STATEMENT OF ICOC PRINCIPLES RELATING TO BIOSIMILARS
May 8, 2009 Draft

1. CIRM and the ICOC should, after careful consideration, take public positions on appropriate legislative and regulatory matters at both the State and Federal level on issues that impact CIRM's ability to achieve its Mission.

    a. The ICOC Chairperson has among his primary statutory duties, responsibility to "interface with the California Legislature and the United States Congress." (California Stem Cell Research and Cures Bond Act, Sec. 125290.45(b)(1)(A)).
    b. Analysis: Legislative and regulatory developments constitute critical elements of the stem cell research and commercial environment. CIRM must work to ensure that legislation and regulations at both the State and Federal level facilitate accomplishment of CIRM's Mission. At a bare minimum, CIRM must guard against statutory enactments which could jeopardize the Mission.

2. CIRM's Mission is, inter alia, to: i) "support and advance stem cell research and regenerative medicine under the highest ethical and medical standards for the discovery of cures, therapies, diagnostics and research technologies to relieve human suffering from chronic disease and injury" and ii) "advance the biotech industry in California to world leadership, as an economic engine for California's future." (California Stem Cell Research and Cures Initiative, Sec. 3)

3. Commercial entities, including biotech companies, must actively participate in research and development efforts for regenerative medicine therapies in order for CIRM to achieve both aspects of its Mission.
    a. Strategic Plan: (5/5/09 Draft): "As the effort to cure or treat disease using stem cell technologies moves closer to the clinic, CIRM will need to call upon expertise in clinical trials, regulatory requirements, and large-scale Good Manufacturing Practices (GMP). The greatest reservoir of these skills resides in pharmaceutical and biotechnology companies. Without injection of such expertise into CIRM programs…CIRM's ability to accomplish its mission will be jeopardized." (p.27)
    b. Strategic Plan (5/5/09 Draft, p.4 "Operational Goals"): Reassess and consider ways to enhance CIRM's relationships with the venture capital, biotechnology and pharmaceutical industries—relationships essential to delivering lifesaving therapies based on stem cell research to patients."

4. The current economic climate threatens CIRM's ability to achieve both aspects of its Mission because prevailing conditions make it very difficult for biotech companies generally to obtain necessary financing from either traditional lenders or venture capitalists.
    a. Venture capitalists are investing significantly less in the current economic climate than was the case just one year ago. See FierceBioTech, April 20,2009, "Venture Capital Investment Plummets in Q1 2009 to 12 year low…" www.fiercebiitech.com/press-release/venture-capiltal-invest.
    b. As a result, cash poor biotech companies-- 37% of whom operate with less than one year's worth of cash-- are cutting back on research programs. http://online.wsj.com/article/SB122522381992117800 5, "Cash-Poor Biotech Firms Cut Research, Seek Aid", October 25, 2008.

5. Companies engaged in stem cell research are particularly challenged to find investors willing to fund research and development in the current economic climate.
    a. Stem cell therapy is a nascent field, marked by great potential but also by great uncertainty regarding outcomes, regulatory standards, reimbursement issues and other critical variables relevant to investment decisions.
    b. The research and development pathway for innovative stem cell therapies is quite lengthy. Thus, development costs for stem cell therapies are very high, even compared to other therapeutics.

6. Patent protection, which can encourage investment in some circumstances, is less likely to motivate investment in stem cell research and development.
    a. Recent changes under U.S. patent law concerning patent life make it less likely that biologics patent owners will achieve meaningful protection from infringement.
        i. Former U.S. law allowed 17 years of patent life from the date a patent issued. Innovators could therefore delay patent issuance until approximately the time when their products launched, thereby achieving nearly 17 commercial years of patent protection for their products.
        ii. Under current law, patent owners receive 20 years of patent life from the date their patent applications are filed. Since patent applications are typically filed many years before product launch (to achieve priority etc.), significant portions of the 20 year period will elapse while the product is still in the development and regulatory phases. By the time a product reaches the market, there may be little patent life left. Statutory provisions which allow recovery of some patent life to compensate for "delays" in the regulatory process do not wholly compensate for this loss.

iii. Moreover, because of the complex nature of biologics, and evolving patentability standards, it may be difficult for Innovators to obtain enforceable claims which will actually provide meaningful patent protection.

7. Providing sufficient periods of data and market exclusivity to Innovators of biologic products is an effective way to encourage necessary investment in stem cell research and development.
    a. In an effort to accelerate the path to market of multiple biologics products thereby reducing price through competition, several pending federal bills propose allowing "biosimilars" applicants to reference the FDA's safety and efficacy findings concerning the relevant Innovator product rather than having to generate the clinical data themselves. Under these proposals, biosimilars would have lower investment costs because 1) the ability to reference Innovator data eliminates some clinical trial expenses; and 2) their development timeline is shorter because they can reference Innovator studies. This lower cost structure means that biosimilars can be priced below referenced Innovator products.
    b. Data and market exclusivity provide Innovators with a period of time within which they can more easily recoup their investment plus a reasonable profit. During this protected period, biosimilar manufacturers are prohibited from referencing the Innovator's data and the FDA is barred from considering a biosimilar application containing a premature reference. Applications seeking approval for new biologics can be filed, but they must provide independently generated clinical data. During the proposed exclusivity periods, Innovators face competition only from others who have incurred similar investment costs.
    c. Exclusivity periods are thus critical to investment decisions: they define the competitive landscape which a successful Innovator product will face. Longer exclusivity periods promote and reward innovative investment. Shorter exclusivity periods discourage investment in innovative technologies.

8. Charged with encouraging innovation that will speedily bring new therapies to market and recognizing the direct connection between the length of market/data exclusivity and the ability of biotech Innovators to obtain investment sufficient to pioneer new technologies, CIRM resolves that any biosimilars regulatory regime must allow a sufficiently long exclusivity period to encourage investment.
    a. Given the lengthy development period for biologics and the comparatively high cost of research and development, CIRM is concerned that a five year exclusivity period (borrowed from the chemical pharmaceutical model) is not sufficient. Five years of

exclusivity will not provide sufficient stability or certainty to motivate investment in stem cell research.

b. CIRM notes that the European Commission, having recently considered this issue allotted a ten year exclusivity period for biologics Innovators.
c. Therefore, to advance its Mission, CIRM supports a data/marketing exclusivity period for biosimilars which (is at least as long as the period allotted by the European Commission (10 Years)) or (is between 12 and 14 years long) or (which is sufficiently long to motivate investment in stem cell research and the biotechnology companies needed to perform it).