

June 15, 2006

BY ELECTRONIC MAIL TO NONPROFITPREGS@CIRM.CA.GOV

Mr. C. Scott Tocher
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Comments to Proposed CIRM Regulation Entitled: Intellectual Property Policy for Non-Profit Organizations, [California Code of Regulations, Title 17. — Public Health, Division 4 — California Institute For Regenerative Medicine, Chapter 3]

Dear Mr. Tocher:

The California Healthcare Institute (CHI) welcomes this opportunity to comment on the California Institute for Regenerative Medicine's (CIRM) interim regulations addressing Intellectual Property Policy for Non-Profit Organizations (IPPNPO) as approved by the Independent Citizens' Oversight Committee (ICOC) on February 10, 2006. 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.

California's highly-developed infrastructure -- including basic science, venture capital, commercial life sciences companies, along with the many support services (e.g. legal, accounting, architectural) essential to transforming scientific discoveries into products -- is the reason our state is the global leader in biotechnology. And it is the reason that public funding of embryonic stem cell research in California can exert enormous leverage. No other state in America -- no other nation in the world -- has the people and experience to capitalize on this new science as quickly as California.

As the advocate for California's biomedical research and development community, CHI appreciates the ICOC's 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). The focus of Prop 71 is to support human embryonic stem cell research with the goal of discovering new diagnostics, treatments and therapies. We therefore support the stated objectives of the IPPNPO to "promote sharing of all types of intellectual property created as a consequence of CIRM funding for use in research conducted by both academic and commercial research and development organizations" and "to facilitate the commercialization of CIRM-funded discoveries without impeding the progress of stem cell research."¹

¹ CIRM Intellectual Property Policy for Non-Profit Organizations, approved by the ICOC on February 10, 2006. pg 4-5.

At the same time, however, CHI is concerned with the IPPNPO objective “to provide a financial benefit to the State of California through revenue sharing in the event that CIRM-funded discoveries lead to valuable diagnostic and/or medical therapies” and specific IPPNPO provisions addressing pricing and access requirements in technology transfer agreements.² Far from promoting technology transfer and commercial product development, these provisions are likely to discourage commercial interest. Because commercialization is essential for the development and production of new medicines, CHI believes that the goal of the IPPNPO should be to *minimize* barriers to technology transfer. Moreover, while we strongly support policies to improve access to advanced medicine, we maintain that IP policies and regulations are not the proper venue for addressing the issues of access and cost.

CHI has consistently encouraged policies to regulate transaction among academic institutions and commercial companies based on the federal Bayh-Dole Act (P.L. 96-517, Amendments to the Patent and Trademark Act).³ While the IPPNPO is generally modeled on federal laws governing technology transfer⁴, it includes several provisions that diverge significantly:

- Product pricing and access provisions that permit licensing “only to organizations with plans to provide access to resultant therapies and diagnostics for uninsured California patients” and only if “licensees will agree to provide to patients whose therapies and diagnostics will be purchased in California by public funds the therapies and diagnostics at a cost not to exceed the federal Medicaid price”;⁵
- March-in rights and grounds for termination of licenses that may be exercised if the pricing and access provisions referenced above are not adhered to;⁶
- Recoupment and revenue-sharing provisions that, beyond a threshold amount and after payments to investors, require grantees to pay 25% of revenues received under a license agreement to the State of California for deposit into the State’s General Fund;⁷ and
- Broad, vague and ambiguous requirements that CIRM-funded inventions must be made available, by grantee organizations and licensees, for research purposes at no cost.⁸

During the past thirty years, California biotechnology companies have licensed hundreds of inventions from academic institutions. The lesson from this collective experience is that stakeholders – researchers and research organizations, industry and other licensees, and venture

² Ibid

³ 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

⁴ Including, in addition to Bayh-Dole, P.L. 96-418, the Stevenson-Wydler Technology Innovation Act (Stevenson-Wydler), as amended

⁵ Proposed Title 17 of California Code of Regulations, section 100306(d)

⁶ Proposed Title 17 of California Code of Regulations, section 100310(a)(2) and section 100306(f)

⁷ Proposed Title 17 of California Code of Regulations, section 100308(b)

⁸ Proposed Title 17 of California Code of Regulations, section 100307 and section 100306(f)

capital investors – value transparency and predictability in licensing and technology transfer agreements. Biotechnology is inherently risky. Any aspect of a technology transfer contract that increases risk, particularly by adding an element of uncertainty, makes it less attractive to potential partners and investors and thus reduces the prospects for successful commercial collaboration.

We address in detail our concerns regarding specific provisions below.

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 potential new medicine from a basic research discovery to a product approved by the FDA. Before FDA product approval, the value of a biomedical company depends on its patents – its intellectual property. 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.

Prior to Bayh-Dole --

“[T]he 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.”⁹

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.**”¹⁰

The licensing and technology transfer mechanisms of Bayh-Dole have had an especially significant impact on the life sciences. In California alone, since Bayh-Dole’s enactment in

⁹ Congressional Research Service (CRS) Report RL32076, *The Bayh-Dole Act: Selected Issues in Patent Policy and the Commercialization of Technology*, by Wendy Schacht. Updated June 10, 2005. p 2.

¹⁰ House Committee on the Judiciary, *Report to Accompany H.R. 6933*, 96th Congress, 2nd Session, H.Rept. 96-1307, Part 1, p3. Emphasis added.

1980, the state's leading academic and non-profit research institutions have spun out over 600 biomedical companies through technology transfer agreements.¹¹

Given the federal technology transfer model's record of success in advancing biomedical research, development, and commercialization, CHI urges the ICOC to adopt an IPPNPO that is more closely in line with federal policy. Where the interim IPPNPO policy differs, we believe that the record of debate, consideration, decision-making, and experience at the federal level offers evidence of the barriers and disincentives that an overly restrictive or ambiguous policy can create.

i. Proposed Title 17 of California Code of Regulations, Section 100306(d)

CHI is concerned that the ICOC may be inappropriately using the IPPNPO to address health care access and pricing issues by requiring exclusive licensing of CIRM-funded inventions "only to organizations with plans to provide access to resultant therapies and diagnostics for uninsured California patients" and only if "licensees will agree to provide to patients whose therapies and diagnostics will be purchased in California by public funds the therapies and diagnostics at a cost not to exceed the federal Medicaid price." 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.

Indeed, CHI strongly 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.¹² Requirements included in the draft IPPNPO would discourage commercial collaboration, technology transfer and licensing by (a) reducing the rate of return on CIRM-related deals in comparison to other academic-industry transactions, and (b) increasing investors' financial risk by imposing state price regulation on downstream products. Considering biotechnology's long product lead times, price regulation makes it all the more difficult to project return on investment.

Experience at the federal level confirms these concerns. 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. ...

¹¹ Source: PricewaterhouseCoopers/California Healthcare Institute surveys, 2002 and 2003

¹² Text of Proposition 71, Sec. 3, "Purpose and Intent"

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.¹³ (emphasis added)

Based on these findings, CHI is concerned that the IPPNPO pricing and access provisions would similarly divert CIRM from its primary missions as outlined by Prop 71. Accordingly, CHI strongly urges the ICOC to remove Section 100306(d) from the final IPPNPO.

ii. Proposed Title 17 of California Code of Regulations, Section 100310(a)(2) and Section 100306(f)

CHI is similarly concerned with the IPPNPO'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 IPPNPO 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 Title 17 of California Code of Regulations, Section 100306(d).¹⁴ CHI maintains that these provisions present an additional disincentive to commercial collaboration.

Bayh-Dole march-in provisions do not include product costs as a triggering mechanism, nonetheless several attempts have been made to persuade the federal government to exercise march-in rights based on the premise that prices of certain pharmaceutical products developed with federal funding were "unreasonable." In each case, the NIH decided not to initiate march-in proceedings.¹⁵ 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. The result would be to 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.

¹³ Congressional Research Service (CRS) Report RL32324, *Federal R&D, Drug Discovery, and Pricing: Insights from the NIH-University-Industry Relationship*, by Wendy Schacht. March 16, 2004. p 15-16

¹⁴ P.L. 96-517, Section 203

¹⁵ 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

CHI also requests, consistent with Bayh-Dole, that “public use” requirements addressed in Section 100310(a)(3) be clearly specified to minimize ambiguity and uncertainty.

Finally, CHI requests that the ICOC very carefully consider how to address march-in proceedings. At a minimum, the ICOC should establish detailed procedures that, in addition to the notice of determination and basis as provided in Section 100310(b), establish the right of the patent holder, licensee, and other interested stakeholders to submit information and arguments opposing and appealing any proposed march-in prior to final action.

iii. Proposed Title 17 of California Code of Regulations, Section 100308(b)

CHI acknowledges that an intent of the research funded by Prop 71 is to “[provide] an opportunity for the state to benefit from royalties, patents, and licensing fees that result from the research.”¹⁶ However, we question IPPNPO provisions that would require grantees to pay, beyond a threshold amount and after payments to inventors, 25% of revenues received under a license agreement to the State of California for deposit into the State’s General Fund. Beyond the request that, for the purposes of this section, the IPPNPO definition of “revenues” be clarified to exclude equity ownership, such as stock, stock options, etc., CHI suggests that direct revenue sharing and/or recoupment 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.¹⁷

¹⁶ Text of Proposition 71, Sec. 3, “Purpose and Intent”

¹⁷ *The Bayh-Dole Act: Selected Issues in Patent Policy and the Commercialization of Technology*, p. 14

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. We further suggest that a recoupment policy will, in fact, divert grantees' financial resources from additional research activities that would otherwise be possible. We therefore request that the ICOC reconsider Section 100308(b) of the interim IPPNPO.

iv. Proposed Title 17 of California Code of Regulations, Section 100307

CHI opposes the draft IPPNPO's extremely broad and unprecedented research use exemption provision. While CHI shares the objective of ensuring that CIRM-funded inventions are made broadly available to the California research community, the provision in the IPPNPO, as written, may have several negative unintended consequences.

First, it eliminates any possibility that a CIRM-funded research tool will be commercialized, because it requires that any licensee make such a research tool available to all California researchers at no cost. If all California customers must be served free, there is no commercial opportunity in embryonic stem cell related research tools. Second, it creates discriminatory treatment of the substantial research tools segment of the California life sciences industry. Prop 71 and CIRM fully recognize that commercial incentives must be preserved to get CIRM-supported therapies and diagnostics to patients in need. The premise that research and development is a two part process, with academic institutions performing basic research and commercial companies conducting applied research, development and commercialization, is fundamental to Prop 71. CHI holds that this principle should apply equally to research tools because commercialization of such inventions accelerates their broad dissemination to the research and commercial communities. Indeed, the academic and non-profit research institutes that initially develop research tools have neither the resources nor the facilities to produce and distribute them in the quantity necessary, making commercialization a fundamentally essential component to research tools dissemination. Just as therapies must reach patients to achieve health benefits, so too must new research tools for stem cell isolation, characterization, and differentiation reach investigators for stem cell research to advance at the fastest possible rate. Finally, the inclusion of such a sweeping research use provision in the IPPNPO sets a dangerous precedent at a time when research use policy is currently being debated in many forums. Given these factors, CHI urges the ICOC to use extreme caution before enacting any research use provisions.

In the rationale for Sec. 100307 outlined in the Statement of Reasons, reference is made to the Patent Act of 1952 and its lack of a "generally applicable research exemption."¹⁸ While exemptions from patent enforcement are rare in U.S. patent law, there are in fact two operative types of research use exemptions that will apply to CIRM grantees even in the absence of any research use provision in the IPPNPO.

¹⁸ CIRM "Initial Statement of Reasons for the Proposed Adoption of Intellectual Property Regulations for Non-Profit Organizations", p 9.

One exemption is the judicially created common law research-use exemption. This exemption provides that it is not an act of infringement to make and use a patented invention if the use is limited to research or experimentation and the user does not obtain any commercial advantage or benefit. There have been only a handful of cases in the 200-year history of this exemption, but in those cases the courts have interpreted this exemption narrowly. In *Madey v. Duke*, the Court of Appeals for the Federal Circuit held that activities that could be construed to have a business-related objective (*e.g.*, publishable research to further a university's prestige, image, and ability to bring in grant money) are considered to be outside the scope of a research use exemption.¹⁹ Thus, academic researchers may be outside the scope of exemption if their activities further the interests of their institutions, such as attracting researchers or securing research grants. As a practical matter however, a patent owner will generally not enforce his patent against a researcher if the research activities in question do not damage the patent owner's commercial interests. While the *Madey v. Duke* decision has raised many concerns in the academic community, a recent study commissioned by the National Academies indicates few instances where patents have constrained commercial or academic biomedical research, even in areas of substantial commercial interest.²⁰ This is true even in the post *Madey v. Duke* environment despite some reported activity aimed at influencing academic research or publication.

A second type of research exemption is a part of the Hatch-Waxman Act of 1984.²¹ It allows making and using a patented pharmaceutical compound or device to collect data for submission to a U.S. government regulatory agency. This is a "safe harbor" for individuals or entities making and using patented materials for uses reasonably related to the development and submission of information to the government (*e.g.*, the FDA). The U.S. Supreme Court recently interpreted this provision very broadly, creating a large statutory drug development-specific research use provision in U.S. law.²² This statutory exemption as well as the common law research use exemption will apply to CIRM grantees absent any additional research use provision in the IPPNPO.

We also point out that researchers can avoid infringement liability by obtaining authorization from patent holders for use of an invention in research.

Finally, it should be noted that good non-patent related alternatives to the research use provision exist. NIH, for example, uses its Research Tool Guidelines to effectively encourage broad dissemination of NIH-funded research tools.²³ Importantly, the NIH approach focuses on the goal of broad access and preserves the flexibility to use commercial forces where they are the

¹⁹ JOHN M.J. MADEY, Plaintiff-Appellant, v. DUKE UNIVERSITY, Defendant-Appellee. UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT. 307 F.3d 1351; 2002 U.S. App. LEXIS 20823; 64 U.S.P.Q.2D (BNA) 1737

²⁰ "Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health", 2006. As available at <http://www.nap.edu/catalog/11487.html>

²¹ 35 U.S.C. §271(e)(1)

²² In decision on Merck KGaA v. Integra LifeSciences I, Ltd. Available at <http://www.supremecourtus.gov/opinions/04pdf/03-1237.pdf>

²³ See "NIH Principles and Guidelines for Sharing of Biomedical Resources" available at <http://ott.od.nih.gov/pdfs/64FR72090.pdf>

best means of achieving broad dissemination. That approach also does not risk undermining the core incentive structure that has motivated the development of so many important life science tools.

Given these factors, CHI suggests that Section 100307 of the IPPNPO be removed or significantly narrowed to acknowledge existing research use exemptions along with the importance and value of commercial research tools to CIRM-funded research, commercial collaboration, and product development. Otherwise, we are concerned that this provision, as written, would eliminate any incentive for private industry to make the additional investments necessary to bring CIRM-funded research-related IP to fruition. Without private sector investment in research innovations, stem cell research and the development of resulting new treatments and therapies will be constrained.

Similarly, CHI suggests that the requirement that grounds for termination of licenses include "failure to keep the licensed invention available to the public for research purposes" included in Section 100306(f) is, as written, vague, overbroad and ambiguous for the same reasons as mentioned above with regards to Section 100310(a)(3). Nor is that language seemingly consistent with the initial requirement of Section 100307, which addresses "California research institutions." Therefore, CHI requests that the ICOC remove or clarify this provision to better explain what purpose it is intended to serve (i.e. what other provisions of the regulations it is intended to support).

Conclusion

CHI appreciates this opportunity to comment on the interim CIRM Intellectual Property Policy for Non-Profit Organizations. We believe that a strong IPPNPO 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 IPPNPO.

In 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:

- Remove Section 100306(d), which permits licensing "only to organizations with plans to provide access to resultant therapies and diagnostics for uninsured California patients" and only if "licensees will agree to provide to patients whose therapies and diagnostics will be purchased in California by public funds the therapies and diagnostics at a cost not to exceed the federal Medicaid price".
- Remove Section 100310(a)(2), which sets pricing and access issues as conditions for the triggering of CIRM march-in rights.

- Clearly specify “public use” requirements addressed in Section 100310(a)(3) in order to minimize ambiguity and uncertainty.
- Remove pricing and access issues as grounds for modification or termination of licenses as provided in Section 100306(f).
- Remove or consider more effective and efficient alternatives to Section 100308(b), which establishes a direct revenue-sharing policy for CIRM-funded commercialized technologies.
- Remove or significantly narrow Section 100307, which broadly requires that CIRM-funded inventions must be made available for research purposes at no cost.
- Clarify, narrow or remove "failure to keep the licensed invention available to the public for research purposes" as grounds for termination of licenses included in Section 100306(f).

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
California Healthcare Institute

cc: Mary E. Maxon, Ph.D.