



Policy Brief

Stanford Institute for Economic Policy Research

The Painful Implementation of California's Stem Cell Research Program

by Roger G. Noll

In November 2004, Californians passed Proposition 71, launching a state-sponsored program to support human embryonic stem cell (HESC) research. The proposition established the California Institute for Regenerative Medicine (CIRM) and authorized a \$3 billion bond issue to finance the program for 10 years. Within two months the governing body of CIRM — the Independent Citizens Oversight Committee (ICOC) — was appointed, and only two months later CIRM's president was selected. CIRM anticipated awarding grants by mid-2005.

Despite this impressive beginning, CIRM faces several challenges that have delayed its research program. Private groups challenge the constitutionality of CIRM, and some politicians propose reforms that would drastically change CIRM's structure, procedures, and financial arrangements. These actions have sufficiently clouded CIRM's future that the bond issue has been delayed indefinitely.

This Policy Brief discusses the controversies surrounding the launch of CIRM. The challenges to CIRM arise from many issues, but here we will focus on the main economic issue that has arisen in the challenges to CIRM: allocating the financial payoff from HESC research. Another economic issue, whether state-sponsored HESC research is worth doing, played only a minor role in the campaign and almost no role in subsequent controversies. Because this issue is central to understanding the others, it deserves to be addressed first.

The Scientific Promise

Biologists agree on two key points about HESC research. First, HESC research could allow scientists to learn how to repair or to replace damaged or destroyed cells. Examples of promising areas for applications of HESC research are traumatic injuries (such as paralysis from an accident), auto-immune diseases (such as juvenile

October 2005

diabetes), and degenerative diseases (such as Alzheimer's). Second, therapies are likely to arise only after numerous small advances, many of which do not involve HESC research. Scientific knowledge about all forms of stem cells is primitive. Scientists must learn much more about how stem cells work and how to control their development before they can develop therapies at commercial scale. Consequently, therapeutic advances are likely to be years in the future.

California's HESC program is comparatively small. In 2003, U.S. universities and colleges spent \$40 billion on research. Federally Funded Research and Development Centers (FFRDCs) operated by universities spent another \$4 billion, and nonprofit institutions spent \$11 billion. Universities and colleges in California spent \$5.4 billion on R&D in 2003, and roughly another \$1.5 billion was spent by FFRDCs and other non-profits in California. Thus, CIRM's planned annual expenditures of \$300 million will account for less than 5 percent of R&D at California basic research institutions.

Biomedical research accounts for about half of R&D at universities and colleges, or about \$20 billion. The National Institutes of Health (NIH) spends roughly \$30 billion on biomedical research. CIRM's expected annual budget is about 1 percent of the NIH budget, and 10 percent of all biomedical research expenditures at California academic institutions. Table 1 shows expenditures on biomedical R&D at the six largest universities in California. Four universities collectively spend more than six times as much on biomedical research as CIRM's budget.

CIRM was created in response to a decision by President Bush to ban federal support for most HESC research. The federal ban is unlikely to be permanent. A bipartisan group of 206 members of the House of Representatives and 58 U. S. Senators formally have asked the President to relax the ban, and 148 legislators are co-sponsors of a bill to authorize a federal HESC program. Although near-term legislation is unlikely, the ban could end soon after President Bush leaves office, even if he is replaced by a Republican. If so, the NIH,

already the 800-pound gorilla in biomedical research, is very likely to march in with expenditures that dwarf CIRM's budget.

For these reasons CIRM is unlikely to cause a major redirection of university R&D, especially in the long run. Even if the program is sufficiently promising to be worth its cost, it is unlikely to revolutionize medicine or even to account for more than a small fraction of biomedical research.

The Economic Implications of the Federal Ban

The ban on using federal funds to support HESC research provides a disincentive to accept CIRM grants and, if accepted, to use them efficiently. The cause is the uncertain status and scope of the ban. In August 2001, President Bush gave a speech in which he stated that he was directing federal agencies to permit HESC research only on stem cell lines that already had been developed. Because of contamination and other problems, the scope of HESC research that is permissible under the ban is extremely limited.

The federal ban never was formally issued as an executive order or fleshed out in regulations. As a result, the ban's legal status and the boundary of permissible activities are unclear, and will remain so until a research institution is charged with violating the ban, which has not yet occurred. Some unanswered questions about the ban are as follows.

- Can a student who receives federal assistance (Pell Grant scholarships and work-study grants for low-income students, National Science Foundation fellowships, NIH traineeships) be involved in HESC research, even though the student's support is not tied to the project?
- If a university uses its recovery of indirect costs to finance seed grants, can these funds be used for HESC research, given that the payments reimburse costs of other research projects?
- Can equipment be used on HESC research if it was purchased with federal funds but is used on federal

projects only part-time, remains useful after the federally supported grant is completed, or was fully depreciated while being used for non-banned purposes?

- Can HESC researchers use libraries that are partially funded as part of indirect costs by government grants?

No federal rules have been promulgated on these and other similar issues. Universities must infer the meaning of the ban, and risk that a zealous government auditor later will interpret the ban differently and declare that federal funds were spent illegally. If upheld in court, such a ruling could cause the university to become ineligible for federal grants, which would be a disaster for any California research university.

Because the potential punishment is so much greater than the amount CIRM grants that an institution will receive, universities will act conservatively to avoid auditing conflicts with the federal government. Universities have a powerful incentive to wall off the people and facilities in HESC projects from all federally sponsored activities, including permitted stem cell research. Because therapies developed from HESC research are likely to make use of the results of many projects, including some that are supported by the federal government, quarantining CIRM's HESC research is likely to delay the development of therapies that use stem cells.

Economic Returns to the State

Another barrier to implementing CIRM's program arises because some state legislators, led by Sen. Deborah Ortiz, seek substantial financial returns to the state government from the program. These legislators see CIRM as a venture capital fund that is likely to create substantial financial value in the near term. They want the state to receive royalties from patents arising from CIRM's research and to require that therapies derived from this research be made available to Californians at discounted prices.

These proposals would permanently undermine CIRM. Seeking a large state payoff from CIRM's research puts the program in conflict with federal policies about patents

that are derived from federal grants. The Bayh-Dole Act of 1980 stipulates that grant recipients have the right to exploit intellectual property that is derived from their federal grants. To implement Bayh-Dole, organizations that receive federal grants established technology transfer offices that license patents that are derived from federal projects. Universities share revenues from patent licensing with their researchers, giving both an incentive to pursue research with commercial promise and actively to seek commercial customers.

Because recipients of CIRM grants also can obtain grants from NIH and other federal agencies, creating a different patent regime for CIRM makes CIRM grants less attractive to researchers. Whereas the wisdom of the federal policy is debatable, the fact remains that if the 800-pound gorilla in biomedical research offers researchers a better deal than CIRM, the latter will have greater difficulty attracting proposals from the best researchers.

A second problem with viewing CIRM as a potential source of a state financial windfall is that substantial financial returns to this research are implausible. Because HESC-based therapies, when and if they are developed, are likely to use many patents emanating from many research projects, the royalties from just the CIRM projects are likely to be small. Moreover, most costs of new-drug development arise in testing alternative formulations and obtaining approval from the Food and Drug Administration to manufacture and to sell the drug. These costs are paid almost entirely by commercial pharmaceutical companies, not government grants to basic research institutions. Thus, a large portion of the profits from HESC therapies is not likely to accrue to the sponsor of some of the basic research that led to it. The most likely effect of an attempt by the state to collect substantial royalties and price concessions from CIRM's research output is simply to cause drug companies not to license CIRM's patents.

The history of technology licensing by universities confirms that royalty revenues are tiny compared to research expenditures. U.S. colleges and universities

receive about \$1 billion in revenue from technology licensing, compared to \$40 billion in annual R&D expenditures and \$20 billion in biomedical research. If CIRM grants are roughly as productive in generating royalties as other university research, CIRM's \$300 million annual expenditures will generate less than \$10 million in royalties, which will not begin for years. Moreover, this assumption is generous. If the state tries to capture this revenue, researchers are likely to seek fewer CIRM grants, and neither they nor their home institutions are likely to attempt to license the results.

If the state succeeds in capturing revenues from licensing CIRM's research output, it could easily cost the state substantially more than the income it receives. Interest on state and local bonds is exempt from federal income taxes only if the bonds are used for purposes that are not tied to specific revenues. State and local governments can collect ordinary taxes from business that arises from these investments, but they cannot impose special taxes on the business that is directly associated with the investments. Although the issue has not yet been tested legally, some state officials believe that CIRM's \$3 billion bond issue would lose tax-exempt status if the state claimed any royalties from the patents emanating from this research. Typically, tax exemption is worth about 1.5 percentage points in the interest rate, which is an initial-year interest cost of \$45 million — far more than plausible royalty income.

Organizing CIRM

The lawsuits against CIRM object to its management structure. The power to make appointments to the ICOC is divided among several government office holders, including the state legislature. The lawsuits claim that enabling state legislators to appoint ICOC members is unconstitutional because it violates the separation of powers between the executive and legislative branches. The lawsuits ask the courts to prevent CIRM from spending any state money until this organizational flaw is repaired, which is tantamount to killing it since Proposition 71 can only be amended by another initiative, not the state legislature.

The issue raised by these lawsuits is not new. Several state entities are headed by boards that include members either from or appointed by the legislature. For example, the Speaker of the Assembly is an ex officio member of the University of California Board of Regents and the California State University Board of Trustees, and both the Speaker and the President of the Senate appoint members to regulatory boards in the Department of Consumer Affairs. A victory against CIRM calls these organizations into questions, and will lead to new lawsuits and new ballot measures to repair the damage.

A second feature of CIRM is slotting of ICOC membership. Except for the chair and vice-chair, Proposition 71 requires that ICOC members represent constituencies - disease advocacy groups, universities, nonprofit institutions and business. This feature of the ICOC creates another criticism of CIRM: Foxes are guarding the chicken coop.

The membership of the ICOC is a departure from other government research agencies. Most ICOC members are from biomedical research institutions, and most of the rest are people who are dedicated to specific diseases. Nevertheless, this structure is less problematic than it appears because of its inclusiveness. The ICOC has 29 members largely because it includes every major research institution and disease advocacy group. A large body, while unwieldy, is unlikely to be biased for or against any significant research institution or disease simply because they all are represented. Moreover, proposal reviews will follow the practice of federal agencies. A committee of experts will recommend projects to the ICOC, based in part on peer review.

Conclusions

CIRM is a temporary vehicle to give California a head start in HESC research before the federal government lifts its ban in a few years. Usually delaying a program does not undermine its purpose, but not so for CIRM. If the federal ban disappears in 2009, CIRM's potential benefits will be far less if it is unable to award grants for another couple of years until its legal and political challenges are resolved.

Most criticisms of CIRM and proposals to restructure it are based on overblown views of its likely significance. CIRM is unlikely to be a major force in biomedical research, to produce research breakthroughs that, without substantial additional research financed by others, will lead to dramatic therapeutic advances, or to generate royalty revenues that are more than a few percent of its expenditures. Thus, the reform proposals are not grounded in either scientific or financial reality. They only delay the start of CIRM's research, and thereby undermine its only purpose.

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Extensive data and analysis about U.S. research and development can be found in U. S. National Science Foundation, *Science and Engineering Indicators 2004* and *Academic Research and Development Expenditures: Fiscal Year 2003*, both available at www.nsf.gov

Table 1
Expenditures on Biological and Biomedical Research at the Largest California Universities, Fiscal 2003

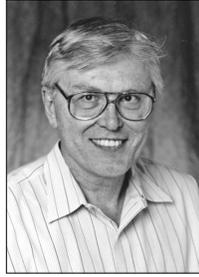
Institution	Expenditures (millions)
UCSF	\$643
UCLA	607
Stanford	333
UCSD	330
UC Davis	248
USC	>201*

Source: US National Science Foundation, *Academic Research and Development Expenditures*, Fiscal Year 2003, Tables 55-56.

* USC data incomplete.

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Roger Noll is the director of the Stanford Center for International Development (SCID) and a Professor of Economics in the Department of Economics at Stanford University. In addition, he is a Senior Fellow at the Stanford Institute for Economic Policy Research (SIEPR). He is a member of the Board on Science, Technology and Economic Policy of the National Research Council.



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SIEPR Policy Briefs
are underwritten by a generous grant from the Taube Family Foundation.



SIEPR *Policy Brief*

A publication of the
Stanford Institute for Economic Policy Research
Stanford University
579 Serra Mall at Galvez Street
Stanford, CA 94305
MC 6015

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