October 5, 2007

Mr. Scott Tocher  
Interim Counsel  
California Institute for Regenerative Medicine  
250 King Street  
San Francisco, CA  94107  


Dear Mr. Tocher:

The California Healthcare Institute (CHI) welcomes this opportunity to comment on the revised California Institute for Regenerative Medicine’s (CIRM) proposed changes to regulations addressing Intellectual Property Policy for For-Profit Organizations (IPPFPO) as released for public comment on Sept. 20, 2007. CHI represents the full biomedical sector of the California economy; our members include more than 250 of California’s leading life sciences companies, universities, and academic research institutions.

As the advocate for California’s statewide biomedical research and development community, CHI appreciates the Independent Citizens’ Oversight Committee’s (ICOC) efforts to develop an intellectual property policy that conforms to the purpose and intent of Proposition 71, the California Stem Cell Research and Cures Act (Prop 71). As you know, CHI has consistently held that policies regulating transactions among academic institutions and commercial companies should be based on the federal Bayh-Dole Act (P.L. 96-517, Amendments to the Patent and Trademark Act). While Bayh-Dole pertains to federally funded research in non-profit organizations, we suggest its basic principles apply to state funded research.

**The Life Sciences Business Model and the Impact of Bayh-Dole**

Intense competition for investment capital places enormous pressures on biopharmaceutical firms, whose products require years of testing to meet U.S. Food and Drug Administration (FDA) standards. On average, it takes 10 to 15 years and more than $800 million to develop a new

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1 See Statement of David L. Gollaher, Ph.D., President and CEO, California Healthcare Institute (CHI) before the Joint Informational Hearing of the Senate Health and Human Services Committee and Assembly Health Committee, Sept. 15, 2004
medicine from a basic research discovery to a product approved by the FDA. Until a company has an approved product, its value depends primarily on its patents – its intellectual property (IP). In fact, for many of the smaller firms that comprise the majority of the biomedical industry, and whose products and technologies are still in pipeline, IP is sometimes their only real asset. The biotechnology industry in California rests fundamentally on IP.

Bayh-Dole, Stevenson-Wydler, and other federal policies regulating intellectual property and technology transfer have been important to the success of California’s biomedical research and development enterprise.

Before Bayh-Dole, according to a Congressional study:

Government [generally] retained title to inventions made with government support whether the research was performed in federal laboratories, in universities, or by individual companies. Licenses to use government patents were then negotiated with firms either on a non-exclusive basis (meaning additional companies could use the technology) or, more rarely, for the exclusive use by one manufacturer. However, it was widely argued that without title (or at least an exclusive license) to an invention and the protection it conveys, a company would not invest the additional, and substantial time and money necessary to commercialize a product or process for the marketplace.²

Enactment of Bayh-Dole, therefore, created a “single, uniform national policy designed to cut down on bureaucracy and encourage private industry to utilize government financed inventions through the commitment of the risk capital necessary to develop such inventions to the point of commercial application.”³

The licensing and technology transfer provisions of Bayh-Dole have had a significant impact on the life sciences. In California alone, since Bayh-Dole’s enactment in 1980, the state’s leading academic and non-profit research institutions have spun out more than 600 biomedical companies through technology transfer agreements.⁴ Considering this record of success, we believe the principles of Bayh-Dole should be applicable to the IPPFPO. Indeed, the record of debate, consideration, decision-making, and experience at the federal level throws much light on the barriers and disincentives that an overly restrictive or ambiguous policy can create.

Our specific comments to the IPPFPO are as follows and in order of their appearance in the regulations:

Section 100406 – Licensing CIRM-Funded Patented Inventions and
Section 100407 – Access Requirements for Products Developed by For-Profit Awardees

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⁴ Source: PricewaterhouseCoopers/California Healthcare Institute surveys, 2002 and 2003
As CHI stated in our comments on the CIRM Intellectual Property Policy for Non-Profit Organizations, we are concerned that the ICOC intends to use the IPPFPO to address health care access and pricing issues beyond the intent of Prop. 71. CHI believes that a stated purpose of Prop 71 – to “[i]mprove the California health care system and reduce the long-term health care cost burden on California through the development of therapies that treat diseases and injuries with the ultimate goal to cure them” assumes that CIRM-funded research and resulting innovation will directly address these goals. While improving health care access and affordability are important goals, they were not the objective of Prop 71 and should, therefore, not be the subject of policies and regulations pertaining to Prop. 71.

With respect to the proposed regulations, the access and pricing mechanisms contained in Section 100406(c)(4) state that “A Grantee may negotiate an Exclusive License for a CIRM-funded Patented Invention that is required for commercialization of a Drug . . . only if the licensee agrees to provide uninsured Californians access to the Drug.” The Section goes on to state “In addition, exclusive licensees must agree to abide by the provisions of subdivision (a) of Title 17, California Code of Regulations, section 100407, regarding discount pricing.”

Regarding uninsured patients, it is unclear what is meant by the term “access.” Is the ability to purchase a drug product or therapy on the open market sufficient to satisfy this requirement? The term could likewise be interpreted as providing a drug product or therapy at no cost to the patient. Without clarification, it would be difficult to attract private investment to develop CIRM-funded technology.

Sections 100406 and 100407 states that “[t]he access plan shall be consistent with industry standards….” There is no evidence today that an industry standard exists. If the drug maker were a small biotech company, would the standard be that of small biotech companies?

The language referring to the pricing mechanism is likewise ambiguous. It is unclear by this language which patients the regulations refer to. How will a company identify the patients that should receive the therapies? The regulation implies that companies that commercialize a therapy will know which patients should receive therapies at a discount. This raises serious privacy concerns, as companies may not be legally allowed to identify the patients whose therapies will be purchased in California by public funds.

The pricing mechanism contained in Section 100407 provides “A Grantee (or its exclusive licensee) must provide a Drug, the development of which was in whole or in part the result of CIRM-funded Research, at a price as provided in the California Discount Prescription Drug Program to eligible Californians under that program.” Both pricing mechanisms contained in Sections 100406 and 100407 are forms of price controls, which we believe will create a substantial disincentive to commercial interest in licensing CIRM-funded inventions from for-profit grantees. In short, we argue that the consequences of these provisions would make industry and investors significantly less likely to consider licensing CIRM-funded technologies. The long-term result

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Text of Proposition 71, Sec. 3, “Purpose and Intent”
could be that promising CIRM-funded research will remain undeveloped, not producing the “life-saving regenerative medical treatments and cures” that are the core purpose of Prop. 71.

As we stated in our comments to the IPPNPO, experience at the federal level confirms these concerns. In the early 1990s, technology transfer and licensing policies at the National Institutes of Health (NIH) attempted to incorporate “fair pricing” requirements, with poor results. According to a report by the Congressional Research Service (CRS) --

Prior to 1995, NIH had included what was known as a “fair pricing clause” in its cooperative research and development agreements [CRADA] and many licensing arrangements. In 1989, the Public Health Service (PHS) instituted a policy addressing the pricing of products resulting from a government-owned patent licensed by NIH on an exclusive basis to industry or an invention jointly developed with industry under a CRADA and then licensed exclusively to the collaborator. …

The clause was removed in 1995 at the request of Dr. Harold Varmus, Director of NIH, after a review of the situation and several public hearings. He concluded that the evidence indicated "...the pricing clause has driven industry away from potentially beneficial scientific collaborations with PHS scientists without providing an offsetting benefit to the public." While sharing concerns over the "potential inaccessibility" of drugs due to costs, "NIH [agreed] with the consensus of the advisory panels that enforcement of a pricing clause would divert NIH from its primary research mission and conflict with its statutory mission to transfer promising technologies to the private sector for commercialization." A study by the Department of Health and Human Services Inspector General found that companies viewed the clause as a major problem in the NIH CRADA approach. Opponents of the clause argued that the uncertainty of the pricing clause exacerbated a process already fraught with risk. According to industry sources, not knowing what the determination of "fair" pricing would be at the end of a long and expensive research, development, and commercialization process was a strong deterrent to entering into cooperative arrangements. Many of the pharmaceutical and biotechnology companies declined to undertake CRADAs. Some firms even declined opportunities for joint clinical trials with NIH in anticipation of future price control demands. 7 (emphasis added)

In the Fall of 2006 CHI surveyed its members to determine what impact the pricing and access requirements proposed by the IPPNPO (and similar language as contained in the IPPFPO) would have on companies and venture capital interest in potential licensing opportunities. The results were dramatic – over 80% indicated that they would be much less likely to consider licensing a technology, or investing in a start-up company based on a technology that carried such pricing and access mandates. The likely consequences of these provisions, therefore, will be fewer new medicines and therapies to the citizens of California.

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At a minimum, the IPPFPO should include a “trigger” or funding threshold that would limit its access and pricing provisions to products for which CIRM funding is a significant and substantial portion of a product’s overall development costs. Such a trigger should apply to CIRM funding whether it involves an invention developed by a company in part through direct CIRM funding to the firm or part of an invention licensed by a company from a CIRM grantee. The principle for the trigger should be the proportion of CIRM funding in the total cost of bringing a product to market, not the process by which CIRM funding is provided.

Failure to incorporate a threshold function in the IPPNPO will, we believe, make licensing and technology transfer of CIRM-funded inventions from both the state’s academic and other non-profit research institutes as well as private firms considerably less attractive in the many instances where a CIRM-funded licensed invention would be but a small part (financial and otherwise) of any downstream commercialized product.

As drafted, the regulations create a great deal of uncertainty. Consider a product not directly derived from CIRM grant funding, but based on the discovery of a biological pathway that was funded by CIRM. Would a company commercializing this product need to have an access plan in place? We believe the regulations should be clarified to apply only to instances where CIRM grant money can be tied directly to a developed product, for example, where a cell line or biological product isolating such cell line was discovered using CIRM grant funding is the actual drug product. To include products that are indirectly related to CIRM funding will discourage corporate partnerships. This is because the access and pricing obligations will not be commensurate with the value added by CIRM grant funding.

Imposing these pricing and access requirements even in instances where CIRM funding is only a minor portion of that which would be required to ultimately commercialize a product will likely lead many for-profit firms to not apply for CIRM funding. And in the case of those firms that do apply, create significant barriers to the additional private sector capital needed to develop and commercialize a product. Simply put, the opportunity cost of placing these requirements on all potential therapies, drugs, and diagnostics will likely be fewer realized therapies, drugs, and diagnostics. To “assure that essential medical research is not unreasonably hindered by the intellectual property agreements,” we therefore urge that the IPPFPO include an explicit threshold function.

Section 100408 – Revenue Sharing

Section 100408 provides that in the event of revenue streams from self commercialized products that result from CIRM-funded patented inventions, awardees must share net revenues in excess of $500,000 with the State of California at a royalty rate of between 2-5% (to be negotiated with CIRM), capped at three times the total awarded money. (Net revenues are defined as gross revenues minus direct costs incurred in the generation and protection of the patents from which the revenues are received; and an invention is defined as a discovery that is or may be patentable or otherwise protectable under Title 35 USC.)
CHI acknowledges and appreciates the inclusion language allowing for a threshold and maximum amount determination of revenue to be returned to the State. We would recommend that funding sources should explicitly include self-funding (i.e., if a company funds a project, that company should get credit for it).

CHI believes the above approach, largely taken from academic settings, substantially underestimates the expenses of drug development to arrive at “net revenue.” Should the CIRM maintain a revenue-sharing provision in the IPPFPO, we suggest the definition of net revenues should be reworked to more closely reflect private sector experience.

We also would maintain, similar to our suggestions for the pricing and access provisions, that the revenue sharing regulations should be clarified to apply only to instances where CIRM grant money can be tied directly to a developed product.

CHI also suggests that direct revenue sharing and royalty provisions may actually reduce the public benefit of Prop 71 funded research. A CRS Report for Congress succinctly summarizes the decision at the federal level not to require direct recoupment provisions.

Providing universities, nonprofit institutions, and small businesses with title to patents arising from federally-funded R&D offers an incentive for cooperative work and commercial application. Royalties derived from intellectual property rights provide the academic community an alternative way to support further research and the business sector a means to obtain a return on their financial contribution to the endeavor. While the idea of recoupment was considered by the Congress in hearings on [Bayh-Dole] legislation, it was rejected as an unnecessary obstacle, one which would be perceived as an additional burden to working with the government. It was thought to be particularly difficult to administer. Instead, Congress accepted as satisfactory the anticipated payback to the country through increased revenues from taxes on profits, new jobs created, improved productivity, and economic growth. For example, according to the MIT Technology Licensing Office, 15% of the sales of licensed products derived from federally funded university research is returned to the government in the form of income taxes, payroll taxes, capital gains taxes, and corporate income taxes. This is estimated to be 6 times the royalties paid by companies to the universities. The emergence of the biotechnology industry and the development of new therapeutics to improve health care are other prominent indications of such benefits. These benefits have been considered more important than the initial cost of the technology to the government or any potential unfair advantage.\(^8\)

CHI suggests that the financial benefits to the state from CIRM-funded research and subsequent technology transfer and product commercialization will come from job creation, exports, increased income taxes, payroll taxes, capital gains taxes, corporate income taxes – in short from a broad range of economic factors.

\(^{8}\) The Bayh-Dole Act: Selected Issues in Patent Policy and the Commercialization of Technology, p. 14
Section 100410 – March-In Rights

CHI is similarly concerned with the IPPFPO’s grounds for termination of licenses and “march-in” rights, provisions and procedures, especially as they pertain to the pricing and access requirements addressed above. While based on provisions in Bayh-Dole, the IPPFPO differs notably by including among the circumstances for triggering march-in rights failure by licensees to adhere to pricing and/or access plans as described in the proposed Section 100410(b)(2). CHI maintains that these provisions, by increasing the risk of litigation, present disincentives to commercial collaboration.

While Bayh-Dole march-in provisions do not include product prices as a triggering mechanism, several attempts have been made to persuade the federal government to exercise march-in rights because prices of certain drugs developed with federal funding were deemed unreasonable. In each case, the NIH decided not to initiate march-in proceedings.9 This history suggests that the ICOC, CIRM and licensees of CIRM-funded institutions would almost certainly face calls for the state to exercise march-in rights. This would add another layer of risk and uncertainty to academic-commercial transactions. CHI therefore suggests that the ICOC remove pricing and access as grounds for both the triggering of CIRM march-in rights and the termination of licenses.

CHI also requests, consistent with Bayh-Dole, that “public use” requirements addressed in Section 100410(b)(3) be clearly specified to minimize uncertainty.

Summary

To promote technology transfer and commercial collaboration on CIRM-funded inventions and to limit barriers to stakeholder participation in research, licensing, and commercialization, CHI suggests that the ICOC edit the IPPFPO as follows:

- Remove Sections 100406(c)(4) and Sections 100407 in their entirety, as we believe health care access and affordability provisions should not be the subject of policies and regulations pertaining to Proposition 71.

- Recognizing the ICOC is likely to maintain pricing and access provisions, we suggest you provide clarity to the term “access” in Section 100406(c)(4).

- With respect to Sections 100406(c)(4) and 100407(a)(2), we suggest clarity on the phrase “industry standards”

- We also suggest a threshold function in Sections 100406 and 100407 that would limit the access and pricing provisions to products for which CIRM funding is a significant and substantial portion of a product’s overall development costs.

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9 See “NIH March-In position paper in the case of Xalatan” and “NIH March-In position paper in the case of Norvir” at http://www.ott.nih.gov/policy/policies_and_guidelines.html
• We suggest amending Sections 100406, 100407 and 100408 to provide that those regulations apply only to products developed as a direct result of CIRM grant funding.

• Provide clarity in Section 100406(c)(4) on how a company that commercializes a product derived from CIRM grant money will identify the patients that should receive access to that product.

• Amend Section 100408 to provide that self-funding be included as a funding source in determining the threshold and maximum amount determination of revenue to be returned back to the state.

• Amend the definition of ‘net revenue’ in Section 100408 to more closely reflect private sector experience.

• Remove pricing and access as ground for triggering march-in rights as contained in Section 100410.

**Conclusion**

CHI appreciates this opportunity to comment on the revised CIRM Intellectual Property Policy for For-Profit Organizations. We believe a strong IPPFPO will advance CIRM-funded stem cell research and, ultimately, treatments for millions here in California and worldwide. This, in turn, will improve California’s health care system, benefit the California economy, and further promote the state’s biotechnology industry as a global leader. We hope that the ICOC will give careful consideration to our comments and incorporate them into the final IPPFPO.

We look forward to working with the ICOC as it finalizes this policy, and we would be happy to further discuss these comments in additional detail.

Thank you for your attention to this important matter.

Sincerely,

David L. Gollaher, Ph.D.
President and CEO