CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

2008 STRATEGIC PLAN UPDATE

STAKEHOLDER DRAFT— 1-28-09

INTRODUCTION

In November 2004 the voters of California adopted Proposition 71 (the California Stem Cell Research and Cures Act) authorizing the issuance of $3 billion in state bonds over at least ten years to support stem cell research in California.[1] The goal of the initiative is:

"To support and advance stem cell research and regenerative medicine under the highest ethical and medical standards for the discovery and development of cures, therapies, diagnostics and research technologies to relieve human suffering from chronic disease and injury."

The Act created the California Institute for Regenerative Medicine (CIRM) and charged the Agency with determining the most effective means of distributing state funds so as to accelerate the entire field of stem cell biology and regenerative medicine.

In December 2006 CIRM published its first Scientific Strategic Plan, which served as the blueprint for CIRM's scientific programs and procedures for program implementation. CIRM's current leadership extends their deepest congratulations and gratitude to the authors, contributors, and science team that developed the 2006 Plan. The 2006 Strategic Plan has served the agency well over the last two years and has been of enormous value in guiding CIRM to remarkable progress. CIRM continues to rely on that Plan as the foundation upon which this update is based.

As a responsible steward of public funds, CIRM must periodically reevaluate both its funding priorities and operations to stay sharply focused on those research opportunities most likely to achieve therapies and cures. The 2006 Scientific Strategic Plan was intended to be a "living plan – flexible in response to its successes and failures, and opportunistic in capitalizing on unforeseen scientific developments." Formal assessment by an outside panel and revision as necessary to the 2006 Plan was recommended at years three and seven. Year 1 for the plan was designated to start July 1, 2007, making the first formal assessment due around July 2010. As we approached the halfway point to this review CIRM leadership felt it was imperative to look at its operations compared to that outlined in the operational section of the 2006 plan [A Fast Start: The First 1,000 Days, page 101] and to consider any strategic adjustments to the plan itself to reflect the current state of the field.

The purpose of this 2008 Strategic Plan Update, "*Accelerating the Movement Toward Cures: The Updated Strategic Plan of the California Institute for Regenerative Medicine*," is to build upon the solid foundation of the 2006 Plan by identifying new research directions for CIRM that reflect the rapidly changing scientific landscape of stem cell science and amalgamate the evolving thinking of CIRM's Governing Board (the Independent Citizens Oversight Committee, ICOC) and of CIRM's staff and many stakeholders regarding the most efficient means of operationalizing CIRM's goals. The governing board and staff have already approved or implemented several strategic and operational diversions from the 2006 plan, particularly the specific steps outlined in "The

[1] An additional $3 billion in interest payments will be spent over 35 years, creating the total investment $6 billion.

First 100 Days Operational Outline." More change is envisioned if CIRM is to maintain consistency with the core values and principals outlined in 2006: accountability, adaptability and innovation.

This document also reflects the vision, priorities, and scientific guidance of Dr. Alan Trounson, who became CIRM's President on December 31, 2007, and who initiated this planning process. Dr. Trounson is eager to move CIRM to its next level of scientific excellence and success by stimulating the development of a scientific "pipeline to cures" that bridges stem cell research from its discovery stages to its clinical applications. The 2008 plan thus calls for significant increases beyond the 2006 Plan in the types of research targeted to elicit therapeutic candidates, and it envisions significantly more investment in "disease team" awards, translational research awards, and collaboration with industry—the final conduit for transforming research advances into commercial therapies for patients.

Additionally, the 2006 Plan focused primarily on CIRM's scientific aspirations, strategic framework and planned scientific initiatives. This update expands on aspects that are relevant to a maturing the agency, cultivating CIRM's leadership role in stem cell research, and CIRM administration. This operational report to the board follows the strategic update.

Building upon the values and foundation expressed in this first Plan, the specific operational goals of the 2008 Strategic Plan Update are as follows:

2008 SCIENTIFIC OPERATIONAL GOALS

- Outline a process for updating CIRM's future research programs in light of the rapidly evolving developments in stem cell science and regenerative medicine.
- Recommend an option for developing robust systems for capturing and evaluating the results of CIRM-funded programs and for sharing these data in ways that accelerate the field.
- Map a plan for accelerating progress to meet CIRM's demanding ten-year therapy goals through the "pipeline to cures" by more efficiently organizing CIRM's portfolio to bridge CIRM-funded basic stem cell research and translational, pre-clinical, and clinical research.
- Reassess and consider ways to enhance CIRM's relationships with the biotechnology and pharmaceutical industry -- relationships essential to delivering to lifesaving therapies based on stem cell research to patients.
- Propose new ways for CIRM to lead stem cell science and regenerative medicine by developing more formal mechanisms for sharing expertise and collaborating with partners in the scientific community, both nationally and around the world.
- Consider methods for monitoring and improving, where appropriate, the medical and ethical regulations governing the conduct of CIRM-funded research.

2008 ADMINISTRATIVE OPERATIONAL GOALS

- Measure and learn from CIRM's successes and shortcomings in achieving the goals set in the 2006 Strategic Plan.
- Evaluate CIRM's internal operations so as to improve efficiency, communication, and integration and to provide an ideal workplace for staff.
- Define ways of establishing a real-time financial reporting system that includes both operational and grant funding, to ensure that CIRM's expenditures are continuously and transparently monitored and to facilitate scientific portfolio management,
- Collect and analyze information on the impact of CIRM as an economic engine and as an additional mechanism for sustaining CIRM financially,
- Encourage the development of a "stem cell science culture" in California by taking a leadership role in educating and informing the general public, including special interest groups and California students of all ages.
- Identify new procedures and methodologies that will expand public transparency, understanding and support of CIRM's operations.

STRATEGIC ADJUSTMENTS UNDER CONSIDERATION

In order to achieve the operational goals noted above some adjustments to the 2006 strategic plan need to be considered. For these CIRM is seeking input from the general public, industry, patient advocates, other stakeholders, and ultimately our governing board. We expect to gather valuable ideas from meetings scheduled with industry leaders February 3 and 20, and from meetings with the general public in early March.

Among areas under consideration:

• the CIRM Governing Board has already approved the allocation of up to $210 million for Disease Team awards, which represents a near doubling of the funds allocated to this award category in 2006. Are these multi-disciplinary teams the best tool for CIRM's efforts on the clinical side of the pipeline, and should they subsume the Clinical and Tissue Engineering RFA's that were forecast in 2006, or do these RFA's need to remain separate?

• while CIRM needs to continue to fund the full spectrum from basic to clinical research, with NIH now able to fund the basic embryonic research, should CIRM consider some reallocation toward clinical?

• CIRM's science office has consolidated many of the RFAs envisioned in 2006, in part because it was not feasible to manage 12 grant cycles per year, but more so, in order to move toward a smaller number of core grants, which are predictable for grantees and can having rolling priorities that reflect that state of the stem cell science at the moment of each RFA (see page 27). Should CIRM continue to move toward reliance on these core grants?

• In light of recent science advances in using stem cells as research tools should CIRM increase the resources it allots to non-cell therapy uses of stem cells? For drug development assays? For disease modeling and small molecule drug discovery?

• CIRM has embarked on a series of MOUs with funding entities from other countries in order to foster collaborations between Californian researchers and top stem cell scientists around the world. Are these MOUs outlined on page 33 the best way to leverage California's investment with the broader scientific community?

• CIRM has started to reach out to industry more proactively recognizing the need and benefit of partnering with California's vibrant biotechnology community to translate basic discovery research into clinical application. Some specific options are outlined beginning on page 29, are these the best approaches.

• Current economic models do not work well for cell-based therapies either for clinical trial funding or for reimbursements for the products that result. Should CIRM fund economic policy research in how your fund phase 3 cell-based trials and how you reimburse for curative therapies?

THE CHANGING SCIENTIFIC LANDSCAPE OF STEM CELL BIOLOGY

Many discoveries, too numerous to cite in detail here, have been made in stem cell biology since November 2004 when California voters created CIRM. For example, research teams have:

- Made major strides in understanding the differentiation pathways that stem cells take as they divide and change into more specialized cells such as neurons or heart muscle;

- Discovered that at least one type of adult stem cell (mesenchymal cells) is itself immunosuppressive and somewhat privileged from attack by the immune system. These cells may avoid some of the roadblocks that other cells face related to immune system destruction of transplanted cells;

- Used stem cells in novel ways to uncover the root causes of disease and, in so doing, revealed targets for traditional drug therapy;

- Found ways to use stem cell lines to screen drug candidates for potential liver and cardiac toxicity.

Four advances in particular stand out, either for transforming the scientific landscape of regenerative medicine or for illustrating the enormous potential of this technology. They are:

1) Induced pluripotent cells

In November 2007, companion papers emerged from the laboratories of Shinya Yamanaka[2] at Kyoto University in Japan and James Thompson[3] at the University of Wisconsin (followed rapidly by the work of George Daley and colleagues[4]) demonstrating that when adult human skin cells are transduced to express genes that are normally active together only in embryonic stem (ES) cells, they can be reprogrammed to become pluripotent (induced pluripotent cells or iPS cells). Like embryonic stem cells, iPS cells have the potential to generate all the cell types of the body.

Research into iPS cells will inform human embryonic stem cell biology and vice-versa. Whether significant developmental differences exist between iPS cells and authentic

2. Takahashi, K. et al. Cell 131, 861–872 (2007).
3. Yu, J. et al. Science 318, 1917–1920 (2007).
4. Park, I-H et.al. Nature 451,141-6 (2008).

human embryonic stem cells, which remain the gold standard for pluripotency, is currently the subject of extensive research. However, it is clear that research must continue on all types of stem and progenitor cells. (See ISSCR Open Letter to the Community, Appendix x). While the original method of generating iPS cells -- using retroviruses to shuttle genes into chromosomes -- is associated with increased cancer risk, further research is rapidly resolving this risk.

CIRM supports the use of iPS cells as models of disease, an approach that has been referred to as 'diseases in a dish.' Several promising opportunities are based on iPS cell research, including establishing patient-specific iPS cells, investigating the heterogeneity of complex disease, and screening for new therapeutic drug candidates to block or delay disease expression.

iPS cells have dramatically changed the landscape of stem cell biology, opening up a new avenue of research. Scientists are just beginning to learn how iPS cells might complement both research into, and medical applications of, embryonic, fetal, placental, and adult stem cells. Ultimately, iPS technology holds great promise for improving the therapeutic options for patients with a variety of conditions.

2) Cancer stem cells

Equally significant are research studies that strongly suggest that certain cancers contain within them a rare population of insidious cancer stem cells. These stem cells were first identified in leukemia, and recent studies suggest that certain solid tumors and other blood cancers contain rare populations of stem-like cells that drive tumorigenesis. Cancer stem cells may well play a role in the recurrence of cancers or in the metastasis of cancer cells in patients who have undergone radiation and chemotherapy treatments. Although "the" solid organ cancer stem cell has not been definitively identified in all cases, research into cancer stem cells will nevertheless promote greater understanding of self-renewal, a trait shared by both tumors and stem cells. If common mechanisms of self-renewal are identified, stem cell research could lead to novel approaches to containing cancer. This merging of the power of stem cell research and cancer biology to target the identification, isolation, and elimination of cells that promote cancer's survival is a major scientific opportunity worthy of CIRM's support

3) Clinical trials based on stem cell research

In April 2008, the Federal Drug Administration (FDA) convened a conference at which the safety of human embryonic stem (hES) cell-derived therapies was discussed. No human embryonic stem cell-derived cell therapies have yet received FDA approval, but the conference was an important landmark in stem cell biology, opening a window on the enormous body of pre-clinical data collected by scientists in biotechnology companies that will ultimately lead to human ES (hES) cell-derived cell therapies.

In recent years the numbers of clinical trials have increased using bone marrow-derived mesenchymal stem cells (MSCs) for severe graft vs. host disease, myocardial infarction and cardiomyopathies, autoimmune diseases such as lupus and Crohn's disease, cirrhosis, and others. These therapies are generally not regenerative, and most experts do not

believe that MSCs themselves generate new heart muscle directly; rather, they appear to provide benefit by improving the endogenous regenerative capacity of the host. Nonetheless, the experiences gained from using these stem cells, as well as cells derived from ongoing fetal and umbilical cord cell therapies, will certainly inform all of stem cell biology.

Stem cells can also be used to elucidate disease pathways and to point to novel therapies, as highlighted by the work of CIRM grantee Catriona Jamieson (UC San Diego), who identified a novel drug therapy for *polycythemia vera* (a disease of the red blood cells that can lead to stroke or leukemia) through her stem cell assay research. This work resulted in a clinical trial less than two years after the assays were initiated, showing the importance of stem cell-based assays to the field of stem cell biology.

4) Expanded federal funding for human embryonic stem cell research

As this updated strategic plan was being drafted, President Barack Obama was expected to reverse the Bush administration's restrictive policies on federal funding of human embryonic stem cell research. CIRM welcomes this development and anticipates it will usher in a period of increased opportunities for collaboration and stronger partnerships targeting stem cell biology and medical applications. The elimination of the restiction on using equipment purchased with federal dollars will alone free up many labs for immediate collaborations, even without new dollars.Through its first two-plus years of stem cell research funding, the Agency and its grantees are well positioned to play a leadership role in this changing national environment, which will help accelerate the development of stem cell-based therapies for patients.

IMPLICATIONS FOR CIRM

While the advances paint an enormously bright future for the stem cell field, they also create significant challenges for CIRM as a funding organization As one of the largest funders of stem cell research in the world and a steward of public funds, CIRM has a unique responsibility to be a national and international leader in stem cell biology and regenerative medicine.

International leadership requires that CIRM be ahead of the curve in stem cell science and capitalize on the most innovative thinking in the field. CIRM must manage its agenda and expectations, recognizing that while some advances may be achieved in a few years, others will take longer, some much longer.

The unknowns in this young field are so vast that, for many goals, predicting a timeframe is difficult. One example is the prospect of transplanting cells derived from pluripotent cells into patients, whether to cure disease or to replace damaged tissues. This therapy will require not only major new insights into generating and differentiating stem cells and controlling their growth and physiology, but also special guidelines crafted by the U.S. Food and Drug Administration (FDA) to regulate the safe use of transplanted cells in patients. FDA's approval of the first such trial January 22 was a major ground breaking

stride for the field. But that trial by Geron Corporation in recent spinal cord injury patients is a first step of a very lengthy process.

The last few years have been marked by groundbreaking new directions in stem cell biology – some of which were impossible to predict. The next few years will likely yield similar, sudden advances. CIRM's flexibility to respond to the attitude changes and new developments in science is essential for these discoveries to pay off in improved patient care.

ACHIEVING OUR GOALS/PROGRESS TO DATE

Because of the rapidly changing landscape of stem cell science and CIRM's progress over the past two years, the CIRM scientific team is even more confident now than in 2006 that the five-year and ten-year goals set in the original strategic plan are achievable. CIRM affirms its commitment to these goals and notes that a few have already been attained.

Ten-Year Goals (to 2017)

CIRM commits to the following ten-year goals:

- Goal I: CIRM grantees will have clinical proof of principle that transplanted cells derived from pluripotent cells can be used to restore function for at least one disease.
- Goal II: CIRM-sponsored research will have generated therapies based on stem cell research in Phase I or Phase II clinical trials for 2-4 additional diseases.

  [*One such trial is underway*.]
- Goal III: CIRM funded projects will have achieve sufficient success to attract private capital for funding further clinical development of stem cell therapies.
- Goal IV: CIRM will have funded new approaches for achieving immune tolerance for transplantation that are in pre-clinical development.
- Goal V: Using stem cell research, CIRM-funded investigators will have established proof of principle in preclinical animal models for the treatment of 6-8 diseases.
- Goal VI: CIRM-funded investigators will have created disease-specific cell lines for 20-30 diseases and used them to gain new information about pathogenesis, to identify new drug targets and to discover new therapeutics.
- Goal VII: CIRM will have enabled development of new procedures for the production of a variety of stem and/or progenitor cells that meet GMP requirements.
- Goal VIII: Through research sponsored by CIRM and others, a thorough description of the steps of differentiation leading to the production of the various cells of the body will have been achieved.

  [Major strides in understanding differentiation, including the roles of RNAi species, in many cell lineages have been made]
- Goal IX: Through research sponsored by CIRM and others, the mechanisms regulating the self-renewal and oncogenic potential of embryonic stem cells and their derivatives will have been identified and characterized.

  [Many of these mechanisms have been identified.]
- Goal X: CIRM will have enabled development of new methods for tissue replacement based on stem cell research.

Five-Year Goals (to 2011)

These five-year goals will be milestones to gauge our progress:

- Goal I: CIRM grantees will have six therapies based on stem cell research in pre-clinical development.
- Goal II: CIRM grantees will have developed new methods for making stem cell lines.

  [*One grantee has used small molecules to induce pluripotency and several have made significant refinements to cell line derivations.]*
- Goal III: CIRM grantees will have successfully created disease-specific stem cell lines for four diseases.

  [*This work is well underway and is expected to be completed during 2009*.]
- Goal IV: CIRM grantees will have developed methods for growing stem cells in defined media.

  [*Several efforts to accomplish this are complete or nearing completion, such as Rock inhibitors*.]
- Goal V: CIRM will have enabled establishment of a stem cell bank.
- Goal VI: CIRM-funded investigators will have demonstrated methods for inducing immune tolerance in animal models.
- Goal VII: CIRM will have increased the workforce of stem cell researchers in California.

  [*CIRM has funded xx graduate students, postdoctoral fellows and clinical fellows through its training grants and has jumpstarted the careers of 45 young faculty through its New Faculty grants. We have also documented that more than 60 stem cell scientists have moved to California's non-profit institutions from around the world since CIRM began operation.]*
- Goal VIII: CIRM grantees will have established tools for toxicity testing based on stem cell research.
- Goal IX: CIRM will have enabled effective partnerships in stem cell research between scientific teams in non-profit and commercial sectors.
- Goal X: CIRM will have established national and international collaborations in stem cell research that will allow us to leverage the comparative advantage of California and our collaborators to advance toward therapies.

  [*CIRM has established a number of such partnerships. See page xx.]*

A good measure of progress to date is a review of the grant schedule proposed in the 20006 strategic plan (left column) compared the actual grant RFAs and awards made by CIRM (right column)

Proposed Schedule for Release of RFAs	
Through June 30, 2007	
Shared Research Laboratories / Stem Cell Techniques Course (January, 2007)	RFA issued January 2007, awarded June 2007
Laboratories / Research Facilities (April, 2007)	RFA issued August 2007, awarded May 2008
Scientific Personnel Development (April - May, 2007)	New Faculty RFA issued June 2007, grants awarded December 2007
Preclinical Product Development (May, 2007)	Determined timing was not right
July 1, 2007 to December 31, 2007	
Tools and Technologies (Development)	RFA issued May 2008, awarded December 2008
Biology of Stem Cells	Included in New Faculty grants awarded December 2007
Stem Cell Research & Society (2 RFAs)	To be handled via conference grants
Translational Research, Stage I	Determined to be premature
Disease Teams, Planning Grants	RFA issued xxx 2007, awarded June 2008
Training Program, II	Decided to offer larger Training II instead of renewal of Training I
Internships	Internships & Tech staff training combined
Technical Support Staff Training	as Bridges grants awarded January 2009
January 1, 2008 to June, 30 2008	
New Methods for Development of Stem Cell Lines	This RFA was combined with the next one as New Cell Lines grants with multiple
Generation and Use of Disease-Specific Cell Lines	priorities in the RFA and awarded June 2008
Economic Impact	RFP responses under review January 2009
Innovation Grants	Included in the Basic Biology RFA issued December 2008
Banks (2 RFA)	Decided fostering a registry of existing lines was more effective
Communities of Science (2 RFAs)	Developed MOUs for collaboration with five countries and one U.S. Foundation
Tools and Technologies (Sourcing)	RFA issued May 2008, awarded December 2008

July 1, 2008 - June 30, 2009	
Immune Tolerance, Initial RFA	Workshop set for February 2009, RFA likely late 2009
Public Outreach (3 RFAs)	Contract for new Web site June 2008 RFP for Public Relations firm awarded July 2008 RFP for high school curriculum project February 2009
Renewal of Training Program I	Offered larger Training II instead, awarded January 2009
Cores (2 RFAs)	Basic Biology RFA issued December 2008 Basic Biology II scheduled for August 2009
Internships	Bridges grants awarded January 2009
Egg and Embryo Research	This was included in New Cell Lines
Disease Teams, Planning Grants	No need to repeat round issued December 2008
Disease Team Grants	RFA expected February 2009
Stem Cell-Based Tissue Engineering (2 RFAs)	Included in Tools and Technology and Basic Biology also covered in some of New Faculty II awards issued August 2008
Clinical Investigation (2 RFAs)	To Be Determined, may be rolled into second round of disease teams
Bio-process Engineering	Held a GMP workshop to determine need and existing capacity
Innovation Grants	Included as a priority in Basic Biology
Translational Research, Stage 2	Early translational RFA issued September 2008, to be reviewed February 2009
Interdisciplinary Research Team Grants	International MOUs designed to capture this intent

As of December 2008 CIRM has awarded the following grants:

- $37.5 million for training 169 pre-doctoral, post-doctoral, and clinical fellows at 16 non-profit and academic research institutions.

- $46 million to fund 73 Leon J. Thal SEED Grants to bring new ideas and new investigators into the field of human embryonic stem cell (hESC) research.

- $72 million for 28 Comprehensive Research Grants to support mature, ongoing studies on human embryonic stem cells (hESCs) by scientists with records of accomplishment in the field.

- $50 million for 17 Shared Research Laboratory Grants (including 6 Stem Cell Techniques Courses) to fund the design and renovation of laboratory space, equipment for the new research facilities, and operating expenses for three years.

- $113 million for 45 New Faculty Awards to encourage and support the next generation of clinical and scientific leaders in stem cell research.

- $271 million to 12 institutions for the construction of major stem cell research facilities.

- $23 million for 16 New Cell Line Awards for the derivation and propagation of new pluripotent stem cell lines for the purpose of understanding, diagnosing, and treating serious human diseases and injury.

- $1.1 million to support 22 Disease Team Planning grants for multidisciplinary teams of scientists pursuing stem cell-based therapies for specific diseases.

- $2x million to support development of Tools & Technologies needed to move the field forward.

- $18 million has been recommended for funding for Bridges to Stem Cell Research Awards.

- $48 million has been recommended for funding for Training Grant 2 Awards.

REPORT ON OPERATIONS

OPERATIONAL HISTORY/PROGRESS TOWARDS CIRM GOALS

This section provides a brief description of CIRM's genesis and administrative organization and outlines the Agency's achievements to date and recommendations for future improvements across the organization.

GENESIS

CIRM had an unusual and eventful beginning. Although Proposition 71 was approved in November 2004 by 59 percent of voters, legal maneuvers by stem cell opponents to declare the Act unconstitutional delayed CIRM's funding from reaching fully authorized levels for almost 30 months. Initial funding for CIRM operations occurred after 16 months, with limited Bond Anticipation Note (BAN) proceeds being made available by generous and visionary private citizens who purchased these BAN securities. In addition, in 2007 Governor Arnold Schwarzenegger authorized a $150 million Pooled Money Investment Fund Loan from the state's General Fund to initiate CIRM-funded research.

Until the litigation resolved, CIRM was forced to operate with a skeleton crew, which did an outstanding job initiating the agency's operations and programs. Indeed, CIRM's small staff multitasked in ways that knowledgeable observers of funding agencies have considered unprecedented.

On May 16, 2007, CIRM emerged victorious from its legal challenges when California's Supreme Court refused to reconsider lower court rulings affirming the constitutionality of Proposition 71. With the legal path cleared, the first tranche of state general obligation bonds was issued on October 4, 2007, allowing CIRM to repay the General Fund and the BAN holders and become fully operational. Given the severely limited resources for almost three years, the accomplishments of CIRM and the Governing Board are remarkable.

ORGANIZATIONAL STRUCTURE

Internally, CIRM is organized into four administrative components: the Science Office, the Administrative Office, and the Chairman's Office, all of which are supported by staff who report directly or administratively to the Office of the President. The Chairman's Office operationally reports to the Chairman and works on a daily basis with the Governing Board Chairman, Robert Klein, to carry out the statutory responsibilities of this office, as defined by Proposition 71.

SCIENCE OFFICE

Much of CIRM's success derives from the enormous talent and effort of the staff in its Science Office. Despite severe understaffing during the first three years of operations, the

Office designed and launched CIRM's scientific programs and policies. Among its achievements, the CIRM Science Office staff has:

- Drafted the scientific concept plans that translate the scientific goals of the 2006 Strategic Plan into scientific and operational grant-award programs.
- Developed Requests for Applications (RFAs) and application forms and instructions that initiated scientific competitions for research, training, and salary grants for California scientists and organizations. As of December 2008, CIRM has awarded 2xx grants at xx institutions through 12 RFAs.
- Staffed the Grants Working Group to facilitate the highly effective peer review process for grant evaluations. This included managing the complex logistics of organizing meetings, recruiting reviewers for each competition, administering the conflict-of-interest disclosure and screening process, distributing grant applications, conducting meetings of the Grants Working Group and collating the data, writing public summaries of the reviews, and presenting the results of each review to the Governing Board and the public.
- Created the initial software programs that allowed CIRM staff and the Grants Working Group to conduct many of the activities of review online. This software facilitated the ranking and funding recommendations for applications to help the Governing Board make its funding decisions.
- Developed policies, including grants administration and intellectual property policies, for both non-profit and for-profit organizations. Established procedures for reporting, monitoring, and assuring compliance with the requirements of these policies, including eligibility determinations and proper budgeting to ensure good stewardship of the state's money over the life of grants.

Scientific competitions. The work of the science team is best reflected in the scientific competitions initiated in response to Request for Applications (RFAs). The scientific adjudication and awarding of grants is a multi-step process that requires the coordination of all of CIRM's resources. Although the process, described below, has worked well, further fine-tuning is anticipated.

At the heart of the process is an effective peer review system established by the Science Office. The Grants Working Group is comprised of an extraordinary group of world-recognized, non-California scientists drawn from the United States and other countries, working alongside a committed group of Patient Advocates who play a critical role in communicating the Group's recommendations to the Governing Board. The Panel has established high standards of excellence, a collaborative working style, and an environment that fosters respectful discussion within a spirit of collegiality. Organized and guided by criteria set by CIRM staff, the scientific experts evaluate grant applications and score them based on the sole criterion of scientific excellence. In making final funding recommendations, the GWG, led by Vice-Chairs chosen from among patient advocate members of the Governing Board, considers the programmatic fit of a research proposal and the potential of the project to advance a particular therapeutic opportunity. The Patient Advocate Vice-Chair and the other patient advocate members of the GWG play an invaluable role leading discussions of the link between scientific excellence and programmatic priorities.

The Grants Working Group panels have also shown remarkable flexibility in providing expert opinions on numerous forms of grant applications, from investigator-initiated basic research proposals to training grants and grants for new investigators, major facilities, the generation of new cell lines, and disease-oriented research groups. CIRM is grateful to the committed members of the Grants Working Group for the long hours they devote to evaluating large numbers of grant applications and for their dedication in traveling to California from distant locations to attend meetings.

ADMINISTRATIVE OFFICE

Staff members in the Administrative Office are critical to CIRM's smooth operations. During CIRM's startup period, they put in place procedures regulating all Agency operations including financial, human resources, information technology, communications, and internal administration. Administrative personnel also worked with Governing Board members and external advisors, in particular in collaboration with the National Academy of Sciences, to establish ethical standards for CIRM investigators and to ensure compliance with state and federal laws and regulations.

CIRM has begun implementing significant improvements in its administrative operations to accommodate an expanding number of programs and operational responsibilities and will continue these efforts going forward. For example:

CHAIRMAN'S OFFICE

The Office of the Chair under Chairman Robert Klein has it primary responsibilities described in the Initiative as follows:

The chairperson's primary responsibilities are to manage the ICOC, the governing board, agenda and work flow including all evaluations an d approvals of scientific and medical working group grants, loans, facilities and standards evaluations, and to oversee the CIRM annual report and public accountability requirements: to manage and optimize the institute's bond financing plans and funding cash flow plan: to interface with the California Legislature, the United States Congress, the California health care system , and the California public; to optimize all financial leverage opportunities for the institute: and to lead negotiations for intellectual property agreements , policies, and contract terms. He also serves on all three of the agencies working groups. The focus of the Office's operational roles – in carrying out these responsibilities – are 1) board policy development; 2) financing challenges of the agency; 3) board legal issues; and 4) inter governmental affairs.

OFFICE OF THE PRESIDENT

The President, aided by the General Counsel to the President and supported by his Executive Assistant, is responsible for setting the direction, breadth of activities, and pace of CIRM's implementation program; its relationships with other institutions; and the scientific vision guiding the Agency's delivery of its mission. Doing so requires continuous knowledge of CIRM's primary activities and involves close communications

with the Chair of the Governing Board, Vice President Operations, Chief Scientific Officer, and other executive staff. The President aims to direct CIRM by drawing the best from all members of staff. Simply put, the agency operates as an integrated, ambitious program, committed to supporting the relationships required to achieve its mission. The president acts to leverage California's scientific and medical assets by creating a national and international network of the worlds leading stem cell research scientists and clinicians, working together to advance the medical and scientific mission of proposition 71.

SUMMARY

CIRM has had an outstanding beginning as the first state-driven organization in the United States to fund stem cell research. As a result, California has emerged as a world leader in stem cell science and regenerative medicine and a model for other states and countries interested in supporting this promising area of research. As a leader, it is incumbent upon CIRM to continue its momentum by promoting knowledge sharing and interdisciplinary approaches on the part of its scientists, by recognizing and funding the most promising avenues of research, and by communicating to the public important progress in the field and realistic hopes for the future. The Strategic Plan Update of 2008 has been conceived to help CIRM achieve these goals.

OPERATIONS GOING FORWARD

SECTION 1: THE SCIENCE PROGRAM

The science program is the heart of CIRM's operations and the catalytic hub for generating CIRM-funded research activities. As CIRM looks to the future, it seeks to (1) drive the basic stem cell discoveries upon which solutions and treatments in regenerative medicine will be based, (2) accelerate the movement of stem cell research towards clinical outcomes, (3) hone our internal processes so they more effectively support the field as a whole, and (4) expand the breadth and depth of CIRM's research portfolio. The anticipated RFA release and assessment program is shown in the figure on page xx.

Recommendations for the future.

Looking towards the future, CIRM's portfolio will expand as efforts are made to accelerate research that will bring stem cell technology closer to the clinic and patient care. For that reason, CIRM will expand the membership of the Grants Working Group to include more reviewers who are able to adjudicate applications for translational and clinical research.

Recognizing that California's biotechnology and pharmaceutical companies have the technical and commercial experience to develop and bring products to the marketplace,

CIRM looks forward to offering these industries numerous opportunities to apply for CIRM grants and loans. Realizing that special expertise is necessary to judge these proposals, CIRM is expanding the Grants Working Group to include scientists with industry experience in biotechnology, drug development, and regulatory processes.

Given that CIRM's Science Office is on the front line of meeting the Agency's evolving needs, other, broader modifications will be needed to enhance and monitor operations. These include:

- Increasing the team's breadth of experience and domain expertise by recruiting to the science team additional highly qualified and motivated scientists to help with RFA writing, grant reviews, and, increasingly, portfolio management and the active management of progress reports with the goal of achieving increased productivity.

- Creating additional programs and RFAs for translational and clinical research that reflects the urgency of CIRM's mission to bring stem cell technology to patient care.

- Preventing reviewer burnout by keeping the grants-review process vibrant, interesting, and effective, and by augmenting the pool of reviewers both in number and in additional areas of expertise.

- Ensuring that CIRM's clinical programs align with evolving FDA requirements for cell-based therapies.

- Implementing a comprehensive, Web-based grants management system that will enable the management of reviews and provide a basis for integrating management and reporting across CIRM's growing grant portfolio.

- Enhancing procedures for monitoring the progress of CIRM-funded investigators to effectively steward CIRM's investments. Active portfolio management by the Science Office will identify the best CIRM-funded science to be advanced under new initiatives and also make scientists aware of pertinent research outside their own institutions.

- Extending CIRM's leadership role in the international community by expanding science-based outreach programs, symposia, and workshops. Proactive outreach is necessary to keep CIRM and its California-based investigators abreast of the new information continuously emerging at the frontiers of stem cell biology and regenerative medicine.

- Creating new mechanisms to leverage CIRM funds through partnerships with other national and international funding agencies and foundations pursuing areas of shared scientific interest.

1. BASIC RESEARCH

CIRM will continue to build California's capacity in stem cell science by issuing Requests for Applications (RFAs) to support the research of scientists at all stages of their professional careers. Recognizing that California has attracted some of the best stem cell scientists in the world, certain RFAs will support the research of these and other established scientists with large research groups. Other RFAs will be designed to serve mid-career scientists who are changing direction or applying new disciplines to the field. Cognizant of the critical and continuous need for new talent, CIRM will also continue to support young investigators who demonstrate the talent and commitment to stem cell basic research.

CIRM's initial lifespan is limited by Proposition 71. Therefore, scientists supported by CIRM will need to have a varied portfolio of grants to drive their laboratories in the event that CIRM funding diminishes or is phased in the years beyond 2017. Accordingly, CIRM recognizes the need to partner with national and international agencies to smooth the transition to collaborative support in the future. In the meantime, the Agency will seek to link with federal agencies such as the NIH and other philanthropic, patient-support, international and state granting organizations to leverage CIRM's research funds.

2. PROGRESS TO THE CLINIC

CIRM has released the first Early Translational RFA to identify candidate molecules or cell types with high potential for use in regenerative medicine. These early-stage translational research awards will support the development of animal models or the discovery of other fundamental information needed by regulatory authorities to support an Investigational New Drug Application that the Food and Drug Administration requires before a clinical trial can begin. CIRM expects these RFAs to be issued annually; they will include a mixture of grants and loans to companies and not-for-profit institutions, with opportunities for awards to multiple co-chief investigators to ensure that the most senior or qualified people in the organizations are intimately involved in the research.

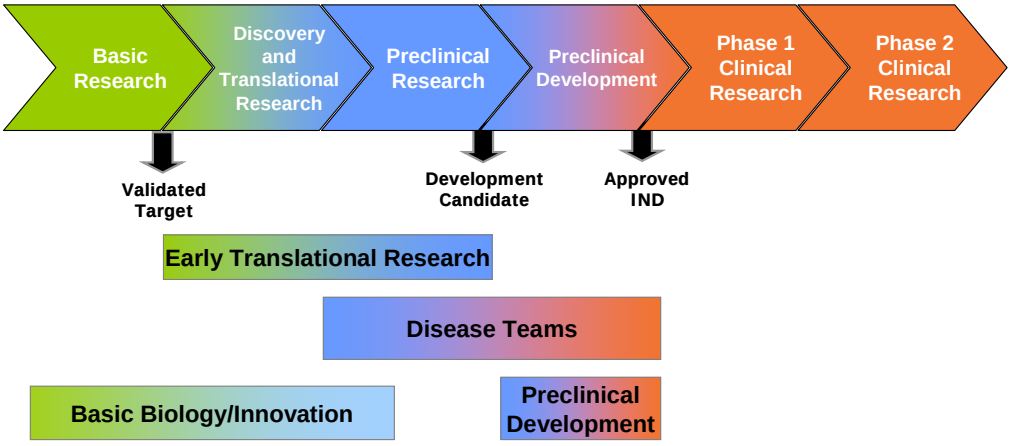
CIRM also recognizes that building the "tools" necessary for basic and translational research is an important step along the path towards the clinic. We anticipate that RFAs supporting the development of tools and technologies will remain an important part of CIRM's research portfolio.

Progress is being made every day in labs around the world, and some promising products are in the pipeline using embryonic, mesenchymal and umbilical cord blood stem cells. These studies represent the frontiers of stem cell therapies, and CIRM is committed to moving them along, particularly those that are under-funded for development and pre-clinical applications.

CIRM will soon issue an RFA for Disease Team grants designed to move research from the laboratory to an IND application within four years. Funding of up to $20 million per

project may be available, assuming that agreed-to milestones are achieved. All teams will be required to use strict project management techniques, and oversight advisory committees will be established to help CIRM staff monitor progress. The projects will have to meet FDA guidelines for cell therapies and treatment protocols. While these have not yet been formalized, requirements for mature autologous and allogenic adult stem cell therapies are now reasonably well established. Because a large number of applications for the Disease Team grants are expected, CIRM plans to triage the "letters of interest" and direct those unlikely to be competitive to consider later RFAs with guidance on their deficiencies. Triaging by CIRM, with the help of external advisors, will make it possible to accept an unlimited number of letters of interest submitted by an institution or company but at the same time result in a manageable number of applications for the Grants Working Group to assess. It will also minimize the time and effort of applicants who are unlikely to be funded and bring the best applications forward for these very special awards.

CIRM is also focusing on the critical need to stimulate research that links immunology with stem cell biology. Since many of the strategies being developed for stem cell therapies involve the use of allogenic cell transplantation (i.e., non-matched donors and recipients), scientists may need to induce immune tolerance to prevent the rejection of the genetically foreign stem cell transplants. This is a far more appealing strategy than current alternatives of exposing patients to long-term immunosuppression therapy. To address this obstacle in clinical applications CIRM will prepare a specific RFA addressing tolerance strategies for allogenic cell therapies that encourages immunologists to work with members of the Disease Teams and other CIRM-supported scientists.



While CIRM's early RFAs focused on training and basic research, those in 2008 began to move into the translational arena. Going forward, RFAs will increasingly cover the entire spectrum of the pipeline, from discovery through clinical development.

3. IMPROVING PROCESSES TO ENHANCE SCIENTIFIC CAPACITY

The Science Team has primary responsibility for delivering CIRM's scientific and clinical mission. The team is comprised of highly qualified and experienced scientists, and as CIRM's research portfolio enlarges the team will have to expand from its current number of XX to 30 or more individuals. Scientists with experience in rapidly growing new areas such as tissue engineering and pharmacology, as well as physicians with clinical trial expertise will be particularly essential to CIRM's expanding support of translational research.

Members of the Science Team have a broad range of specific expertise, including neurosciences, neurodegenerative disorders, mitochondrial function and membrane biology, embryology and mouse genetics, immunology, surgery and immunosuppression, signal transduction, cancer biology, anesthesiology, critical care, stem cell microenvironments, visual systems, animal and human embryology, human embryonic stem cell biology, stem cell differentiation and transplantation, and product development. CIRM strongly encourages their continued specialization and supports their attendance at primary conferences of their discipline and their ongoing communication with scientists working in their area of specialization.

Setting the CIRM Research Agenda

CIRM relies on multiple sources of information to monitor progress in the stem cell field, frame issues, and identify specific areas of opportunity or roadblocks to research progress, all of which form the basis of new RFAs.

In order to develop interesting and relevant RFAs, CIRM's Science Officers must remain on the cutting edges of stem cell biology and regenerative medicine. Toward this end they read and debate the scientific literature, attend national and international scientific meetings, host research seminars, meet with investigators at their home institutions, and participate in frequent scientific discussions with their peers.

Members of the Science Office maintain their specialty research interests by hosting presentations by visiting scientists from California and elsewhere. CIRM leverages technology like video conferencing to facilitate communication with scientists worldwide. The Chief Science Officer is actively involved in NIH grant reviews and other major new programs in cell biology and regenerative medicine and, like CIRM's President, serves as a reviewer to scientific journals and international research institutions.

Other sources and resources that inform the CIRM research agenda include:

> **3.1 CIRM workshops**. Workshops provide a valuable venue for learning about scientific fields and for convening experts to advise on how to advance various research agendas. For example, in July 2008, a workshop on the use of stem cells in predictive toxicology brought together scientists and engineers from the

pharmaceutical and biotechnology industries, national and state environmental health and regulatory agencies, and academia.

Other recent workshops have addressed cancer stem cells and cell production in good manufacturing practice (GMP) facilities. Upcoming workshops will address topics such as immunology, stem cell transplantation, autism and mental health, and joint research by investigators in California and scientists of other countries under agreements that have been negotiated (e.g. United Kingdom and Japan)

3.2 Progress reports. The Grants Administration Policy (GAP) requires that CIRM grantees submit progress reports detailing the research carried out during each funding year. Science officers are responsible for evaluating these reports as they relate to the original goals of the project.

To manage the flow of information, CIRM is developing and implementing the categorization systems and database that will store information according to disease relevance, cell types and technologies employed, research results, questions raised and answered, and possible next steps. In discussing these reports, the Science Office will suggest ways to expand on promising results and will identify areas of potential future investigation. Some of this information will flow from records kept by the ***Grantium*** grants management program now being implemented.

Analysis of progress reports may suggest the need to launch entirely new programs or reveal opportunities to make adjustments in current programs, for instance, by encouraging collaborations among investigators pursuing similar or related work in different organizations. The Science Team will facilitate communication and collaborations among investigators, including sponsoring symposia and mini-workshops to accelerate collaborative progress. The Science Office may also recommend to the Board additional funding to research teams for especially successful or promising programs that are directly related to achieving CIRM's mission.

Conversely, the Science Office is also responsible for recommending termination of failing projects. Grants will be terminated if (a) milestones were not achieved, (b) the proposed research was abandoned in favor of more promising lines of research without pre-consultation with CIRM, or (c) the research has hit a dead end. Given the high-risk nature of many of CIRM's programs, we expect 'negative' results, but these do not necessarily represent failure; indeed, CIRM will share instructive negative results – which are often unpublishable – with CIRM's research community. These results yield substantial value in directing future research as well as in helping to understand the development of disease.

For milestone-driven clinical research projects (such as the Disease Team grants), beyond providing detailed data, investigators will be required to outline their go/no go decisions in evaluating stem cell-based therapeutic candidates, and to submit Gant charts to help CIRM and other monitoring committees assess progress. CIRM will also use progress reports, in conjunction with evaluations by

designated monitoring committees, to identify candidate drugs, treatments, or assays that deserve additional funding for follow-on stages of pre-clinical development.

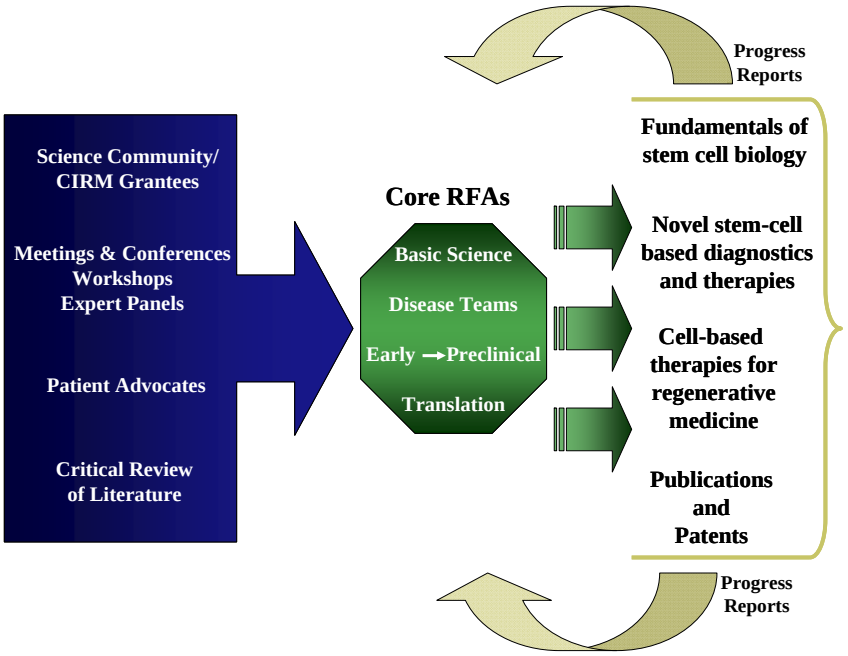
Progress reports also serve a communication function, providing information that CIRM's Communications Office can use to update its audiences about research progress arising from CIRM-funded projects. Additionally, the reports create a record of what types of science CIRM has funded, how well this funding aligns with CIRM's strategic goals, and whether the interests of stakeholders have been fully realized and balanced.

3.3 CIRM Annual Conference. CIRM hosted its first grantees conference in September, 2008 with more than four hundred CIRM-funded scientists attending. The meeting featured lectures, posters, and interactive science sessions. Prominent U.S. and international scientists attended by invitation and led stimulating discussions on subjects of high priority, including iPS cells. The conference was held under "Cold Spring Harbor Rules" whereby data are not communicated outside the conference except at the initiation of the authoring scientist. The meeting will be held annually, providing CIRM's Science Officers with opportunities to interact with grantees in a stimulating environment and allowing CIRM-funded scientists to forge connections and learn about each other's work. The initial Conference was enthusiastically supported by grantees, with many new connections and informational exchanges made between California scientists and an obvious strong morale existing among all grantee laboratories.

3.4 Investigator-initiated Conferences. Conferences initiated by CIRM investigators, which can now be funded through applications to CIRM, are also extremely valuable forums for information sharing and initiation of new collaborations.

3.5. Patient Advocacy. Input from patient advocates is incorporated into CIRM's decision-making at many levels. As members of the Grants Working Group, patient advocates have a formal role in formulating recommendations to the Governing Board regarding project funding. CIRM's science officers attend clinical conferences as a means of interacting not only with researchers, but also with patient advocates from around the country. As stem cell biology progresses from the laboratory to the clinic, ongoing dialogue with patient advocates, both from within California and from national disease foundations, will become increasingly important in the application of stem cell therapies.

The vast majority of patient advocates understand that each individual disease interest group is best served by following the best science no matter what disease it is studying. So they generally have a desire to keep abreast of the field as a whole. We will be sharing lay-level summaries of CIRM research results with patient advocate groups to enable them to provide informed input.



This figure diagrams how data are fed forward into generation of RFAs, and the primary importance of feedback from progress reports in fine-tuning RFAs to advance CIRM's scientific mission.

3.6 Stakeholder Guidance. To achieve a balanced portfolio, the Science Office responds to guidance from various stakeholders, including research institutes, companies, clinical centers, patient groups, research foundations, government, and the general community. Achieving research balance means funding a broad range of projects that will lead to clinical trials, as well as research focused on specific diseases or diagnostic tools. Of particular interest are programs that address areas of high medical need, those ready for translational applications, and those with the potential to be prototypes for other fields in regenerative medicine.

4. Enlarging the Breadth and Depth of the Research Portfolio via a System of Core Grants Offered Periodically

To ensure that opportunities for rapid and significant progress in both basic and clinical science are identified and pursued, and to be certain that technologies are evaluated and renewed periodically, CIRM intends to categorize most RFAs into five major research activities. Organizing grants in core areas will facilitate CIRM's ability to monitor research progress and to measure progress along the pathway from discovery through development and onto clinical application. It will also enable the agency to schedule RFAs for new and renewed programs more predictably, reducing the number of GWG meetings and workload on grant reviewers.

CIRM's core or primary grant areas are as follows:

4.1 Basic Innovation in Stem Cell Biology

Basic stem cell research conducted by a broad spectrum of researchers is an essential first step in moving this technology from the bench to the bedside. In its short four-year history, CIRM has aggressively funded innovative basic research projects that are likely to advance the field and CIRM's mission. CIRM will continue to build on the critical mass of scientific excellence and to fund creative projects with the potential to lead to clinical applications.

4.2 Early Translational Research

These awards will support research that advances stem cell-derived candidate therapies or assays to a development candidate stage ready for consideration for preclinical development and enabling a regulatory filing. The candidate therapies may be stem cells or their derivatives, small molecules, proteins, antibodies, genetic manipulations, or any pharmaceutical that is identified using stem cell technologies.

4.3 Preclinical Research

Preclinical research awards cover subspecialty activities following successful early translational research that points to a promising development or cell therapy. Examples include animal toxicology and pharmacology studies, manufacturing processes for drugs or cell therapies, clinical protocol development, and strategies for overcoming bottlenecks that impede the development of cell therapies.

4.4 Disease Teams

As described elsewhere, CIRM plans a major investment to support Disease Team Grants aimed at achieving an IND within the four-year grant/loan funding period.

CIRM recommends a $210,000,000 investment for the first round of Disease Team Grants to initiate approximately 10-12 projects. This is a significant shift in CIRM's strategic plan, and represents increasing the commitment to this initiative in 2009 alone by 75 percent over that proposed in the 2006 Strategic Plan for 2009 through 2011.

The scope (and therefore funding) for Disease Teams will differ, depending upon the maturity of the candidate therapy. Disease Team Grants will be milestone driven and monitored on a regular basis by project managers and oversight committees. CIRM will make a special effort to identify teams making singular progress toward a clinical application and to accelerate their translational research efforts by facilitating appropriate collaborations and further funding.

4.5 Research Fellowships and Training Programs

CIRM training grants have greatly expanded the cadre of California researchers skilled in the techniques of growing and manipulating stem cells, and thus have played a critical role in accelerating stem cell research capacity in the state. Funding for the first round of training grants will end during the winter and spring

of 2009, just as a new, slightly larger round of training grants is to be awarded. While CIRM has determined that continuity in these training opportunities provides value, the agency will consult with the research community to determine whether more trainees are needed to drive the CIRM mission and if additional young stem cell researchers can reasonably expect the field to accommodate them.

Similarly, the first two rounds of New Faculty Awards have given talented young faculty the security of five years of steady funding. Before considering another round of New Faculty Awards, however, CIRM will review the funding landscape. While a main goal of the Agency remains ensuring a sufficient pipeline of scientists to pursue all viable avenues of regenerative therapies, CIRM must balance this aim with the capacity of the field to utilize new talent.

The Bridges program is designed to introduce students in community and state colleges to careers in the biomedical sciences in general and stem cell science in particular. The Governing Board is expected to approve the first round of these grants in January 2009. Because of anticipated ongoing needs to grow the pool of research personnel and diversify the community of researchers, CIRM expects this program to continue.

SECTION 2. COLLABORATING WITH INDUSTRY

As the effort to cure or treat disease using stem cell technologies moves closer to the clinic, CIRM will need to call upon expertise in clinical trials, regulatory requirements, and large-scale Good Manufacturing Practices (GMP). The greatest reservoir of these skills resides in pharmaceutical and biotechnology companies. Without the injection of such expertise into CIRM programs, either independently or through formal collaborations between industry and universities and other not-for-profit organizations, CIRM's ability to accomplish its mission will be jeopardized. Therefore, one of CIRM's primary goals is to promote and facilitate the involvement of corporations in CIRM's programs so as to harness the resident expertise and resources in regulatory, clinical, manufacturing, and R&D arenas.

To achieve these goals, CIRM proposes four strategies:

Strategy 1: Ensure that CIRM's internal programs, policies and regulations embrace industry participation. In each aspect of its work, CIRM will be mindful of the benefits of industry participation as well as the impact of CIRM policies and practices on such participation, removing obstacles where appropriate. Towards that end, CIRM must ensure that:

- Its grant programs are conducive to industry participation, amending them as necessary to facilitate collaboration with pharmaceutical and biotech companies.

- CIRM's business loan program is implemented on terms that encourage industry participation while including provisions to assure preferential pricing for California local and state government entities and access to the uninsured.
- CIRM's rigorous peer review encourages industry participation. For example, by including on the Grants Working Group industry experts who are qualified to assess science and who recognize what is necessary for commercial success.

Strategy 2: Reach out to the pharmaceutical and biotechnology industry to better understand its needs and encourage its participation in CIRM programs. CIRM recognizes that the not-for-profit and business communities, while sharing the goal of using stem cell research to improve the lives of patients, have different missions, capabilities, and cultures. To promote industry involvement, CIRM must:

- Establish a "Biotech Advisory Group" comprised of representatives from the pharmaceutical and biotechnology sector to advise CIRM on industry trends and needs and to help evaluate CIRM's interactions with this sector.
- Join or establish a formal liaison with industry groups with a stake in stem cells at the state, national, and international levels, such as BIO, PhRMA, BayBio and BIOCOM**.**
- Include, as appropriate, topics with industry focus in CIRM-hosted and sponsored events and make sure industry representatives are included as participants and speakers.
- Take visible leadership roles at conferences, panels, and professional meetings addressing industry participation in stem cell research.

Strategy 3: Serve as a resource to support industry involvement in stem cell research and development. CIRM should provide:

- Tools and access to resources that are not easily obtainable from other sources and that are valuable to industry.
- Opportunities and guidance for joint collaborative projects involving industry and not-for-profit entities.
- Information and updates on best practices in intellectual property (IP) licensing and trade secret issues.
- Information on, and guidance in, grant writing and best practices in CIRM-specific grant management.
- Information on IP prosecution and other relevant legal developments. CIRM will consider establishing a network or panel of IP and licensing attorneys with strong client bases in the commercial stem cell arena. The group could meet periodically to share best practices and advise the Agency.
- Help in both monitoring "blockers" to industry participation and using CIRM resources and influence judiciously to resolve logjams. Examples might include reviewing the European Union's views on patentability of stem cell inventions and their impact on the commercial sector, and identifying factors that have led to failures in exploiting stem cell technology and recommending solutions.
- Opportunities to facilitate the exchange of information between companies regarding stem cell manufacturing and regulatory experience, with the aim of

avoiding duplication of effort and repetition of mistakes. CIRM regulations already require the exchange of certain types of materials, once results are published by grantees; the Agency should monitor that exchange to ensure its benefits are being maximized.

- Advocacy for policy changes and clarifications of various state and federal agency rules that hinder industry involvement in stem cell research and development. Such advocacy might involve submitting *amicus* briefs in various legal proceedings, submitting "white papers" to government agencies, and testifying before governmental bodies.

Strategy 4: Educate key stakeholder constituencies about industry's critical role in accomplishing CIRM's mission. Key constituencies should be educated about the close links and cascade effects between health/economic benefits for Californians on the one hand, and industry innovation/intellectual property protection on the other. To improve understanding, CIRM should:

- Regularly update the Governing Board about relevant developments in the pharmaceutical and biotechnology sector.
- Help raise public awareness about biotechnology's unique ability and extensive track record of success in bringing valuable therapies to patients and the need for industry involvement to help drive similar stem-cell based therapeutics. This education can be implemented through information on CIRM's Website and in its annual report, publications and statements, and public events.
- Raise the awareness of state legislators about the importance of industry involvement in CIRM's mission.
- Encourage other funding organizations, especially those with whom we have established memoranda of understanding (MOUs), to fund industry research and development efforts.

Strategy 5: Providing loans to support later stages of research leading to clinical trials and new therapies. Bringing new and more effective treatments and therapies into practice is a complex, expensive process, and financing is becoming more difficult for small biotech companies. Since CIRM believes these companies will be important partners for California's world class academic and non-profit research institutions in bringing stem cell therapies to market, finding ways to support their efforts is essential.

CIRM is already providing opportunities for for-profit companies to apply for support of basic science research through its grant programs. In the next year the Agency will introduce a loan program that will provide significant new funding to biotech companies while maximizing CIRM's ability to achieve its goals by recycling monies re-paid from loans into new research programs. Key features of the loan program:

- RFAs for preclinical and clinical development will make loans available for for-profit companies.
- Applications for loans will undergo the same rigorous peer-review process as applications for grants.

- Standards will be developed for assessing financial feasibility and risks associated with loans.
- Underwriters will be identified to manage the financial aspects of the loan program.
- Loan funds repaid to CIRM will be recycled and used to support additional research RFAs.

To summarize, California's biotechnology and pharmaceutical companies are among the best in the world in their ability to develop innovative technologies and products to meet the needs of patients. In collaboration with Caliofrnia's leading non-profit research sector, they represent an invaluable and essential resource to bring stem cell therapies to patients; and they are enthused about CIRM and eager to contribute to the Agency's success. Working together, CIRM and its industry partners have unlimited potential to realize CIRM's lifesaving mission. To maximize this potential, CIRM must remain aware of the sector's specific needs for technology and information and work diligently to provide opportunities for industry to engage – without hurdles -- with both CIRM and its not-for-profit partners.

SECTION 3. NATIONAL AND INTERNATIONAL LEADERSHIP

Thanks to the vision, generosity, and foresight of California voters who overwhelmingly supported the passage of Proposition 71, and due to the growing success and impact of CIRM's programs, California is rapidly becoming recognized as an international hub of stem cell research. Stem cell scientists from around the country have identified California as the most desirable location for their research (Sidebar 1), and many leading scientists have moved here from other states and countries to carry out their work (Sidebar x).

The tasks and challenges CIRM faces in bringing stem cell technology to patients within ten years loom large by any estimation. Additional assets, both intellectual and financial, will accelerate the march to success, as will leveraging CIRM programs through interactions with talented people outside California.

COLLABORATIONS AND JOINT PROGRAMS

Collaborations with scientists from outside California play a valuable role in advancing CIRM's research agenda. International collaborations allow California to significantly leverage both its financial and intellectual investment in the field. These collaborations will be facilitated by agreements with external funding agencies via competitive RFA programs. A number of agreements have either already been forged or are in late-stage discussions with research agencies in other countries, philanthropic foundations, patient-advocacy organization, and private agencies that support research in specific diseases. These arrangements will be expanded over time to create a worldwide network of scientists working together to accelerate progress on stem cell therapies and their transition to the clinic.

These collaborations will:

- Allow CIRM to expand its research portfolio by involving scientists from institutions and companies located in other states in the U.S. and abroad in joint study and research programs.

Stem Cell Researchers Around the Country Are Noticing CIRM's Role

When a Georgia Tech researcher asked scientists from around the country to rank the top states in their discipline, nearly 90 percent of stem cell scientists ranked California in the top three, compared with about half the non-stem cell scientists. A similar percent of stem cell scientists were aware of California's commitment to fund stem cell research on a large scale.

See Nature Reports Stem Cells 10 July 2008 - Levine A (2008) Policy considerations for states supporting stem cell research: evidence from a survey of stem cell scientists. Public Admin. Rev. 68: 681-94. 2008

CIRM Funding is Attracting Researchers to California

- Twenty-four national and international leaders in stem cell research have moved to California from 10 U.S. universities and six foreign countries.
- Thirty-three young investigators have decided to launch their careers in the state after studying in labs in 16 different U.S. institutions and three foreign countries.
- A sample of five CIRM-funded institutions has increased the number of stem cell researchers from 134 in 2004 to 463 by November of 2008, a 455 percent increase.

- Create opportunities for CIRM funding to leverage additional support from other organizations.
- Reduce duplication of both effort and facilities in projects of shared interest.
- Accelerate opportunities for clinical applications. Sidebar 3 lists existing CIRM collaborations with executed memoranda of understanding.
- Engage other funding agencies and biotechnology and pharmaceutical companies in developing environmental toxicity testing and in designing and screening drugs.

Sidebar 3.

Organization	**Collaboration**
State of Victoria, Australia	Broad in scope, immunology strengths
Canadian Stem Cell Consortium	Cancer stem cells
Medical Research Council, UK	Broad in scope
Juvenile Diabetes Research Foundation	Diabetes
Japanese Science and Technology Agency	Broad in scope, iPS cell focus from Japan
Spain	Broad in scope

CIRM will pursue collaborations with the NIH that may accelerate research capacity in a wide spectrum of areas, including basic cell biology, molecular biology, translational medicine, and clinical trials. The Agency is also exploring joint research and clinical trial programs with international agencies representing regional medical interests in Europe, the Middle East, and Asia. In these discussions CIRM seeks a wide variety of unique expertise, medical programs, and specific patient input, to amplify and complement the work being done in California. Certainly, as these efforts progress, CIRM will gain experience that will enhance its ability to advance effective clinical treatments for California's citizens.

CIRM has received numerous inquiries from organizations eager to engage in collaborative funding. As CIRM considers entering into partnerships it is:

- Establishing standards and criteria for determining appropriate partners and circumstances.
- Ensuring that all joint-funding arrangements are consistent with CIRM's scientific and ethical standards and with all of CIRM's governing statutes and regulations, including rigorous peer review.
- Strengthening mechanisms for monitoring progress, to enable CIRM to rapidly identify and seek new partnerships in promising research areas.

In summary, with CIRM programs and operations now firmly established in California, the Agency is extending its reach and influence both nationally and internationally, playing a leadership role and benefiting from the scientific progress of others.

SECTION 4. COMMUNICATION AND EDUCATION

CIRM'S RESPONSIBILITY TO THE PUBLIC

California's public and financial support comes with a responsibility to keep the entire community informed about CIRM's activities and accomplishments. This requires more than a passive posting of grants awarded. To be well informed about CIRM's scientific mission and how funds are being invested to improve human health, the public must first understand some basic information about stem cell research and why broad and sustained funding is critical to advancing this research from the laboratory to patient care. Armed with sufficient background information and realistic reports of progress, citizens can put into perspective the research results achieved through CIRM funding and recognize the true hope they represent.

To this end, CIRM has launched a broad-based communication and public education effort. The aim is to address the general public and several niche audiences, including the media, patient advocacy organizations, researchers, legislators, and business leaders. CIRM plans to reach each audience through multiple channels: face-to-face communication, print media, and especially the Web. Many members of the Science Office, as well as CIRM grantees, are being called upon to increase opportunities for face-to-face education and outreach.

Since March 2008, CIRM has been enhancing the content on its Website to include more information about stem cell research in general and CIRM-funded research in particular, with links to related content on many of the CIRM-funded institutions' Websites. During December 2008, CIRM brought online an entirely new website that represented the first phase in building a mini stem cell university on the Web. CIRM hopes to engage enough outside resources and new, in-house-produced content to make its Website a definitive resource for anyone who wants to learn where new research results have taken the field and to put those results into perspective. Because many people have become accustomed to learning by video, the CIRM Website now also includes information in this format from leaders in the field on a wide range of topics and issues within stem cell science.

REACHING OUR AUDIENCES

For patient advocates: CIRM expects the new "For the Public" landing page off the Website to become a valued resource. Much of its content will be searchable by disease, and individual stories will maximize Web learning by providing links to researchers' home pages and related video, images, research papers, and press releases. CIRM plans to collate materials related to specific diseases and use them as a basis for in-person meetings with advocate leaders, to enlist them in further disseminating CIRM content and to create links back to CIRM. The eAlerts list serve system and a new Really Simple Syndication (RSS) feed system will play key roles in this effort.

For business leaders: CIRM is reviewing the knowledge about and attitudes toward the Agency among business leaders to help direct communication activities within this niche.

Two information-exchange sessions for industry held in September 2007 were rated as valuable and will be repeated, as required. CIRM's leadership frequently accepts and seeks opportunities to speak to business groups in California. For the biotech community, CIRM expects the "For Researchers" landing page on the new Website to be a useful tool for tracking RFAs and grant awards.

For State Executive Officers: The office of the Chair and the Director of Communications will organize briefings for the constitutional officers and their staff, many of whom will be encouraged to sign-up for the RSS feed to stay appraised of CIRM activities. In-person meetings will continue on a frequent basis with CIRM's government relations representative, and periodically with CIRM senior executives.

For the legislative community: CIRM plans to conduct advocacy workshops on pending federal and state legislation to assemble information on the potential influence of these legislative measures on stem cell therapies and the ability to access patients. CIRM will organize briefings for legislators and their staff, many of whom will be encouraged to sign-up for the RSS feed to stay appraised of CIRM activities. In-person meetings will continue on a frequent basis with CIRM's government relations representative, and periodically with CIRM senior leadership and board members. CIRM is building a rapid response team to answer legislative requests and to effectively assimilate legislative input.

For the media: CIRM will begin augmenting its traditional press releases, and those produced by grantee institutions, with video segments. These clips will feature certain faculty describing science at a lay level and employ compelling visual images suitable for TV to convey the excitement that stem cell science holds for the future of medicine.

The media are a significant conduit of information to the general public, and journalists need to understand a broader perspective of the field than that afforded by daily news coverage. Thus, an important component of CIRM's mission is to offer the media educational opportunities. More than 30 journalists attended CIRM's first writer's seminar on September 17, 2008, where 9 guest speakers presented on a wide variety of topics in stem cell research. Beyond educational seminars designed specifically for media, we will also consider implementing mini-fellowship programs offering hands-on lab experience.

For the science and medical community: CIRM communicates with grantees and partners through a grantee conference and by posting critical information online. CIRM encourages the involvement of scientists in education programs for elementary, high school, and undergraduate students, postgraduates, and the general community and plans to include early-stage career scientists in a wide range of communication and education activities.

For the Governing Board: Continuing education of the Board is an important component of CIRM's communications strategy. Efforts include regular "Spotlight on Disease" sessions in which clinical and basic scientists, alongside patients, discuss current progress

in the research and treatment of specific diseases and injuries. In addition, snapshots of research advances in stem cell science are provided regularly at Board meetings by the President, with summaries of the presentations posted on the Website. The CSO and other members of CIRM staff also provide updates on new discoveries, clinical developments, IP, and other important developments in the field as they occur.

For the general public: The CIRM Website will serve as the primary communication tool between the Agency and general public. In addition, CIRM will look for and create opportunities for leaders and researchers in the field to speak before live audiences. For example, CIRM will organize at least one town forum each year in the Bay Area, Los Angeles Basin, and San Diego regions.

To promote interactive learning, CIRM is considering issuing an RFP to develop a portable, multimedia display on stem cell research that can be used prior to and after the Town Forums, at grantee institutions, and in CIRM's lobby.

CIRM will work directly with the educational community, and in particular with high school science teachers, to create educational modules that can be used broadly in the schools at multiple levels. A Request for Proposals to develop these materials will be issued in 2009.

To reach international audiences, CIRM's Chief Communications Officer serves on the International Society for Stem Cell Research's (ISSCR) public education committee. The committee fosters the dissemination of teacher materials and the development of Web educational content and also organizes a public symposium at the annual ISSCR meeting.

MAKING COMMUNICATIONS HAPPEN

CIRM has hired a three-person communications staff, bringing to the agency significant experience in science communication, media relations, Web content development, and video storytelling. An additional communication expert on contract handles special projects, and a public relations agency enhances targeted media placement.

In addition, CIRM's communication team has significantly extended the reach and impact of its communications efforts by enlisting the public information officers of grantee institutions, thereby creating a virtual statewide public education effort focused on stem cell communications. Press releases are cross-posted on both CIRM's and these institutions' Websites and collaboration across institutions makes most of the video products possible. Liaisons extend to national and international scientific organizations and patient advocacy organizations with which CIRM coordinates communication and key messaging.

SECTION 5. ETHICS AND COMPLIANCE

ETHICAL STANDARDS AND PROCESSES FOR REVISION

Before CIRM developed its own policies, the Governing Board adopted the National Academies' Guidelines for Human Embryonic Stem Cell Research as interim regulations for its grants. The Academies' guidelines were considered the gold standard for the ethical conduct of hESC research when they were announced in April 2005. When these guidelines were adopted by CIRM's Governing Board in May 2005, California became the first state to employ them as interim regulations.

In just over a year, the Standards Working group held eight public meetings to develop its final recommendations for CIRM's own guidelines. They represent the first comprehensive set of state regulations to implement and build on the Academies' guidelines.

CIRM's Medical and Ethical Standards (MES), which took effect in October 2006, provide comprehensive regulation of CIRM-funded research. Proposition 71 requires CIRM's Medical and Ethical Standards Working Group (SWG) to meet at least four times per year to consider the need for new standards and to periodically re-evaluate existing standards in light of developments in stem cell science and in national standards for research ethics.

The SWG has recommended a number of revisions to CIRM regulations that have enhanced CIRM-funded researchers' ability to use tissues, cells, cell lines, and blastocysts. For example, in 2008 the Group recommended amendments to make CIRM's regulations more consistent with the Guidelines of the National Academy of Sciences regarding access to human embryonic stem cells (hESC) lines, embryos, and somatic cells.

ACCESSING CELLS AND TISSUES

In the near term, CIRM anticipates two levels of activity regarding its materials procurement policy. First, CIRM staff will continue a policy development and implementation strategy established in 2008. Activities will include finalizing:

- The development of regulations and administrative procedures for evaluating cell lines intended for use in CIRM-funded research,
- The development, consistent with the National Academy's Guidelines, of regulations authorizing the use of cell lines, and
- The development of regulations authorizing the use of IVF-embryos in which one of the gamete donors received compensation.

The second level of activity involves re-evaluation of existing policy regarding the procurement of oocytes for research. Some observers have suggested that Medical and

Ethical Standards regulations have constrained efforts to develop stem cell lines through somatic cell nuclear transfer (SCNT). To discuss this important issue further, CIRM will convene a meeting with a range of participants, including those directly affected by oocyte donation and those with special interests in this process.

The advent of induced pluripotential stem (iPS) cells also raises new issues that merit consideration and evaluation. iPS cells appear to have many of the properties of embryonic stem cells, including the potential to form embryos and gametes. Thus, CIRM needs to refine appropriate policies for the consent, donation, use, and application of cells to be induced to pluripotency in CIRM-sponsored research.

CLINICAL TRIALS

As CIRM moves towards clinical application of cell therapies, the SWG will increasingly focus on medical and ethical considerations related to early clinical trails. Doing so will require ongoing consultation with a range of stakeholders, including the Food and Drug Administration, the Office of Human Research Subjects Protection in the U.S. Department of Health and Human Services, and patient advocacy organizations.

CIRM will continue to work to foster collaboration and exchange between national and international organizations regarding ethical, human subject, and clinical trials issues. The SWG will provide a forum for considering how oversight mechanisms for current stem cell research might be applied to the conduct of clinical trials.

PARTICIPATION IN CLINICAL TRIALS AND BASIC RESEARCH

The governing board will actively engage the patient advocacy community to consider how to enhance their participation in research and clinical trials. The board will examine how basic research and trial development can dovetail with the needs and expectations of potential participants. A primary goal will be to identify mechanisms that engender both participation and participant empowerment in CIRM-funded research.

COMPLIANCE WITH CIRM REGULATIONS AND CONTRACTS

CIRM has emphasized compliance with its grants administration policy to its grantees; individual members of the Science Team have made numerous visits to grantee institutions as part of an ongoing process to communicate, support, and underscore the need for compliance.

In 2008, CIRM initiated a new in-depth program to evaluate grantee compliance with CIRM regulations and policies. The program entails an internal review of grantee records as well as site visits to evaluate compliance with the requirements of CIRM's Medical and Ethical Standards regulations and the Grants Administration Policy. Site visits include the review of CIRM grantees' stem cell research oversight programs and of specific grant applications for compliance with MES regulations and the Grants Administration Policy. CIRM's evaluation will help recipient organizations correct any shortcomings. Conversely, compliance visits to institutions and companies will provide

CIRM with opportunities to receive valuable input from grantees and their administrators so as to further improve the agency's procedures and regulations.

In 2009-10, CIRM anticipates completing site visits to all institutions receiving funding in excess of $5 million. CIRM may also evaluate any specific application or institution on an as-needed basis to ensure compliance. CIRM will also continue to refine broader programmatic approaches to ensure compliance with all regulations and policies, including the development of materials designed to provide guidance to grantees, sponsorship of workshops and training, and ongoing technical assistance to grantee intuitions.

RECOGNIZING OUR ROLE IN SETTING NATIONAL AND INTERNATIONAL STANDARDS

CIRM is actively involved in the development of national and international standards through its participation in state, national, and international organizations oriented towards research ethics and policy development. Specific affiliations include:

- Membership in the International Stem Cell Forum's Ethics Working Party,
- Membership in the Interstate Alliance for Stem Cell Research,
- Partnership with the International Society for Stem Cell Research Registry Initiative, and
- Participation in an international network to establish interoperable stem cell registries.

Through these organizational affiliations, CIRM will pursue a number of activities intended to improve international exchange and access to research materials. Specific activities will include:

- Working within the Interstate Alliance for Stem Cell Research to identify opportunities for enhancing regulatory compatibility across states and with the National Academies Guidelines.
- Working within the Interstate Alliance for Stem Cell Research to develop consensus approaches for documentation of research oversight.
- Collaborating with the International Society for Stem Cell Research to identify hESC lines and other research materials that conform to state, national, and international standards.
- Creating interactions between CIRM's organizational affiliates and the SWG to consider best practices for research ethics.

CIRM intends for these activities to maximize the diversity of research materials and paths available to CIRM grantees, while at the same time creating a timely and efficient system to assure utmost compliance with all relevant ethical standards.

LEGAL OVERSIGHT OF SCIENTIFIC OPERATIONAL FUNCTIONS

CIRM's General Counsel (GC) has the role of shaping the Agency's legal strategies relative to operations, relationships with business, and new initiatives to ensure compliance with state and federal laws and, where appropriate, with state, national and international regulations. To be an effective instrument for delivering new discoveries to the clinic, CIRM needs to remain an innovative agency able to capitalize on changes in science and in governmental policies and regulations. In this fast-moving area of research, evolving opportunities need a swift response by CIRM that remains both legal and within the margins of community support. The GC and legal officers of CIRM are integral to keeping CIRM an effective instrument of the community's desire to embrace stem cells in regenerative medicine.

The primary responsibility of CIRM's legal team is to be seamlessly integrated into operations so that it readily identifies potential problems and puts processes in place to avoid them before they arise. The legal staff strives to ensure that all legal concerns that may be raised by operations are handled as part of an efficient, integrated effort. The legal team acts as a check–and-balance resource for other departments, documenting the processes that support the innovative practices described throughout this Strategic Plan. The team's specific internal strategy include:

- Handling legal complexities that may arise from the national and international alliances in which CIRM participates.
- Furthering the understanding of CIRM's intellectual property policies as CIRM grantees move towards translational work and begins to make grants and loans to for-profit entities.
- Assuring that accounting and funding practices are continuously reconciled legally to bond funding requirements.
- Integrating operations with the Finance Officer to ensure that appropriate contracting controls are enforced and that documentation of transactions is appropriately maintained per CIRM's policy.
- Providing guidance to the Compliance team in reviewing CIRM Grantees for compliance with CIRM's regulations and policies.
- Clarifying and improving CIRM's regulations in a responsive manner.
- Sustaining CIRM's compliance with relevant state and federal laws and regulations.
- Managing and advising on the numerous audits of CIRM's operational, financial, governance, and conflict-of-interest matters.
- In the process of CIRM's daily operations, CIRM's General Counsel advices the president and the president directs all scientific compliance activities of the legal office.

SECTION 6. THE CIRM STAFF PROFILE AND ORGANIZATIONAL PLAN

CIRM's Governing Board, the Independent Citizen's Oversight Committee (ICOC) holds final decision-making authority on all research funded by CIRM, and as such has ultimate responsibility for the mission of Proposition 71 and for driving CIRM's scientific and

administrative programs. For these reasons the President and staff of CIRM need to have a seamless, mutually supportive working relationship with Chairman Klein and other members of the Board.

At the same time, Chairman Klein, his staff, and Board members carry out responsibilities that are independent of the President's Office but central to CIRM's mission, including, for example, working closely with all the state's constitutional officers, State legislators, the Federal Executive Branch, the US Congress; overseeing CIRM's participation in the bond financing that provides funds for CIRM's research and administrative programs; and serving as CIRM ambassadors in the multiple communities vested in CIRM's mission.

The vision and aspirations of Proposition 71 are being realized through the dedicated efforts of CIRM's professional staff. Integral to CIRM's success has been choosing the right people to work in the Agency and giving them the tools they need to succeed.

To ensure that most of CIRM's funds flow towards research, Proposition 71 mandates that CIRM employ no more than 50 staff employees, plus the chair and the vice chair of the board. This cap requires high performance by all CIRM employees, and for that reason CIRM seeks to hire and develop staff members who are not only expert in their field, but also flexible, motivated, and capable of transferring skills in ways that support CIRM's operating goals.

As of November 2008, CIRM had 3x employees. The Agency's hiring practices have worked well: a strong team has been forged, comprised of individuals who are talented, committed, knowledgeable, and sufficiently flexible to execute the Agency's goals. To retain these talented individuals, CIRM strives to provide a professionally challenging work environment, policies that recognize and support work/life needs, a culture of professional collegiality, and a competitive compensation and benefits package. CIRM is also eager to provide staff with professional development opportunities, including but not limited to conference attendance, classes, and professional networking. Two percent of the overall fiscal-year salary budget is set aside for professional development.

Over the next several years, CIRM will need to hire additional employees to carry out its scientific and administrative functions. The anticipated staffing need at steady state is 30-32 science officers and support staff. Since CIRM's aggressive science programs will result in approximately 400-500 grants and loans being managed and monitored at any one time, sufficient staffing of the Science Office will be essential to ensure quality control and appropriate investing of CIRM funds in the best science. Hiring additional science staff will also increase the workload on administrative staff in all departments.

New employees must be chosen carefully. In addition to talent, expertise, and commitment, CIRM employees must have the flexibility and the capacity to work in a constantly changing environment. Job descriptions for CIRM employees go beyond the standard, benchmarked job descriptors found within larger, established institutions, and potential employees must be willing to transfer skills to support CIRM's operating goals.
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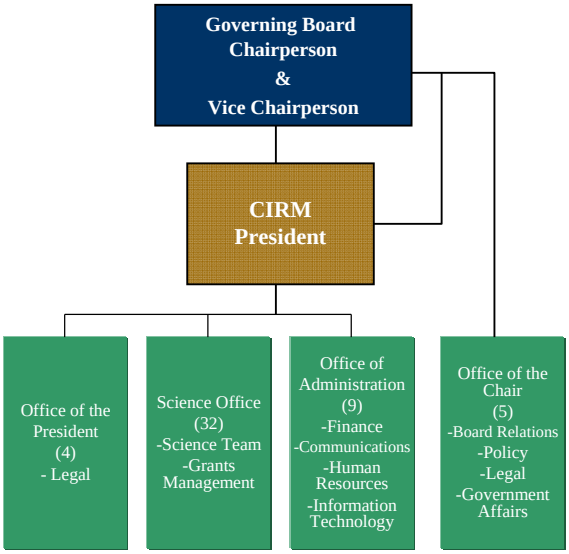
SECTION 7. CIRM ADMINISTRATIVE OPERATIONAL PROGRAM

CIRM OPERATIONAL STRUCTURE

CIRM operations fall into four functional areas, the Office of the President, the Science Office, Office of Administration, and the Office of the Chair. The functions within each office are outlined in the organizational chart below.



In addition to its internal staff, CIRM affords opportunities for external collaboration, both to augment the Agency's intellectual resources and to develop partnerships. CIRM also provides volunteer opportunities, internships, fellowships and speaking engagements to promote information sharing with CIRM staff. CIRM cannot work in a vacuum and must allow for new perspectives and insight from others in the field.

In order to remain within the prescribed cap on full-time positions, CIRM is constantly judging whether work should be carried out internally or through the use of outside experts. In some cases, outsourcing is less expensive and more efficient. A good example of this is payroll administration, which is currently handled by a partner state agency with expert staff members dedicated to this function.

FINANCES AND BUDGETING

CIRM's financial services are managed by CIRM's Director of Finance through a contract with the Department of General Services. The state's Contracted Fiscal Services Unit provides ongoing dispersement and accounting services, including recordkeeping and reporting vehicles.

CIRM operations are based on an annual budget that is capped at six percent, excluding legal fees. The Governing Board and its Finance Committee are ultimately responsible

for monitoring and approving the budget, which covers costs for the Office of the President, Science Office, Administration, and Office of the Chair.

During its startup phase CIRM has functioned well within its approved budgets, and significantly below its statutory budget caps, but more needs to be done to ensure that the Agency's budget and expenditures are transparent to CIRM and to the public. Towards that end, CIRM intends to:

a) Develop a cash-flow methodology to ensure sufficient funding for both administrative needs and grant/loan awards,
b) Enhance budgeting tools to ensure timely and accurate forecasting,
c) Facilitate timely financial reporting to all cost centers,
d) Be a repository of key state agency contacts, and
e) Maintain the documentation and updating of all financial processes.

GRANTS MANAGEMENT SERVICES

Quality control in CIRM's grants administration function is essential to keeping CIRM's mission on track and to ensuring that funds are being spent efficiently and according to expectations. The Grants Management (GM) Team which is responsible for this function strives for accuracy, consistency, and efficiency. Towards that end, the GM team has set five key goals:

- Develop and implement a fully functional Web-based grants management system (*Grantium*).
- Create and provide standardized, regular reporting vehicles that are available to all CIRM constituents.
- Keep CIRM turnaround time to a minimum.
- Achieve 100% grantee compliance with CIRM policies and regulations.
- Become a leader in innovative grants management practices.

To accomplish these goals, CIRM will implement electronic internal reviews and approvals for award payments and create an interface that provides a secure electronic route for transferring award payment data from the *Grantium* system to CalStars. The plan is to move to a paperless Grants Management office by establishing electronic fund transfers of award payments to recipients. Only the Notice of Grants Awards [NGAs] will require paper documentation. The GM team is working with the Science Office to ensure consistent data capture, tracking, and reporting, and to establish a methodology for the annual assessment of projecting and budgeting awards.

In short, the GM Team is committed to establishing clear, consistent processes for grantees in order to minimize the administrative burden and maximize the time spent on research. Within CIRM, the team will work to strengthen the identity of the grants management office as a resource for grantees and staff.

INTERNAL PROCESSES AND REVIEWS

As a California State Agency, CIRM recognizes the need for frequent audits of internal and external financial procedures. Accordingly, CIRM has:

- Established internal processes and timetables designed to facilitate financial and procedural reviews,
- Established a reporting calendar for financial activities,
- Established systems to assure that all state procedures for contracting are followed,
- Arranged a single repository for all information, subject to review, and
- Developed an operational recovery plan designed to keep to a minimum any disruption to the functioning of CIRM's offices and computer equipment resulting from a natural or manmade disaster.

GRANTS SCHEDULE 2008 - 2011

The table below illustrates the high-level schedule through 2011, noting when RFA's will be issued, when applications are due and when the CIRM Governing Board (ICOC) is scheduled to review applications for approval. Also noted are some key CIRM workshops and industry meetings that have already been scheduled. 2009 will be the year that CIRM transitions to Grantium, a Web-based grants management program. CIRM anticipates that the Basic Stem Cell Biology Initiative – RFA II, will be the first program run completely in Grantium and that the RFA issued in the fourth quarter of 2009 (perhaps on immunology) will be the second program run in Grantium.

RFA	3Q08	1Q09	2Q09	3Q09	4Q09	1Q10	2Q10	3Q10	4Q10	1Q11	2Q11	3Q1
		year of transition to Grantium										
Training II & Bridges Tech. Training		Present to ICOC for Approval Jan. 29/30										
Early Translational Research	Apps due Nov. 20		Present to ICOC for Approval Apr. 28/29			Post RFA		Applications due early Sept.		Present to ICOC for Approval Jan.		
Basic Stem Cell Biol. Initiative: RFA I	Post RFA		Applications due April 23	Present to ICOC for Approval August 19/20								
Basic Stem Cell Bio. Initiative: RFA II		Post RFA				Applications due Feb.	Present to ICOC for Approval June					
RFA TBD (Immunology?)					Post RFA		Applications due April	Present to ICOC for Approval mid-August				
Basic Research (annually)						Post RFA				Applications due Feb.	Present to ICOC for Approval June	
RFA TBD						Post RFA			Applications due Nov./Dec.		Present to ICOC for Approval April	
Disease Team		Post RFA	Applications due June 24 (est)		Present to ICOC for Approval October 15					Post RFA	Applications due end of June	
Workshops/Meetings		Immunology Workshop (February)		ISSCR (July 8-11)		Grantee Annual Meeting (February)						