will consider whether the review was conducted in a fair manner and was free of undue bias.

REQUESTED ACTION

Recommend that the Board approve the proposed amendments to the Grants Working Group Bylaws.

Attachment

Bylaws of the Scientific and Medical Research Funding Working Group

Originally adopted by the ICOC on
09/09/05; amended on 3/15/07,
06/27/08, 12/09/09,10/25/12,
03/19/13, 03/26/15 and 5/21/15.

ARTICLE 1. Authority.

The Scientific and Medical Research Funding Working Group ("Grants Working Group or GWG") of the Independent Citizen's Oversight Committee ("ICOC") to the California Institute for Regenerative Medicine ("Institute") is established by Part 5, Division 106, Chapter 3, section 125290.50 and section 125290.60 of the Health and Safety Code, also known as the California Stem Cell Research and Cures Bond Act ("Act").

ARTICLE II. Purpose.

The GWG is created for the purpose of providing recommendations to the ICOC regarding standards, criteria, requirements, funding, and oversight of grant and loan applications and awards. This purpose will be accomplished through the review of grants and loan applications, based on standards and criteria adopted by the ICOC, in order to make recommendations to the ICOC for the awarding and continued funding of training, research, therapy development, and clinical trial grants and loans. Finally, this purpose will be accomplished through oversight reviews of grantees to ensure compliance with the terms and conditions of the award in order to fulfill the mission of the Act, and to report and make recommendations for subsequent actions to the ICOC or the CIRM President, as appropriate.

ARTICLE III. Functions.

The duties of the GWG shall include the following:

(A) Recommend to the ICOC interim and final criteria, standards and requirements for considering funding applications and for awarding grants and loans;

(B) Recommend to the ICOC standards for the scientific and medical oversight of awards;

(C) Recommend to the ICOC any modifications of the criteria, standards and requirements described in sections (A) and (B) above as needed;

(D) Review grant and loan applications based on the criteria, requirements and standards adopted by the ICOC and make recommendations to the Application Review Subcommittee of the ICOC for the award of grants and loans to promote training, research, therapy development, and clinical trials;

(E) Oversee peer-group reviews of grantees to ensure compliance with the terms of the award, and report to the ICOC or the President of CIRM, as appropriate, any recommendations for subsequent action;

(F) Recommend to the ICOC standards for the evaluation of grantees to ensure that they comply with all applicable requirements. Such standards shall mandate periodic reporting by grantees and shall authorize the GWG to audit a grantee and forward any recommendations for action to the ICOC.

ARTICLE IV. Membership, Selection, and Terms of Service.

Section 1 (Method of Appointment). Members of the GWG shall be appointed by the ICOC.

Section 2 (Appointment). The GWG shall be composed of: (1) seven ICOC members from the ten (10) disease advocacy group members ("Patient Advocate Members") described in paragraphs (3), (4), and (5) of subdivision (a) of Section 125290.20 of the Act; (2) scientists nationally recognized in the field of stem cell research who are not California residents and who are not employed in the State of California ("Scientist Members"), 15 of whom shall be invited to participate in each peer review, and; (3) the Chairperson of the ICOC.

Section 3 (Term of Service). GWG members shall normally serve for six (6) years except that after the first six-year term the Scientist Members' terms will be staggered so that one-third of the members shall be appointed for a term that expires two years later, one-third of the members shall be appointed for a term that expires four years later, and one-third of the members shall be appointed for a term that expires six years later. Subsequent terms are for six years. In the event that a Scientist Member resigns prior to completing his or her term of service, incoming members appointed by the ICOC shall be invited to serve for a term of two (2), four (4), or six (6) years. GWG members may serve a maximum of two consecutive terms. A GWG member who has served two consecutive terms is eligible for re-appointment after two years have passed since the member's previous term ended.

Section 4 (Expiration of Term). When a member's term expires, the ICOC shall appoint a new member within 90 days. GWG members shall continue to serve until their replacements are appointed.

Section 5 (Alternate Patient Advocate Members). In the event that a Patient Advocate Member of the GWG cannot attend all or a portion of a meeting of the GWG, that Patient Advocate Member may designate an alternate from among any of the patient advocates who are members of the ICOC to serve as an Alternate Patient Advocate Member in the absence of the appointed Patient Advocate Member.

Section 6 (Specialists). Individuals with scientific expertise on a particular issue may occasionally be invited to attend meetings of the GWG for the purpose of providing evaluation or expertise with respect to specific grant(s) or research fields. Specialists do not have voting privileges and their presence is not counted towards a quorum.

Section 7 (Review Chairs of the GWG).

(A) **(Appointment)** For each peer review, the President shall appoint a Scientist Member to serve as Review Chair of the GWG for all matters that are specific to that review. The President shall select a Review Chair with the knowledge and background necessary to lead that review.

(B) **(Duties)** A Review Chair of the GWG shall preside over the scientific evaluation of applications accepted for review , as described herewith in Article VII, Section 2, and other GWG business associated with that review meeting. The duties of a Review Chair shall commence upon appointment by the President, and shall conclude when final action has been taken on all applications considered under that review.

(C) **(Alternate Review Chair)** In the event that a Review Chair of the GWG cannot attend all or a portion of a scientific review meeting pertaining to the designated RFA or PA, the President may designate another Scientist Member to serve as an alternate Review Chair in the absence of the Review Chair.

Section 8 (Vice-Chair of the GWG).

(A) **(Appointment)** The ICOC shall appoint as co-Vice-Chairs of the GWG two Patient Advocate members of the ICOC.

(B) **(Duties)** The Vice-Chairs of the GWG shall moderate the Application Review Subcommittee's consideration of programmatic issues pursuant to Article VI, Section 6 of the Board Bylaws.

Section 9 (Compensation and Expenses of GWG Members).

(A) **ICOC Members** – ICOC members of the GWG, except the Chair and Vice Chair of the ICOC, shall be entitled to a daily consulting rate and reimbursement for expenses, as established by the ICOC.

(B) **Scientist Members** – Scientist Members of the GWG shall be entitled to a daily consulting rate and reimbursement for expenses, as established by the ICOC.

Section 10. (Conflict of Interest). All Scientist Members and Specialists shall be governed by conflict of interest rules and economic disclosure requirements adopted by the ICOC. ICOC members shall be governed by California conflict of interest laws, as set forth in Health and Safety Code section 125290.30(g) and the conflict of interest policy for ICOC members adopted by the ICOC.

Section 11. (Confidentiality). Members of the GWG shall comply with CIRM's Confidentiality Policy, which is attached as Appendix A.

Section 12. (Grounds for Removal of Members). Any Scientist Member of the GWG may be removed by the ICOC for cause. The grounds for removal are as follows:

(A) An intentional violation or violations of the conflict of interest policy applicable to the member;

(B) Two or more grossly negligent violations of the conflict of interest policy applicable to the member;

(C) Consistent failure to perform the assigned duties of the member or unexcused absence from three consecutive GWG meetings;

(D) Violation of medical or ethical standards by the member in his or her professional capacity as determined by the appropriate research institution or the appropriate professional group;

(E) Residency or employment by an institution located in the State of California;

(F) The conviction of a felony or act involving serious moral turpitude.

Section 13. (Procedure for Suspension of Members). The President of the CIRM may suspend a Scientist Member of the GWG based on any of the grounds enumerated above by giving the member written notice of his or her suspension, including the grounds for the suspension. The suspension shall remain in effect until it is terminated by the President, the member resigns from the GWG, or the ICOC has considered the permanent removal of the member pursuant to Section 15.

Section 14. (Procedure for Removal of Members). The President of CIRM may recommend to the ICOC the removal of a Scientist Member of the GWG based on any of the grounds enumerated above. The President must inform the member in writing that he has requested that the ICOC consider removal of the member at least 10 days prior to the ICOC's consideration of the matter. The notice must include the grounds for the recommendation. The member may address the ICOC in writing or in person during the meeting of the ICOC at which the removal of the member is considered.

Section 15. (Procedure for Temporary Leave of Absence). The President of CIRM or the Administrative Chair shall consider and may, at his or her discretion, grant requests, from Scientist Members for temporary leaves of absence, not to exceed six months, due to family or personal illness, death of a loved one, or other extenuating circumstances.

ARTICLE V. Duties of GWG Members and Role of CIRM President and Scientific Officers.

Section 1 (Scientist Members). The Scientist Members of the GWG are responsible for evaluating and scoring grant and loan applications for scientific merit, and for voting, along with the other members of the GWG, on grant and loan funding recommendations to the Application Review Subcommittee of the ICOC. Scientist Members, along with the other

members of the GWG, will also vote on recommendations regarding active awards in the CIRM portfolio.

Scientist Members of the GWG are full members and participate in all aspects of the GWG's review of applications. They provide the essential scientific expertise to inform the recommendations of the full GWG and the decisions made by the ICOC.

The review is led by the Review Chair, a Scientist Member. During the review, Scientist Members of the GWG are responsible for assessing the scientific merit of each application, according to the criteria stated by CIRM, based on their own scientific expertise and the expert opinion of the other scientific reviewers. In written critiques and during review meetings, they should be willing to explain their reasoning to assist Patient Advocates in fulfilling their responsibilities on the GWG and the ICOC, to allow CIRM scientific team members to prepare summaries for the ICOC, applicants and the public, and to provide guidance or recommendations that will be useful in the management of approved awards. During the scoring of applications, Scientist Members may ask questions, probe the views expressed by other participants, and express their own views. Scientist Members are expected to consider the views expressed by other participants, but their confidential scores should reflect their own independent scientific judgment.

After the scoring of applications concludes, Scientist Members of the GWG join the Patient Advocate Members to make and vote on motions concerning the final funding recommendation to the Application Review Subcommittee of the ICOC. If thirty-five percent (35%) of the members of the GWG join together in a minority position, a minority report may be submitted to the Application Review Subcommittee of the ICOC.

Section 2 (Patient Advocate Members). The seven (7) Patient Advocate members of the GWG, together with the Scientist Members, are responsible for voting on grant and loan recommendations to the Application Review Subcommittee of the ICOC.

Patient Advocate Members of the GWG are full members and participate in all aspects of the GWG's review of applications, except for assigning scores. They represent the patients whose needs drive all CIRM-funded research. As members of the ICOC, they provide a continuum for the flow of information and insights between the two bodies.

A Patient Advocate Member of the GWG will be invited to participate as a reviewer for each application accepted for review. During the review of applications, the Patient Advocate reviewer will be invited to offer his or her views of the merits of the application, but will not score the application. In addition, all Patient Advocate Members may ask questions, probe the views expressed by other participants, and express their own views.

After the scoring of applications concludes, the Patient Advocate Members join the Scientist Members of the GWG to make and vote on motions and minority reports concerning the final recommendation to the Application Review Subcommittee of the ICOC. In addition, the Patient Advocate Members shall participate in a motion after the completion of the review to provide the Application Review Subcommittee with their assessment as to whether or not, based on their participation in the review, the review was fair and free from undue bias.

Section 3 (Specialists). Specialists may be invited by the CIRM team to participate in meetings of the GWG for the purpose of providing scientific expertise on a particular issue(s), area, or field and/or for a specific grant application.

Section 4 (Role of CIRM President). CIRM's President serves on the GWG as a non-member participant in all GWG discussions, but does not assign scientific scores, make motions, or vote. As the leader of CIRM's scientific and professional team members, the President may ask GWG members to consider how an application will address scientific issues that have come up in the field or in the execution of CIRM-funded research, respond to questions by GWG members on science matters, and provide information within his/her expertise.

The President should alert the GWG and the Application Review Subcommittee of the ICOC to matters that have been found to be inconsistent or incorrect in the review of a grant application.

Section 5 (Role of CIRM Scientific Team). Members of CIRM's scientific team, under the leadership of the President, support the GWG, by managing and coordinating the review process, including but not limited to tracking conflicts of interest, ensuring observance of confidentiality rules, setting the schedule of review, and ensuring that applications are appropriately evaluated and scored. To this end, the scientific team members provide guidance and information regarding CIRM's programs, portfolio and procedures, including explaining the scope and requirements of the RFA or PA and the review criteria and responding to requests for information regarding awards or applications that aid the GWG in making informed evaluations. The scientific team also ensures that review criteria, priorities and requirements are appropriately applied to the evaluations and discussions of applications, and help the Review Chair ensure that all GWG members contribute to the proper evaluation and scoring of applications. Scientific team members should, on request of the Review Chair, provide information to the GWG in their areas of expertise.

The scientific team members are responsible for monitoring scientific progress of CIRM-funded research projects, and may be called upon to report on that progress if it is relevant to the review of an application before the GWG or for the GWG to provide recommendations on progress of an existing award. They are responsible for summarizing, for the Application Review Subcommittee of the ICOC, applicants and the public, the reasoning behind the scientific scores and GWG recommendations. Accordingly, scientific team members may ask GWG members to clarify their views or address specific issues in order to present a complete and useful report.

Prior to Application Review Subcommittee's consideration of GWG recommendations, the President and scientific team should consider whether there are applications which they believe warrant particularly close review, or whether specific modifications may be needed to successfully execute a particular proposal.

ARTICLE VI. Meetings.

Section 1 (Regular Meetings). The GWG shall hold at least four meetings per year, one of which will be designated as its annual meeting. The GWG may hold additional meetings as the CIRM determines are necessary or appropriate. The annual meeting shall be attended **in person** by GWG members.

Section 2 (Teleconference Meetings). At the discretion of the CIRM team, members of the GWG may participate in meetings of the GWG, with the exception of the annual meeting, by teleconference, provided that the public has the opportunity to participate in public sessions of the GWG that are conducted by teleconference. Significant medical needs of members of the GWG will be given a high priority in arranging teleconference meetings.

Section 3 (Open Meetings). The GWG shall meet in public session except for discussions related to evaluation of grant applications and recommendation of applications to the Application Review Subcommittee of the ICOC, discussions related to appeals or requests for reconsideration of GWG recommendations, discussions related to the review of a grantee's progress and compliance with the terms of the award, and discussions of other matters that may be considered in closed session under the Bagley-Keene Open Meeting Act or under Health and Safety Code section 125290.30. The GWG may recommend additional exceptions to the ICOC as necessary to carry out the mission of the GWG.

Section 4 (Special and Emergency Meetings). Special and emergency meetings may be called by the CIRM President if necessary.

ARTICLE VII. Procedure for Recommending Grant and Loan Applications.

Section 1 (Quorum). Sixty-five percent of the GWG members who are eligible to vote shall constitute a quorum of the GWG.

Section 2 (Recommendation Procedures).

(A) Unless excused due to conflicts, both ICOC and non-ICOC members of the GWG shall be present in-person or via teleconference during the entire GWG meeting, and may participate in all discussions.

(B) Scientific Evaluation and Scoring

1. The Review Chair of the GWG shall preside over the scientific evaluation and scoring process, and the process to arrive at the final recommendations to the Application Review Subcommittee of the ICOC.

2. The fifteen (15) Scientist Members of the GWG shall evaluate each application for scientific merit and assign a numerical value to each application based on standards and criteria adopted by the ICOC. The criteria and standards for evaluation are hereby incorporated by reference into these Bylaws.

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Section 3 (Applications for Non-Clinical Programs).

(A) For purposes of making funding recommendations to the Application Review Subcommittee of the ICOC for applications for non-Clinical Program awards, each individual score and the average numerical score for each application shall be assigned to one of two tiers as follows:

1. Tier 1 = score 85 and above, representing applications that have exceptional merit and that warrant funding; or
2. Tier 2 = score below 85, representing applications that are not recommended for funding.

(B) The grants review office will inform reviewers of these tiers in advance of the GWG meeting so that this guidance may be incorporated into their reviews and scores.

(C) At the conclusion of the consideration of all applications, the Scientist Members will have a final opportunity to review their individual scores and make any changes they wish as to any application in which they are able to participate (not in conflict). After an appropriate amount of time, the Scientist Members will then submit final scores. After final submission, the scores may not be changed. For programs for which only one application will be funded, the application receiving the highest average scientific score will be deemed to be the GWG's recommendation for funding.

Section 4 (Applications for Clinical Program).

(A) For applications for Clinical Program awards (CLIN1, CLIN2, and CLIN3, and any subsequent amended versions or new Clinical Program PAs), Scientific Members shall assign a score of 1, 2, or 3, as signified below:

1. A score of "1" means that the application has exceptional merit and warrants funding;

2. A score of "2" means that the application needs improvement and does not warrant funding at this time but could be resubmitted to address areas for improvement;

3. A score of "3" means that the application is sufficiently flawed that it does not warrant funding, and the same project should not be resubmitted for review.

(B) Funding Recommendations for Clinical Program Awards

The CIRM team will tally the numbers of Scientist Members who assigned a score of 1, 2 and 3, respectively, and will present that information for each application to the entire GWG. If a plurality of Scientist Members has assigned a score of 1 or 2, then that score shall constitute the recommendation of the GWG. If a majority of Scientist members has assigned a score of 3, then that score shall constitute the

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(2) For applications for clinical stage program awards, t

recommendation of the GWG. However, if there is no plurality and there is a numerical tie between two or more scores, then any member of the GWG may make a motion to break the tie by assigning the application a score of 1, 2, or 3 and transmitting that score to the Application Review Subcommittee as the recommendation of the GWG. In addition, if a plurality of Scientist Members, but fewer than a majority, have assigned a score of 3, then any member of the GWG may make a motion to assign the application a score of 2 or 3 and to transmit that score to the Application Review Subcommittee as the recommendation of the GWG.

Section 5 (Oversight Reviews).

When reviewing progress on existing awards, any member of the GWG may make and second a motion to make a recommendation to the ICOC or the President, as appropriate, for subsequent actions.

Section 6 (Recommendations and Minority Reports).

(A) Recommendations of the GWG to the Application Review Subcommittee of the ICOC shall be made by a majority vote of a quorum of the members of the GWG, except for recommendations involving "vital research opportunities," which require a two-thirds vote of a quorum of the members of the GWG pursuant to Health and Safety Code section 125290.60(c)(1)(D). If thirty-five percent (35%) of the members of the GWG join together in a minority position, a minority report may be submitted to the Application Review Subcommittee of the ICOC.

(B) Upon completion of the review, the members shall consider a two-part motion with respect to the review. All members shall vote as to part (1); only the Patient Advocate members shall vote as to part (2):

1. The review was scientifically rigorous, there was sufficient time for all viewpoints to be heard, and the scores accurately reflect the recommendations of the GWG.
2. The review was carried out in a fair manner and was free from undue bias. (PAs only).

(C) The outcome of the vote on both parts of the motion shall be made available to the Application Review Subcommittee, along with the GWG's recommendations.

Section 7 (Vital Research Opportunity).

(A) Through the eligibility criteria specified in RFAs and PAs, CIRM gives priority to applications involving pluripotent stem cell and progenitor cell research that cannot, or is unlikely to receive timely or sufficient federal funding, unencumbered by limitations that would impede the research. However, the GWG may recommend funding for vital research opportunities. A "vital research opportunity" means scientific and medical research and technologies and/or any stem cell research that is not recommended for funding pursuant to (A) of this section but which provides a substantially superior research opportunity vital to advance medical science as

determined by at least a two-thirds vote of a quorum of the members of the GWG. Human reproductive cloning shall not be considered a vital research opportunity.

ARTICLE VIII. Rules of Order.

Debate and proceedings in the GWG shall be conducted in accordance with Robert's Rules of Order (Newly Revised) when not in conflict with rules of the GWG or other statutory requirements.

ARTICLE IX. Amendments.

These Bylaws may be amended or repealed by the ICOC at any regular or special meeting by a majority vote of a quorum of the ICOC. The GWG may recommend amendments to these bylaws to the ICOC for its consideration.