

**REPORT OF THE OFFICE OF THE CHAIRMAN
TO EXTERNAL REVIEWERS**

Prepared by the Office of the Chairman of the Governing Board
of the California Institute for Regenerative Medicine

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REPORT OF THE OFFICE OF THE CHAIRMAN OF THE GOVERNING BOARD OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE TO EXTERNAL REVIEWERS

I. Background on Proposition 71

A. Drafting the Measure

In 2002, a group of patient advocates who were frustrated with the restrictions on stem cell research imposed by the Bush Administration joined forces in an effort to convince the California Legislature to appropriate funds to the California Department of Health for stem cell research. After the bill stalled in the second policy committee, the group decided to examine other options for advancing stem cell research in California. Based on the recommendation of several groups and the Juvenile Diabetes Research Foundation, the group sought the advice of Robert Klein. Mr. Klein had served as the lead U.S. Senate patient advocate for the Juvenile Diabetes Research Foundation's successful efforts in Congress to secure a \$1.5 billion mandatory supplemental appropriation to the National Institutes of Health. The appropriation, which required the unanimous consent of both the House and the Senate, funded research involving Type 1 and Type 2 diabetes after the White House directed Congress to shut down all new appropriations to maximize the funding available for the Iraq War.

In 2003, the group contacted Robert Klein by telephone while he was traveling in Peru. Mr. Klein suggested that they consider using the proceeds of state general obligation bonds to fund an independent stem cell research agency, rather than attempting to appropriate funds on an annual basis through the California Department of Health. Although the group's consultants advised him that this idea was not feasible, Klein consulted with Chas Cardall, senior partner at Orrick, Herrington and Sutcliff (a nationally recognized bond law firm), who advises the State and the University of California on tax issues relating to bonds and who confirmed that the State could issue bonds to fund intellectual capital in addition to infrastructure. When Klein returned from Peru, the group asked him to lead their effort to secure funding for stem cell research in California.

Klein identified several goals for the group's effort. First, in light of the limited scope of research for which federal funds could be used and the ideological opposition to human embryonic stem cell research, a stable source of funding was essential to sustain active researchers and to lure new scientists into the entire range of stem cell research. Second, the assignment of the burden for the costs of supporting such research should be aligned with the long-term benefits they expected would arise from it. Third, the research should create an engine to drive California's innovation economy in the biotechnology sector. Fourth, the effort required a mission-driven institute whose singular focus was to speed the delivery of stem cell research-driven therapies and cures to patients suffering from chronic disease and injury. Finally, this mission should be protected from political interference while at the same time ensuring public accountability.

Although the California Legislature had adopted a bill to authorize research involving human embryonic stem cell research in 2002, Klein recognized that a bill that sought funding for human embryonic stem cell research would face insurmountable barriers, including ideological opposition to such research. Furthermore, an approach that would require annual appropriations would not provide the stability of funding that was necessary to jump start this new field of research. As a result, the group agreed to explore the possibility of proposing a ballot measure and Klein established a Scientific Advisory Committee chaired by Dr. Irv Weissman and including Dr. Jeffrey Bluestone, Dr. Larry Goldstein and Dr. Paul Berg, with participation by Dr. David Baltimore and other leading scientists.

To educate himself further, Klein attended meetings of the International Society for Stem Cell Research and seminars on stem cell research at Stanford University, Harvard University and other academic and nonprofit research institutions on the East Coast. Klein also consulted with the Chief Financial Officers at the Salk Institute, the City of Hope, Stanford University and the Juvenile Diabetes Research Foundation to validate program elements including the feasibility of imposing limits on the administrative budget and staff and other restrictions. The campaign committee also commissioned a poll to identify the voters' interests and areas of concern. As a result of the polling, the group learned that the voters viewed accountability, including limits on overhead, and scientific, medical and ethical standards as critical elements of the measure.

After conducting exhaustive research, including consulting with scientists, academic leaders, biotechnology experts, among others, Klein began to draft a ballot measure. Klein worked with a team of lawyers, including: Chas Cardall and Bob Feyer, who helped with the bond and tax issues; Steve Merksamer, Dick Martland and John Mueller, who provided regulatory, governmental and strategic counsel; and James Harrison, who provided advice regarding constitutional issues, including the structure of the agency, based on his experience defending a similar measure (Proposition 10) against a challenge. Amy DuRoss coordinated the scientific, legal and policy components of the drafting effort. Klein wrote the draft Initiative and the working group crafted the implementing statutory and constitutional language.

- First, to ensure stability of funding, the Initiative amended the California Constitution to create a right to conduct human embryonic stem cell research, including somatic cell nuclear transfer, and to establish the California Institute for Regenerative Medicine.¹ (Cal. Const., art. XXXV, §§ 2, 5.) They also protected CIRM's funding by providing for a continuous appropriation and prohibiting the funds allocated to CIRM from being transferred or appropriated by the Governor or the Legislature for another purpose. (*Id.*, § 4.)
- Second, in order to align the costs of the research with the expected benefits over time, Klein decided to fund CIRM through the issuance of \$3 billion in long-term bonds. (Health & Saf. Code, §§ 125291.10 et seq.) As a result, the bonds will be paid off over time as the anticipated benefits of the research are realized. At the same time, to protect California's general fund during a time of economic uncertainty, they capitalized interest on the bonds for the first five years, thereby protecting the general fund against any costs during this period of time. (*Id.*, § 125291.20.)
- Third, to stimulate the biotechnology sector in California, the Initiative established a program to provide research and facilities funding through grants and loans. (Health & Saf. Code, § 125290.70.) The research funding and facilities funding provide the intellectual and capital infrastructure, respectively, that is necessary to stimulate the development of a stem cell research industry in California.
- Fourth, the Initiative created a statutory framework for CIRM that reflects the agency's mission of delivering therapies and cures to patients as quickly as possible. Thus, they authorized funding for all research along the development spectrum from basic research to translational research to clinical trial research and created the infrastructure for a world-class peer review system that ensures that the best science is funded and that the programmatic goals of the agency are achieved. (Health & Saf. Code, § 125290.60.)
- Fifth, the Initiative established a 29-member Board composed of leading scientists and physicians, patient advocates and life sciences industry executives. (Health & Saf. Code, § 125290.20.) Members of the Board are appointed by four constitutional officers and the leaders of the Senate and the Assembly to serve fixed terms, thereby ensuring broad representation and protecting the agency from political

¹ The measure also amended the Constitution to prohibit the use of public funds for research involving human reproductive cloning. (Cal. Const., art. XXXV, § 3.)

interference. (*Id.*) Furthermore, the Initiative charged the Board with providing oversight of CIRM, including requiring the Board to adopt an array of public accountability standards ranging from conflict of interest rules to medical and ethical standards for research. (*Id.*, §125290.40.) The Board's oversight role and the standards which the Board was charged with adopting ensure accountability to the public.

After spending months consulting with experts, drafting the measure, and vetting it with patient advocate groups and others, including Dr. James Battey at the National Institutes of Health, who provided advice in his **private capacity**, Klein submitted the draft measure to the campaign's executive committee. After obtaining their approval, the measure was submitted to the Attorney General and circulated for signatures among the voters. Ultimately, the proponents of what became Proposition 71 collected more than 1.1 million signatures to qualify the measure for the November 2004 ballot, thereby demonstrating the board base of support for stem cell research in California. (In 2004, 598,105 valid signatures were required to qualify a constitutional amendment for the ballot.)

B. Coalition of Patient Advocacy Groups

After drafting Proposition 71, the proponents turned their attention to the challenging task of building a large coalition of supporters and raising the money necessary to conduct a statewide campaign in California, which is heavily dependent upon television advertising to communicate with the voters. This effort culminated in endorsements by approximately 70 national and/or state patient advocacy organizations. The campaign's Chairman, Robert Klein, and his executive staff supported principally by Amy DuRoss and Amy Lewis, raised more than \$34 million from patient advocate organizations, patient families, and their direct supporters. The committee did not accept funding from biotech or pharmaceutical organizations, or individuals representing those organizations, unless the individual family contributed as a patient family.

Under the leadership of the patient advocates' campaign, Chambers of Commerce – representing all of the major urban centers along the coast from San Diego to San Francisco – endorsed Proposition 71; and, at the request of patient advocates, major cities like Los Angeles and San Francisco, passed council resolutions endorsing the initiative. The California Medical Association and Children's Hospitals of California, numerous other medical societies, scientific organizations, 40 Nobel Prize winners, all of the State constitutional officers, and the Democratic Party leadership in the California State Assembly and the State Senate endorsed the measure. In addition, all of the major metropolitan newspapers throughout the population centers on the coast, from the San Francisco Chronicle to the San Diego Union-Tribune, endorsed the measure. Only one major newspaper – the Sacramento Bee, which refused to meet with the proponents and which opposes most ballot measures – took a stand against Proposition 71. (The Sacramento Bee has continued to be a critic of CIRM.) By contrast, the Bakersfield Californian endorsed Proposition 71.

In the 10 days before the election, the campaign committee inspired California citizens, patient advocates and their supports to send 3 million affinity group emails within the state supporting Proposition 71, and approximately 3 million affinity group emails out of the State of California, discussing the necessity for this research and funding. Across the state of California, in every major media market – in fact, in every urban and rural center – patient advocates and organizations identifying with the needs of the chronically ill reached out to their local civic groups and media to support Proposition 71. On November 2, 2004, more than seven million California voters (59% of the voters) voted in favor of Prop. 71.

While patient advocates in the United States had previously supported scientists by leading requests for major increases in funding for the National Institutes of Health (federal funding of scientific research), Proposition 71 represented a new paradigm: patient advocates leading a funding initiative supported by scientists and medical societies, business leaders and progressive religious leaders, with the goal of state funding of scientific and medical research from basic scientific discoveries through the entire medical and regulatory pipeline to phase two human trials and proof of human efficacy.

C. National Academies 2004 Workshop

Immediately prior to being elected Chairman of CIRM's Governing Board (after nomination by the Governor, Lieutenant Governor, Treasurer and Controller), Robert Klein worked with the President of the National Academies of Science, Engineering and Medicine to convene a two-day workshop of the nation's leading scientists, ethicists, and governance/legal experts at the University of California, Irvine National Academy Building. This invitation-based workshop, which included members of the press, scientific and medical leaders and patient advocates, set the intellectual foundation for later policies on conflicts of interest; grants program priorities; medical and ethical standards; intellectual property administration and ownership; and general agency procedures. In particular, Robert Klein asked the General Counsel of the National Academy of Science to address policies that would protect against conflicts of interest and achieve the highest scientific and ethical standards. In response, the General Counsel of the NAS recommended that CIRM consider adopting a policy to exclude California scientists from CIRM's peer review group to assure the public that recommendations to the Board would be based on scientific merit. In addition, as discussed below (section __), Mr. Klein asked Bruce Albers, the President of the National Academy of Sciences, to accelerate the work of the Academy's task force on medical and ethical standards for human embryonic stem cell research in order to provide a foundation for the development of CIRM's standards. The NAS was instrumental in providing guidance for the development of CIRM's medical and ethical standards and conflict standards and for its initial research programs, including the Training Grant and SEED Grant programs.

The Chairman's intent in establishing this immediate relationship with the NAS was: (a) to make it clear that the leadership of Prop. 71 was reaching out to the NAS for best practices, and (b) to create a prestigious validation and shield against alternative pressures that were not consistent with the best scientific practices, by incorporating the NAS's recommendations.

D. Post-Election Legal Challenges

Then-State Controller Steve Westly and then-State Treasurer Phil Angelides convened the first meeting of CIRM's Governing Board on December 17, 2004, and the Board conducted its first business at a meeting in January 2005, including hiring its first staff. One month later, in February 2005, opponents of Proposition 71 filed original writ petitions in the California Supreme Court to challenge the constitutionality of Proposition 71. The California Supreme Court declined to hear the petitions, but the opponents re-filed their claims in Alameda County and Sacramento County Superior Courts and expanded the scope of their action to encompass allegations regarding CIRM's performance and compliance with the law. At the direction of Chairman Klein, attorneys for CIRM filed a motion to consolidate both actions in Alameda County Superior Court to take advantage of the court's single assignment system, which improved the prospects for a quick resolution of the case. The desire for a speedy resolution of the case was particularly strong because the lawsuits effectively prevented the State of California from issuing bonds in support of CIRM by challenging the legal authority for the bonds' issuance.

The cases involved extensive discovery, including hundreds of interrogatories and requests for admission, the production of tens of thousands of pages of documents, and more than 25 depositions. In February 2006, the cases proceeded to trial before Alameda County Superior Court Judge Bonnie Lewman Sabraw who, after considering the documentary evidence and trial testimony, rejected each and every claim advanced by the plaintiffs, including claims that challenged CIRM's compliance with California law.

The Court of Appeal upheld the trial court's judgment in a strongly worded decision:

After careful consideration of all of appellants' legal objections, we have no hesitation in concluding, in the exercise of "our solemn duty to jealously guard the precious initiative power" (CART, supra, 109 Cal.App.4th at p. 808), that Proposition 71 suffers from no

constitutional or other legal infirmity. Accordingly, we shall affirm the well-reasoned decision of the trial court upholding the validity of the initiative.
(California Family Bioethics Council v. California Institute for Regenerative Medicine
(2007) 147 Cal.App.4th 1319, 1373.)

The California Supreme Court declined to review the Court of Appeal's well-reasoned and thorough opinion. The litigation launched by the opposition was completely defeated, on every facet of the complaint, by May, 2007 – just short of 2 years after it began in the trial court. By comparison, validation actions brought by the California Housing Finance Agency took approximately four years to complete and the constitutional challenge to Proposition 10, which raised many of the same issues as the challenges to Proposition 71, took more than four years to come to an end. The strategic decision to consolidate the cases in Alameda County permitted the accelerated consideration of the case, thereby saving approximately two years in the process. The Chairman's Office managed the litigation, including gathering information in response to discovery requests, preparing responses to interrogatories, and scheduling depositions and preparing Board members for their depositions. Melissa King acted as the administrative coordinator for the litigation and James Harrison, board counsel, served as co-counsel with the Attorney General's Office, which served as lead counsel in defending Proposition 71. CIRM also benefited from the participation of a group of amici, including Cal Tech, Stanford, USC, the Burnham Institute, Cedars Sinai, City of Hope, the Salk Institute and numerous other research organizations and patient advocate groups in California. The law firm of Munger, Tolles & Olson represented the amici, led by Mark Epstein and O'Malley Miller.

Opponents filed a third case in Alameda Superior Court challenging CIRM's award of Training Grants under state conflict of interest laws. In response to a motion to dismiss and based on the strength of the Court of Appeal decision, the trial court dismissed the case.

A fourth case challenged the constitutionality of funding stem cell research under the federal Constitution. The federal court dismissed the case on jurisdictional grounds and the Ninth Circuit confirmed the decision. The U.S. Supreme Court declined to review the case.

Although these early lawsuits impeded the State's ability to issue bonds on CIRM's behalf, CIRM used the delay to lay the foundation for the agency's research program, adopting medical and ethical standards, intellectual property standards and conflict of interest rules, among others. In addition, the agency created the infrastructure necessary to make, manage and monitor its grants and loans. Additionally, CIRM funded its original grant program during the litigation.

II. Overview of Legal Structure of CIRM

A. Organization of Agency

1. Governing Board and Board Subcommittees

CIRM is governed by a 29-member Board composed of Californians with expertise in: (1) managing large research grants and complex institutions and conducting cutting edge medical research; (2) understanding the critical path for the development of successful experimental medical treatments and directing the approval process through the Food and Drug Administration and other regulatory bodies and ethical committees; and (3) advocating on behalf of Californians who suffer from a variety of chronic diseases and injuries, including participating in the review of applications for medical research grants.

To prevent a single elected official from exercising undue influence, the appointments to the Board are divided among four constitutional officers (the Governor, the Lieutenant Governor, the Controller and the Treasurer), each of whom appoints five members of the Board and each of whom has the right to nominate candidates for

Chair and Vice-Chair. In addition, the President *Pro Tem* of the Senate and the Speaker of the Assembly each appoint one member. The Chancellors of the University of California at San Francisco, Davis, San Diego, Los Angeles and Irvine each appoint an executive officer from his or her campus. A majority of a quorum of the Board, defined as 65 percent of eligible members, is required to take action on an issue. Although this threshold presents a challenge, it also ensures full participation and a diversity of perspectives.

The members of the Board must be appointed from among the executive officers of California's leading universities, research institutions and life science commercial entities, as well as leaders among California's patient advocacy groups. (Health & Saf. Code, § 125290.20.) As the Court of Appeal recognized, "[t]here are stringent qualifications for appointment designed to ensure that all members possess appropriate experience and expertise and the persons knowledgeable in the various disease groups that may benefit from the research are represented." (*California Family Bioethics Council v. California Institute for Regenerative Medicine* (2007) 147 Cal.App.4th 1319, 1332-1333.) The appointment scheme ensures that members are appointed based on their expertise, not based on political influence or financial contributions and it provides the public with the assurance that decisions are made based on scientific merit. Service by patient advocates on the Board and on the Working Groups, as required by Proposition 71, also plays an important role in maintaining the public trust because the patient advocates act as surrogates for the public and help to keep the agency focused on its mission.²

To provide stability to the Board and CIRM, the members serve fixed terms of six or eight years (meaning that they do not serve at the pleasure of their appointing authority). (Health & Saf. Code, § 125290.20(c).) Aside from the Chair and Vice-Chair of the Board, who are treated as employees for the purposes of receiving compensation, the members of the Board volunteer their time, with some electing to receive only a modest *per diem* of approximately \$116 per day. A sizeable number of Board members have participated in more than 100 meetings since the voters' approval of Proposition 71, many without compensation.

Among other responsibilities, the Board is charged with: (1) adopting all scientific, medical, ethical and intellectual property policies; (2) making final decisions on all grant and loan awards; and (3) overseeing the operations of CIRM and handling governmental (state and federal), legal and state finance issues.

The Board has created several subcommittees and taskforces to permit the Board to use members' time and expertise efficiently. These subcommittees and task forces include: (1) the Governance Subcommittee, (2) the Legislative Subcommittee, (3) the Intellectual Property Task Force, (4) the Finance Subcommittee, (5) the Loan Task Force, (6) the Science Subcommittee, (7) the Evaluation Subcommittee, and (8) the Presidential Search Subcommittee, and (9) the Communications Subcommittee.³ These subcommittees have conducted numerous public meetings to focus attention on important subjects, and each makes recommendations to the full Board in its particular area of expertise. For example, the Intellectual Property Task Force has conducted 18 public meetings and hearings to explore complex issues relating to intellectual property generated by CIRM-funded research. Based on the recommendations of the IP Task Force, the Board has adopted regulations governing both non-profit and for-profit grantees. These regulations are now a model for other states that are investing public funds in scientific and medical research.

Attached to this report are a list of Board members and their short biographies, as well as the Board membership of the Working Groups and the Board Subcommittees. Chairman Klein requested that this information be provided to reviewers because each member of the Board has made an extraordinary contribution to the success

² In other jurisdictions, the public has resisted scientific inquiries led by pharmaceutical companies. Although the leadership of the pharmaceutical industry is dedicated to improving public health, the public remains skeptical of efforts led by pharmaceutical companies.

³ The most recent subcommittee to be established, the Communications Subcommittee, has not yet met; its purpose is to understand how the obligation of the Board and CIRM to meet their mandate to communicate with the citizens of California can be substantially enhanced. Currently, it is the Board's perception that the communications efforts primarily serve the research community, which although laudable, do not adequately address the broad responsibility to communicate with the California public.

of CIRM and all references to the Chairman or the Chairman's Office must be viewed within the context of the extraordinary work of the Board, Board counsel, the Chairman's staff and CIRM staff. The Board members' biographies illustrate the talent and experience upon which the Board, the Working Groups and the Board subcommittees have relied to advance the mission of CIRM.

2. The Agency

The agency, led by the President, provides scientific expertise and leadership, implements the policies and programs adopted by the Board, and manages the standards and grant-making processes, including overseeing grant and loan recipients. As a result of the highly specialized and urgent nature of CIRM's mission, substantial differences exist between CIRM and other state agencies. For example, CIRM is limited to no more than 50 employees, while comparable funding organizations often have staffs that are more than twice as large.⁴ As a result, CIRM staff perform a variety of specialized functions that would ordinarily be handled by a much larger number of employees at other agencies and that are unique to running an institute dedicated to scientific discovery and the delivery of therapies. Because of their need for specialized expertise and flexibility, CIRM staff members are exempt from civil service and are compensated based on the salary levels for comparable positions at California medical schools and research institutions from which members of the Board could be appointed. (Health & Saf. Code, § 125290.45(b)(4).) The compensation of CIRM employees reflects not only the heavy demands placed upon them, but also the limitations on employment with CIRM; employees serve at the will of the President and the duration of CIRM's current funding stream is 12-13 years before considering any loan repayments, which rules out the possibility of the long-term career track available for many civil service positions. To be clear, however, CIRM was established in the California Constitution and does not have a defined time limit on its lifespan. CIRM's ability to continue awarding grants and loans could be extended if the voters were to approve new bond funding in 2014 or 2016. As a private citizen, Chairman Klein has indicated that his goal is to seek an additional \$3 to \$5 billion for CIRM. He believes the public will require clear evidence of CIRM's contributions to medical advances before approving additional bonds in a State election. This proof of progress will need to be made through the record of published discoveries, new research and therapeutic tools, as well as Phase 1 and Phase II human clinical trials in progress.

3. Working Groups

a. Establishment of Working Groups

To assist the Board in carrying out its duties, Proposition 71 established three expert advisory groups: (1) the Scientific and Medical Research Funding Working Group ("Grants Working Group"), which makes recommendations regarding research standards and awards; (2) the Scientific and Medical Research Facilities Working Group ("Facilities Working Group"), which makes recommendations regarding facilities standards and awards; and (3) the Scientific and Medical Accountability Standards Working Group ("Standards Working Group"), which makes recommendations regarding scientific, medical and ethical standards.

Early in 2005, Chairman Klein established a number of board search subcommittees to populate the Working Groups with leading national experts and to establish the policies and procedures of each Working Group. The Chairman proposed and the Board debated, refined and approved the original policy and operating objectives (the mission statement) for each of these search subcommittees and established all of the initial working procedures for the "Working Groups." These policies and procedures were presented to the Board and further refined in the approval process. The search committees included:

⁴ SB 1064, which was recently signed by the Governor and which will go into effect on January 1, 2011, will remove this cap. See the discussion of SB 1064 in section ___, below.

The Grants Working Group Search Subcommittee, originally chaired by Dr. Ed Holmes (then Dean of UCSD School of Medicine), which reviewed over 800 nominations;

The Standards Working Group Search Subcommittee, chaired by Dr. David Kessler (then Dean of UCSF School of Medicine); and,

The Facilities Working Group Search Subcommittee, chaired by Dr. Michael Friedman (President and CEO of the City of Hope).

The broad national outreach for scientific leaders, conducted through a public process, brought a diversity of perspectives to CIRM.

b. Composition and Role of Working Groups

CIRM's three working groups ensure that CIRM benefit from the expertise and advice of the leading scientists, clinicians, ethicists, real estate experts and patient advocates in the United States and the world.

The Grants Working Group

The Grants Working Group, composed of 15 scientists and clinicians drawn from outside California (upon the recommendation of the National Academy of Sciences), seven Board patient advocate members, and the Chair of the Board, engages in a rigorous peer review and programmatic review of each application. Proposition 71 is designed to ensure that scientists would work hand-in-hand with patient advocates in pursuit of CIRM's mission to find therapies and cures for chronic disease and injury. To ensure that the Grants Working Group has the expertise required to review a wide variety of proposals, from basic research to clinical research, CIRM has recruited a variety of experts as alternate and specialist members of the Grants Working Group. For example, more than 60 alternate members are available to assure appropriate expertise in any grant cycle. In addition, from time to time, CIRM calls upon over 70 specialists to lend their expertise to CIRM. While these specialists share their expertise and analysis (including a benchmark score) with the Grants Working Group, they do not formally score applications, nor do they participate in programmatic review.

Pursuant to Proposition 71, the Grants Working Group is responsible for recommending standards for the review and oversight of applications and for reviewing grant and loan applications and making funding recommendations to the Board, which is required to make the final decision on all awards. (Health & Saf. Code, §§ 125290.40(c), 125290.60.) The scientific members of the Grants Working Group review and assign a scientific score to each application.

Although the patient advocate members of the Board are not generally physicians or scientists and do not participate in the scientific scoring of applications, they participate in all other aspects of CIRM's grant review, including the discussion of applications that precedes scientific scoring. In addition, two patient advocate members – Joan Samuelson and Jeff Sheehy – serve as Vice Chairs of the Grants Working Group. Similarly, the Chairman of CIRM's Governing Board serves as an ex officio member of the Grants Working Group, and in that capacity, he participates in the scientific and programmatic discussion but does not score or vote. This allows the Chairman to obtain an understanding of the issues addressed in peer review and assists him in leading the discussion of applications in the Governing Board's Executive session reviews of proprietary scientific and privileged medical information and in open session and to provide insights to the scientific members of the peer review group on issues and/or information such as Board policies, Board priorities and statutory interpretations, and/or facilities and finances of the public or private institutions sponsoring the scientist's application. The role of the patient advocates is particularly important during the programmatic review of applications. One of the two patient advocate Vice Chairs of the Grants Working Group, Jeff Sheehy,

leads this discussion and the patient advocates serve as an important link between the Governing Board and the Grants Working Group, providing a continuum for the flow of information and insights between the two bodies. Programmatic review is designed to give the Grants Working Group an opportunity to consider issues, such as portfolio balance, in making funding recommendations to CIRM's Governing Board. For example, a member of the Grants Working Group, including a patient advocate member, may make a motion to move an application from one tier to another. The patient advocates vote on these motions, along with the scientific members of the GWG. Patient advocate members also participate in the consideration of the Grants Working Group's final funding recommendations, which are sent to CIRM's Governing Board for its review.

The Standards Working Group

The Standards Working Group is composed of nine scientists and clinicians, four medical ethicists and five patient advocate members of the Board. (Health & Saf. Code, § 125290.55.) Sherry Lansing, a patient advocate member of the Board, serves as Co-Chair of the Standards Working Group, along with Dr. Bernard Lo. The Standards Working Group is responsible for recommending scientific, medical and ethical standards to the Board, including standards for safe and ethical procedures for obtaining materials and cells for research. (*Id.*) Under Proposition 71, the Governing Board is responsible for approving all standards. (*Id.*, § 125290.40(c).) The Standards Working Group played a pivotal role in the development of CIRM's medical and ethical standards, which are discussed below.

The Facilities Working Group

The Facilities Working Group is composed of four real estate specialists and six patient advocate members of the Board. (Health & Saf. Code, § 125290.65.) David Lichtenger, a real estate expert, and Board member David Serrano Sewell, a patient advocate, serve as Chair and Vice-Chair, respectively, of the Facilities Working Group. The Facilities Working Group is responsible for recommending standards for the review of facilities applications and for reviewing such applications and making recommendations to the Board. (*Id.*) Under Proposition 71, the Board is responsible for making all final decisions on facilities awards. (*Id.*, § 125290.40(c).) The Facilities Working Group was instrumental in developing and implementing the Shared Labs and Major Facilities Grant programs, which are discussed in more detail below.

B. Approval of Accountability Standards

Proposition 71 requires CIRM's Governing Board to adopt a public accountability and medical and scientific accountability standards, including: (1) conflict of interest rules; (2) intellectual property standards; and (3) medical and ethical standards. These standards ensure that: (1) funding decisions are made based on scientific merit, free from conflicts of interest; (2) CIRM-funded research is conducted according to the highest ethical standards; and (3) the State of California has an opportunity to obtain a return on its investment in stem cell research, including medical savings and access to therapies for those with limited financial resources.

1. Conflict of Interest Standards

a. Governing Board and Agency

CIRM's Governing Board has adopted rigorous conflict of interest standards for Board members, for CIRM staff and for members of the working groups. **CIRM policies exceed the requirements of state law. For example, Board members are precluded from receiving any financial support through a CIRM grant or loan and the scientific members of the Grants Working Group all come from outside California to ensure they cannot personally benefit from CIRM funding, which is restricted to research conducted in the state. In addition, conflict of interest policies for working group members cover financial conflicts of interest as**

well as professional and personal conflicts of interest. State law, by contrast, is limited to financial conflicts of interest.

The Board also has an extensive process to avoid conflicts. In advance of each meeting at which the Board will be considering applications for funding, CIRM staff provides each Board member with a list of all applicant institutions, principal investigators and collaborating organizations and investigators that would receive funding pursuant to the application. Along with this list, counsel provides a memorandum to the members describing the Board's conflict of interest rules and state conflict of interest laws and asking members to identify those institutions and investigators in which the member has a financial interest. Board members then submit a certified list identifying their conflicts to CIRM staff prior to the scheduled meeting. CIRM staff members also review each Board member's statement of economic interests (Form 700) to screen for additional conflicts that a member may have overlooked. With this information in hand, staff compiles: (1) a master list identifying by application those members who have financial interest in the application, and (2) a list for each member identifying the member's conflicts by application number. Each member receives a copy of his/her conflict list prior to the meeting.

At the Board meeting, the Board considers the rankings and recommendations of the Grants Working Group in three categories: (1) recommended for funding (Tier 1); (2) recommended for funding if funds are available (Tier 2); and (3) not recommended for funding (Tier 3). The Board can and has funded and denied the funding of grants from all three categories; by utilizing the combined expertise of all 29 members, the Board – at times – perceives opportunities or obstacles to specific grants, that the members of the peer review committee may not have fully appreciated. Generally, the Board first considers motions to move individual applications from one tier to another (e.g., from Tier 3 to Tier 1). Before a particular application is discussed, the Chair of the Board asks counsel to screen for members who are ineligible to participate in the discussion. Counsel reminds members to consult their conflict list before participating in the Board's discussion of a particular application. Staff then monitor the discussion and the vote to ensure that disqualified Board members abstain, and when a roll call vote is taken on a specific application, conflicted Board members are not called.

Nothing, including these stringent rules and procedures can completely eliminate the possibility of an unintended conflict of interest, but they represent CIRM's best efforts to ensure that decisions are made solely on the merits of an application and to eliminate even the appearance of impropriety. Furthermore, if an unintended conflict is discovered, the approval process affected by the conflict is repeated, with recusals, to produce a final decision that is conflict-free.

b. Working Groups

The Board and CIRM take extraordinary steps to ensure that conflict of interest policies are enforced. For example, to ensure the grant-making process is free of conflicts of interest, members of the Grants Working Group are required to file annual disclosure forms identifying their financial interests. In addition, Working Group members certify, prior to the grant review, those applicant institutions and investigators in which they have a financial, professional or personal conflict of interest. When an application in which a member has an interest is discussed in a working group session, the member leaves the room under the supervision of a staff monitor. At the end of the session, each member certifies, under penalty of perjury, that he/she has not participated in the review of an application in which the member has a financial, professional or personal conflict of interest. CIRM staff members are also screened for conflicts prior to grant review. After reviewing these standards, the Controller found that CIRM has "extensive conflict of interest policies that are modeled after and, in some cases, go beyond the National Institute[s] of Health requirements."

2. Medical and Ethical Standards

a. Development of Standards

Proposition 71 required CIRM's Governing Board to adopt medical and ethical standards for CIRM-funded research, including standards for informed consent modeled on standards promulgated by the National Institutes of Health. (Health & Saf. Code, §§ 125290.35((b)(1), 125290.55(b).) At the request of the Chairman of the Proposition 71 campaign (now the Chairman of CIRM's Governing Board), the National Academy of Sciences expedited its development of model standards for human embryonic stem cell research by one year. When the NAS approved these standards on April 26, 2005, CIRM's Governing Board adopted these standards as its interim standards on May 23, 2005, **one month later**. Using the NAS standards as a springboard, CIRM then developed the first comprehensive set of governmental regulations governing the conduct of human embryonic/pluripotent stem cell research, as required by Proposition 71. The Standards Working Group developed and the Governing Board approved final standards in a one-year period. Some of CIRM's provisions vary from the NAS standards because of specific requirements contained in Proposition 71. For example, CIRM's regulations include a 12-day limit on cell division while NAS has a 14-day limit. In some cases, CIRM's regulations exceed the requirements of NIH guidelines; for example, CIRM's informed consent requirements exceed the current NIH guidelines for consent.

CIRM adopted these standards under California's strict open meetings rules and administrative law requirements. CIRM and the Standards Working Group held 9 public meetings to develop specific policy recommendations. During these meetings, the Standards Working Group and the Board considered extensive public comment. In addition, CIRM staff responded in writing to over 100 written comments from research institutions, patient advocates, interest groups and the public. **The process culminated in the Board's approval of final standards making California the first state to have comprehensive ethical standards for basic and clinical human embryonic stem cell research.** These standards have served as a model for other states.

b. Consistency with NIH

CIRM has also worked with the National Institutes of Health to promote the adoption of NIH standards that are compatible with CIRM's standards. Thus, CIRM provided comments to the draft NIH guidelines. The Board established an NIH Guidelines Response Task Force to provide immediate feedback and input to an effort led by Dr. Geoff Lomax and CIRM General Counsel Elona Baum. Melissa King, the Board's Executive Director, managed the Task Force, which included Dr. Floyd Bloom, Dr. Susan Bryant, Dr. Michael Friedman, Dr. Jeannie Fontana, Dr. Francisco Prieto, Jeff Sheehy, Sen. Art Torres and Robert Klein. Under CIRM's standards, all hESC lines approved by NIH are acceptable for use by CIRM funded researchers. CIRM revised its medical and ethical standards to ensure that they are operationally consistent with NIH guidelines (e.g. hESC lines derived from embryos for which the gamete donor was paid for reproductive purposes are acceptable), with a few exceptions.

c. Coordination with CAMR and IASCR

CIRM staff member Geoff Lomax co-chairs the Interstate Alliance on Stem Cell Research ("IASCR"). The IASCR's mission is to advance stem cell research (human embryonic, adult and other) by fostering effective interstate collaboration, by assisting states in developing research programs, and by promoting efficient and responsible use of public funds. The IASCR was established to facilitate coordination among states that wish to advance stem cell research. Stem cell research programs in these states vary considerably in scope and the regulatory requirements that underpin them. This diversity of approaches could impede collaboration and the sharing of research materials or raise overall costs. The IASCR provides a forum for information exchange and collaborative planning in an attempt to facilitate the sharing of data, resources and cell lines across state borders

to ensure the efficient development of research programs. CIRM has played a leadership role in the organization to promote consistency.

3. Intellectual Property Standards

a. Development of Standards through IP Taskforce

Proposition 71 requires CIRM's Governing Board to adopt intellectual property standards that balance the State's opportunity to benefit from patents, royalties and licenses, with the need to ensure that essential research, including therapy development, is not unreasonably hindered by IP agreements. (Health & Saf. Code § 125290.30(h).) To that end, ten members of the Governing Board formed a subcommittee, the Intellectual Property Task Force, to develop a policy that would strike this balance. The Task Force, which is chaired by Ed Penhoet, conducted more than 15 public meetings devoted to policy development, surveyed the best practices of more than 20 funding entities, conducted over 100 interviews, received nearly 20 presentations by experts and stakeholders and conducted a dozen public comment rounds. This work culminated in the development of intellectual property regulations applicable to CIRM's non-profit grantees, which were approved by CIRM's Governing Board in 2006. Since then, the Task Force has developed four intellectual property policies applicable to for-profit grantees and a set of consolidated regulations applicable to all CIRM grantees. John Simpson, a consumer advocate who attended many of these meetings, referred to the Intellectual Property Task Force's work as "an excellent example of how public policy should work." (John Simpson, Consumer Watchdog, December 12, 2007 Board Meeting [<http://www.cirm.ca.gov/transcripts/pdf/2007/12-12-07.pdf>].)

b. Summary of IP policies

The primary components of the IP policies require: (1) revenue sharing when CIRM grantees license their CIRM-funded inventions; (2) sharing of biomedical materials for research purposes where they are published by the grantee; (3) revenue sharing tiered to the success of a drug where the grantee self-commercializes the CIRM-funded IP; (4) the submission of access plans for uninsured Californians by grantees, collaborators and exclusive licensees; and (5) discount prescription drugs for low-income Californians. CIRM monitors development and compliance through reporting requirements and ultimately by exercising march-in rights, if necessary.

C. Public Transparency

1. Open Meetings and Public Records

The Board complies with the Bagley-Keene Open Meeting Act and the Public Records Act. Indeed, for a young agency, CIRM has offered a virtually unprecedented opportunity for public participation in its processes. The Board, for example, has met more than 60 times since it first convened in December 2004. At each meeting, members of the public are invited to comment on every action item on the agenda, and at the end of the meeting, the Chair invites general public comment.

CIRM has also involved the public in the conduct of its business. For example, in developing the agency's first scientific strategic plan, CIRM held six public hearings and, prior to adopting each of its regulations, conducted public hearings over and beyond the opportunities for public comment provided at Board and subcommittee meetings where the proposed regulations were discussed. CIRM has also invited the public to participate in meetings on important scientific and ethical subjects, such as oocyte donation. The Board's subcommittees also offer an important opportunity for the public to participate in the development of CIRM's policies on matters ranging from intellectual property to CIRM's loan program.

The public also has an opportunity to participate in the meetings of CIRM's Working Groups. Although the Working Groups are not bound by the Bagley-Keene Open Meeting Act, the Board made a policy decision to open these meetings to the public, with the exception of scientific peer review. As the National Academy of Sciences has recognized,

Scientific peer review has long been a feature of decision making at key government funding agencies, such as the National Science Foundation and the National Institutes of Health, as well as at other government agencies and private foundations that support research. In virtually all cases, including the leading federal agencies just mentioned, evaluations of the strengths and weaknesses of specific proposals are carried out in sessions that are closed to the public.

(January 2, 2008 Letter from Ralph J. Cicerone, Ph.D., President, National Academy of Sciences, and Harvey V. Fineberg, M.D., PH.D., President, Institute of Medicine, App. 15.)

With the exception of scientific peer review, the Working Groups have conducted more than 50 public meetings involving matters ranging from the criteria for the evaluation and award of grants to the standards for informed consent for embryo donors. Indeed, all of the meetings of the Standards Working Group and the Facilities Working Group have been conducted in public.

CIRM has also complied with the Public Records Act, responding to dozens of Public Records Act requests. In addition, CIRM responded to two Administrative Procedure Act petitions. Most recently, the Board approved a petition requesting that the agency adopt a regulation defining the term "California Supplier." After several public hearings and meetings, the Board adopted a policy that was widely supported by consumer groups, grant recipients and the commercial sector. CIRM also maintains a robust website that offers members of the public a wealth of materials relating to CIRM's grant awards, policies and upcoming programs and meetings.

2. Communication with the Public

a. Annual Report

The Chairman of CIRM's Governing Board has general oversight of the annual report, giving him the responsibility to communicate with the public regarding CIRM's mission, operations and performance in this report each year. Chairman Klein has continuously championed the inclusion of patient advocates and their stories in the report given the importance of reporting to the public regarding the personal, human terms of suffering and potential hope which the public can understand and empathetically identify as a vital and urgent human need for therapies.

The annual report has also provided a forum for Board members, including Dr. Floyd Bloom who made a special contribution to last year's annual report in the commentary entitled "Disease Team Initiative." In addition, Dr. Harvey Fineberg, President of the Institute of Medicine, and Ralph Cicerone, President of the Academies of Science – at the Chairman's request - jointly wrote a commentary on the importance of confidential peer review for the annual report. The annual report has been a critical tool in communicating CIRM's progress to the Legislature, the Governor, grantees, collaborators and the general public.

b. Spotlights

The Board, under the leadership of Chairman Klein, continually strives to keep patients and patient advocates at the forefront of CIRM communications. The Chairman's Office has organized presentations by scientists, physicians and patients (referred to as "Spotlights on Disease") before most of the meetings of CIRM's Governing Board. These presentations, which, as the name suggests, focus on a particular disease or injury, are

a potent reminder to the Board and the public of CIRM's mission. Each Spotlight presentation is videotaped, posted on CIRM's website, and made available to the public upon request. These videos have proven to be an important tool in CIRM's public communications effort.

c. Press Conferences/Interviews

To enhance the public's understanding of Proposition 71 and CIRM's progress, the Chairman and other members of the Board have helped to organize, and have participated in, press conferences tied to major Board actions, including press conferences with the Governor, the Controller, Speakers of the Assembly Nuñez and Perez, the Mayor of Los Angeles, and other state leaders who have helped raise the level of awareness of CIRM's tremendous progress in advancing scientific research. The Chairman and members of the Board have also participated in press conferences with both state and international governmental, scientific and medical leaders, including: The Governor of Maryland, the Governor of Wisconsin, the Governor of Michigan, the Texas Legislature, State of Victoria Premier Brumby, Premier Bracks and Minister of Innovations Jennings, the Minister of Health for Canada, Lord Drayson (Minister of Science of the United Kingdom), California Senate Majority Leader Dean Florez, Senator Feinstein, Senator Boxer, and Congressman Dreier. Press conferences that feature elected leaders often act as a draw of television news crews, thereby increasing CIRM's ability to communicate with the public.

3. Audits

a. Annual Financial Audit and Citizens Financial Accountability Oversight Committee

Proposition 71 requires CIRM to commission an annual independent financial audit. (Health & Saf. Code, §125290.30(b).) In addition, Proposition 71 established the Citizens Financial Accountability Oversight Committee ("CFAOC"), which is chaired by the Controller, to review the audit and CIRM's financial practices and issue an annual report. The CFAOC has conducted four oversight hearings, supported by reports from the outside auditors and documentation on CIRM's programs, policies, and practices. (See <http://www.sco.ca.gov/eo/cfaoc/>.)

b. Bureau of State Audits

CIRM has also been subject to an extensive performance review conducted by the Bureau of State Audits ("BSA"). BSA staff spent hundreds of hours reviewing CIRM's policies and records and meeting with CIRM staff. BSA staff examined CIRM's strategic plan and policies governing grants management, conflicts of interest, travel, compensation, contracting, and intellectual property. CIRM worked closely with BSA to address each of the issues raised in the review and adopted many of BSA's recommendations before the report was released. CIRM has now implemented each of the recommendations made by the BSA, with one exception.⁵

c. Controller

The Controller conducted a thorough review of CIRM's conflict of interest policies, grant administration, administrative expenses and expenditures in a performance audit that was completed in 2008. Significantly, the Controller found that CIRM has "extensive conflict of interest policies that are modeled after and, in some cases, go beyond the National Institute[s] of Health requirements" and that CIRM had complied with those policies. The Controller also found that CIRM's grant administration policies were based on "best practices" and that CIRM was administering its grants in compliance with Proposition 71 requirements and CIRM policies

⁵ BSA suggested that CIRM seek a formal opinion from the Attorney General regarding the interplay between Proposition 71 and a state conflict provision. Because CIRM is confident of its position, it declined to seek a formal opinion.

and procedures. Finally, the Controller confirmed that CIRM's expenditures were in compliance with Proposition 71 and CIRM's policies and procedures.

d. Little Hoover Commission

The Little Hoover Commission, a state agency whose focus is reinventing government, held public hearings regarding CIRM at the request of the Legislature. Chairman Klein and President Trounson testified before the Commission and submitted written testimony. Although the Commission recommended several structural changes which CIRM's Governing Board opposed, CIRM has adopted several of the Little Hoover Commission's recommendations to improve the performance of the agency. Some of these recommendations are included in SB 1064, which as discussed below, CIRM endorsed.

D. Engaging with the Legislature and Governor

1. 2005 Policy Enhancements

In 2005, as CIRM was being established, Chairman Klein worked with legislative leaders, including the President Pro Tem of the Senate, Senator Dunn (Chair of the Senate Judiciary Committee), Senator Speier (Chair of the Senate Insurance Committee), and Senator Ortiz (Chair of the Senate Health Committee), along with representatives from the Office of the Speaker of the Assembly and relevant Assembly committees to devise policies that ensure public participation and accountability in the grant review process. Through more than 30 hours of meetings and discussions, a consensus developed with the legislative leadership. Chairman Klein presented a comprehensive proposal describing this consensus to the Board at its July 2005 meeting in Sacramento. The Board adopted the proposal endorsed by the legislative leaders and the Chairman. Thus, CIRM strengthened the conflict of interest policies for Working Group members and required disclosure of the members' personal, professional and financial interests. As noted above, these policies go well beyond state conflict of interest laws, which are limited to financial conflicts, and exceed the standards set by the NIH. The Board also agreed to make available for a confidential audit the Working Group members' conflict of interest forms to ensure that CIRM's processes were strong and effective. In addition, the Board agreed to open the meetings of CIRM's Working Groups to the public, with the exception of sessions involving confidential peer review. The Board also agreed that the records of the Working Groups would be subject to the Public Records Act, with the limited exceptions of scientific and medical applications for grants and loans and their peer-reviewed evaluations. To ensure that members of the public have access to the information in all funded applications, the Board requires that every funding recommendation include a public summary of the proposal, the evaluation and the potential benefit to the State of California. Finally, the Board agreed not to amend specific policies adopted in collaboration with the Legislature without a supermajority vote (70% of a quorum to amend policies) and without first providing notice to the Legislature.

2. SB 1064

CIRM, led by Vice-Chairs Art Torres and Duane Roth, worked closely with Senator Elaine Alquist (Chair of the Senate Health Committee) to reach a compromise regarding SB 1064, which incorporates some of the recommendations of the Little Hoover Commission as well as several CIRM practices and regulations. In brief, the bill eliminated the 50-employee cap (while requiring CIRM to remain within the 6% cap on administrative expenditures), permitted the Board to provide reasonable compensation to the patient advocates for their service on the working groups, and codified certain practices and regulations that are already in effect while maintaining the agency's flexibility to make changes in the future. Relief from the 50-person cap was institutionally necessary as the scientific staff expands to provide oversight and guidance over the greatly enlarged portfolio of on-going research, including imminent human trials.

Governor Schwarzenegger signed SB 1064 into law on Thursday, September 30, 2010. The bill will take effect on January 1, 2011.

E. Engaging with the U.S. Congress and Executive Branch

As recent events in Washington demonstrate, federal funding for human embryonic stem cell research remains a controversial topic. Because of the importance of federal support for stem cell research in accomplishing CIRM's mission, Chairman Klein and Vice Chairs Torres and Roth have actively engaged with members of Congress and the Executive Branch in support of CIRM's mission. In addition, CIRM's Governing Board has adopted resolutions supporting federal legislation to protect and/or enhance stem cell research and therapy development activities. These resolutions include extending work product protection periods for biosimilars because of the extremely long development period for cellular therapies. For example, in 2006, Board members worked with the U.S. House and Senate leadership on key legislation to authorize embryonic stem cell research. Also in 2006, the Speaker of the House invited Chairman Klein to be her guest in the Speaker's gallery when she convened her first session as Speaker of the United States Congress. In her first days as Speaker, she declared the Embryonic Stem Cell Bill as one of her top 3 priorities (HB3).

III. Finances

A. Two Competitions for Free Office Space

1. Interim Headquarters

CIRM strives to be an innovative state agency and to look for opportunities to leverage the agency's limited resources. Chairman Klein, sensing an opportunity in excitement generated by the passage of Proposition 71, approached the State Department of General Services, which is responsible for leasing office space on behalf of state agencies, to request the department's approval to create a competition seeking headquarters space without rent, utilities, tenant improvement costs, or furnishing costs. The interim headquarters competition resulted in one year without these costs and an extension for an additional six months was obtained without cost.

The Department of General Services initially resisted the Chairman's request because these terms had never before been achieved for a State agency. The free interim headquarters office space strategy was important to preserve scarce working capital of the agency during the early period of the then-threatened litigation.

2. Permanent Headquarters

To search for permanent headquarters, the Board established the Site Search Subcommittee, which was chaired by Robert Klein and which conducted the search through a competition between cities (and their philanthropic champions) to determine which city could offer CIRM the greatest savings. This competition provided the strategic advantage of combining the strength of philanthropic champions of science with the leaders of California's major city-states as champions of science. This strategic alliance became one of the pillars upon which the major facilities competition was built, including the capacity of applicant institutions to meet the two-year goal for completion of construction and to accelerate the entitlement process.

Ten competing cities offered CIRM office space, conference facilities, and other subsidies with a total value of more than \$100 million. These cities included:

- Alhambra
- Emeryville
- Long Beach
- Los Angeles

- Peninsula cities
- Richmond
- San Diego
- San Jose
- San Francisco
- Sacramento

Through the competitive process, the Board selected San Francisco as CIRM's headquarters based on benefits originally valued at \$17 million for 10 years of free rent and free operating costs on 20,000 square feet of office space, plus 16,000 hotel rooms with 2,000 free and 14,000 substantially discounted over 10 years, and free access to seven conference venues from 300 seats to 50,000 seats for 10 years, as the main benefits. In addition, the Chairman negotiated a supplemental contribution to the tenant improvement work for the agency's headquarters of approximately \$1.55 million. The contract negotiations and the contract terms resulted in the office space providers later having to contribute an additional amount of subsidy, estimated by them at a value of approximately \$3 million, to meet all of the terms negotiated, raising the total benefit to the agency to \$20 million.

No agency in the history of California has ever received a major city subsidy for locating its headquarters in that jurisdiction; this is particularly noteworthy given that, at the time, CIRM could not hire more than 50 employees.

B. Start-Up Loan

To provide the agency with working capital, during the initial stages of the litigation, CIRM drew on a \$3 million loan from the State General Fund as authorized by Proposition 71. In addition, the Chairman (through a referral from Mayor Newsom of San Francisco) negotiated a \$5 million donation from the Dolby family to the agency.

C. Bond Anticipation Notes

As a result of litigation challenging the constitutionality of Proposition 71, the State was unable to issue bonds on CIRM's behalf. The ideological opposition to Proposition 71 intended to prove that they could destroy any democratically-mandated medical research (that they opposed on religious grounds) by merely tying up the initiative with litigation. CIRM, therefore, had to demonstrate that the agency could operate right through the litigation period or the ideological opposition would have exported this model of obstruction to numerous other states. As a result, the Chairman worked with the Office of State Treasurer Phil Angelides Office to create the State of California's first "Bond Anticipation Note" program to issue \$45 million of State of California notes to drive the mission agenda for stem cell research forward, despite the litigation that blocked the sale of state bonds.

Through financial and legal presentations of the Chairman, with the support of Sherry Lansing, Ed Penhoet, Richard Murphy and other Board members, these bonds were privately placed with seasoned investors. The Chairman identified potential investor placements and made presentations on the legal issues to the investors' counsel and participated in follow-up discussions between the investors' counsel and Board counsel.

Bond anticipation notes had never been sold in California's history and, certainly, their sale during constitutional litigation challenging their validity had never been attempted. If the court case had been lost, the investors buying the Bond Anticipation Notes and their attorneys understood that their funds would become a donation to the State of California. Nevertheless, the Bond Anticipation Notes were sold and on April 16, 2006, the first sale closed.

During the litigation, members of the Board and CIRM staff worked together to advance the first grant competition to train stem cell scholars, a program priority first proposed during the NAS meeting in December 2004. The Board approved the selection of the institutions that would be funded for the scholars' program in September 2005. The proceeds from the closing of the Bond Anticipation Note private placement funded 169 stem cell scholars at 16 California research institutions and universities in 2006, more than a year before the litigation ended.

California demonstrated to the nation that a mandate from the state's voters for biomedical research could not be defeated by the legal strategies of ideologically-driven obstructionists. The private placement of \$45 million in bonds also demonstrated to the Governor and to the state's political leaders that the philanthropic leadership of California in each of the major population centers was deeply dedicated to moving this program forward.

D. General Fund Loan

After numerous civic leaders from San Diego to San Francisco communicated their confidence in a positive litigation outcome and their commitment to Proposition 71 by buying \$45 million in bond anticipation notes, Governor Schwarzenegger, at Sherry Lansing's request, agreed to assist with the agency's bridge funding as permitted under Proposition 71. (Health & Saf. Code, § 125291.60.) David Crane, Senior Advisor to the Governor, worked with the Chairman to design and implement this plan. As a result, CIRM received a \$150 million loan from the General Fund pending the end of the litigation. This funding permitted CIRM to begin its research programs in earnest.

The Governor's loan sent a message to California's researchers and patients and to the nation that the implementation of Prop. 71 would now move forward at a very high level despite the fact that the California Supreme Court had not yet considered the challenge to Proposition 71. Governor Schwarzenegger announced his authorization of the funding as a counter-balance to President Bush's veto of the 2006 congressional vote to permit human embryonic stem cell funding, once again putting California at the forefront of this emerging technology.

E. Bond Funding

1. PMIA Loans

Proposition 71 allows CIRM to participate in interim loan funding through the State's Pooled Money Investment Account ("PMIA"). When the financial and economic crisis began in 2008, locking California out of the general obligation bond market for an extended period of time, the Chairman recognized, despite official statements by the State of California to the contrary, the possibility that the State would seek to recapture the proceeds of PMIA loans that had not been expended. As a result, he established a plan to prioritize the spending of the proceeds of the PMIA loan – under a structure designed to leverage the value for the State – before drawing down bond funds, which under Proposition 71 are not subject to transfer.

In early 2008, CIRM requested and received a \$250.64 million PMIA loan that was used to finance CIRM's single largest Request for Applications – the \$271 Major Facilities Grant program. The Chairman, with the approval of the Facilities Working Group and the Board, also devised a discounted upfront payment award pursuant to which eight of the twelve institutions received upfront funding of their research building program in exchange for their agreement to discount the amount of their grant request. This resulted in payments to these institutions in June 2008, roughly 18 months earlier than would have been expected under a last-dollars-in approach. To qualify for the program, the institutions had to have an AA bond rating from Moody's or Standard and Poor, or be part of the University of California system, and unconditionally commit to funding the balance – approximately 75 percent – of the construction costs not covered by CIRM.

This decision proved to be of critical importance for several reasons. First, it permitted several of the major facility grant recipients to begin construction immediately and to take advantage of reduced construction and other costs during the economic downturn. All of these facilities are now in the final phases of opening for research. Second, it permitted CIRM to use the proceeds of its PMIA loan in a manner that maximized the value for the State and provided a substantial infusion to the construction industry in California at a time that it was desperately needed. By the end of December 2008, the Department of Finance had ceased making new PMIA loans and froze the unused funds in agencies' PMIA accounts. If CIRM had not already spent the funds, therefore, it would have lost the ability to use them and CIRM's grantees may have had to halt or abandon construction due to the lack of reliable funding. Without access to this interim funding or bond sales, many state agencies had to shut down projects and non-essential operations. CIRM, by contrast, was able to continue funding all of its commitments without any interruptions.

CIRM, unlike other state agencies, was able to utilize 95% of its PMIA funds (thereby saving access to \$57 million) before those accounts were frozen. Because the Chairman's Office had accelerated the bond sales substantially in advance and in anticipation of this possibility, CIRM funding continued on a timely basis, without interruption. CIRM had a working capital fund of approximately \$200 million (an important level for assurance of institutional and private company participation) throughout this period, funded from bonds; the Chairman negotiated a renewal of the bond private placement program with State Treasurer Lockyer's Office, in case this became necessary to ensure uninterrupted funding. This is in contrast to school district construction programs, other agency construction projects and the state's transportation and housing programs which suffered shutdowns for months.

2. Issuing Bonds

Unlike most state agencies, which are funded through annual appropriations made by the Legislature (and subject to the Governor's line item veto), CIRM is funded through the issuance of state general obligation bonds. In order to authorize the sale of these bonds, Proposition 71 created the California Stem Cell Research and Cures Finance Committee, which is comprised of the Treasurer, the Controller, the Director of the Department of Finance, the Chair of CIRM's Governing Board and two other members of CIRM's Governing Board appointed by the Chairman. (Health & Saf. Code, § 125291.40.) The Committee is charged with authorizing the issuance of the bonds approved by the voters and directing the Treasurer to sell the bonds from time to time to meet CIRM's needs. (*Id.*, § 125291.45(a).) On May 9, 2005, the Committee adopted a resolution approving the issuance of \$3 billion of state general obligation bonds on behalf of CIRM. Before each issuance of bonds, the Committee meets to direct the Treasurer to make a sale.

In the fall of 2007, the State issued \$250 million of bonds on CIRM's behalf – the nation's first sale of Stem Cell Bonds. The sale was met with overwhelming success with more than 40% of the bonds purchased by retail (individual) investors, a nearly unprecedented level of retail demand for this time period. These bonds represented the financial realization of the paradigm shift of California in recognizing scientific and medical research as an intellectual capital infrastructure asset that builds a future for California's healthcare system and job base infrastructure.

Since the fall of 2007, the State has issued \$505 million in federally subsidized Build America Bonds (2009) and \$161.545 million (2009) and \$112 million (2010) in taxable bonds, all of which has permitted CIRM to provide stable funding to its grantees and to assure CIRM's international collaborators that CIRM has the funds necessary to support joint research programs. Each bond sale required CIRM to present detailed information regarding its current and future grant programs and expenditures. The Chairman's Office coordinated closely with the Governor's Office, the Department of Finance and with the State Treasurer's Office, on each of these bond sales.

3. Continuous Appropriation and Stability of Funding

A long-term commitment of the funding source is critical to provide adequate assurances to attract the best scientific talent and to permit complex long-term scientific challenges to be undertaken. The stability of the funding – its insulation from interruption – is critical, providing the security to embark on challenging, innovative research with a long development path, and to attract major philanthropic, biotech and institutional matching fund commitments.

Proposition 71 provides this stability. First, it added Article XXXV to the California Constitution to create the constitutional authority to conduct stem cell research and to ensure that funds authorized by the voters would be used exclusively for the purposes specified in Proposition 71. Second, article XXXV, section 4, of the California Constitution expressly states that the proceeds of the bonds authorized by Proposition 71 **“shall be continuously appropriated without regard to fiscal year, be available and used only for the purposes provided in this article, and shall not be subject to appropriation or transfer by the Legislature or the Governor for any other purpose.”** Thus, neither the Legislature nor the Governor has the authority to transfer or appropriate CIRM’s funds for another purpose, such as balancing the State’s budget.

4. Aligning Burden of Costs with Benefits of Research

Any process of appropriations or funding that draws down current funding resources to pay for intellectual medical research capital creates a misalignment between the intended medical benefit group and the group paying for the investment. Consider the Salk vaccine as an example: it created massive improvements in health and cost savings through the avoidance of broad scale polio over the last 50 years. For the United States alone, in the late 1950s, it was estimated that by 2005 it would cost US\$100 billion per year just to maintain polio victims in iron lungs, housed in hotels, specifically developed to meet the scale of victims anticipated. Clearly, American society has benefited over a number of generations from the successful research investment in Intellectual Capital made in the 1950s. Yet, the cost of developing the vaccine was borne solely by the generation of that time.

To bring the costs of medical research and the benefits in alignment, the research investment, under the Proposition 71 political-economic philosophy, should be funded through long-term capital financing structures such as state, national or international bonds that amortize the cost over the benefiting generations. By utilizing bonds that spread the cost over 30-50 years, the critical mass of financial assets that can be marshaled in the near-term increases enormously. California’s Proposition 71 demonstrates the power of this concept, even at a state level, to lift an entirely new field of medical Intellectual Capital – Stem Cell Research – from an exploratory phase, into an intense medical revolution. Proposition 71 also demonstrates the positive ripple effect that can occur when one jurisdiction undertakes to align the research cost structure with the benefiting group. Once one major state or nation demonstrates a commitment to raise vast sums of capital through long-term bonds, other states and nations will be encouraged, if not compelled, to raise their investment in Intellectual Capital to remain competitive in the future research advances and commercialization of this broad-based Intellectual Capital Asset: the development of Stem Cell Therapies for Chronic Disease and Injury.

5. IRS Private Letter Ruling

Aside from California, until Texas copied part of this model with a 2006 initiative and a 2008 bond sale, there had been no state in the United States and there is no country that has been identified which has sold general obligation bonds to fund comprehensive scientific and medical research programs: the intellectual infrastructure of the 21st century. The Chairman’s Office worked with the Treasurer’s Office, and the State’s bond counsel, to structure the first intellectual capital general obligation bond issue in this country.

With the exception of bonds sold to finance the construction of facilities, CIRM's bonds have been sold as taxable bonds, which offer a higher rate of interest than a comparable tax-exempt bond. Recognizing the need to optimize the Institute's bond financing structure and reduce the state's borrowing costs, the Chairman has worked with the State Treasurer's Office and bond counsel to seek an IRS private letter ruling (PLR) determination that CIRM's bonds qualify for tax-exempt status. The Chairman, along with Lynn Harwell, Scott Tocher, representatives from the Treasurer's Office, bond counsel and Board counsel, met with the IRS to discuss the private letter ruling request. Based on the information obtained during this meeting, the Chairman and his staff are working with bond counsel to finalize the request. If the IRS were to rule in CIRM's favor, it would further reduce the State's borrowing costs by approximately \$300 million for the interest paid on the \$3 billion bond proceeds. The Legislative Analyst's project of state interest costs in the ballot pamphlet has, nevertheless, been highly consistent with the actual interest rates incurred over the first \$1 billion in bond borrowings, despite the impact of state budget politics on the state's bond rating in the interim.

F. Cap on Administrative Expenses (General Administration and Grants Administration)

As a mission driven agency with defined goals, unlike other state agencies, CIRM's administrative expenses (i.e. overhead or operating expenditures) are expected to rise to a plateau, level off, and then decline over a phase-out of the program if no additional bond authorization is approved to continue the mission. As CIRM continues to ramp up and increase its funding commitments, it is expected that additional staff and overhead expenses will be necessary to ensure accountability of public funds as well as to enable compliance with CIRM regulations. Proposition 71 expressly limits administrative expenses to no more than six percent (6%) of the \$3 billion in authorized bond sales (i.e. three percent [3%] for general administration and three percent [3%] for grant administration). These operating expenditures must be balanced to ensure that CIRM can meet its mission and remain staffed until its research funding programs close out (CIRM anticipates that its final grant program funding will terminate in FY 2019-2020, with the last Governing Board approval of grant and loan awards in approximately 2017). Because of an expected exposure to litigation and numerous statutory and legal regulatory processes, legal costs are excluded from this limitation, although they have remained moderate exclusive of the early litigation period.

To date, CIRM's operating expenditures have been significantly below the six percent (6%) maximum as compared with total bond sales and/or funding commitments. CIRM's expected total operating expenditures from inception through FY 2010-2011 represent approximately 4.9 percent. Additional constraints on CIRM's operating expenses include the salaries that CIRM may pay its employees. The Governing Board is required to set salaries for CIRM's employees based on the salaries paid to employees in comparable positions at University of California medical schools and other non-profit research institutions in California described by qualitative criteria in Proposition 71. Thus, CIRM's efficiency is a model for state government and is unrivaled in the private sector where average operating costs for the highest rated private foundations are typically in the 12 percent range for a comparable operating scope of responsibilities.

G. Funds Available for Research and Facilities

1. Allocation of Funds

In addition to restricting administrative costs, Proposition 71 specifies the allocation of funds for research and facilities, and limits the amount of funds that CIRM may commit in a year. (Health & Saf. Code, § 125290.70.) Thus, Proposition 71 specifies that 97 percent of the net proceeds from the sale of bonds must be used for grants, loans and grant administration costs. Additionally, of the amount available for grants and loans, no less than 90 percent must be used for research. For the first ten years, CIRM's research funding commitments are

subject to a yearly cap, but unused capacity may be carried over to one or more following years. A diagram depicting the allocation of CIRM's \$3 billion authorization is attached to this report.

Given the lack of adequate support for several years from the federal government in the nascent field of stem cell research and regenerative medicine, critical funding gaps arose for the financing of facilities to house and enable this critical research. To address this gap, up to 10 percent of CIRM's net bond proceeds (less general administrative costs and bond issuance and capitalized interest costs) are available to build scientific and medical research facilities.

2. Research Awards

To date, CIRM has committed \$1.013 billion to multi-year grants and loans for research. These programs cover the entire spectrum of research funding from basic research to translational research. CIRM has also funded training programs for young researchers and for technical staff. For more information about CIRM's scientific programs, please refer to "A Brief History, Current Status Report, and Options for Next Steps."

Proposition 71 imposes a cap on indirect costs of twenty-five percent (25%). (Health & Saf. Code, § 125290.70(a)(5).) Unlike the National Institutes of Health, however, facilities costs are considered "direct" costs. (*Id.*, § 125292.10(u).) Thus, CIRM more closely follows the Howard Hughes Medical Institute in connection with the reimbursement of facilities costs.

3. Facilities Awards

a. Shared Labs

The primary goal of the Shared Labs program is to provide dedicated laboratory space that is free of NIH support, equipped to grow and maintain hESCs, where investigators can conduct research on hESC lines including those that are prohibited by federal policy. Funds were provided for renovation of laboratory space and for major equipment necessary for culturing and analyzing hESCs. The laboratories serve as a shared resource with available core equipment and trained personnel; available not only to stem cell scientists at the grantee institution but also to those from nearby institutions without such facilities. These dedicated, common laboratories encourage optimal sharing among individual investigators, research groups and departments, foster a collaborative, multidisciplinary research environment, and promote cost effectiveness.

b. Major Facilities

CIRM also created a major facilities program to provide dedicated research facilities that are free of NIH support where investigators could conduct research on the whole range of stem cell research, including hESC research. These new facilities were intended to protect against a recurring risk of legislative or judicial changes to federal policy governing the use of federal funds for hESC research, as well as a platform to accommodate the substantial expansion of stem cell research in California. CIRM's Governing Board allocated \$270 million for construction and equipment as part of the major facilities program, resulting in the funding of a \$1.15 billion facilities and equipment program.

The CIRM Major Facilities Program involved a two-part review. First, applicant institutions were required to submit an application to justify the scientific need for a new research facility. The Grants Working Group reviewed the scientific merit of the proposals and made recommendations to the Board, which invited select institutions to submit a second application describing the proposed facility in great detail. The Facilities Working Group reviewed these applications to evaluate the merits of the facilities proposal, including leverage.

In 2007, the Board created a rating system for the second part of the major facilities competition that included leverage as a key rating factor. (In writing Proposition 71, Robert Klein specifically established that the Chairman would “optimize all financial leverage opportunities for the Institute”. In 2006, in a public session on the strategic plan, he introduced “financial leverage” as one of the “strategic principals” and goals of the agency, and the Board specifically adopted this goal.) As a result, the institutions throughout the state understood that they would have to meet very high leverage/matching fund standards to qualify for a major allocation of the \$270 million set-aside for the major facilities competition. When the final decisions were made, the agency’s \$270 million of bond funds was matched by \$880 million in the combined total of facilities funding of \$560 million and an additional \$320 million for major facilities fixturation, equipment, and faculty hiring support.

The Board worked with a number of institutions and/or donors to assist in raising funds, including assisting a number of institutions with creative structures and/or problem solving to support their CIRM Major Facilities. For example, the Sanford Consortium for Regenerative Medicine and the Buck Institute each faced substantial challenges in proceeding with their projects. The Chairman worked closely with both institutions in an effort to remove the barriers to the projects. In the case of the Sanford Consortium, for example, the Chairman worked with Board counsel and Board staff as well as the leadership of the Consortium, including Dr. Ed Holmes, T. Denny Sanford, Irwin Jacobs, John Moores and Louis Coffman, to establish an escrow account and a unique multi-tier funding program in order to assure the Consortium’s lenders that CIRM had the resources necessary to satisfy its commitment under the grant award and reciprocally to assure the Board of the Consortium’s performance.

Given an estimated shortfall of major facilities funds and secondarily to reach quality scientific and clinical projects beyond the funding capacity of the Board’s \$270 million funding set-aside, even with the known matching funds, the Chairman introduced for Board consideration and adoption two innovative concepts: By working with facilities’ sponsors on their discrete needs for facilities and class-one equipment, as compared to class two equipment, an additional \$30 million of class two equipment funds was added to the total available funds for the competition to bring the total to \$270 million.

By developing an innovative front-end funding program for high credit quality institutional sponsors of major facilities, the institutions were able to save sufficient funds prospectively to provide a \$16 million discount to their requests to the agency. Effectively, \$286 million in funding was provided with \$270 million from the agency.

H. Leveraging CIRM Funds

1. Philanthropy

In addition to the private donor leverage that CIRM generated in support of its headquarters and major facilities program, CIRM has also drawn significant support from philanthropists and ordinary citizens. CIRM has received substantial gifts from the Dolby and Goldman families and smaller gifts from dozens of other members of the public who support CIRM’s mission. These funds enhance CIRM’s ability to accomplish the mission with which the voters entrusted it.

2. Collaborations and International

CIRM has established joint research funding programs with other states, countries, and provinces and states within countries. Pursuant to these collaborations, CIRM funds researchers in California while the other countries and states fund their own researchers in collaborative research projects.

In 2006, after the President of the University of California system asked the Chairman to participate in a California-Canadian conference on scientific and industrial collaboration, Robert Klein was named co-chair of the California-Canadian Joint Task Force on Cancer Stem Cell Research. In 2007, at Robert Klein's request, Governor Schwarzenegger added a stop to his official trip to Canada to visit the Toronto Mars Biomedical Research Center and to deliver a major address, with Ontario Premier McGuinty and Robert Klein as supporting speakers, focusing on the potential cancer stem cell collaboration between California and Canada.

In 2007 and 2008, to advance this collaboration with Canada and to develop cooperative resources for bilateral funding with CIRM, Robert Klein accepted an appointment to the Board of Genome Canada, a \$1.8 billion genetics research funding public corporation created by the Canadian federal and provincial governments and their funding agencies to understand their best practice standards and their administrative practices governing large multi-year grants for research while providing Canada with information regarding California's new models and best practices for biomedical research funding. As a member of the Genome Canada board, the Chairman advocated for and voted on Canadian funding for a collaboration with CIRM, but he recused himself from voting on CIRM's bilateral agreement with Canada. Subsequently, the senior staff of Genome Canada has assisted the California agency in exploring best practice models for administration of the disease team grants. In the summer of 2008, Robert Klein resigned from the Genome Canada Board to avoid potential conflicts with joint funding proposals with the agency. Genome Canada is now part of the collaboration of the Canadian Cancer Stem Cell Initiative and California cancer stem cell research scientists funded by CIRM.

In 2008, with the leadership and collaboration of Dr. Alan Trounson, this effort culminated in a bilateral agreement with Canada to put up \$100 million for Canadian scientists working with California researchers on cancer stem cell research.

In 2006, 2007, and 2008, the Chairman worked with the leadership of the State of Victoria, Australia, and Dr. Alan Trounson, originally on the passage of federal legislation in Australia to fully authorize embryonic stem cell research. Shortly after Dr. Trounson was recruited as president in 2007, the Premier of the State of Victoria, John Brumby, asked Robert Klein and Dr. Trounson if a vibrant intercontinental scientific exchange could be created between Victoria and California. Robert Klein suggested that this relationship could follow the model of the bilateral funding then proposed for Canada and California. Klein and Trounson called this proposal the "Scientific AirBridge to Australia." Now, with Dr. Alan Trounson as President of the agency, this relationship has evolved into a bilateral agreement with the State of Victoria to support Australian scientists collaborating with California stem cell researchers funded by CIRM.

CIRM has entered into collaborative funding agreements with Spain, the Spanish Province of Andalucía, the United Kingdom, Japan, Germany and China. These collaborative funding arrangements leverage CIRM's funds by requiring CIRM's collaborators to fund researchers in their own countries or states to work with CIRM-funded researchers to push CIRM's mission forward. Scientists in these world-leading stem cell research nations can file team applications with their California counterparts; grant awards for the research approved for each jurisdiction is funded by that jurisdiction. The scale of the portfolio that permits large-scale grants and the broad-based developments of scientific capacity in California, with the assurance of long-term stable funding, incentivizes and enables a sustained level of comprehensive international collaboration on translational medicine that has rarely been achieved. Once the threshold transactional costs of building a funding relationship have been invested, additional collaborative relationships on complementary research in immunology and/or basic science can also be advanced.

3. Other States

Besides the benefit of scientific leverage and the potential to advance therapies more quickly through interstate collaborations, it is critical that California not become an isolated leadership outpost for stem cell therapies in the United States. A major political coalition of states backing the full range of stem cell research is essential to

retain the support of Congress, the President, the FDA and the American public who must be broadly prepared to understand and accept this new research and the cellular therapies that arise from it.

In 2005, 2006, 2007 and 2008, the Chairman's Office worked with the Governor of Wisconsin and Wi-Cell, affiliated with the University of Wisconsin, to advance federal legislation permitting embryonic stem cell research with NIH funding. In addition, a collaborative relationship was established that facilitated Wi-Cell announcing that California stem cell researchers could utilize Wi-Cell patents for research purposes, without financial payments and elaborate documentation.

Also, the agency worked with the Governor of Maryland to establish a collaborative, bilateral funding relationship between the two states' stem cell programs. Similarly, early meetings have been held with the Governor of New York to encourage a New York stem cell initiative; a collaborative funding agreement between the New York Stem Cell Foundation and CIRM is now in place. The Chairman has also met with the Governor of Michigan and the Lieutenant Governors of Ohio and North Carolina to assist them in the early stages of planning for potential bilateral funding agreements with California.

Given the critical stem cell research leadership in Wisconsin, and the vital patent holdings of Wisconsin on human embryonic stem cells, the Chairman has continued to meet and work with the Governor of Wisconsin on bilateral scientific exchanges and a potential bilateral funding agreement.

I. Loan Program - Evergreen and Leverage

To achieve the goal of commercialization of stem cell research-related products, CIRM will fund for-profit (commercial) research institutions in California through and loans. These loans will be targeted at the funding gaps in product development that will serve to leverage participation by follow-on investors, such as venture capital and other capital markets, and result in more products that enter the market. For the state and CIRM, the advantage of a loan program versus a grant is the ability to recycle CIRM research funds, enlarging the return for each CIRM research dollar expended. In addition to loan principal and interest, loans also feature warrant coverage, depending on the type of loan, which will provide a risk premium for CIRM's commitment.

IV. Loan Program

A. Policy

The Chairman's Office and the Loan Task Force, chaired by Duane Roth, along with the Board Finance Subcommittee, chaired by Michael Goldberg, and CIRM staff developed CIRM's loan program. It is estimated by PricewaterhouseCoopers that the loan program is sustainable with a recovery of capital and 20% growth, even with a 30-50% nonperformance rate for research and therapy development loans. The loan portfolio will grow from capital recovery, interest income and stock warrant proceeds from successful products. It is expected that in the first 14 years, this program of \$500 million can result in over \$1.1 billion in program funding, adding substantial leverage to the agency funding assets. Significant matching funds are already apparent in the involvement of several biotech companies in CIRM grants or loans and in the international companies involved in CIRM's international funding collaborations.

B. Loan Program Objectives

The goal of a loan program is to fund the translation of research into research tools, medical diagnostics and devices and therapeutic products. These loans will be targeted at the funding gaps in product development that will serve to leverage participation by follow-on investors, such as venture capital and other capital markets,

and result in more products that enter the market. With clinical trial period matching funds, the loan program may add an additional \$500 million to \$1 billion in capacity.

C. Review of Loan Applications

The review of a loan application is conducted in the first step in the same manner as an application for a grant, with the application being evaluated and scored on its scientific merit by the Grants Working Group. A loan application must also submit detailed financial information with regards to the company's financial status and management team. An outside consultant verifies this information and performs due diligence regarding the loan applicant. To date, CIRM has funded only one loan. However, the agency is continuing to improve the loan program to make it attractive to potential companies and it anticipates that the volume of loans will increase as CIRM funds more clinical research.

CONCLUSION

The Stem Cell Revolution Is Launched

The tragedy of George Bush's restriction of federal funding for embryonic stem cell research (beyond 10-12 viable cell lines) created a gift for California. While virtually all United States' stem cell research was hobbled by ideological restrictions, California voters passed Proposition 71, funding a substitute national program across the entire range of stem cell research and propelling California into national and international leadership. A recent study funded by The National Science Foundation (NSF) stated, "California has established itself as a major center for stem cell research. Recruitment of world-class stem cell scientists from across the globe has been a direct result of CIRM funding." The study summarizes Proposition 71's impact by stating: "In its short history, the CIRM has taken on a vigorous life of its own. It is apparent that the shift of a major focus for stem cell research to California will have a significant effect into the future on the geographic distribution of biological science and biotechnology infrastructure in the United States; on the location of university, biotechnology, and pharmaceutical research and start-up firms; and on the investment of venture capital. Evidence for this is the \$300 million the CIRM has invested in stem cell facilities, already leveraged to more than \$1 billion in linked donations."