

Perspective

Stem Cell Research: A Platform for Science-Policy Innovation

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I. INTRODUCTION

The California Stem Cell Research and Cures Initiative and related state-based funding programs are designed principally to advance research and regenerative medicine. In pursuing this mission, the California Institute for Regenerative Medicine (CIRM) has engaged in ongoing deliberations concerning a diverse array of science policy issues. As evidenced by this symposium’s program, state-based stem cell policy development has included consideration of (1) appropriate research oversight, (2) intellectual property and access mechanisms for therapies, (3) strategies for governance and financing, and (4) safety evaluation and clinical trials.

These issues are not unique to stem cell research as they have been the topic of ongoing science and health policy deliberations. What is unique is the particular combination of law and science policy issues that have emerged in a “space” with sustained capacity for deliberation and development coupled with organizational capability for implementation. In effect, the mission-driven nature of CIRM and other state programs creates an imperative that has served to drive policy innovation in multiple domains. This policy innovation is noteworthy and was touched upon in the various sessions of the symposium.

A. Research Oversight

State-based programs rapidly developed policies to ensure the ethical and responsible conduct of research.¹ In the CIRM example, funds could not be released until standards for oversight were in place. Emphasis was given to establishing frameworks for the oversight of research not eligible for federal funding, including derivation of human embryonic stem cell (hESC) lines from embryos and somatic cell nuclear transfer.

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¹ Susan Stayn, *A Guide to State Laws on hESC Research and a Call for Interstate Dialogue*, 5 BUREAU OF NAT’L AFF. MED. RES. L. & POL’Y REP. 718, 718-24 (2006).

In 2007, Connecticut convened a meeting of state based programs to initiate the Interstate Alliance on Stem Cell Research (IASCR). The alliance has subsequently served to provide ongoing deliberative capacity to support collaborative development of oversight policies. Particular attention was given to incorporating the National Academies Guidelines for hESC Research into state regulations and contracts. Compatible standards for hESC derivation emerged among California, Connecticut, Massachusetts, Maryland and other IASCR members. Symposium participants noted that these derivation standards incorporate donor consent and hESC use policies that appear compatible with the more recent National Institute of Health (NIH) Guidelines for hESC research. This compatibility is important because federal funds may not be used for hESC derivation. Consequently, states are in a position to fund the development of hESC lines that may be utilized in NIH-funded research. The early adoption of compatible standards suggests foresight and efficacy in the collaborative state-based approach.

B. IP and Access to Therapies

Proposition 71 contains provisions designed to provide benefit to the state from royalties and patent licensing fees from CIRM-funded research. These provisions have become manifest in CIRM's intellectual property (IP) and revenue sharing requirements.² In the process of developing these requirements there was a consensus that CIRM should enact policies to promote access to therapies. Specifically, grantees must develop plans to provide access to resultant therapies and diagnostics for uninsured, or state-insured California patients. These groundbreaking policies represent new models for how state-sponsored initiatives can provide wide public benefit. California is unique with regard to policies related to IP and revenue sharing, because the enabling legislation governing other state programs does not include such provision. Other states recognize the pre-eminence of federal law and have been restrained in the development of unique IP requirements. Partners in the Interstate Alliance suggest this may change if the California approach proves efficacious.

C. Financing and Governance

Proposition 71 established a stable and long-term financing and governance mechanism to support stem cell research. Participants suggested the term and stability of funding has served to leverage additional investment in California and other states. The CIRM Major Facilities program, where \$272 million in public investment served to leverage \$884 million in donor and institutional funding, was cited as an example. This approach is not unique to California; in 2009, New York State announced funding to support the development of core stem cell research facilities. Another example of innovation in financing is CIRM's Loan Program, which is being designed to create a recurring funding pool intended to serve as a sustainable financing mechanism. While efficacy of this approach remains to be tested, it is another potential mechanism "leveraging" public funds for research and economic development.

State funding programs have governance structures designed to support long-term program development. California, Connecticut, and New York have advisory committees or governing boards that oversee funding decisions and/or the development of ethical standards. These boards and committees operate in accordance with state "sunshine" (public meeting) laws, adding process transparency and opportunities for public participation.

² See CAL. CODE REGS. tit. 17, §§ 100300-10; CAL. CODE REGS. tit. 17, §§ 100400-10.

D. Clinical Trials

Proposed clinical trials, involving the use of hESC-derived progenitor cells, are driving procedures for the safety and efficacy evaluation of cell-based therapeutics by the FDA. Participants described the iterative evaluation process required to develop cells for commercial scale use. Issues such as product purity, end-stage differentiation, migration of administered cells, and immunological properties of transplantation products are ongoing concerns. While primary responsibility for safety and efficacy of clinical trials lies with the U.S. Food and Drug Administration (FDA),³ state programs provide added capacity and expertise that have led to collaborative partnerships to support the development of safe and effective therapies.

II. STEM CELL POLICY CONVERGENCE

In a comparatively short timeframe, the stem cell field has been a source of innovation in the domains of research oversight, financing and governance, and intellectual property policy. There may be disagreement on the efficacy of specific policies, but the field has demonstrated the ability to respond to an array of policy challenges in a coherent, deliberative, and transparent manner. Prior funding has been focused primarily on training of personnel, development of core facilities, and supporting basic research. As research now expands to include state, interstate and international initiatives for translation and clinical medicine, it is worth considering the capacity of the stem cell field for addressing future scientific and legal challenges.

The symposium highlighted how in the domain of research oversight and regulation, policies have been developed at the state, national, and international level. Commentators have historically been concerned about a “patchwork” effect where the proliferation of rules in state and national jurisdictions would be detrimental to research.⁴ Certainly, there are jurisdictions, such as some U.S. states, where opposition to hESC research has resulted in punitive policies. In jurisdictions supportive of hESC research, however, there has been a convergence of policy resulting in a high degree of compatibility. Such collaboration enables participants to leverage organizational capacity and expertise to support effective policy development.

This compatibility has been enhanced by the development of networks such as IASCR and the International Society for Stem Cell Research (ISSCR). This network capacity has facilitated the development of a complimentary policy framework among jurisdictions seeking to advance stem cell research. This point was evidenced by the presentation on the recent NIH Guidelines for hESC research. The NIH Guidelines provide a process for registering hESC lines derived in accordance with the consensus framework endorsed in many supportive jurisdictions.⁵ In the context of U.S. policy, it is heartening that state policies governing the derivation of hESC lines appear complimentary with federal NIH Guidelines governing the use of such lines.

III. EMERGING CONSIDERATION FOR TRANSLATIONAL RESEARCH

As the symposium participants noted, the emergence of a clinical trajectory has created new scientific and legal challenges. Foremost were issues related to clinical evaluation of cell

³ Donald. W. Fink Jr., *FDA Regulation of Stem Cell-Based Products*, 324 SCIENCE 1662, 1662-3 (2009).

⁴ Timothy Caulfield et al., *The Stem Cell Research Environment: A Patchwork of Patchworks*, 5 STEM CELL REV. REP. 82, 82-88 (2009).

⁵ National Institutes of Health Guidelines for Human Stem Cell Research, 74 Fed. Reg. 32,170, 32,170-75 (July 7, 2009).

and cell-derived therapies. The same network capacity that has served to support the development of policies to guide basic research is now addressing these challenges. The symposium highlighted ISSCR's effort to develop guidelines for stem cell clinical trials. Further, it was noted that a range of national and international regulatory issues related to clinical safety and efficacy of cell therapies will be a special topic for consideration in advance of the 2010 ISSCR annual meeting in San Francisco. In addition, the FDA has forged partnerships with the research community, including state-based programs, to consider effective methods for assuring the safety and effectiveness of cell products. The development of international funding collaborations has brought renewed commitment to advancing research in accordance with the highest standards. Translating these commitments to results will require research sponsors to continue to develop consensus policy frameworks.

IV. THE VALUE OF RENEWED FEDERAL COMMITMENT

In general, symposium participants were extremely positive about the prognosis for future success. They described how issues related to cell differentiation, clinical administration, and immunology were being addressed in controlled experiments, and with the implementation of good manufacturing practices. A picture emerged of these issues being hurdles rather than insurmountable barriers. Contributing to this sense of optimism is the renewed commitment by federal partners, including the FDA and NIH. While states can effectively develop basic research programs, a full commitment from federal partners is required to support the clinical development of cell therapies. The scientific and legal challenges for the field are greatly attenuated by this renewed commitment particularly when contrasted to the less supportive federal policy environment of the past.

V. POLICY INNOVATION THROUGH ORGANIZATIONAL DESIGN

This sense of optimism should not be construed to understate the scientific challenges for the field. Rather, the thrust of this commentary is to recognize scientific challenges lie ahead, and to suggest the stem cell field as a whole is comparatively well positioned, in a historic sense, to address related legal and policy concerns. This comparative field strength appears to have emerged from an environment that provided sustained capacity for deliberation and research program development coupled with organizational capability for implementation. A recent study funded by the National Science Foundation concludes that California has established itself as a major center for stem cell research affecting both distribution of biotechnological infrastructure and start up firms and investment of venture capital in the United States.⁶

State programs supported policy innovation at a time when financial and organizational resources were constrained at the national level. The mission-driven nature of the state-based stem cell enterprises created a space for collaboration and policy innovation. This environment is now enhanced by an effective federal presence. While this symposium highlighted the scientific and legal challenges remaining, the field is well prepared to address them in a coordinated and systematic manner.

⁶ Joel W. Adelson & Joanna K. Weinberg, *The California Stem Cell Initiative: Persuasion, Politics, and Public Science*, 100 AM. J. PUB. HEALTH (forthcoming Mar. 2010), available at <http://ajph.aphapublications.org/cgi/content/full/100/3/446>.