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BY FEDEX AND ELECTRONIC MAIL

Ms. Elaine M. Howle
California State Auditor
Bureau of State Audits
555 Capital Mall, Suite 300
Sacramento, CA 95814
NormC@bsa.ca.gov

Dear Ms. Howle:

We are pleased to submit our one year response outlining our efforts to implement the recommendations your office made in its February 2007 report, "California Institute of Regenerative Medicine: It Has a Strategic Plan, but It Needs to Finish Developing Grant-Related Policies and Continue Strengthening Management Controls to Ensure Policy Compliance and Cost Containment."

When the audit began, the agency had been in operation barely 18 months, had a staff of just 20, and was hindered in its growth and in its mission by litigation challenging Proposition 71. A year after publication of the audit, CIRM has been operating for three years, the litigation has fully and finally resolved in CIRM's favor, the first issue of $250 million in general obligation bonds has been sold, staff has increased to 28 full time equivalent, and all the recommendations of your report have been implemented or otherwise resolved.

We want to thank you and your fine staff again for the care and effort that went into preparation of the audit and in the way staff has continued to work with us over the past year. The audit process made a useful and important contribution to our effort to operate the Institute effectively and efficiently in the service of our mission, and in full compliance with state law. As a young state agency, we are still establishing and refining key procedures and policies. The audit process has provided us a framework in which to

consider new issues as they arise. We recognize that to effectively serve our scientific mission to advance stem cell science to therapies, we must build public trust in our ability to be responsible stewards of public funds.

Chapter 1: ***The California Institute for Regenerative Medicine Developed a Detailed Strategic Plan to Guide its Use of Funds***

Recommendation:
To provide accountability and assess annual progress in meeting its strategic goals and initiatives, the institute should fulfill its plans to develop a process to track management information reported annually by grantees.

CIRM agreed with this recommendation and has implemented three processes for tracking information to assess progress in meeting our strategic goals: a comprehensive computerized grants management system, annual progress reporting requirements that will be incorporated into that system, and annual meetings for CIRM grantees.

You will recall that our initial effort to create a comprehensive grants management system suffered a set-back when the vendor encountered serious financial difficulties, leaving CIRM without a work product. We learned from that experience and conducted a comprehensive bidding process to select a new vendor. First, we carefully defined our functional requirements, including those for scientific information capture, tracking and management reporting. When fully configured, the system will allow the following: "tagging," to allow Institute staff to tie an RFA to specific goals in the Strategic Plan; the ability to track outcomes of CIRM-funded scientific research, such as publications, patent applications and awards, Investigational New Drug applications, and license agreements; and the ability to code grants to categories such as disease focus, type of research and stage of research.

On May 25, 2007, we issued a detailed Request for Proposals (RFP) that requested responses based on a pay for performance schedule. Five firms submitted responsive proposals. (An electronic copy of the RFP is attached.) These were scored by a team of staff and invited experts, based on criteria stated in the RFP. Based on the scoring, during the summer of 2007 CIRM invited three firms to respond to specific questions, and to make a four-hour presentation to staff to highlight the attributes of their proposed systems. In October 2007, CIRM's governing board, the Independent Citizens Oversight Committee (ICOC), approved Institute staff's recommendation and awarded the contract to Grantium. (The agenda item for this approval and links to the corresponding documentation presented to the ICOC can be found at http://www.cirm.ca.gov/meetings/2007/10-03-07.asp.) Since that time, we have been negotiating the precise terms of the contract, to insure that we achieve a true pay for performance standard. We hope to execute that contract next month.

Under the terms of the CIRM Grants Administration Policy, all recipients of CIRM research grants must submit annual progress reports; recipients of facilities grants must submit quarterly reports. These progress reports will be a crucial part of our management reporting system and of our grants management system. (CIRM's Grants Administration Policies can be found at http://www.cirm.ca.gov/policy/policy.asp.)

In addition, in September 2007 CIRM held its first annual meetings for CIRM scholars, who were the first recipients of CIRM grants -- the Training Grants, which were awarded and funded in 2006 – and the only grantees who have had funding for a full year. CIRM held two meetings, one in Northern California and another in Southern California, to provide the trainees the opportunity to present preliminary data, engage in scientific discussion, and exchange ideas. Both meetings included three basic elements: short oral presentations from one trainee per institution funded; a two-hour poster session during which all trainees were encouraged to display and discuss their research with others one-on-one; and a session during which trainees led and participated in discussion groups on topics of interest including Stem Cell Self-Renewal and pluripotency, Translational Challenges, and Career Transitions. In preparation for the meetings CIRM published a compendium of the 115 abstracts submitted by the trainees. (This compendium can be found at http://www.cirm.ca.gov/pub/pdf/annual_mtg.pdf.)

In the fall of 2007, CIRM also published a booklet titled *Awards and Applications Approved for Funding 2007* which included abstracts of all applications approved for funding and that cleared administrative review through CIRM's first four Requests for Applications (RFAs): the CIRM Training Program (RFA 05-01), which in 2006 funded 16 of 26 applications received; the Leon J. Thal SEED Grant Program (RFA 06-01), which in 2007 funded 73 of 231 applications received; the Comprehensive Research Grants Program (RFA 06-02), which in 2007 funded 28 of 70 applications received; and the Shared Research Laboratory and Stem Cell Techniques Program (RFA 07-01), which funded 17 of 22 applications received for shared labs, and six of nine applications received for stem cell techniques courses. (A copy of this booklet can be found at http://www.cirm.ca.gov/pub/pdf/Compendium.pdf.)

Responsible Staff: Patricia Olson, Director of Scientific Activities; Ed Dorrington, Director of Grants Management Systems.

Chapter 2: *Some Key Tasks Remain for the California Institute for Regenerative Medicine in Developing and Strengthening Grant-Related Policies and Controls.*

Recommendation:
The committee should ensure that it follows through with its plan to identify the appropriate standard for providing uninsured Californians access to therapies developed

using institute funds and to convey clearly to grantees its expectations for providing access in its intellectual property policies. In addition, the committee should identify practical benchmarks to use as a standard for discount prices for therapies and apply the standard to its policies for grants to nonprofit and for-profit organizations.

CIRM agreed with this recommendation and has implemented it. In connection with development of its intellectual property policies for non-profit organizations, beginning prior to the audit and thereafter CIRM held a series of public meetings to discuss ways to identify benchmarks for discount prices for uninsured California patients and those whose drugs and non-drug therapies may be purchased with public funds.

On July 14, 2007, CIRM's Intellectual Property Policies for Non-profit and Academic Institutions became final and codified at Title 17, California Code of Regulations sections 100301-100310. Section 100306(d) provides in pertinent part that CIRM grantees may grant exclusive licenses "only to persons that agree to have a plan in place at the time of commercialization to provide access to resultant therapies and diagnostics for uninsured California patients. In addition, such licensees will agree to provide drugs at prices negotiated pursuant to the California Discount prescription Drug Program (commencing with California Health & Safety Code section 130500, et seq.) to eligible Californians under that program." In addition, these regulations require annual reporting to CIRM regarding any such licensing activity, so that CIRM can monitor performance. (The intellectual property regulations applicable to non-profit and academic institutions can be found at http://www.cirm.ca.gov/reg/pdf/IP_Regs_100300.pdf.)

In March 2007, the ICOC initiated the administrative law process for adoption of Intellectual Property Policies for For-Profit Organizations. These draft regulations have completed several rounds of public comment and include similar, but more specific requirements for access and discount pricing. These can be found in draft regulation for Title 17, California Code of Regulations section 100407 Access Requirements for Products Developed by For-Profit Awardees. The final regulations have been adopted by the ICOC and are awaiting final approval by the Office of Administrative Law (OAL). (The intellectual property regulations applicable to for-profit organizations can be found at http://www.cirm.ca.gov/reg/pdf/IP_CompRegs.pdf.)

The for-profit regulations execute a three-pronged policy with respect to access and pricing. First, at the time of commercialization, they require grantees to develop and provide a plan for access by uninsured Californians. Second, the regulations require that CIRM-funded therapies be available according to CalRX benchmarks to institutions purchasing such therapies with public funds. Third, the regulations anticipate state efforts to offer a discount prescription drug program to underinsured Californians, and require grantees to participate in this type of program.

Once the for-profit regulations have been approved by OAL (forecast for March 2008), the Institute intends to propose to the ICOC modifications to the non-profit regulations where appropriate to harmonize them with the more specific requirements contained in the for-profit regulations.

Responsible Staff: C. Scott Tocher, Interim Associate Legal Counsel to the Vice Chair

Recommendation:
The committee should monitor the effectiveness of its policy to make institute-funded patented inventions readily accessible on reasonable terms to other grantee organizations for noncommercial purposes to ensure that it does not inhibit the advance of stem cell research.

CIRM agreed with this recommendation and has implemented it. Scientific advances depend on the ability of researchers to replicate and extend the results of prior research findings, and access to materials described in scientific publications facilitates this process. Indeed, it is customary for scientists to share materials described in their published research, and some journals require it as a condition of publication. Similarly, the intent of CIRM's regulations is to promote rapid advancement of the field. These regulations require CIRM grantees to give other researchers access to biomedical materials discussed in published research, at cost, for non-commercial purposes. See Title 17 California Code of Regulations section 100304, and draft regulation 100404. CIRM monitors compliance with these regulations by requiring grantees to submit annual progress reports that identify publications and licensed patented inventions, as well as any requests for access by other scientists for non-commercial research purposes.

Responsible Staff: C. Scott Tocher, Interim Associate Legal Counsel to the Vice Chair

Recommendation:
The institute should complete the development of its grants administration policy targeted toward for-profit organizations.

CIRM agreed with this recommendation and has implemented it. Following a series of interested persons meetings held by Institute staff in the fall of 2007, the ICOC adopted an Interim Grants Administration Policy for For-Profit Organizations on December 12, 2007. These regulations are now beginning the administrative law process. As a result of the adoption of these interim regulations, CIRM opened its two most recent RFAs – the New Cell Lines Awards (RFA 07-05) and the Disease Team Planning Awards (RFA 07-04) – to for-profit organizations. (The for-profit GAP can be found at http://www.cirm.ca.gov/reg/pdf/Reg100501_IX.pdf.)

Responsible Staff: Patricia Olson, Director of Scientific Activities

Recommendation:
To provide increased accountability over the grants award process, the institute should ensure that the grants review working group follows the new procedures to record its votes to recommend funding for stem cell research grants, and maintains those records.

CIRM agreed with this recommendation, implemented the recommendations of your staff before issuance of the audit, and has continued to maintain those records. In 2006, CIRM adopted new procedures to record the votes of each member of the Grants Working Group participating in a given meeting, and to identify members recused from discussing or voting on applications under consideration due to potential conflicts of interest. At every Grants Working Group meeting held since November 2006 each participating member signed a statement that documents their voting record and recusal record at those meetings. In addition, CIRM staff records the member's participation and presence inside and outside the meeting room for discussion of particular applications, and maintains these records. CIRM retains these records as part of its documentation of the grant award process. The names of working group members recused from discussion are provided to the ICOC before their vote on grant funding, are publicly disclosed in the summary reviews of each application (which are available on our Web site), and are part of the public record. We have also implemented similar procedures for the confidential scoring of the Facilities Working Group.

Responsible Staff: Gilberto Sambrano, Senior Officer to the Grants Working Group; Tamar Pachter, General Counsel

Recommendation
To monitor the performance of grantees effectively, the institute should complete the implementation of a grants monitoring process, including audits, and the development of related procedures.

CIRM agreed with this recommendation and has implemented it. CIRM takes very seriously its obligation to monitor the performance of its grantees. As part of the grants monitoring process, CIRM conducts a complete administrative review prior to issuing formal Notices of Grant Award and before funds are released. CIRM also has written procedures for the process of that review, and for auditing of that process. In addition to its other capabilities, the new grants management system will allow CIRM to track grantees to make sure they have certified current compliance with ethical review and notification requirements for funded research. For facilities grants (including the approved shared laboratories grants and major facilities grants that are expected to be approved in May 2008) CIRM has developed a set of performance milestones that require review throughout the life of the grants. (An electronic copy of the administrative review procedures is attached.)

CIRM has also designed an audit process with spot checks to ensure that grantees comply with required medical and ethical standards. A similar audit process with spot checks is being designed for financial compliance, and is expected to be in place by summer of 2008, when research grantees will have completed the first year of funding. (An electronic copy of the procedures for standards audit is attached.)

In addition, CIRM has added special provisions to the Grants Administration Policy for Non-Profit and Academic Institutions that govern facilities grants, specifically the Shared Laboratory Program and the Major Facilities Program. These additions establish criteria and benchmarks specific to the demands of capital grant programs. (These amendments to the Grants Administration Policy can be found at http://www.cirm.ca.gov/reg/pdf/FGAP_policy.pdf and http://www.cirm.ca.gov/reg/pdf/Reg100701_MFGAP.pdf.)

Responsible Staff: Patricia Olson, Director of Scientific Activities; Amy Lewis, Grants Management Officer; Rick Keller, Senior Officer to the Facilities Working Group; Geoff Lomax, Senior Officer to the Standards Working Group

Recommendation:
The institute should seek a formal opinion from the attorney general regarding whether the exemptions created for working groups from conflict-interest laws are intended to exempt them from the conflict-of-interest provisions that apply if the recommendations of an advisory body are routinely and regularly adopted by the decision-making body to whom they are made.

We have given careful consideration to your recommendation and have decided that the concerns raised have been fully resolved by subsequent events and court decisions. First, as you noted in the audit report at page 47: "As of December 2006, it was too early to assess whether the working groups will make recommendations on grant funding or other substantive recommendations that the committee will accept without significant amendment or modification . . . ." We now have a record of more than three years of operation and approval of five rounds of grants, in which the recommendations of the CIRM working groups have never been routinely and/or regularly adopted by the ICOC.

Second, you noted in the audit report at page 48 that the Superior Court's legal conclusion that the ICOC, not the working groups, is the "ultimate decision-making body" for CIRM was not binding because, at that time, the case was pending on appeal. Since then, however, the Court of Appeal affirmed the decision of the Superior Court, and the decision became binding on May 16, 2007, when the Supreme Court denied review. In its opinion, the Court of Appeals expressly affirmed the Superior Court's conclusion that the ICOC, not the working groups, exercises all decision-making authority. (See *California Bioethics Council v. California Institute for Regenerative*

Medicine (2007)147 Cal.App.4th 1319, 1364; an electronic copy of the Court of Appeals opinion is attached.)

CIRM now has an authoritative, binding legal ruling that as a matter of law, the working groups do not exercise decision making authority. We hope that your counsel will agree that no opinion of the attorney general could provide greater authority or confidence on this point, and therefore there is no longer any reason to request it.

Responsible Staff: Tamar Pachter, General Counsel

Recommendation:
[T]he institute should follow its plans to amend its conflict-of-interest policies to include specialists invited to participate in stem cell research program activities, such as grant application review.

CIRM agreed with this recommendation, has interpreted its policies to include specialists, and has implemented the recommendation. In March 2007, the ICOC amended the conflict of interest policy for the Grants Working Group to specifically include specialists. (The amended conflict of interest policy can be found at http://www.cirm.ca.gov/meetings/pdf/2007/021507_item_16.pdf.)

Responsible Staff: Gilberto Sambrano, Senior Officer to the Grants Working Group; Tamar Pachter, General Counsel

Recommendation:
To provide employees with the information they need to disclose all potential conflicts of interest, the institute should develop the necessary procedures to ensure that its employees are aware of the companies that apply for funding.

CIRM agreed with this recommendation and has implemented it. At the time of our earlier responses, CIRM had not yet opened any RFA to for-profit organizations. The first two RFAs open to for-profit organizations were RFA 07-05, the New Cell Lines Awards and RFA 07-04, the Disease Team Planning Awards. There are two processes in place to ensure that employees are aware of for-profit companies that apply for CIRM funding.

These two RFAs required all applicants to submit Letters of Intent (LOIs) by a deadline prior to the application deadline. Once CIRM received these LOIs, General Counsel requested a list of the for-profit applicants from the Science Office. At a staff meeting held the week after the LOI deadline, General Counsel reminded all employees of the divestiture provisions in the Conflict of Interest Policy for CIRM Employees, and followed up by sending an email to all employees with the list of for-profit organizations that submitted LOIs in response to these RFAs. (An electronic copy of this email is

attached.) This procedure will be followed with all future RFAs open to for-profit organizations.

In addition, the agency has in place a conflict of interest procedure that follows receipt of actual applications. Specifically, CIRM employees must review a list of all entities that have applied for funding pursuant to a particular RFA, note any conflicts, and sign the result. Employees are then disqualified from participating in the review of applications as to which they have identified a conflict. They are not given access to any such applications, and they must leave the room during review of any such application.

Responsible Staff: Gilberto Sambrano, Senior Officer to the Grants Working Group; Tamar Pachter, General Counsel

Recommendation:
To ensure compliance with its conflict-of-interest policies, the institute should revise its procedure for reviewing grants to include a review of the Statements of Economic Interest for committee members of the working groups before every grants review meeting. Moreover, it should revise its procedures for grants review meetings to ensure that it retains documentation regarding conflicts of interest of the working groups, including information that it took appropriate recusal actions.

CIRM agreed with this recommendation and has implemented it. Since November 2006, staff has performed a back-up review of all working group members, including ICOC members, by reviewing their pre-meeting disclosures against their Statements of Economic Interests. In addition, as specifically noted above, since November 2006, CIRM staff has documented actual disqualification actions at meetings of the Grants Working Group and all working groups, and maintains these records.

Responsible Staff: Gilberto Sambrano, Senior Officer to the Grants Working Group; Tamar Pachter, General Counsel

Chapter 3: *To Improve Cost Containment, the California Institute for Regenerative Medicine Modified its Contracting and Travel Policies and Plans to Conduct Another Salary Survey, but It Needs to Do More.*

Recommendation
The institute should ensure that it follows its newly revised policies, which address some of the concerns raised in our audit. The institute also should amend its policies further to include the rest of the concerns that we have raised.

Although the institute now monitors staff members who attend its meetings, it should implement a preapproval requirement for travelers that want to claim meals separately.

CIRM agreed with this recommendation and has implemented it. Under CIRM's Travel Policy and Business Meeting Expenditure Policy and practice, employees are not reimbursed for meals at meetings where meals are provided without prior authorization. CIRM continues to monitor the travel claims of staff who attend meetings to insure that reimbursement is not claimed when CIRM provides a meal. (The Travel Policy and Business Meeting Expenditure Policy adopted by the ICOC at its January 2008 meeting can be found at http://www.cirm.ca.gov/faq/pdf/TravelPolicy.pdf and http://www.cirm.ca.gov/policy/pdf/Business_Policy.pdf.)

Responsible Staff: Richard Murphy, Interim President; Alan Trounson, President

Recommendation
The institute should revise its travel reimbursement claims form for working groups to require sufficient information that would allow an adequate review of the amounts claimed.

CIRM agreed with this recommendation and has implemented it. Since March 1, 2007, members of CIRM working groups have submitted all travel reimbursement claims on the standard state travel claim form (STD 262). CIRM reviews and allows these claims pursuant to the same policy and procedure applicable to CIRM employees.

Responsible Staff: Richard Murphy, Interim President; Alan Trounson, President

Recommendation
The committee should adopt a travel reimbursement policy for its members that will result in the reimbursement of reasonable and necessary expenses, as stated in the act, and that address the concerns we raised in the report.

CIRM agreed with this recommendation and has implemented it. At its January 17, 2008 meeting the ICOC amended the Travel Policy previously adopted for CIRM employees and working group members (and observed by the ICOC) to apply to members of the ICOC. Under this policy, ICOC members are governed by the same rules applicable to employees, working group members, and indeed, anyone filing a travel claim with CIRM. Other amendments adopted at the January meeting were designed to align CIRM policy more closely to that of the Regents; deviations from the policy of the Regents were adopted where Regents policy did not address the requirements of CIRM's mission, or did not make sense in the context of CIRM's organization. (The CIRM Travel Policy can be found at http://www.cirm.ca.gov/faq/pdf/TravelPolicy.pdf.)

Responsible Party: Robert Klein, ICOC Chairman; Richard Murphy, Interim President; Alan Trounson, President

Recommendation
To ensure that the methodology to set salary ranges complies with the act, the institute should follow through with its plan to resurvey any positions whose salary ranges were affected by the errors, omissions, and inconsistencies in its initial salary survey and salary-setting activities.

CIRM agreed with this recommendation and has implemented it. CIRM issued an RFP to contract with an experienced firm for the review and survey of all budgeted CIRM positions, including those about which your report expressed concerns. CIRM received two responsive bids and signed a contract with Mercer Human Resources Consulting on April 30, 2007. In addition, based on the requirements of Proposition 71, CIRM has documented its salary administration philosophy and practice. Under its Total Compensation Philosophy, adopted in January 2008, CIRM will target base pay at the 80th percentile of relevant market data. (The Compensation Philosophy can be found at http://www.cirm.ca.gov/meetings/pdf/2008/022008_item_3b.pdf.)

Mercer delivered its final report to CIRM on January 14, 2008. (The Mercer report, including a list of the participating organizations, cane be found at http://www.cirm.ca.gov/meetings/pdf/2008/022008_item_3a.pdf.)

It is important to note that since your audit report was published, the Institute has significantly changed its staffing model and in the process eliminated positions that were among the eleven you thought required a new survey. In addition, our review of functional needs have suggested that some blending and integrating of responsibilities would allow for the most robust and efficient use of our limited staff resources. As a result, CIRM has several hybrid positions that encompass responsibilities that cross multiple positions at other institutions. (CIRM's current Organization Chart can be found at http://www.cirm.ca.gov/meetings/pdf/2007/121207_item_19.pdf.) The Mercer report nevertheless surveyed those positions, and includes information about new positions that were created during data gathering, but does not include data for new positions created after Mercer's data gathering process closed. A list of surveyed positions is in the Mercer report.

In addition, the Institute has updated its job descriptions to improve accuracy and consistency. CIRM is in the process of evaluating Mercer's data to ensure that the job descriptors used were accurate based on current expectations.

Based on Mercer's data, the positions of Executive Assistant to the ICOC Chair and Senior Executive Assistant to the President are the only positions about which your report expressed concerns for which salary exceeds the 75th percentile reported. In addition, there are two other positions not mentioned in your report, Director of Grants Management Systems and Grants Management Specialist II that were surveyed, for which salaries exceed the 75th percentile (for historical reasons or because it was

necessary to successfully recruit). Under Mercer's methodology, there was insufficient data reported to allow it to calculate the 80th percentile. CIRM is comparing actual job descriptions and responsibilities with the survey job descriptors to ensure they were benchmarked against proper criteria.

CIRM staff plans to discuss the Mercer survey with the ICOC at its March 2008 meeting, and at that time to propose any changes to salary ranges indicated by the survey report, in keeping with CIRM's Compensation Philosophy. (A list of CIRM's current salary ranges can be found at http://www.cirm.ca.gov/jobs/pdf/Salary_Structure.pdf.) Where there is insufficient data available from UC and private research institutions, CIRM will use relevant general market data if available from established salary surveys, giving emphasis to non-profits and/or California health science organizations to establish an appropriate metric.

Responsible Staff: Alexandra Campe, Human Resources Officer

We are very pleased to be able to report full implementation of your recommendations. Again, we very much appreciate the diligence and professionalism your staff has demonstrated and continues to demonstrate throughout this process, the contributions they have made to improving the processes of the agency, and to ensuring that Californians can have full confidence in the integrity of the processes that we use to commit public funds to stem cell research. We at CIRM are confident that your input has significantly improved important operational components of the Institute, and for that we thank you.

Sincerely,

Alan O. Trounson, Ph.D.
President and Chief Scientific Officer
California Institute for Regenerative Medicine