Ref. 1

Alliance for Research Innovation

April 30, 2007

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

RE: Comments to Proposed CIRM Regulation Entitled: Intellectual Property Policy for For-Profit Organizations (IPPFPO)

Dear Mr. Tocher:

The Alliance for Research Innovation welcomes this opportunity to comment on the California Institute for Regenerative Medicine's (CIRM) interim regulations on the Intellectual Property Policy for Profit Organizations (IPPFPO) as released for public comment on March 15, 2007. The Alliance represents multiple trade associations and companies focused on preserving and enhancing innovation in biomedical research. Many of our members are actively involved in the research, development, and commercialization of biomedical materials and research tools, including materials and tools related to stem cell research.

Our comments focus on Section 100404 – Publication-Related Biomedical Materials Requirements.

This section requires a CIRM grantee to "share biomedical materials described in published scientific articles for research purposes in California… without cost or at no cost." The section allows exceptions to this rule, including "special circumstances" and if it "would endanger the competitive position of the company." Illustrative "special circumstances" include an exception if providing the biomedical materials is "onerous" or "in direct conflict with the business of the awardee." Negotiation with the CIRM is necessary to determine whether these exceptions apply to any particular grantee or circumstance.

We appreciate the intent of this language. The existing provision, however, creates only the *possibility* that a commercial biomedical materials grantee will be exempted from the requirement of sharing its products at cost or at no cost. The uncertainty as to when CIRM would determine a grantee's eligibility for an exception as well as the risk that CIRM may not grant the exemption are certain to reduce the participation of commercial firms in CIRM's programs. As the CIRM has acknowledged on many occasions that the development of advanced tools and materials for stem cell research is one of the most important early goals of the Institute, this outcome would be unfortunate.

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The CIRM successfully tackled the issue of preserving commercial incentives while ensuring researcher access to CIRM funded research tools in the context of the IPPNPO, and we suggest you use a similar construct here.

We suggest that an explicit exemption be provided in this section if a grantee company commercializes a CIRM-funded biomedical material on reasonable terms, and would suggest adding the following sentence at the end of Section 100404:

> **"Commercial suppliers of biomedical materials can satisfy the requirements of this paragraph by making the materials commercially available on reasonable terms for research use in California."**

By adding such an amendment, commercial entities will not be discouraged from working with the CIRM to develop important new biomedical materials, yet would be required to meet the needs of California researchers on terms consistent with those in the pending IPPNPO licensing regulations. Time consuming negotiations would not be required of CIRM or potential commercial awardees. Under the amendment, CIRM would remain the entity, as in the IPPNPO, to determine whether the "reasonable" standard is being met.

We appreciate this opportunity to comment on the interim CIRM Intellectual Property Policy for Profit Organizations. We hope that the ICOC will give careful consideration to our comments and we look forward to working with the ICOC as the policy is finalized. As always, we would be happy to discuss these comments in additional detail.

Sincerely,

Applied Biosystems, an Applera Corporation business

BIOCOM

Invitrogen Corporation

Isis Pharmaceuticals

Sangamo BioSciences

Target Discovery

Ref 2

BIOCOM

April 30, 2007

Members of the Independent Citizen's Oversight Committee
California Institute For Regenerative Medicine
210 King Street
San Francisco, CA 94107

Dear Members of the Committee:

BIOCOM leads the advocacy efforts of the Southern California life science community with more than 520 members including biotechnology and medical device companies, universities and basic research institutions, and service support firms. We appreciate the continued opportunity to offer comment on the "Intellectual Property and Revenue Sharing Requirements for For-Profit Organizations." Specifically, we remain troubled by certain aspects of the policy as submitted.

Access Requirements

Under the terms of the IP and Revenue Sharing Requirements For-Profit Organizations, grantees must agree to a royalty sharing formula, an access plan for uninsured Californians for therapies developed with CIRM funds, and a discount for purchase of therapies using "public funds".

Further, Section 100407(a) states that awardees "will provide (at time of commercialization) to CIRM a plan to provide access to resultant therapies for uninsured Californians for therapies developed with CIRM funds." It should be noted this provision is not clear whether a grantee would be responsible only for the cost of the therapeutic agent or for all costs of the therapy and should be clarified.

In Section 100407 (b) (pg 13, line 8), it states:

> *(b) Awardees agree to provide therapies resulting from CIRM funding purchased in California by public funds at a discount price. For drugs generated as a consequence of CIRM funding, awardees agree to provide drugs purchased in California by public funds at any benchmark price described in the California Discount Prescription Drug Program (commencing with CA Health and Safety Code section 30500, et seq.).*

As "public funds" does not appear in the definitions section, BIOCOM asks that the term "public funds" be clarified and narrowly defined. Further, as BIOCOM raised in testimony before the ICOC on December 7, 2006, it is unclear how CIRM expects to

have access to the CA Discount Prescription Drug Program pricing, as it is considered statutorily confidential and corporate proprietary information. Section 130506 (f) of the CA Health and Safety Code reads:

> *(f) All information reported by a manufacturer to, negotiations with, and agreements executed with, the department or its third-party vendor pursuant to this section, shall be considered confidential and corporate proprietary information. This information shall not be subject to disclosure under the California Public Records Act (Chapter 3.5 (commencing with Section 6250) of Division 7 of Title 1 of the Government Code). The Bureau of State Audits and the Controller shall have access to pricing information in a manner that is consistent with their access to this information under the Medi-Cal program and under law. The Bureau of State Audits and the Controller may use this information only to investigate or audit the administration of the program. Neither the Bureau of State Audits, the Controller, nor the department may disclose this information in a form that identifies a specific manufacturer or wholesaler or prices charged for drugs of this manufacturer or wholesaler. Information provided to the department pursuant to subdivision (e) of Section 130530 shall not be affected by the confidentiality protections established by this subdivision.*

As confidential and corporate proprietary information, by statute the Department of Health Services cannot release this information. Regulation cannot undo this statutory protection for the companies.

Revenue Sharing

The policy outlined in Section 100408 (pg 14, line 2) does not account for compound products; products which involve multiple patented technologies (e.g. systems with software, systems with software and reagents and/or drug-device combinations). In such cases, provisions must be made so that "royalty stacking", in which a company could incur separate financial liabilities to CIRM and other entities for multiple discoveries utilized in a single product, does not become an onerous financial burden.

March-in Rights

Regarding the implementation criteria for march-in rights contained in Section 100410 (a)(4) (pg 18, line 16), according to Section 100410(b) (pg 18, line 18) CIRM may exercise these rights "at any time in the event of a public health or safety emergency declared by the Governor." This provision is so overly broad and all-encompassing that it would present an unacceptable level of risk to most companies. BIOCOM asks that this provision be narrowed significantly so as to preserve public safety without the level of uncertainty inherent in the present language. This is an area much better left to the federal government, as it is possible this provision could, in a national health emergency

situation, set up conflicting demands on companies in the face of a regional and national public health emergency. It is imperative that the bar to invoke march-in rights be a high one, with very clearly defined triggers, and one that can be implemented in only the most extraordinary of circumstances. Anything less will be a tremendous impediment to investment in CIRM-funded discoveries.

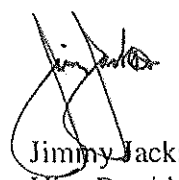
Publication Requirements

In the Section 100404 (pg 9, line 3), the proposed policy states:
Unless a special case could be made that doing so would endanger the competitive position of the company, an awardee shall share biomedical materials described in published scientific articles for research purposes in California within 60 days of receipt of a request and without bias as to the affiliation of the requestor unless legally precluded. Under special circumstances, exceptions to the above are possible with approval by CIRM; if requests become onerous or are in direct conflict with the business of the awardee, awardees can appeal to CIRM for alternative arrangements. Alternatively, authors may provide requestors with information on how to reconstruct or obtain the material. Materials are to be shared without cost or at cost.

In past IP Task Force Subcommittee meetings, it has been acknowledged that one of the earliest revenue streams CIRM may capture is from the research tools industry. As currently written, this provision would effectively remove a major potential market from that industry, making the pursuit of CIRM grants or CIRM-grantee discoveries significantly less attractive to them. If the for-profit entity does not feel it can attain a fair rate of return, that tool will not be pursued via CIRM and the state will lose a potential revenue stream. An alternative that protects the essence of this proposed provision while not erecting an obstacle would be to specify that one "special case" would be if the materials are made broadly commercially available on reasonable terms for research purposes in California.

BIOCOM thanks you for your consideration of these very difficult and complex issues. If I may answer any questions on the issues raised in this letter, please feel free to call me at 858-455-0300x102 or email me at jjackson@biocom.org.

Sincerely,



Jimmy Jackson
Vice President of Public Policy
BIOCOM

Ref. 3

CHI

CALIFORNIA HEALTHCARE INSTITUTE

BY ELECTRONIC MAIL TO FORPROFITIPREGS@CIRM.CA.GOV

April 30, 2007

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

RE: Comments to Proposed CIRM Regulation Entitled: Intellectual Property Policy for For-Profit Organizations (IPPFPO)

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 For-Profit Organizations (IPPFPO) as released for public comment on March 15, 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).[1] While Bayh-Dole pertains to federally funded research in non-profit organizations, we suggest its basic principles should 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 medicine, from a basic research discovery to a product approved by the FDA. Until a company

[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

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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 mechanisms of Bayh-Dole have had an especially 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 100404 – Publication-Related Biomedical Materials Requirements

This section requires an organization receiving CIRM grant money to "share biomedical materials described in published scientific articles for research purposes in California… without cost or at no

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[2] 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.
[3] House Committee on the Judiciary, *Report to Accompany H.R. 6933*, 96th Congress, 2nd Session, H.Rept. 96-1307, Part 1, p3. Emphasis added.
[4] Source: PricewaterhouseCoopers/California Healthcare Institute surveys, 2002 and 2003

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cost." The section allows exceptions to this rule, including "special circumstances" and if it "would endanger the competitive position of the company." Defining "special circumstances," the section allows an exception from providing biomedical materials if doing so is "onerous" or "in direct conflict with the business of the awardee."

We appreciate the apparent intent of this language. Our concern, however, is that the language is vague, setting no clear standard to determine whether or not a commercial biomedical materials firm would be exempted from this requirement. A company might invest substantial resources drafting a CIRM proposal or working on a CIRM-funded program before being able to determine through negotiations with CIRM if this exception language applies.

We therefore suggest that the requirement to provide biomedical materials not apply if a company commercializes the product on reasonable terms, and would suggest adding the following sentence at the end of Section 100404:

> Commercial suppliers of biomedical materials may satisfy the requirements of this paragraph by making materials commercially available on reasonable terms for research use in California.

By adding this amendment, commercial entities will not be inadvertently required to provide biomedical materials (which may be described in published scientific papers) free of charge, and would be required to meet the needs of California researchers on terms consistent with those in the pending IPPNPO licensing regulations.

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

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.[5] 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.[6] 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(d) state that "awardee organizations shall grant exclusive licenses involving CRIM-funded patent inventions relevant to therapies to organizations with plans to provide access …for uninsured California patients." The Section goes on to state "licensees will agree to provide to

[5] Letters from D. Gollaher, President and CEO, CHI, to S. Tocher, CIRM, regarding CIRM regulation entitled: Intellectual Property Policy for Non-Profit Organizations, June 15, 2006, August 22, 2006, September 15, 2006, October 4, 2006, and December 4, 2006.

[6] Text of Proposition 71, Sec. 3, "Purpose and Intent"

patients whose therapies will be purchased in California by public funds the therapies at a discount price."

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.

Section 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 "for drugs generated as a consequence of CIRM funding, awardees agree to provide drugs purchased in California by public funds at any benchmark price described in the California Discount Prescription Drug Program (commencing with California Health & Safety Code section 30500, et seq.)." 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 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.

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.

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[7] 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

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.

Another issue with Section 100406 relates to subsection (f) which requires negotiation of "grounds for modification or termination of the license." This clause specifically sets forth the example where modification or termination would be appropriate as including "failure to meet agreed-upon commercialization benchmarks." The example does not take into consideration unexpected setbacks, which are encountered in most drug development programs. While maintaining our overall objection to the pricing and access provision, we propose revising this provision to read:

> Examples would include failure to use commercially reasonable efforts to meet agreed-upon commercialization benchmarks and to cure any such failure using commercially reasonable efforts, whereby such cure may include reasonably alternative means or negotiating alternative benchmarks....

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.

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

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

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(a)(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(a)(3) be clearly specified to minimize 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 100410(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. While we appreciate Section 100410(b) allows for an "opportunity to cure," the section is written so as to presume there is a deficiency in the actions of the licensee. We think there should be provision enabling the patent holder, licensee, or other interested stakeholders to oppose and/or appeal a determination that they have been deficient.

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:

- Include language in Section 100404 that would eliminate the requirement to provide biomedical materials if a company commercializes the product;

- Remove Sections 100406(d) 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(d).

- With respect to Section 100407(a), we suggest clarity on the phrase "industry standards"

[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 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.

- 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(d) 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.

- Establish detailed procedures in Section 100410 for march-in proceedings, including establishing 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.

Conclusion

CHI appreciates this opportunity to comment on the interim 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 is 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 Gollaher

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

Ref. 4

STEMCELLS INC

Via Facsimile (415-396-9141)

April 30, 2007

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

Re: Proposed CIRM Regulations for Intellectual Property and Revenue Sharing by For-Profit Organizations

Dear Mr. Tocher:

I am writing on behalf of StemCells, Inc. to raise some questions and concerns we have about the CIRM's proposed regulations for intellectual property and revenue sharing by for-profit organizations (the "Draft Regulations"). Because StemCells is both an acquirer and creator of stem cell technologies, know-how and talent, we share the CIRM's interest in promoting stem cell research locally in California. Like many in our industry, we agree that recipients of CIRM funding owe special obligations both to CIRM and to Californians more generally because of the statutory mandates of Proposition 71. We sincerely hope a regulatory framework can be established in a way that encourages meaningful innovation in California and the development of successful stem cell therapies, while at the same time generating a fair return for CIRM and California taxpayers.

To this end, let me start by mentioning a few basic principles important to us. If you share our belief that either StemCells or a company like StemCells will be the most likely organization to successfully develop, clinically test and launch a stem cell therapy within the next 10 years, then it is in our mutual interest to make the Draft Regulations sufficiently attractive to companies like ours. Anything that undercuts these principles could very easily make CIRM funding prohibitively unattractive to us (and presumably to other for-profit organizations), thereby marginalizing the CIRM to everyone's detriment.

First, whatever the CIRM adopts must be clear, easy to understand and consistently applied. If the final regulations are ambiguous or unpredictable, then established and conservative companies will likely shy away from CIRM funding, leaving only risky ventures interested in the "high risk" money. It is not in anyone's interest for the CIRM to be viewed as a source of last ditch funding.

Second, whatever the CIRM adopts must be bounded. In other words, the obligations imposed upon recipients of CIRM funds must not extend beyond the funded projects or be disproportionate to the benefits received. For example, if CIRM funding creates obligations on companies with respect to their pre-existing technologies or IP (or technologies or IP developed independent of CIRM funding), then companies with substantial intellectual property (in other words, those most likely to be successful in the long term) will likely avoid CIRM funding as well as the acquisition of CIRM-funded companies. Similarly, a million dollar grant from the CIRM

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into a $20 million dollar program should carry different obligations than a million dollar grant from the CIRM into a $500 million dollar program. If not, companies with well funded programs (in other words, those most likely to be successful in the long term) will likely avoid CIRM funding except for programs of lesser importance or those less likely to succeed.

Our HuCNS-SC program, for example, has cost us many tens of millions just to get us to our first Phase 1 trial (our Batten's Disease trial currently being conducted at OHSU), and this does not include sizeable license fees paid for foundational technologies. It's doubtful we would ever accept money from the CIRM into our neural stem cell program if doing so would taint our base IP or create obligations widely disproportionate to the benefits of incremental funding.

Third, whatever the CIRM adopts must acknowledge the fundamental need companies have to keep certain information confidential, especially early in a company's development. If not, companies and their investors will find it strategically advantageous to avoid CIRM funding and CIRM-funded companies. Private companies will resist being forced to operate as if they were publicly traded. And all for-profits will resist disclosing their long term strategic objectives, which they would be doing if they were forced to publicly disclose planned clinical trials or potential licenses, for example.

Fourth, whatever the CIRM adopts must be workable. In this regard, we encourage the CIRM to consider carefully the experiences of the NIH, NASA and other federal agencies leading up to the enactment of the Bayh-Dole Act.

With these principles in mind, we spent a considerable amount of time reading through and discussing the Draft Regulations. We are presently preparing a more detailed response, including some suggested changes to the Draft Regulations. But here are some of our preliminary questions and concerns. We greatly appreciate your consideration of these points as you continue to deliberate and refine these very important regulations.

A. Ambiguity and Risk

Whatever the CIRM adopts must be unambiguous, easy to understand and predictable. If the Draft Regulations are perceived as a thicket of ambiguities and uncertainties, no for-profit organizations of quality would accept CIRM funding. "Good science" would instead access less risky sources of capital, such as venture fund financing, NIH grants, business collaborations, debt, and public markets. "High risk science" lacking these options would be more willing to accept risky money. This would necessarily discourage meaningful stem cell innovation in the state and handicap the likelihood that CIRM funding directly contributes to a successful stem cell therapy.

We see the following as some of the most significant ambiguities and risks in the Draft Regulations, as currently written:

(1) Section 100400 suggests that future amendments to the Draft Regulations would apply retroactively to CIRM-funded programs even if the CIRM funds have already been spent ("New or amended regulations adopted after the expiration of the Project Period of a grant, loan or contract and after all CIRM funds for the grant, loan or contract have been expended will apply

on January 1 following the effective date of the new or amended regulation, unless specified otherwise in the regulation."). Not only would this be on questionable constitutional footing, but it creates considerable uncertainty. See, e.g., Bowen v. Georgetown University Hospital, 488 U.S. 204 (1988). The regulations in effect at the time of an award should apply throughout the applicable Project Period.

(2) The terms that are most important for the Draft Regulations are not expressly defined, such as "CIRM-funded patented inventions," "CIRM-funded research" and "CIRM-funded inventions." The lack of consistent definitions creates unnecessary ambiguity. For example, is the meaning of "CIRM-supported research" under Section 100403 different from the meaning of "CIRM-funded research" under Section 100410, "CIRM-funded scientific research" under Section 100401(d) and "CIRM-funded projects" under Section 100408(c)? Presumably a "CIRM-funded invention" is an invention conceived or first reduced to practice during the performance of research that is partially or fully funded by the CIRM. Meanwhile, a "CIRM-funded patented invention" must necessarily be a CIRM-funded invention that is claimed by a valid, unexpired U.S. patent. And "CIRM-funded research" must necessarily be the research funded by the CIRM, as described in the CIRM grant request. Clarifying these definitions and using them consistently throughout the Draft Regulations, would make the regulations less troubling and more predictable.

(3) The first sentence of Section 100406(b) appears to be sweeping and absolute ("Awardee organizations shall negotiate non-exclusive licenses of CIRM[-]funded inventions to third parties whenever possible."). It's unclear whether this preference for non-exclusive licensing is intended to be at the expense of self-commercialization efforts. Our presumption is that the CIRM has no bias in favor of licensed rather than self-commercialized technologies.

(4) Section 100406(h) instructs Awardees to "take administrative action to modify or terminate license rights where necessary." But what does "administrative action" mean? And what does "where necessary" mean?

(5) The public access requirements under Section 100407 create a tremendous amount of uncertainty. How deep must the discount be? What "industry standards" are you referring to? To our knowledge, there are no such standards because this would be the first regulation of its kind. In this regard, we share the view of groups like the California Healthcare Institute that price controls are both beyond the scope of the CIRM's statutory authority and ultimately unworkable and stifling to business formation, innovation and investment.

(6) We do not understand the 17% payment obligations under Section 100408(a). Does the CIRM intend the effective royalty rate for licensed technologies to be between 19-22% for revenue in excess of $500,000? This seems prohibitively high given that CIRM funding will almost always be a small percentage of any successful stem cells development effort.[1]

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[1] We've learned secondhand that the 17% royalty rate under Section 100408(a)(2) is intended by the CIRM as a ceiling and that the ultimate royalty rate for any given CIRM-funded patented invention will be proportionate by virtue of Section 100408(a)(3). Changes to make this express would be a good step forward.

(7) Section 100408(c) provides: "For grants that lead to very successful commercial products, a one-time blockbuster payment equal to three times the total awarded money is expected when revenues exceed $250 million per year and when revenues exceed $500 million per year." We can not tell whether the "blockbuster" payments under Section 100408(c) are expected to be one time payments for the life of the product or payable each year of blockbuster sales.

(8) Also, in order for the 1% blockbuster payment to apply under Section 100408(c) a CIRM-funded patented invention must have been "involved in the achievement of blockbuster revenues." If this different from simply saying that the additional payment is owed only if a CIRM-funded patented invention generates revenues in excess of $500 million in a given year? If not, then why isn't this particular revenue sharing obligation disproportionate to the benefit conferred by the CIRM funding because it potentially extends to pre-existing technologies and programs that in fact did not result in protectable CIRM-funded patented inventions?

(10) Also, it's unclear whether the blockbuster payments are triggered from the Awardee's perspective only. Put another way, we assume the blockbuster payment obligations do not apply if a licensee enjoys "blockbuster" revenues, but an Awardee receives less than $500 million in revenues (royalties, milestones, etc.). It would be strange to put the Awardee into a position of losing money should a product's sales ever climb over $500,000 in a given year. We also assume milestone and R&D payments, such as through funded research collaboration agreements, are not counted towards the $500 million trigger. The determination of whether a product is a "blockbuster" should be whether the product itself generates sales revenue in excess of $500 million in a single year.

(11) It's unclear whether the press release obligations under Section 100409 only apply to press releases about either CIRM-funded research or CIRM-funded patented inventions. The phrase "events that arise as a consequence of CIRM funding" could be inappropriately broad to include press releases about financial statements of position and other newsworthy things having nothing to do with scientific research funded by the CIRM.

(12) The march-in rights of Section 100410 create a lot of uncertainties. For example, what does "practical application of a CIRM-funded patented invention mean"? We suspect this means that a product either has or has not been commercialized anywhere in the world, but this is not clear. And what does "broad availability in California (for reasons other than price)" mean? Also, will the march-in rights because of a public health emergency only last for so long as the emergency is ongoing?

(13) In addition to these points, we have a slew of other related questions, such as:

> (a) Will the revenue sharing obligations be worldwide even if the patent protection is on a nation-by-nation basis? (b) Will CIRM impose revenue sharing obligations on sales from jurisdictions where no patent protection exists?
>
> (c) Does the obligation to share Biomedical Materials under Section 100404 include an obligation to share materials that are proven to be ineffective or potentially dangerous? (d) Does the obligation to supply the Biomedical Materials at cost or free continue on if an Awardee begins commercializing the Biomedical Materials? (e) Must the person

requesting Biomedical Materials tell the Awardee what the research will be? (f) Must the request be bona fide? (g) If an Awardee considers the proposed research dangerous, immoral, illegal, or otherwise improper what should it do?

(h) Have you considered adding a dispute resolution mechanism for challenging the CIRM's determination that a reason to exercise march-in rights exists? This might save all interested persons significant litigation costs.

(i) Under the access requirements of Sections 100406 and 100407, does the clause "provide access to . . . uninsured Californians" mean free access, discounted access or access at the Average Selling Price ("ASP"), as defined under federal law? (j) If the resultant therapy requires third party drugs, devices or surgical procedures, must an Awardee "provide access to" those, too? Presumably Awardees will only need to provide access to whatever the Awardee manufactures and not to the sum total of all costs to the combined therapy (for example, surgery costs).

B. Constraints and Proportionality

To be viewed as fair and not over-reaching, whatever the CIRM adopts must be constrained—obligations must not be disproportionate to the benefits conferred or extend beyond the programs actually funded by the CIRM. Despite this, a number of the provisions within the Draft Regulations could impose certain obligations, whether intentionally or not, on Awardees that reach beyond the funded programs and any resulting inventions. Furthermore, a number of the obligations seem to apply with equal force whether the CIRM funds $1 million or $100 million towards a specific research program.

The most troubling of these unconstrained provisions are the following:

(1) The public access requirements of Section 100407 seem to apply irrespective of whether an Awardee receives $1 or $100 million from the CIRM. Furthermore, subparts (a) and (b) refer to therapies "resulting from CIRM funding" and therefore the obligations seem to extend beyond CIRM-funded patented inventions. As I mentioned above, this creates a risk of tainting pre-existing technologies and IP, which discourages companies from seeking CIRM funding for clinical trials or existing research programs.

(2) There are no caps to an Awardee's revenue sharing obligations with respect to licensed technologies. This actually creates a disincentive to license, which is at odds with the CIRM's desire to have stem cells technologies shared broadly.

(3) Section 100408(a)(3) suggests that if both CIRM funds and other funds are used to create a CIRM-funded patented invention, then the "return to the State of California of any resultant revenues shall be proportionate to the support provided by CIRM for the discovery of the invention." Unfortunately, it is unclear how this provision interrelates with the earlier provisions of Section 100408. For example, does this proportionality provision allow for a royalty rate below 17% notwithstanding Section 100408(a)(2)? (see footnote 1) But how about a royalty rate below 2% notwithstanding Section 100408(a)(1)? And should proportionality be based solely upon money contributed to a particular program? Timing can also be critically important

and have bearing on the perceived fairness of the regulations. For example, there would seem to be a fundamental unfairness in requiring the same consideration from an Awardee regardless of whether the CIRM funding went into a pre-Phase 1 program or a Ph 3 program. For this reason, within the industry, a license to a Phase 2 technology costs less than a Phase 3 technology. If the burden remains the same in the final regulations, the CIRM will be "priced" out of the market for Phase 3 programs—unable to fund late stage clinical work, and therefore much less likely to be able to participate in a successful stem cells therapy within the planned 10-20 year horizon.

(4) The revenue sharing obligations of Section 100406 seem to apply regardless of whether a particular therapy includes both CIRM-funded patented inventions and other inventions. Likewise, will revenue streams from licensees be proportionately adjusted when a licensee takes a license to both CIRM-funded patented inventions and other inventions? And what about offsets for royalty stacking?

(5) Because the march-in rights extend to "CIRM-funded research projects," could the CIRM require the licensing of pre-existing IP? This risk alone would make the Draft Regulations toxic to companies with substantial patent portfolios. Likewise, perpetual march-in rights seems overly burdensome. Consider instead terminating one or more of these march-in rights once the CIRM has received revenue from an Awardee, once an Awardee has begun Phase 3 clinical, or once an Awardee has successfully commercialized a CIRM-funded patented invention. Without question, the first trigger for march-in (i.e., that an Awardee has not "made reasonable efforts in a reasonable time to achieve practical application of a CIRM-funded patented invention") should disappear once an Awardee has commercialized a product containing a CIRM-funded patented invention; but this isn't clear in the Draft Regulations.

C. Confidentiality

Whatever the CIRM adopts must allow companies to keep certain information confidential, especially early in a company's development. If not, then CIRM funded companies will be at a strategic disadvantage and investors will opt instead for other sources of funding. In this regard, the reporting obligations under Sections 100402 and 100406(a) raise a number of important questions:

(1) Will these reports be held in confidence by CIRM? Is the CIRM willing to commit to this, by guaranteeing that the reports will not be publicly disclosed unless disclosure is required by law?

(2) Are the reporting obligations limited to CIRM-funded inventions and the results of CIRM-funded research?

(3) Must Awardees disclose confidential and/or ongoing negotiations, past, present or future?

(4) Must Awardees disclose trade secrets?

D. Unworkable Obligations

Whatever the CIRM adopts must be perceived as workable and not prohibitively burdensome. Here are some potential challenges we'd face implementing the Draft Regulations:

(1) Virtually all of the obligations seem to run forever. For example, do the reporting obligations continue after a CIRM-funded patent has expired? Do the revenue sharing obligations continue after all patent protection has expired?

(2) As presently drafted, Section 100403 appears to place obligations directly onto an Awardee's principal investigator(s). This creates a risk of potential conflicts of interest within an Awardee organization and raises the specter of personal liability. Awardees can (and should) take on whatever obligations ultimately get adopted.

(3) Under Section 100406, Awardees interested in licensing CIRM-funded inventions must "include terms in the license agreement addressing all relevant therapeutic and diagnostic uses for which [an] invention is applicable." But how can this be accomplished when license agreements are often entered into early in the research and development stage and certainly before all potential therapeutic uses are known? Won't this be especially true for a novel area of research such as stem cell biology?

(4) Under Section 100407, an Awardee must provide to the CIRM an access plan at the time of first commercialization. In contrast, under Section 100406(d), it seems that an Awardee can only grant an exclusive license to a CIRM-funded patented invention to an organization that already has "plans to provide access at the time of commercialization to resultant therapies for uninsured California patients." Is this supposed to be the same sort of plan? If so, how can a licensee prepare a plan for access before the therapy itself is understood? Won't this obligation be impossible to comply with for a pre-clinical technology? Perhaps this is supposed to be just a commitment to provide the CIRM with such a plan at the time of commercialization. In other words, can a potential licensee satisfy this obligation by contractually agreeing to comply with Section 100407 as if it were the awardee organization?

(5) The discount pricing mechanisms of Section 100407 seem confusing and difficult, if not impossible, to administer. With many different payors, both public and private, operating in the state, it's unclear to us how any manufacturer would offer discounts to a specific subset of patients. Our customers will be the hospitals and our therapies will likely be a small component of one or more hospital procedures, presumably billed to payors on a DRG basis. Perhaps everyone would be better served by clear and consistent standards, such as a commitment to sell CIRM-funded therapies in California at no more than the ASP.

(6) The cure period under the march-in rights is presently set at 12 months. And yet these technologies take years to develop. An Awardee should not lose exclusivity if it is diligently working to address any issue identified by the CIRM.

(7) The march-in rights give the CIRM the right to force the grant of exclusive licenses to CIRM-funded inventions, but what if these inventions have already been licensed? Must all licensees permit a claw back right? What if the reason for the forced license is that the licensing Awardee

itself has failed to adhere to its own public access plan? If the CIRM can claw back and nullify a licensee's license in order to force an exclusive license to another party, won't this, as a practical matter, make it almost impossible for an Awardee to license CIRM-funded inventions?

(8) Presumably an invention is no longer a CIRM-funded patented invention once the applicable patent expires or is finally adjudged to be invalid—otherwise the Awardee would be unable to compete against those companies that didn't take CIRM-funding. Only when an Awardee enjoys patent protection, can it afford to carry the burdens being proposed by the Draft Regulations. But this dichotomy isn't clear from the Draft Regulations. For example, as presently written, it seems an Awardee might have "blockbuster" sales payment obligations even though all other competitors are free to commercialize the technologies without any such obligations weighing them down.

E. Conclusion

As you can tell, StemCells has a number of questions and concerns about the Draft Regulations, as currently proposed. We realize that drafting regulations "by committee" is extremely difficult to do. So we welcome and appreciate the opportunity to participate in this process.

Unless substantial changes are made to the Draft Regulations, StemCells is unlikely to seek CIRM funding, and certainly not for any of our most advanced programs. This is unfortunate, because each of us will necessarily be tied to the successes and failures of our industry in California and the CIRM is in a position, both with its available funds and with these regulations, to either pull our entire industry up or drag it down. Meanwhile, stem cell advancements and therapies promise to be a blessing to all of us if given a chance to grow. For these reasons, we respectfully ask that you consider doing the following:

(1) Make future changes to the regulations not apply retroactively to grant recipients.

(2) Define narrowly the terms "CIRM-funded research," "CIRM-funded inventions," and "CIRM-funded patented inventions," so that Awardees can avoid tainting their other programs and pre-existing inventions.

(3) Strike the public access requirements altogether, whether because they exceed the scope of Proposition 71 or because they are unworkable and unduly burdensome. Absent this, make them easier to apply and understand and less burdensome and arbitrary. For example, "Awardee Organizations must not sell CIRM-funded patented inventions at a price above their applicable Average Selling Price to uninsured Californians."

(4) Limit the reporting obligations to information about the results of CIRM-funded research, executed license agreements, and issued patents arising out of CIRM-funded research.

(5) Put caps onto all revenue sharing obligations, so that managers can weigh the relative costs and benefits of different financing alternatives with certainty.

(6) Narrow the march-in rights by providing for an efficient third party dispute mechanism and by making it clear that the CIRM would have no right to force the licensing of anything other than CIRM-funded patented inventions.

We appreciate your consideration of these matters. In turn, we will propose some specific modifications to the Draft Regulations within the next few weeks with the hope of getting you something to help you address at least some of the foregoing points. Meanwhile, we look forward to your response.

Sincerely,

StemCells, Inc.

By: Kenneth B. Stratton, Esq.
Its: General Counsel

Cc: Martin McGlynn

Rd. 5

April 30, 2007

VIA FACSIMILE 415-396-9141
and email: forprofitipregs@cirm.ca.gov

C. Scott Tocher
Interim Legal Counsel
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RE: Proposed Regulations: Intellectual Property and Revenue Sharing Requirements for For-Profit Organizations

Dear Mr. Tocher:

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We are pleased to provide our comments on CIRM's recently published proposed regulations for intellectual property and revenue sharing requirements for for-profit organizations. We greatly respect and appreciate the work that CIRM is doing to support stem cell research in California. We also recognize the challenges that CIRM faces in addressing a range of diverse interests as it works to implement the goals of Proposition 71. However, the goal of bringing new therapies to patients suffering from degenerative diseases is shared by all California citizens. We firmly believe that if CIRM is to succeed in stimulating the translation of basic research on stem cells into such therapies, it will need to engage with biotechnology companies that are leading the development of these therapies.

Our goal in submitting the comments that follow is to provide a biotechnology company perspective. The regulations governing the obligations that would accompany CIRM funding to a biotechnology company must be both clear and realistic. If they are, then biotechnology companies will engage in the process and CIRM funds will contribute to the development of stem cell therapies in California. Our comments below are intended to help CIRM develop such clear and realistic regulations.

1. **The obligations imposed on CIRM funding awardees must be clear.** It is vital that the costs and obligations that attend CIRM funding be clearly defined and certain. Any company considering seeking CIRM funding will need to weigh the costs and obligations of applying CIRM funding to a project against the costs and obligations associated with other available capital (e.g., venture capital, public markets, debt instruments). If the costs and obligations of CIRM funding are unclear then responsible companies will be deterred from taking CIRM funding. There are a number of areas in the proposed regulations where the obligations are not clear.

C. Scott Tocher
California Institute for Regenerative Medicine
April 30, 2007

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- **Definitions.** Throughout the regulations, a variety of undefined terms are used to describe products and patents arising from CIRM funding. We suggest utilizing the following definitions and employing them consistently when setting forth obligations with respect to products and inventions that arise from CIRM funding:

  "CIRM-Funded Patented Invention" means a patent application or patent granted thereon for an invention developed in the course of a project or activity funded in whole or in part by a CIRM award.

  "CIRM-Funded Self-Commercialized Product" means a therapy manufactured or sold by an awardee that was developed in whole or in part under a CIRM award.

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- **Access for uninsured patients.** The proposed regulation for access requirements (§100407(a)) provide companies with very little guidance as to what expectations will be placed on them at the time of commercialization. The first sentence refers broadly to "therapies developed with CIRM funds." There is a separate access provision in §100406(d) for situations where an awardee grants an exclusive license to a "CIRM-funded patented invention." Does §100407(a) then apply only to self-commercialized products? §100407 could be read to impose an access obligation on any product which, during the course of its development was touched by CIRM funding, but that seems unlikely to be the intent. For example, do the access provisions apply to a product either developed under a non-exclusive license to a CIRM Funded Patented Invention, or developed by a commercialization partner of an awardee where there was no CIRM Funded Patented Invention? Who will determine whether an access plan is "consistent with industry standards?" To what aspects of a therapy must awardees provide access? For example, if an awardee manufactures and sells a cell therapy that requires surgical delivery and the use of a medical device, is the awardee responsible for ensuring that an uninsured patient has access to the surgical procedure and the delivery device?

  In the absence of a clearer definition of awardees' obligations, even those awardees with the most comprehensive access plans may face lawsuits alleging that their plans are insufficient. The cost of such litigation alone could quickly dwarf the funding provided by CIRM in many cases. We suggest that section §100407(a) be clarified by: (i) explicitly limiting access requirements to CIRM-Funded Self-Commercialized Products and products developed under exclusive licenses to CIRM Funded Patented Inventions, and (ii) replacing the vague "consistent with industry standards" language with an explicit guidance or cap on awardees' access

obligations (e.g., as a percent of product revenue or a multiple of the funding provided by CIRM).

- **Discount pricing.** Similarly, companies will need further guidance from CIRM regarding the potential scope and impact of the discount pricing provisions in §100407(b) on their businesses. We suggest: (i) explicitly limiting discount pricing requirements to CIRM-Funded Self-Commercialized Products and products developed under exclusive licenses to CIRM Funded Patented Inventions, (ii) developing definitions for "therapy" and "drug" to clarify the intended meaning of these terms, and (iii) providing more explicit guidance with respect to the discount pricing requirements for non-drug therapies.

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- **Revenue sharing for licenses under CIRM-funded inventions.** It appears that the 2-5% payment amount set forth in the last sentence of §100408(a)(1) is a drafting error, and that the revenue sharing rate applying to licensing revenues in excess of $500,000 is 17% if CIRM fully funded the invention, or proportionally less for inventions funded from multiple sources (§100408(a)(3)). The language describing the threshold amount, revenue sharing rate, and application of proportionality to that rate should be clarified. It appears that the 2-5% rate should be incorporated into §100408(b)(1). We also understand that the limitation of §100408(b) to CIRM-funded patented inventions is a drafting error that will be corrected in the next iteration of the regulations.

- **Blockbuster payments.** The description of blockbuster payment requirements in a separate section §100408(c) as opposed to a subsection of §100408(b) implies that such payments are due for both outlicensed and self-commercialized products. The language of this section does nothing to narrow the requirement, tying blockbuster payments only to total product revenues, regardless of whether it is the awardee or their licensee who realizes the $250 million in revenues. We understand that CIRM's intent was that blockbuster payments apply only to self-commercialized products. Given that outlicensing revenues are already subject to an uncapped 17% revenue share (and hence revenues to CIRM will already scale with product success), we agree that limiting blockbuster payments to self-commercialized products is the only reasonable approach. To clarify this intent, the description of blockbuster payments should be moved to a subsection of §100408(b), and the language of this subsection should also be modified to clearly tie blockbuster payments to revenues from CIRM-Funded Self-Commercialized Products instead of "CIRM-funded projects." It is our understanding of the language that each of the two payments is payable once annual revenues for a CIRM-Funded Awardee Commercialized Product reach $250M and then $500M. But,

what if a CIRM funded project yielded multiple products or if the same cell therapy were sold in different formulations for different indications?

- **March-in rights.** March-in rights provisions in §100410 refer to "CIRM-funded patented inventions *or CIRM-funded research projects*." March-in rights on patented inventions have precedent in Bayh-Dole (35 USC Section 203), and a clear mechanism exists for the exercise of such a right. However, it is unclear what is encompassed in a march-in right for a "CIRM-funded research project." Could an awardee be required to provide licenses under all patents covering a product developed under partial funding from CIRM, even if the invention of those patents was in no way funded by CIRM? Could an awardee be required to cede control of manufacturing facilities for a product developed in part under a "CIRM-funded research project?" An appropriately constrained approach might be to provide that if a march-in right is triggered, CIRM could require access to both CIRM funded patent inventions through licensing as well as data generated under the CIRM funding. We suggest clarifying language to reflect this as follows: ". . . to grant a nonexclusive, partially exclusive, or exclusive license to CIRM-Funded Patented Inventions and/or data generated under CIRM funding in any field of use . . ."

  §100410 is also broader and less clear than 35 USC 203 in at least three other respects. First, 35 USC 203(1)(a) limits federal march-in rights to the field of use in which the patent holder is determined to have not made sufficient effort. The language of §100410(a)(1) has no such limitation, leaving open the question of whether a march-in right could be exercised against an awardee in one field of use based on their insufficient efforts in a different field. Second, 35 USC 203(1)(c) clearly states that "requirements for public use" must be "specified by Federal regulations" to trigger march-in rights. The equivalent CIRM regulation in §100410(a)(3) contains no such clarification, but instead requires "broad availability in California" without specifying the meaning of that phrase. Finally, 35 USC 203(2) specifies the process for appeals, a provision that is notably absent in the CIRM document.

- **Possibility of changing costs and obligations.** An additional barrier to clarity is the risk that CIRM could retroactively change the requirements placed on awardees. The proposed regulations in §100400 governing scope provide companies with little assurance that the regulations they agree to comply with by accepting an award will continue to be the regulations to which they are held in the future. §100400 states "Any new or amended regulations adopted by the ICOC will be applied to currently active grants, loans or contracts on the start date of the next non-competitive renewal period after the effective date of the regulations." If an awardee elects not to apply for a non-competitive renewal based on an

assessment that the revised regulations would impose too great a burden on their business, would the revised regulations then not apply to products and inventions developed under the previous funding period? If an awardee elects to apply for the renewal, would the revised regulations apply only to developments under the new project period, or also to previous developments?

§100400 also appears to provide for retroactive application of revised guidelines even to projects for which the funding period has expired: "new or amended regulations adopted after the expiration of the Project Period of a grant, loan or contract and after all CIRM funds for the grant, loan or contract have been expended will apply on January 1 following the effective date of the new or amended regulation, unless otherwise specified in the regulation."

Thus, this aspect of the proposed regulations would preclude an awardee of CIRM funding from obtaining a clear and certain understanding of the costs and obligations associated with the funding. This is something that most companies would find unacceptable.

2. **The obligations imposed on awardees must be proportionate to CIRM's contribution.** The discovery and development of a new therapy has been estimated to cost in excess of $800 million. In addition to grants from CIRM, funding for the development of therapies is almost certain to come from many other sources, including venture capital, public markets, debt instruments, reinvestment of corporate revenue, and grants from other agencies. The revenue sharing requirements of the regulations appropriately recognize this fact and require returns that are proportional to CIRM's investment. In contrast, as currently proposed, the regulations relating to access provisions and march-in rights place a burden on awardees that is likely to be highly disproportionate to the relative contribution of CIRM funding to the development of a therapy. If left unchanged, these provisions will have the unfortunate effect of discouraging applications by for-profit organizations for any grant amount that does not represent a very significant fraction of the overall development costs of a product.

   One solution to this problem would be to apply a minimum threshold funding level (either as a dollar amount or as a percent of total product development costs) below which these provisions do not apply. Alternatively, the cost of access programs to an awardee could be capped at a multiple of the funding provided by CIRM. With respect to the march-in rights, this problem would largely be addressed by adding language limiting CIRM's march-in rights to inventions and data generated under CIRM funding (as suggested above).

3. **The regulations must take into account the importance of partnering in bringing biotechnology products to market.** Commercialization of a pharmaceutical or biological therapy requires substantial investment in sales and marketing infrastructure, and a sophisticated understanding of the medical landscape for the indication in question. Most biotechnology companies do not have the resources or the expertise to successfully commercialize the products they develop. As a result, the overwhelming majority of small and medium-sized biotechnology companies have historically opted to partner their products with a large pharmaceutical or biotechnology company prior to commercialization. This typical biotechnology "product licensing" model is quite distinct from the "patent licensing" model typically adopted by universities and other non-profit organizations. In the "patent licensing" model, a university typically seeks to license a single patent family soon after filing and without any further investment in development of products covered by the patents in question. In the "product licensing" model, a biotechnology company will invest significantly in the development of a therapeutic product, often bringing a product to the point of late stage clinical trials prior to partnering. As a result, the partnership agreement between the biotechnology company and its commercialization partner will typically involve awarding of licenses under a large number of patent families covering the product (some of which may have been developed under CIRM funding and some of which likely were not), transfer of product manufacturing know-how, awarding of rights to use preclinical and clinical data in regulatory submissions and marketing materials, and perhaps even an agreement of the two parties to collaborate for co-development and/or co-promotion of the product in question.

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- **Application of uncapped 17% revenue share in a "product licensing" model.** The revenue sharing requirements outlined in §100408(a) appear to use the terms "revenues received . . . under a license agreement that involves CIRM-funded patented inventions" (subsection (1)) and "revenues received under a license agreement . . . of any CIRM-funded patented inventions" (subsection (2)) interchangeably. In the "product licensing" model typically adopted by biotechnology companies, the value of a license agreement entered into by an awardee will likely encompass value captured not just from an individual CIRM-funded patented invention, but also from many other sources. The language of subsection (1) implies that the 17% revenue share applies to the entire value of any license agreement involving a CIRM-funded invention, in which case 17% is inappropriately high. The language used in subsection (2) implies that that the 17% revenue share is intended to apply only to the value ascribed to the CIRM-funded invention, which is a more appropriate model.

- **Possibility of triggering both revenue share and royalty provisions.** In the proposed regulations, an awardee would likely trigger both the 17% revenue share of §100408(a) and the 2-5% royalty obligation of §100408(b) if it awarded a license under a CIRM-Funded Patented Invention to a partner, but also co-promoted the partnered product. We would suggest adding a statement that licenses to CIRM-Funded Patented Inventions relating to a collaboration for a CIRM-Funded Self-Commercialized Product will not trigger both the royalty and revenue sharing provisions of the regulations. Given that CIRM's stated intention in applying a cap to royalties but not to revenue sharing is to encourage companies to develop products themselves, we suggest that the capped royalty (and not the uncapped revenue share) should apply in such co-commercialization partnerships.

- **Need for flexibility.** Attracting commercialization partners will likely be a requirement for the successful development and availability of CIRM-funded products in all but the smallest of commercial markets. As such, it is not in the interest of CIRM, awardees, or patients to hinder awardees' ability to partner products with companies capable of expediting or enabling their commercialization. We suggest that CIRM should establish a mechanism for appeal of any requirement of the regulations if an awardee encounters difficulty in partnering a CIRM-funded product because of a potential partner's concerns regarding a provision of the CIRM regulations.

Thank you for the opportunity to contribute our comments for CIRM's consideration. If you have any questions, please feel free to contact us. We would be pleased to provide any further clarification or comment that would be helpful to you.

Sincerely,

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