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UNITED STATES REGULATION OF STEM CELL RESEARCH: RECASTING GOVERNMENT'S ROLE AND QUESTIONS TO BE RESOLVED

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Every progress in science in the last decades, from the moment it was absorbed into technology and thus introduced into the factual world where we live our everyday lives, has brought with it a veritable avalanche of fabulous instruments and ever more ingenious machinery. All of this makes it more unlikely every day that man will encounter anything in the world around him that is not man-made and hence is not, in the last analysis, he himself in a different disguise.¹

- Hannah Arendt

I. INTRODUCTION

Humans, like many other animals with central nervous systems, run under the control of biological clocks distributed among the various organs of their bodies and synchronized by a master clock located in their brains.² Like an organism in which these clocks have been disconnected from their master, the many arms of United States federal and state law governing stem cell research and medicine exhibit a profound lack of synchronicity and varying degrees of “soft” and “hard” touch. This situation, we believe, results largely from the United States National Institutes of Health (“NIH”) having been stymied since the late 1970s from becoming a fully formed “master clock” for a nationwide,

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1. Hannah Arendt, *The Conquest of Space and the Stature of Man*, NEW ATLANTIS, Fall 2007, at 43, 52.

2. See generally COLD SPRING HARBOR SYMPOSIA ON QUANTITATIVE BIOLOGY: CLOCKS AND RHYTHMS (2007) (discussing the biological clock mechanism of humans and other living beings).

perhaps worldwide, human embryology research program—one that includes the study of human embryonic stem cells (“hESCs”) and regenerative medicine.³ This is a role that the NIH has successfully achieved in many other areas of health science.⁴ A solution to this problem may be the invention in 2007 of induced pluripotent stem cells (“iPSCs”).⁵ Beyond iPSCs, the tantalizing potential looms for reprogramming adult somatic cells directly into other types of adult somatic cells without having to revert to pluripotent status.⁶ But even if these innovations may help resolve decades of ethical and religion-based debates over hESCs, a larger problem not specific to any technology remains: addressing the conflicts that now exist among federal and state governments over how best to regulate stem cell research and medicine—conflicts that arose in an environment without the NIH being able to play its historic lead role in shaping ethical, legal, and socially acceptable practices for this emerging area of health science.

3. On April 17, 2009, subsequent to the submission of this Article, the NIH announced the availability for public comment of Draft Guidelines containing policies and procedures by which it proposes to fund extramural and conduct intramural human stem cell research. The publication of these Draft Guidelines marks the first step in the NIH’s implementation of President Barack Obama’s Executive Order, the stated purpose of which is to promote human stem cell research. *See* Draft National Institutes of Health Guidelines for Human Stem Cell Research Notice, 74 Fed. Reg. 18,578 (Apr. 23, 2009); Exec. Order No. 13,505, 74 Fed. Reg. 10,667 (Mar. 9, 2009); *see also infra* note 131.

4. *See* National Institutes of Health, www.nih.gov/about/NIHoverview.html (last visited Mar. 3, 2009) (“With the support of the American people, the NIH annually invests over \$28 billion in medical research. More than 83% of the NIH’s funding is awarded through almost 50,000 competitive grants to more than 325,000 researchers at over 3,000 universities, medical schools, and other research institutions in every state and around the world. About 10% of the NIH’s budget supports projects conducted by nearly 6,000 scientists in its own laboratories, most of which are on the NIH campus in Bethesda, Maryland.”).

5. iPSCs are pluripotent stem cells derived from human adult somatic cells and that exhibit many characteristics of, but are not identical to, human pluripotent stem cells derived from human blastocysts. *See* Junying Yu et al., *Induced Pluripotent Stem Cell Lines Derived from Human Somatic Cells*, 318 *SCIENCE* 1917, 1917 (2007); Kazutoshi Takahashi et al., *Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors*, 131 *CELL* 861, 868 (2007). For the political significance of iPSCs, *see*, for example, President George W. Bush, State of the Union Address (Jan. 28, 2008) (“On matters of life and science, we must trust in the innovative spirit of medical researchers and empower them to discover new treatments while respecting moral boundaries. In November, we witnessed a landmark achievement when scientists discovered a way to reprogram adult skin cells to act like embryonic stem cells. This breakthrough has the potential to move us beyond the divisive debates of the past by extending the frontiers of medicine without the destruction of human life.”).

6. *See, e.g.*, Bruce Goldman, *Smash the (Cell) State!*, *NATURE*, Aug. 27, 2008, <http://www.nature.com/stemcells/2008/0808/080827/full/stemcells.2008.115.html> (last visited Feb. 4, 2009). Adult somatic cells are cells in the body of an organism other than those that will become gametes (eggs and sperm). The word “adult” is somewhat of a misnomer in that the bodies of organisms ranging from newborns to what are normally considered to be adults are composed of adult somatic cells.

This Article probes this question of conflicts between present federal and state regulation of hESC research by comparing the federal Bayh-Dole Act (“Bayh-Dole” or the “Act”) regime for licensing patents claiming inventions funded by agencies of the U.S. government (such as the NIH) with the patent licensing regime of the California Institute for Regenerative Medicine (“CIRM”). CIRM is the agency of the State of California authorized and directed to fund hESC research through the issuance of \$3 billion of general obligation bonds at an estimated cost of at least \$6 billion payable over the next thirty years.⁷ Although, to date, eight other states have also adopted stem cell research funding programs, this Article centers on CIRM as the most ambitious state effort to fill a science-funding vacuum created through federal government law and policy.⁸

Part II of this Article provides an overview of the roles, relationships, and norms of government, academia, and industry in federal funding of research that evolved in the United States during the second half of the twentieth century, with particular emphasis on the passage of the Bayh-Dole Act of 1980.⁹ Part III covers the emergence, beginning as early as the 1970s, of federal laws and regulations relating to the study of human embryology and hESC research, the emergence of state law and regulation following the turn of the twentieth century into the twenty-first, and the resulting patchwork quilt that currently prevails. This discussion echoes a centuries-old theme of the impact on scientific progress when politics based on imperfect perception holds the purse strings tied around scientific research. Part IV explores in some detail how the trends, developments, stakes, and stakeholders described in Parts II and III intersect in the patent licensing regulations adopted by CIRM. This discussion particularly illustrates an unending debate on how to best translate patentable inventions funded by government into medicines and therapies for promoting the public health—a debate that goes back at least as far as the adoption of Bayh-Dole and to the debates

7. Dean E. Murphy, *Defying Bush Administration, Voters in California Back \$3 Billion for Stem Cell Research*, N.Y. TIMES, Nov. 4, 2004, at P10.

8. New York, by way of the Empire State Stem Cell Board created in 2007, has committed \$600 million to stem cell research. EMPIRE STATE STEM CELL BOARD, STRATEGIC PLAN 7, http://stemcell.ny.gov/plan_comment_form.php. Massachusetts, overriding the veto of Governor Mitt Romney, plans to create an institute for stem cell research and regenerative medicine at the University of Massachusetts. Nat'l Conference of State Legislatures, Stem Cell Research, www.ncsl.org/programs/health/Genetics/embfet.htm (last visited Jan. 15, 2009). New Jersey was the first state to appropriate funds for both adult and embryonic stem cell research, and in 2005 and 2006 it allocated a total of \$23 million to the New Jersey Stem Cell Institute. *Id.*

9. See *infra* notes 44-59 and accompanying text.

in the 1970s over federal funding of fetal tissue research.¹⁰ Through a comparative discussion of Bayh-Dole and CIRM, Part IV also illustrates a larger-scale problem—the jurisdictional conflicts that will exist in the field of stem cell research and regenerative medicine irrespective of whether hESCs, iPSCs, or any applicable substitute serves as its foundation. The Article concludes by asking stakeholders in stem cell research and regenerative medicine on a worldwide scale to consider adopting a more proactive approach to addressing these multi-jurisdictional conflicts in policy and regulation that have arisen in the United States, as well as beyond the United States, over the past thirty years, owing in large part to a lack of coordination among the various government actors.

II. UNITED STATES FEDERAL FUNDING: FROM ATOMIC BOMBS TO BIOTECH

The threat of annihilation by technology during World War II (“WWII”)¹¹ inspired aggressive United States investment to raise the base of science, which continues to this day.¹² The impact on American research universities was profound—a definitive before and after:

10. See *infra* notes 84-99 and accompanying text.

11. The uranium atom was split successfully in 1938. See National Atomic Museum, The Manhattan Project, <http://www.atomicmuseum.com/Tour/manhattanproject.cfm> (last visited Mar. 3, 2009). Fearing that the Nazis could and would develop an atomic bomb, the United States undertook the Manhattan Project to pre-empt them. *Id.*

12. See Titus Galama & James Hosek, *U.S. Science Is Holding Its Own*, PITT. POST-GAZETTE, July 9, 2008, at B7. According to one recent report on the state of United States investment in science relative to other nations:

Although China, India and South Korea are starting to account for a significant portion of the world’s science and technology activities, and are showing rapid growth, they still account for a very small share of patents, science publications and citations. The United States, meanwhile, continues to invest in science and technology infrastructure, is creating significant employment in science and engineering, and benefits from the immigration of foreign-born science and engineering students and workers.

Id. For detailed, timely data on research and development (“R&D”) expenditures, see National Science Foundation, Research and Development, <http://www.nsf.gov/statistics/showpub.cfm?TopID=8> (last visited Mar. 9, 2009). The two largest R&D efforts of the war were the Manhattan Project and the Radiation Laboratory at the Massachusetts Institute of Technology (“MIT”). ROGER L. GEIGER, RESEARCH AND RELEVANT KNOWLEDGE: AMERICAN RESEARCH UNIVERSITIES SINCE WORLD WAR II 7 (Transaction Pub. 2004) (1993). As Geiger notes of these two projects:

In their objectives and management, they were almost mirror opposites. The first began as a rather diffuse undertaking, but gradually concentrated an enormous amount of science, engineering, and material resources upon the single goal of producing an atomic bomb. The second began with a single device—a British designed magnetron, the basis for effective microwave radar—and gradually proliferated into an entire industry with multiple products and applications.

Id.

Research universities before World War II and research universities afterward are two different stories. The first is one of a (growing) handful of institutions seeking to advance to world-class standards in basic science and receiving an enormous boost from the great philanthropic foundations. The second is a story of a system of universities impelled forward by the demands and the resources of the federal government, but also guided by their own academic ambitions.¹³

In fact, as discussed below, the American science research experience during and since WWII encompasses three distinguishable eras: the military-industrial complex (“MIC”) establishment era (1939 into the 1940s); the academia-industry separation era (mid-1940s into the 1980s); and the academia-industry integration era (1980s to the present).¹⁴ The following discussion addresses each with a focus on the roles of and relationships among government, academia, and industry, and the resulting technology transfer and research and development infrastructure and norms.

A. *Military-Industrial Complex Era*

The Great Depression inspired generous government funding of civil works—roads, airports, bridges, buildings, and beyond—to put America back to work and stimulate the economy.¹⁵ Still, the United States entered WWII without a standing army or a meaningful

13. GEIGER, *supra* note 12, at xiii.

14. Although beyond the focus and scope of this Article, there is another chapter in government science funding that must be mentioned—the “earmark era.” See generally Jeffrey Mervis, *U.S. Research Earmarks: Building a Scientific Legacy on a Controversial Foundation*, 321 SCIENCE 480 (2008); see also Interview by Robert Frederick with Jeffrey Mervis, Deputy News Editor, Science Magazine, Science Magazine Podcast (July 25, 2008), available at http://podcasts.aaas.org/science_podcast/SciencePodcast_080725.mp3 (transcript on file with the Hofstra Law Review). This era was launched by two projects funded by Congress decades ago: a \$32 million appropriation in the late 1970s that allowed Tufts University to build a nutrition center in downtown Boston, and a \$14.2 million appropriation in 1983-84 that enabled Catholic University of America to erect a four-story science building in Washington, D.C. See Mervis, *supra*, at 480. Earmarks, often referred to as “pork barrel projects,” are funding directives by Congress without agency involvement, peer review, or substantial scrutiny by congressional committees. See *id.* “Most scientists, and their professional organizations, look down their noses at earmarks. They see them as a threat to the merit review process that most federal agencies use to fund basic science.” *Id.* Nevertheless, science earmarks have increased steadily and significantly since the Tufts appropriation, culminating in \$4.5 billion in 2008. *Id.*

15. See Steven A. Ramirez, *The Law and Macroeconomics of the New Deal at 70*, 62 MD. L. REV. 515, 517-19 (2003). These direct project appropriations were the predecessor for the earmark era in government science funding, which is addressed *supra* note 14.

infrastructure of military weapons manufacturers.¹⁶ In science and technology, the war effort necessitated direct, intense interaction among government, industry, and academia with complete focus on application.¹⁷ The federal government became a contract purchaser of inventions from both academia and industry.¹⁸ The country left WWII with established, expansive, and ongoing relationships between the armed forces and private industry suppliers, and financial support of the same became a permanent, major expenditure and budget priority.¹⁹ President Eisenhower appreciated the scope of this Rubicon-like crossing and its impact on future generations,²⁰ which he shared in his Farewell Address to the Nation broadcast by radio on January 17, 1961:

Akin to, and largely responsible for the sweeping changes in our industrial-military posture, has been the technological revolution during recent decades.

In this revolution, research has become central; it also becomes more formalized, complex, and costly. A steadily increasing share is conducted for, by, or at the direction of, the Federal government.

Today, the solitary inventor, tinkering in his shop, has been overshadowed by task forces of scientists in laboratories and testing fields. In the same fashion, the free university, historically the fountainhead of free ideas and scientific discovery, has experienced a revolution in the conduct of research. Partly because of the huge costs involved, a government contract becomes virtually a substitute for intellectual curiosity. For every old blackboard there are now hundreds of new electronic computers.

16. At the time of the nation's founding, the country called up troops only when needed or used militias, but did not make an organized military a permanent fixture until after WWII. Jesse Smith, *Introduction to JESSE SMITH, THE MILITARY-INDUSTRIAL COMPLEX: PRESIDENT DWIGHT D. EISENHOWER'S FAREWELL ADDRESS TO THE NATION* 3, 3 (2006). According to the Department of Defense's Fiscal Year 2007 Baseline Report, there are 1,899,074 military personnel in the United States and its territories, and the United States military is present at more than 823 installations outside of the United States. U.S. DEP'T OF DEF., *BASE STRUCTURE REPORT, FISCAL YEAR 2007 BASELINE* 22, 76 (2007), available at http://www.defenselink.mil/pubs/BSR_2007_Baseline.pdf.

17. GEIGER, *supra* note 12, at 7 ("Given the absolute priority of the war effort, the usual academic tasks of universities were largely displaced for the duration."). Moreover, it is important to note that "[t]he basic relationship between the federal government and universities for conducting wartime research was governed by contracts negotiated according to the principle of no-loss and no-gain. Universities were reimbursed for the direct costs they incurred and also given some allowance for overhead." *Id.* at 6. This relationship provided the precedent for "administrative overhead" that later became commonplace with federal grant funding for bench research.

18. *See id.* at 7.

19. *See* Smith, *supra* note 16, at 3-4.

20. *See id.* at 3-4. President Dwight Eisenhower coined the phrase "military-industrial-complex" in his Farewell Address, which was broadcast to the American people via radio. *Id.* at 5.

The prospect of domination of the nation's scholars by Federal employment, project allocations, and the power of money is ever present—and is gravely to be regarded.

Yet, in holding scientific research and discovery in respect, as we should, we must also be alert to the equal and opposite danger that public policy could itself become the captive of a scientific-technological elite.

It is the task of statesmanship to mold, to balance, and to integrate these and other forces, new and old, within the principles of our democratic system—ever aiming toward the supreme goals of our free society.²¹

As President Eisenhower predicted, the MIC has continued and expanded post-WWII, raging through the Cold War and today culminating with the War on Terror.²² However, to prevent the “domination of the nation's scholars by Federal employment, project allocations, and the power of money[,]”²³ the federal government also has been a strong supporter and generous funder of peer-reviewed, civilian-focused research by academic and government laboratories—especially in the human health sciences.²⁴ For decades this duality contributed to separation between academia and industry, but now, following a change in federal technology transfer law and policy in the 1980s,²⁵ we are decades deep into an era of extensive integration and unprecedented advancement in biomedical science.²⁶

B. *The Era of Separation*

Academia and industry worked in tandem during WWII as part of the national war effort. With the war over, they largely separated,²⁷ as their traditionally different cultures and priorities re-emerged; supportive

21. Farewell Radio and Television Address to the American People, 1 PUB. PAPERS 1038-39 (Jan. 17, 1961).

22. See Smith, *supra* note 16, at 7-8.

23. Eisenhower, *supra* note 21, at 1039.

24. See generally GEIGER, *supra* note 12. Generous NIH funding of biomedical research was introduced in the 1950s, and increased exponentially during the final decades of the last century to remain constant with the price of biomedical R&D. For an NIH chart illustrating this, see http://report.nih.gov/award/research/RG_Current_Constant_Dollars_Chart.ppt (last visited Feb. 17, 2009).

25. See *infra* Part II.C.

26. See Alan E. Guttmacher & Francis S. Collins, *Realizing the Promise of Genomics in Biomedical Research*, 294 JAMA 1399, 1401-02 (2005); see also Symposium, *Proceedings of “The Genomics Revolution? Science, Law, and Policy,”* 66 LA. L. REV. 1 (2005).

27. These relationships did not separate entirely, for academia-industry relationships were established by the MIC that continued on, while more were forged as the MIC expanded, and the general base in science and technology rose. See *infra* note 34 and accompanying text.

federal science policy supported and funded separate tracks of engagement with each; and United States intellectual property law and policy pushed them apart.²⁸ During WWII, the federal government had been a contract purchaser of inventions from both academia and industry.²⁹ Industry was cautious about commingling its investments in researchers and institutions with government funding through mutual relationships, which raised a risk of government claims to invention.³⁰ Also, many in academia were eager to return to the funding and cultural norms that predated WWII: enablement of land grant and other public universities by significant state government funding and tuition, and enablement of private schools from higher tuitions and major philanthropic funding.³¹ Tuition coverage from the GI Bill expanded enrollment and increased tuition revenue, which benefited universities in general.³²

Still, in some parts of academia a lingering appetite for federal government funding and associated applied research opportunities had developed.³³ Norms were set during the War for the supplement of occasional government contract engagements to sustain the technological revolution—especially to remain competitive with the Soviet Union. Some institutions comfortable with an emphasis on application in science—most notably MIT, which for years had placed applied science at the center of its curriculum and had been deeply involved in the Radiation Laboratory³⁴—embraced these and other opportunities to work directly with industry.³⁵

28. See James Stuart, *The Academic-Industrial Complex: A Warning to Universities*, 75 U. COLO. L. REV. 1011, 1032-35 (2004).

29. GEIGER, *supra* note 12, at 6.

30. The United States government has suggested and actually made claims to several pharmaceuticals post-development and market entry. A noted fairly contemporary example is the breast cancer drug Taxol. See Ron A. Bouchard, *Balancing Public and Private Interests in the Commercialization of Publicly Funded Medical Research: Is there a Role for Compulsory Government Royalty Fees?*, 13 B.U. J. SCI. & TECH. L. 120, 153-54 (2007) (discussing how the federal government funded the development of Taxol, but granted the pharmaceutical company the right to sell the drug to the public). We see analogous behavior today when research institutions that receive federal funding apply the requisite Common Rule infrastructure—compliance with the regulations to protect human subjects that federal funding triggers—to their privately-funded basic research endeavors. See generally PRICEWATERHOUSECOOPERS LLP, INSTITUTIONAL REVIEW BOARD (IRB) REFERENCE BOOK (Michele K. Russell-Einhorn & Thomas Puglisi eds., 2001) (providing an overview of federal regulations regarding the oversight of human subjects research).

31. Jed Scully, *The Virtual Professorship: Intellectual Property Ownership of Academic Work in a Digital Era*, 35 MCGEORGE L. REV. 227, 241-42 (2004).

32. GEIGER, *supra* note 12, at 41.

33. *Id.* at 13.

34. See *supra* note 12.

35.

The 1950s ended with yet another major escalation in federal funding of science research—this time in response to the technological prowess of the Soviet Union. On October 4, 1957, the Soviet Union outpaced the United States in space technology by launching Sputnik 1, the first man-made object to orbit the earth.³⁶ The United States increased its own government laboratory research in space science and beyond, and also introduced more programs to support university development, infrastructure, and graduate education.³⁷

However, the 1960s, which began with the Bay of Pigs Invasion and Cuban missile crisis and ended with the government's own space science program placing a man on the moon, saw greater demand that federally-funded science produce tangible applications.³⁸ The federal government grew impatient with academic research, and its funding of academic research diminished. "The *annus horribilis*, 1968, brought an end to the expansion of academic research and anguish over the role that universities had assumed."³⁹ This trend continued, making the 1970s a decade of stagnation in federal support for academic research:

The MIT Technology Licensing Office (TLO) was established in 1945, many years before most universities were encouraged to take similar steps by the Bayh-Dole Act. The TLO office plays a very proactive role in technology transfer activities. Rather than waiting for a technology pull, reacting to requests for licenses from interested companies, the TLO encouraged faculty to promptly disclose inventions, then quickly and carefully evaluate the market value of inventions, and obtain protection of intellectual property. It also meets with venture capitalists to discuss new technologies and ongoing research at the Institute that may be appropriate for a start-up venture. This approach began at MIT at a time when such an approach was viewed as 'unseemly' by some of MIT's peer institutions.

Rory P. O'Shea et al., *Creating the Entrepreneurial University: The Case of MIT 12* (2005), available at www.umssystem.edu/ums/departments/ed/documents/EntrepreneurialUniversityMIT.pdf. In contrast, at other academic institutions establishment of policies and administrative procedures required for working within the Bayh-Dole regime took at least a decade following its enactment.

36. See Barton Beebe, Note, *Law's Empire and the Final Frontier: Legalizing the Future in the Early Corpus Juris Spatialis*, 108 *YALE L.J.* 1737, 1744 (1999). To summarize:

The immediate effect of the Sputnik Crisis in America was a call for total mobilization, for "blood, sweat and tears," in pursuit of scientific and technological superiority. This call extended to the nation's educational system, to its industrial base, to its commodity culture, and, of course, to its methods of governance. Ever prudent, Eisenhower refused to be carried away by the panic. In his 1958 State of the Union Address, he declared that the Soviet Union had begun to wage "total cold war," but proposed only modest reforms. It was left to the Kennedy and Johnson Administrations, to the New Frontier and the Great Society, to wage total cold war in return.

Id. at 1745 (footnotes omitted).

37. GEIGER, *supra* note 12, at xv.

38. *Id.*

39. *Id.*

For the next ten years universities endured stagnation in research support, the end of enrollment growth in higher education, a crash in the job market for new Ph.D.'s, intrusive government regulation, and fiscal distress. Universities largely reacted to student rebellion and public chastisement by withdrawing to the ivory tower. Higher education rhetoric and university actions disdained entanglements with the defense establishment or the corporate world, extolling instead the role of unsullied social critic. Egalitarianism and social justice informed the new zeitgeist as a powerful campus polity sought to enlist the university in such virtuous causes as racial and social gender equity, third world liberation, urban revitalization, and environmental preservation. . . . [B]y the late 1970s it was becoming increasingly apparent that there was too little research, academic or otherwise, reaching the productive economy.⁴⁰

C. *The Era of Integration*

By the end of the 1970s, the decade-long bout with “stagflation” (coined at the time to capture the combination of a stagnant economy, a floundering stock market, and inflation) led to demand for more R&D and translation of the fruits of that R&D into economy-stimulating technology. In Congress, more than any other problem, the energy crisis, characterized by staggering oil prices and long lines at gas pumps, generated accusations that big business was not investing enough in research, and that the federal government, mired in bureaucracy, was allowing academic research funded by the government to remain locked in file cabinets.⁴¹ This latter criticism was well-founded. The lack of any uniform federal policies on patenting government-sponsored inventions or the transfer of technology from the government to the private sector left agencies to act case-by-case as they encountered instances of invention.⁴² This generated agency-specific inconsistencies, multiplied among the agencies with which individual universities and corporate entities had to deal. The result was uncertainty and tremendous administrative burdens for all involved.⁴³ “At the time, fewer than 5

40. *Id.*

41. *See id.*, at xv-xvi; U.S. GEN. ACCOUNTING OFFICE, TECHNOLOGY TRANSFER: ADMINISTRATION OF THE BAYH-DOLE ACT BY RESEARCH UNIVERSITIES 2-3 (1998) [hereinafter GAO REPORT]; Chester G. Moore, Comment, *Killing the Bayh-Dole Act's Golden Goose*, 8 TUL. J. TECH. & INTELL. PROP. 151, 153-54 (2006).

42. GAO REPORT, *supra* note 41, at 3.

43. *Id.*; *see also* Lorelei Ritchie de Larena, *The Price of Progress: Are Universities Adding to the Cost?*, 42 HOUS. L. REV. 1373, 1378 (2007) (“Naturally, that created undue bureaucracy as universities (and other contractors) and their funding agencies attempted to sort through ownership issues both *ex ante*, in the grant applications, and then again, *ex post*, once inventions were

percent of the 28,000 patents being held by federal agencies had been licensed, compared with 25 percent to 30 percent of the small number of federal patents for which the government had allowed companies to retain title to the invention.”⁴⁴

Congress responded in 1980 by passing legislation intended to promote economic development, enhance United States competitiveness, and benefit the public through commercialization of government-funded research—the Bayh-Dole Act⁴⁵ and the Stevenson-Wydler Act.⁴⁶ The legislative intent of Bayh-Dole was, through reform of patent policy related to government-sponsored research: (1) to enable and encourage “universities, not-for-profit corporations, and small businesses to patent and commercialize their federally-funded inventions and (2) to allow federal agencies to grant exclusive licenses for their technology to provide more incentive to businesses.”⁴⁷

created.”); Stuart, *supra* note 28, at 1034-35 (“However, under the pre-1980 regime, the government retained intellectual property rights to such research; thus, a firm would have to go through the unwieldy process of trying to license inventions from the federal government. . . . [T]he Act was aimed at corporate underwriters who, because of these newly added layers of legal protection, would be encouraged to underwrite university research so as to turn inventions into marketable products.”).

44. GAO REPORT, *supra* note 41, at 3; *see also* Stuart, *supra* note 28, at 1034 (“Whereas the major principle in the decades after World War II was that technology owned by the government was for ‘everyone’s benefit,’ supporters of the Act claimed that this policy effectively rendered government-owned technology for ‘nobody’s benefit.’ It simply gathered dust in government repositories.”).

45. University and Small Business Patent Procedures Act of 1980, Pub. L. No. 96-517, § 6(a), 94 Stat. 3019 (1980) (codified as amended at 35 U.S.C. §§ 200-212 (2000)); *see also* COUNCIL ON GOVERNMENTAL RELATIONS, UNIVERSITY TECHNOLOGY TRANSFER: QUESTIONS AND ANSWERS (1996), available at <http://206.151.87.67/docs/bayhdoleqa.htm> (providing background information on the Bayh-Dole Act).

46. Technology Innovation Act of 1980, 15 U.S.C. §§ 3701-3715 (2006).

47. GAO REPORT, *supra* note 41, at 3; DEP’T OF HEALTH & HUMAN SERVS., NAT’L INST. OF HEALTH, NIH RESPONSE TO THE CONFERENCE REPORT REQUEST FOR A PLAN TO ENSURE TAXPAYERS’ INTERESTS ARE PROTECTED (2001) [hereinafter NIH REPORT], available at <http://www.nih.gov/news.070101wyden.htm>; *see also* Matthew Herder, *Asking for Money Back—Chilling Commercialization or Recouping Public Trust in the Context of Stem Cell Research?*, 9 COLUM. SCI. & TECH. L. REV. 203, 207-12 (2008) (providing a detailed discussion of the proposed recoupment provisions and associated testimony); Moore, *supra* note 41, at 153-54. As explained by the NIH, the collective goal of these acts “is to promote economic development, enhance U.S. competitiveness, and benefit the public by encouraging the commercialization of technologies that would otherwise not be developed into products due to lack of incentives.” NIH REPORT, *supra*. Later, Congress added to these Acts with enactment of the Federal Technology Transfer Act of 1986 (“FTTA”), which authorizes federal agencies to enter into cooperative research and development agreements (“CRADA”) with non-federal partners to conduct research. *See* Federal Technology Transfer Act of 1986, 15 U.S.C. §§ 3710a-3710d (2006). In 1987, federal regulations were issued by the Department of Commerce, codified at 37 C.F.R. § 401 (2008), to fully implement the provisions of the Bayh-Dole Act. GAO REPORT, *supra* note 41, at 3-4 (providing a clear summary of the requirements set forth in these regulations).

Originally, Bayh-Dole did not apply to large firms, its benefits being limited to “any contractor who is a non-profit research institution or a small business.”⁴⁸ This concession was to balance the lack of a recoupment provision⁴⁹ and the Act’s grant of title to the grantee with the United States holding only a license.⁵⁰ Although those seeking a recoupment provision pressed hard, ultimately the day was carried by their opponents who argued that any amount collected by recoupment might be outweighed by the administrative costs⁵¹ and would certainly be dwarfed by the indirect returns from funding scientific research.⁵² The

48. H.R. REP. NO. 96-1307, pt. 1, at 5 (1980).

49. See Herder, *supra* note 47, at 207-12 (detailing the discussion of the proposed recoupment provisions and associated testimony). Many in Congress were apprehensive about giving away inventions made with taxpayer investments.

Until shortly before its passage, the Bayh-Dole Act contained language to recoup the federal investment for federally funded technologies that reach commercialization. The proposed language included a formula for the repayment process. The Government would receive 15 percent of income over \$70,000 gross income after a patent application was filed and up to an additional 5 percent if the gross income exceeded \$1 million, up to the amount of government contributions under the funding agreement, pegged to the Consumer Price Index.

NIH REPORT, *supra* note 47.

50.

Throughout, there remained tension over the question of whether the government should own resulting inventions, or merely have a right to use them. This title-versus-license debate was ultimately resolved by the Bayh-Dole Act in favor of the latter system, whereby the contractor may elect ownership, but the government obtains an automatic, fully paid-up grant-back on federally funded inventions.

de Larena, *supra* note 43, at 1379 (footnote omitted).

51. NIH REPORT, *supra* note 47.

52. See *id.*; see also Herder, *supra* note 47, at 214. Opponents of the recoupment provision argued that an increase in federal, state, and local tax bases from resulting commercial activity and jobs would far exceed taxpayer investment, and this position was supported by the United States Congressional Joint Economic Committee. NIH REPORT, *supra* note 47. According to the Congressional Economic Joint Committee:

The benefit of increased life expectancy in the U.S. as a result of advances in health care creates annual net gains of about \$2.4 trillion (using 1992 dollars). . . . “[I]f only 10 percent of these increases in value (\$240 billion) are the result of NIH-funded medical research, it indicates a payoff of about 15 times the taxpayers’ annual NIH investment of \$16 billion.”

Id. (quoting JOINT ECONOMIC COMM., U.S. SENATE, THE BENEFITS OF MEDICAL RESEARCH AND THE ROLE OF THE NIH 17 (2000)). Also, a commissioned study concluded that:

The total economic value to Americans of reductions in mortality from cardiovascular disease averaged \$1.5 trillion annually in the 1970-1990 period. So if just one-third of the gain came from medical research, the return on the investment averaged \$500 billion a year. That’s on the order of 20 times as large as average annual spending on medical research—by any benchmark an astonishing return for the investment.

LASKER/FUNDING FIRST, MARY WOODWARD LASKER CHARITABLE TRUST, EXCEPTIONAL RETURNS: THE ECONOMIC VALUE OF AMERICA’S INVESTMENT IN MEDICAL RESEARCH 8 (2000), <http://www.laskerfoundation.org/advocacy/pdf/exceptional.pdf>.

issue has been addressed and the same conclusion reached globally.⁵³ As explained by the NIH in its 2001 report on technology transfer:

To obtain passage of the [Bayh-Dole Act], members of Congress agreed that recoupment provisions would be dropped. However, due to concerns of some members of Congress that large companies would benefit from public dollars without a return to the taxpayer, large companies were removed from eligibility in the final bill. With these changes, the bill was passed and the Act today remains applicable to universities, nonprofit organizations and small businesses. In 1983, by Presidential Memorandum, President Ronald Reagan extended the implementation to large companies. And, in 1987, implementation of the Act was extended to these companies as part of an Executive Order issued by President Reagan.⁵⁴

The new dispensation of the Bayh-Dole Act did not come free of all limitations, but these are not very onerous, particularly as the Act has been put into practice over the three decades since its passage. Chiefly the limitations require that the funded invention be responsibly protected and pursued. They state a preference for American industry in any relevant products to be made or sold in the United States.⁵⁵ Grant recipients must report promptly all inventions to the funding agency. Grantees must also timely elect whether to seek patents on the inventions and, if they decline or fail to do so, the funding agency may take title to them.⁵⁶ Whether or not the funding agency takes title to the invention or the patent, the United States is given the right to practice the invention, worldwide and at no charge, for its own use.⁵⁷

53.

Countries around the globe attempting to emulate Bayh-Dole have, whether by design or default, reinforced the underlying logic against recoupment, which is essentially as follows: obligations to provide direct financial returns undermine the commercialization process and therefore threaten what the public cares about most, i.e. the production of new goods.

Herder, *supra* note 47, at 203.

54. NIH REPORT, *supra* note 47.

55. The accompanying burdens and obligations are found at 35 U.S.C. §§ 200-212 (2000 & Supp. V 2006) and the implementing regulations are at 37 C.F.R. § 401.1-1.17 (2008).

56. 35 U.S.C. § 202(c)(1)-(2); 37 C.F.R. § 401.14(c)-(d). If the contractor elects to seek patents, it must do so timely and, if it declines or fails to do so, the funding agency can take title to them. 35 U.S.C. § 202(c)(2); 37 C.F.R. § 401.14(d)(1). The contractor's ongoing efforts to achieve practical application of the invention are not ignored. It must report annually to the funding agency on the invention's utilization. 37 C.F.R. § 401.14(h). The content of that report should include "information regarding the status of development, date of first commercial sale or use, gross royalties received by the contractor, and such other data and information as the *agency* may reasonably specify." *Id.* However, the agency is urged to accept the information, to the extent feasible, in the contractor's usual internal format. 37 C.F.R. § 401.8(a).

57. 35 U.S.C. § 202(c)(4); 37 C.F.R. § 401.14(b).

Finally, and importantly, Bayh-Dole provides the government with a “trump card,” the march-in right. Insofar as the grantee fails to achieve practical application of the invention and make its benefits reasonably accessible to the public, the funding agency may march in on the patented invention and license it to others.⁵⁸ Because the march-in right is so powerful and could exert an *in terrorem* effect on grantees and those with whom they hope to work to develop inventions arising from funded research, the Bayh-Dole Act regulations hedge the exercise of any march-in right with due process protections to the grantee.⁵⁹ And the actual practice of funding agencies under the Bayh-Dole Act’s march-in provisions is consistent with the regulatory intent not to disturb the settled expectations of grantees and their commercial counterparties.⁶⁰

58. 35 U.S.C. § 203(a).

59. For a description of these due process protections, see 37 C.F.R. § 401.6(b)-(j); *see also* Michael S. Mireles, Jr., *States as Innovation System Laboratories: California, Patents, and Stem Cell Technology*, 28 *CARDOZO L. REV.* 1133, 1138, 1143, 1155-59 (2006) (describing the march-in rights under the Bayh-Dole Act and noting that the process is so cumbersome that, to date, they have not been exercised by the government). For instance, if the funding agency receives information that might warrant exercise of the march-in right, it must give the contractor written and specific notice, and afford the contractor the chance to respond with comments and relevant information. At this informal stage, the agency may drop the matter and, if so, it must timely notify the contractor. If the agency decides to proceed, it must initiate a formal proceeding, which is replete with safeguards against error, bias, or caprice. The contractor may submit evidence and if the evidence raises a genuine dispute over material facts, the agency must undertake the necessary fact-finding. The contractor may appear with counsel and submit documentary evidence, present witnesses, and confront such witnesses as the agency may present. The contractor has the right to a written transcript of the proceeding and official written findings of fact and may submit written argument and make oral arguments. The head of the agency is responsible for making a final written determination, and this must be sent to the contractor by certified or registered mail within ninety days of the completion of fact-finding or oral argument. If the agency reaches a determination adverse to the contractor, the result is held in abeyance pending final resolution in the United States Court of Federal Claims, to which anyone adversely affected by the march-in determination may petition. *See* 35 U.S.C. § 203(b); 37 C.F.R. § 401.6. This abeyance applies unless there is a public health emergency under 35 U.S.C. § 203(a)(2) or the contractor has failed to honor the substantial United States manufacture requirements of 35 U.S.C. § 203(a)(4).

60. In the twenty-eight years since the Bayh-Dole Act was enacted, there have been three occasions when a funding agency (in each case, the NIH) was petitioned to exercise its march-in powers against a grantee. The first of these was the petition by CellPro, Inc. against patents on stem cell purification and suspension technology, which were held by Johns Hopkins University and Baxter Healthcare Corporation. Nat’l Inst. of Health, Office of the Dir., Determination in the Case of Petition of CellPro, Inc. (Aug. 1, 1997), *available at* <http://www.nih.gov/news/pr/aug97/nih-01.htm>. The second and third petitions were companion petitions directed against Abbott Corporation’s Norvir and Pharmacia Corporation’s Xalatan drugs. Nat’l Inst. of Health, Office of the Dir., In the Case of Norvir (July 29, 2004), *available at* <http://www.ott.nih.gov/policy/March-in-norvir.pdf>; Nat’l Inst. of Health, Office of the Dir., In the Case of Xalatan (Sept. 17, 2004), *available at* <http://www.ott.nih.gov/policy/March-in-xalatan.pdf>. The NIH has not chosen to exercise the march-in power in any of these three petitions. This lack of action has not pleased some, who argue that patented products cannot be said to have been “reduced to practical application” as Bayh-Dole requires, if they are available to the public at a price that is too expensive

Federal technology transfer law and policy has had a profound impact on academia, industry, biomedical R&D, the American economy, and, potentially, the future of human health.⁶¹ As it sought to do, the “give away” of federally-funded invention “unlocked all the inventions and discoveries that had been made in laboratories throughout the United States with the help of taxpayers’ money.”⁶² The immediate impact was to integrate different parts of the R&D community.⁶³ “A fruitful collaboration between academic researchers and industry promised to fuel not only economic development but also new sources of revenue for universities. A vast movement of privatization was underway by the mid-1980s, and it reinvigorated research universities.”⁶⁴ Since the 1990s, this integration of academia and industry has proceeded in an explosive manner, giving rise to all the benefits, concerns, and controversies that accompany such dramatic and rapid change.⁶⁵ Arguably, this integration

(although any price above zero will be open to this criticism). *See, e.g.*, Statement of James Love, President of Essential Inventions Inc., NIH Meeting on Norvir/Ritonavir March-In Request (May 25, 2004), available at <http://www.ott.nih.gov/policy/meeting/James-Love-Pres-Essential-Inventions-Inc.pdf>. Thus, there is pressure to amend the Bayh-Dole Act to make march-in less “cumbersome,” and that pressure has come to bear on the California system, as discussed *infra* at Part IV.C. *See* Mireles, *supra* note 59, at 1155 (stating that Bayh-Dole march-in is “encumbered by a complex set of regulations, including provisions allowing for appeal of any decision to exercise such rights, and could serve as a disincentive to use those rights”).

61. The GAO evaluated the impact of technology transfer in a report issued in 1998 and the NIH did the same in 2001. *See generally* GAO REPORT, *supra* note 41; NIH REPORT, *supra* note 47. Reports also have been done by consulting groups such as the Boston Consulting Group, and on the national and state levels. *See generally* PETER GOLDSBROUGH ET AL., BOSTON CONSULTING GROUP, THE PHARMACEUTICAL INDUSTRY INTO ITS SECOND CENTURY: FROM SERENDIPITY TO STRATEGY (1999); Biotechnology Industries Organization, www.bio.org (last visited Mar. 31, 2009) (follow “State by State Initiatives” hyperlink). *See also generally* Michael J. Malinowski & Radhika Rao, *Legal Limitations on Genetic Research and the Commercialization of Its Results*, 54 AM. J. COMP. L. 45 (2006) (noting the progress of biopharmaceuticals).

62. *Innovation’s Golden Goose*, ECONOMIST, Dec. 14, 2002, at 3.

63. *Id.*

64. GEIGER, *supra* note 12, at xvi.

65. As stated by one observer, “It has turned universities into commercial entities, created a multibillion-dollar industry of technology transfer, and subsidized virtually every biotechnology company and discovery of the past twenty-five years.” de Larena, *supra* note 43, at 1375. For another evaluation of the Bayh-Dole Act, see generally DAVID C. MOWERY ET AL., IVORY TOWER AND INDUSTRIAL INNOVATION: UNIVERSITY-INDUSTRY TECHNOLOGY TRANSFER BEFORE AND AFTER THE BAYH-DOLE ACT IN THE UNITED STATES (2004). For thoughtful discussion of what major medical centers should consider before entering into alliances with industry, see Hamilton Moses, III, et al., *Industrial Collaboration*, 348 NEW ENG. J. MED. 863, 864 (2003). Perhaps the major point of controversy is the assertion that federal technology transfer law and policy has resulted in frantic patenting in biotechnology, creating a thicket of patents and administrative burden in licensing that threatens to shut down the field. Professors Rebecca Eisenberg, Arti Rai, and others have centered their careers on this argument. *See, e.g.*, Rebecca S. Eisenberg & Arti K. Rai, *Harnessing and Sharing the Benefits of State-Sponsored Research: Intellectual Property Rights and Data Sharing in California’s Stem Cell Initiative*, 21 BERKELEY TECH. L.J. 1187, 1197 (2006); *see also* Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The*

was a categorical imperative: In some fields, particularly life science, neither universities nor industry could reach and remain at the leading edge of scientific research and product development, respectively, without engaging with each other. The rapid pace of the science, and its complexity, meant that any given research project depended on many different tools and skill sets, on many scales and schedules; and many of these were constantly being superseded or expanded. No single participant or R&D sector could afford to develop and maintain all of these complementary technologies without help from other participants both within and outside its particular sector. In some cases, this collaboration was personified by individuals moving between academia and industry and acting as agents for both simultaneously.⁶⁶ Remaining at the forefront of technology is innate to universities' combined missions of teaching, research, and service: "By no means is all new knowledge discovered in universities, but most of it soon finds its way there. Universities serve as the warehouse and distribution center for the most advanced and theoretical forms of knowledge."⁶⁷

In particular, "[b]iotechnology manifested its commercial potential in unmistakable fashion. Pure biological research had yielded the tools to transform life itself, with enormous implications for medicine and agriculture."⁶⁸ An entire domestic-based sector, today well over 1000 companies,⁶⁹ has unfolded in about the time it takes to develop one innovative new biopharmaceutical.⁷⁰ The global pharmaceutical sector

Anticommons in Biomedical Research, 280 *SCIENCE* 698, 698-99 (1998). Certainly, the rocketed acceleration of the state of the art in biotech fueled by the unprecedented progression of the underlying science leaves us with many patents issued early in the genomics revolution that would not sustain reexamination, and this has driven those in the field to an obsessive-compulsive drive to patent. Perhaps the United States Patent and Trademark Office should exercise the mechanism of reexamination and clear much of this perceived thicket. See Michael J. Malinowski & Maureen A. O'Rourke, *A False Start? The Impact of Federal Policy on the Genotechnology Industry*, 13 *YALE J. ON REG.* 163, 233 (1996). Nevertheless, to date, biotech R&D is unique in its tendency to inspire competitors to collaborate, and, in general, those engaged in biopharmaceutical R&D have demonstrated a strong predisposition to license over patent conflicts and to conservatism and judgment in the enforcement of issued patents. This collaborative effect is the shared practice and field experience of the authors.

66. MOWERY ET AL., *supra* note 65, at 166.

67. GEIGER, *supra* note 12, at xvii.

68. *Id.* at xvi; see also Guttmacher & Collins, *supra* note 26, at 1400.

69. BIOTECHNOLOGY INDUS. ORG., GUIDE TO BIOTECHNOLOGY 2 (2007), available at <http://www.bio.org/speeches/pubs/er/BiotechGuide.pdf> (providing data as of 2005).

70. Industry estimates, based on largely proprietary data, provided by industry voluntarily and processed by the Tufts Center for the Study of Drug Development (a center sponsored by the industry), are ten to fifteen years at \$800 million for one innovative new drug. *Id.* at 42. However, "technological advances have lowered the cost of sequencing at a fairly constant rate, halving it approximately every 22 months." Guttmacher & Collins, *supra* note 26, at 1400. Thus, it is likely

and biotechnology sectors have become part of a continuum,⁷¹ with biopharmaceuticals replacing pharmaceuticals in development.⁷² The United States has experienced a tremendous biopharmaceutical R&D influx, making it the concentrated epicenter of the global endeavor to translate the map of the human genome into medical utility and, more generally, to realize the human health and other application benefits of contemporary biotechnology.⁷³

III. THIRTY YEARS OF STEM CELL DEBATE

Legislation and regulation of stem cell research and medicine operates at multiple levels of government and along two fundamental dimensions. In the United States, these multiple levels include federal, state, and local. Of the two fundamental dimensions, the first speaks normatively to that which may be absolutely prohibited, permitted, or mandated by statute or regulation; and the second, to that which the government may or may not be willing to fund.⁷⁴ Within the normative dimension, assuming at least some form of human stem cell research or medicine is permitted, various sub-dimensions arise relating to matters

that the development of new technologies will continue to “accelerate this rapid decrease in sequencing costs.” *Id.*

71. BIOTECHNOLOGY INDUS. ORG., *supra* note 69, at 2, 6-15; PHARM. RESEARCH AND MFRS. OF AM., 2007 ANNUAL REPORT 4 (2007), *available at* <http://www.phrma.org/files/2007%20Annual%20Report.pdf> (“The pharmaceutical industry is one of the most R&D intensive businesses in the United States. Last year, America’s pharmaceutical and biotechnology companies invested \$55.2 billion in biopharmaceutical research.”). For example, Global Research and Development at Pfizer, Inc. funds a Biotherapeutics and Bioinnovation Center based in the San Francisco Bay area that combines “cutting-edge biology, new platform technologies, and advanced research tools to discover and develop new medicines” and has been mandated to “collaborate broadly with the academic, biotech, and venture communities to focus on discovering and developing new medicines.” *See* WorldPharmaNews.com, *Pfizer Launches Independent Biotherapeutics and Bioinnovation Center*, Oct. 5, 2007, <http://www.worldpharmanews.com/content/view/147/30>.

72. For the purpose of this discussion a “small molecule compound” is comprised of a few dozen atoms, typically carbon, oxygen, hydrogen, nitrogen, and some others, produced through chemical synthesis or purified from substances found in nature. A “biologic” is typically a larger molecule or complex of molecules, such as a protein or an antibody, and is usually produced by bacteria or yeast through the process of fermentation and then purified. *See* BIOTECHNOLOGY INDUS. ORG., *supra* note 69, at 42.

73. A 2004 report issued by the Milken Institute predicted that by 2014 the biopharmaceutical industry’s impact on the United States would mean over 3.6 million jobs and \$350.1 billion in real output. MILKEN INST., BIOPHARMACEUTICAL INDUSTRY CONTRIBUTIONS TO STATE AND U.S. ECONOMICS 158-59 (2004), *available at* <http://www.milkeninstitute.org/publications/publications.taf?function=detail&ID=377&cat=ResRep>.

74. *See generally* LOUIS M. GUENIN, THE MORALITY OF STEM CELL USE (2008); RUSSELL KOROBKIN & STEPHEN R. MUNZER, STEM CELL CENTURY 26-91 (2007) (providing a systematic exploration of this range of issues).

such as informed consent,⁷⁵ payments and reimbursements to subjects and participants in such research,⁷⁶ and the use and commercialization of the various instruments, reagents, tissue samples, cell lines, and cells through which research, medicine, or both are undertaken.⁷⁷

Within each of these dimensions, the national debates took a separate course, but they arose long before hESCs were even available. The debate within the funding dimension arose in the late 1970s in the context of the NIH's consideration of whether and how it would support research in embryology, including in vitro fertilization ("IVF"). IVF is related to hESC research by virtue of the fact that pre-implantation embryos created in IVF clinics for treating fertility problems but not used for implantation—referred to as "excess preimplantation embryos"—are a source of hESCs,⁷⁸ and several cell-handling techniques in IVF are also employed in somatic cell nuclear transfer ("SCNT") technology.⁷⁹

75. An important element of all legislative and regulatory rules and guidelines for the use of excess human embryos to create pluripotent stem cell lines has been the informed consent of the donors of those embryos. For several years, commentators have expressed concerns about the adequacy of informed consent used for existing pluripotent stem cell lines derived from excess human embryos. *See, e.g.*, Timothy Caulfield et al., *Informed Consent in Embryonic Stem Cell Research: Are We Following Basic Principles?*, 176 CAN. MED. ASSOC. J. 1722, 1724 (2007); *see also* Rosario M. Isasi & Bartha M. Knoppers, *Beyond the Permissibility of Embryonic and Stem Cell Research: Substantive Requirements and Procedural Safeguards*, 21 HUM. REPROD. 2474, 2478 (2006). The informed consent issue has captured increasing attention with some controversy as to whether certain pluripotent stem cell lines derived from excess human embryos prior to August 9, 2001, were derived with adequate informed consent. *See, e.g.*, Monya Baker, *Consent Issues Restrict Stem-Cell Use*, 454 NATURE 556, 556 (2008); Robert Streiffer, *Informed Consent and Federal Funding for Stem Cell Research*, HASTINGS CTR. REP., May-June 2008, at 40, 42-43.

76. For a list of state laws relating to payment and reimbursements for donation of eggs, zygotes, embryos, and fetal tissue, see Nat'l Conference of State Legislature, *supra* note 8.

77. For an explanation of the application of human subject protection rules to cancer treatment clinical trials, including stem cell transplant, see generally INST. OF MED., A REPORT ON THE SPONSORS OF CANCER TREATMENT CLINICAL TRIALS AND THEIR APPROVAL AND MONITORING MECHANISMS (1999). For an example of the impact of federal funding policies on stem cell research facilities at American universities, see Stanford Report, *5 Questions: Longaker on Stem Cell Research* (Apr. 6, 2005), <http://news-service.stanford.edu/news/2005/april6/med-longaker-040605.html> (last visited Mar. 11, 2009) (describing how state funding for the purpose of creating new stem cell lines must first be used to build separate facilities so that no federal funding is inadvertently spent on such research).

78. *See* THE NATIONAL ACADEMIES, UNDERSTANDING STEM CELLS: AN OVERVIEW OF THE SCIENCE AND ISSUES FROM THE NATIONAL ACADEMIES 5-6, available at <http://dels.nas.edu/bls/stemcells/what-is-a-stem-cell.shtml>. Because of the stochastic nature of IVF, multiple eggs are fertilized during the IVF procedure. Those fertilized eggs that are not implanted in the mother are referred to as "excess" embryos and are stored under cryogenic conditions. *Id.* at 5.

79. In SCNT, the nucleus of an egg cell from an organism of a particular species is replaced with the nucleus from an adult body cell, or somatic cell, taken from an organism of that or another species. This procedure came to be referred to as "cloning" and has historically been viewed as an important research tool within the fields of embryology and developmental biology. *Id.* at 7.

In contrast, within the normative dimension, the debate began to boil in the 1990s over the issue of creating human pluripotent stem cell lines.⁸⁰ These cell lines could be produced from (a) excess preimplantation embryos; as well as from (b) “research embryos” produced by fertilizing donated human eggs (called “oocytes”) with donated human sperm specifically for research purposes outside the context of IVF-based fertility treatment; and (c) SCNT-produced blastocysts.⁸¹ As the debate first arose, a distinction existed between research embryos produced and SCNT-produced blastocysts, but this distinction blurred after August 9, 2001, when the White House issued a fact sheet on hESC research (the “2001 Fact Sheet”).⁸² In the wake of the NIH’s implementation of the policy set forth in the 2001 Fact Sheet, the debate grew confused and important distinctions were suppressed between and among terms and phrases such as “human embryonic stem cells,” “somatic cell nuclear transfer,” “human cloning,” “human cloning for reproductive purposes,” and “human cloning for research purposes.”⁸³ As noted, elements of the normative debate were combined,⁸⁴ and that combined debate conflated with the funding debate. The conflated normative and funding debate spread from the federal arena to the states, and the confusion and controversy has continued unabated at both the federal and state levels. By combining and merging these technological concepts and debates, important distinctions may have been lost, or perhaps never achieved. Without clear distinctions, honest and constructive debate—even if impossible to resolve—cannot be accomplished.

80. Pluripotent stem cells are found in the interior of a blastocyst and are referred to as such “because they can differentiate into all of the cell types of the body.” *Id.* at 4.

A blastocyst . . . is a pre-implantation embryo that develops 5 days after the fertilization of an egg by a sperm. It contains all the material necessary for the development of a complete human being In its interior is the inner cell mass, which is composed of 30-34 [pluripotent] cells. . . . In common usage, ‘embryo’ can refer to all stages of development from fertilization until a somewhat ill-defined stage when it is called a fetus.

Id.

81. See, e.g., Nicholas Wade, *Clinton Asks Study of Bid to Form Part-Human, Part-Cow Cells*, N.Y. TIMES, Nov. 15, 1998, at L31.

82. Press Release, President George W. Bush, Fact Sheet: Embryonic Stem Cell Research (Aug. 9, 2001) (on file with the Hofstra Law Review).

83. *Id.*; see also Richard Pérez-Peña, *Broad Movement Is Backing Embryo Stem Cell Research*, N.Y. TIMES, Mar. 16, 2003, at N20.

84. Richard Pérez-Peña, *supra* note 83, at 20 (“In the last year, the stem cell debate has merged with the one over human cloning.”).

A. *The Funding Dimension at the United States Federal Level*

1. The 1970s

Touching a complex issue on which the American public is deeply divided, the Supreme Court's 1973 holding in *Roe v. Wade*⁸⁵ marked neither the beginning nor the end of the debate on early termination of pregnancy; rather, the Court's holding fueled the controversy.⁸⁶ Responding to the policy issues presented in *Roe*, together with concerns over the protection of human subjects in government-funded research, Congress in 1974 established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research ("Commission").⁸⁷ One of the Commission's missions⁸⁸ was "to investigate and study research involving the living fetus, and to recommend whether and under what circumstances such research should be conducted or supported by the Department of Health, Education, and Welfare."⁸⁹

In 1975, the Commission concluded, among other things, "that some information which is in the public interest and which provides significant advances in health care can be attained only through the use

85. 410 U.S. 113 (1973).

86. See generally EVE HEROLD, *STEM CELL WARS* (2006) (discussing connections between the stem cell debate and the debate about elected early termination of human pregnancy); see also Janet L. Dolgin, *Embryonic Discourse: Abortion, Stem Cells, and Cloning*, 31 FLA. ST. U. L. REV. 101, 161-62 (2003) (Discussing the "larger history of ideas" spanning centuries as the continuing source of fuel for this particular debate: "[T]he most important questions arising within the debate about embryonic research and therapeutic cloning (and more widely about genetic information and its uses) concern the character of the *individual* person in a universe with the capacity to prolong life long beyond current expectations, to alter people's minds and bodies—and perhaps their souls—through technology, and to select physical and affective traits prenatally. . . . Both the debate about abortion and that about embryonic research are also debates about social transition. The future is murky, but these conflated debates provide the analyst with a view of society contemplating itself and its most deeply held convictions.").

87. See National Research Act, Pub. L. 93-348, 88 Stat. 342, 348 (1974); see also NAT'L COMM'N FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH, REPORT AND RECOMMENDATIONS: RESEARCH ON THE FETUS I (1975) [hereinafter NAT'L COMM'N FOR THE PROTECTION], available at http://www.bioethics.gov/reports/past_commissions/research_fetus.pdf.

88. A primary mission for the Commission was to address how it was possible for the United States government to have funded for decades the infamous Tuskegee Study, a study of black men suffering from syphilis in which the men were not given standard antibiotic therapy. See, e.g., Ctrs. for Disease Control and Prevention, U.S. Public Health Service Syphilis Study at Tuskegee, <http://www.cdc.gov/tuskegee/index.html> (last visited Mar. 12, 2009).

89. NAT'L COMM'N FOR THE PROTECTION, *supra* note 87, at 1 (indicating Congress's concern, among others, "that unconscionable acts involving the fetus may have been performed in the name of scientific inquiry, with only proxy consent on behalf of the fetus"); see also Marjorie Sun, *Another Threat to Fetal Research*, 218 SCIENCE 981, 981 (1982) (noting that as early as 1973, the NIH had instituted rules relating to research with human fetuses).

of the human fetus as a research subject.”⁹⁰ The task for drawing regulations consistent with the ethical principles required for conducting and funding research on the human fetus fell to the Ethics Advisory Board (“EAB”) of the Department of Health, Education, and Welfare (“HEW”).⁹¹ The demise of this powerful board in September 1980, two months prior to the presidential election of that year, may be a root cause of the stymied progress in stem cell research to the present day.⁹²

Following the July 1978 report from England of the first human birth using IVF,⁹³ the EAB took up the attendant scientific, ethical, legal, and social issues, and, in May 1979, reported that IVF research was “ethically acceptable” and could be supported with federal funds.⁹⁴ Under 45 C.F.R. § 46.204(d), the EAB would be responsible for reviewing IVF and related embryologic and fetal research to be conducted or funded by the NIH. But, as at least one source explains, the then Secretary of HEW, Patricia Harris, viewed infertility as a problem suffered by the middle and upper classes and not one to be studied with HEW funds.⁹⁵ And as other sources indicate, Secretary Harris was also influenced by letters from the public strongly opposed to federal funding of embryologic and fetal research.⁹⁶ Consequently, Secretary Harris allowed the EAB charter to lapse, without renewal, in September 1980.⁹⁷ This decision resulted in a “de facto moratorium” on any funding for

90. NAT’L COMM’N FOR THE PROTECTION, *supra* note 87, at 62.

91. See STEPHEN S. HALL, *MERCHANTS OF IMMORTALITY: CHASING THE DREAM OF HUMAN LIFE EXTENSION* 100 (2003).

92. From 1974 to 1978, the EAB issued several reports that formed the basis of the federal regulations set forth in 45 C.F.R. § 46 (2007), a four-part set of regulations, with each part aimed at protecting a specific population of subjects in specified areas of research conducted, supported or otherwise subject to regulation by any federal department or agency. Part B focused on research involving pregnant women, human fetuses, neonates of uncertain viability, and nonviable neonates. *Id.*

93. See, e.g., *Woman Gives Birth to Baby Conceived Outside the Body*, N.Y. TIMES, July 26, 1978, at A1.

94. *Ethics Advisory Board: In Vitro Fertilization is ‘Ethically Acceptable,’* IRB, Apr. 1979, at 7, 7.

95. HALL, *supra* note 91, at 100-01 (“[Harris] said infertility was a middle-class and upper-class problem,’ [according to former NIH bioethicist John C. Fletcher]. . . . ‘The official view was, and probably still is, that infertility wasn’t a disease.’ Harris refused to approve . . . IVF research in general. Then, when the EAB’s charter lapsed, ‘it was summarily disbanded’ by Harris in September 1980, according to former EAB member Albert Jonsen, who [stated], . . . ‘The Ethics Advisory Board still hovers as a ghostly presence in the Federal Regulations, charged with mandatory review of certain types of research, but it exists nowhere in reality.’”).

96. See Richard Doerflinger, *A New Assault on the Smallest Humans?*, U.S. Conference of Catholic Bishops, Aug. 5, 1988, <http://www.usccb.org/prolife/issues/ivf/lif8588.shtml> (“HEW Secretary Patricia Harris nevertheless decided not to fund the research, in part because she received thousands of letters against it from citizens concerned about the risks to the human embryo.”).

97. JUDITH A. JOHNSON, CONG. RESEARCH SERV., *HUMAN CLONING* 4 (2001), available at <http://www.law.umaryland.edu/marshall/crsreports/crsdocuments/RS21096.pdf>.

IVF and embryology research.⁹⁸ This breakdown in the administrative process, coupled with “political winds [growing] chillier still for government-financed research after the 1980 election,”⁹⁹ led to an exodus from the NIH of the expert embryologists and fetal development scientists who had assembled there to advance their fields.¹⁰⁰

2. Revitalization of the NIH

Shortly after taking office in 1993, President Clinton selected Nobel Laureate Harold Varmus as the new NIH director.¹⁰¹ Determined to revitalize the NIH’s study of human fetal tissue and stem cell biology as important potential sources of new therapies, Dr. Varmus saw to it that the National Institutes of Health Revitalization Act of 1993 (“NIHRA”) included provisions conducive for that research—principally among these, a single sentence that abolished the requirement that IVF research proposals be reviewed by the EAB (an entity that had then been dead for thirteen years).¹⁰² Replacing that review process would be one that required the Secretary of Health and Human Services (“HHS”) to apply the same risk standard in assessing research proposals for fetuses.

98. *Id.*

99. HALL, *supra* note 91, at 101.

100. See, e.g., *Scientist Quits NIH Over Fetal Rules*, 223 SCIENCE 916, 916 (1984) (“The absence of an ethics advisory board is ‘frustrating some of our scientists who can’t work on very important problems,’ says Mortimer Lipsett, director of the Institute of Child Health and Human Development. . . . Oddly enough, although antiabortion groups have been the strongest critics of in vitro fertilization, many of the scientific problems Lipsett alludes to can be construed as ‘pro-life’ because they are aimed at improving an embryo’s chances for survival.”). The requirements for EAB approval of research with embryos also applied to research with fetuses. While embryology and human fetal tissue research at the NIH may have been quick to deteriorate during the 1980s, by the turn of the 1980s into the early 1990s, several other areas of research at the NIH were also suffering. See, e.g., David Korn et al., *The NIH Budget in the “Postdoubling” Era*, 296 SCIENCE 1401, 1401 (2002) (“In the late 1980s and early 1990s, the federal budget deficit, a recession, and administrative changes within the NIH caused oscillations in funding. . . . The net effect was to destabilize established research teams, to create uncertainty in young people contemplating research careers, to stimulate investigators to slice research projects into smaller grant proposals, and to shift a larger share of funded research costs onto awardee institutions.”).

101. Barbara Looney, *Should Genes Be Patented? The Gene Patenting Controversy: Legal, Ethical, and Policy Foundations of an International Agreement*, 26 LAW & POL’Y INT’L BUS. 231, 232 & n.8 (1994).

102. National Institutes of Health Revitalization Act of 1993, Pub. L. No. 103-43, § 121(c), 107 Stat. 122, 133 (1993) (nullifying 45 C.F.R. § 46.204(d) (2007) (requiring EAB review of IVF proposals) and overturning Exec. Order No. 12,806, 57 Fed. Reg. 21,589 (May 21, 1992)). The overturned Executive Order by President George H. Bush established a fetal tissue bank “to provide a source of human tissue to develop treatments and research methods for various diseases. . . . The fetal tissue in the bank [was to] to be obtained exclusively from ectopic pregnancies and spontaneous abortions.” Exec. Order No. 12,806, 57 Fed. Reg. 21,589. The Order also directed the Secretary of Health and Human Services to “develop human fetal cell lines in a manner consistent with current policy” and to ensure that the activities directed under the Order were “carried out in accordance with all other applicable legal requirements related to fetal tissue.” *Id.*

The policy underlying this approach was to protect unsuspecting women and their fetuses from unethical manipulation.¹⁰³

Serving this same objective, in September 1994, the NIH's Human Embryo Research Panel reported its conclusion that federal funds should be provided for research that would use excess preimplantation embryos, and that, because studies requiring fertilization of oocytes were "needed to answer crucial questions in reproductive medicine," it "would therefore not be wise to prohibit altogether the fertilization and study of oocytes for research purposes."¹⁰⁴ The Panel stressed, however, that all such research should be done in accordance with careful regulation and consistent monitoring entailed by moral respect for the qualities possessed by preimplantation embryos.¹⁰⁵ These conclusions were unanimously accepted by the Advisory Committee to the Director of NIH, but not by President Clinton, who, in a December 2, 1994 statement specifically rejected federal funding for creating embryos for research.¹⁰⁶ The NIH thus proceeded to develop guidelines to support research using excess preimplantation embryos, with overall public consensus still far away.

3. The Dickey-Wicker Amendment

The enthusiasm for increased NIH funding exhibited by the 104th Congress—the "Contract with America" Congress elected in 1994—did not extend to SCNT with human cells and hESC research.¹⁰⁷ Several representatives in Congress were particularly concerned that the December 2, 1994 presidential directive had only opposed the use of federal funds to create human embryos for research purposes and not, as well, the use of excess preimplantation human embryos for creating pluripotent cell lines. This concern led to the adoption of the "Dickey-Wicker Amendment" (also referred to as the "Dickey Amendment"), a

103. See 42 U.S.C. § 289g(b) (2000). The regulations that ensue from the authority in 42 U.S.C. § 289g(b) are set forth in 45 C.F.R. § 46.205(b)(1)(ii) (2007), which states that: (a) No fetus in utero may be involved as a subject in any activity covered by this subpart unless: (1) The purpose of the activity is to meet the health needs of the particular fetus and the fetus will be placed at risk only to the minimum extent necessary to meet such needs, or (2) the risk to the fetus imposed by the research is minimal and the purpose of the activity is the "development of important biomedical knowledge which cannot be obtained by other means." *Id.*

104. AD HOC GROUP OF CONSULTANTS TO THE ADVISORY COMM. TO THE DIR., NAT'L INST. OF HEALTH, 1 REPORT OF THE HUMAN EMBRYO RESEARCH PANEL, xi-xii (1994).

105. *Id.* at x.

106. President William J. Clinton, Statement on Federal Funding of Research on Human Embryos, (Dec. 2, 1994), available at <http://www.presidency.ucsb.edu/ws/index.php?pid=49545&st=embryo&st1=>.

107. Phillip B.C. Jones, *Funding of Human Stem Cell Research by the United States*, 3 ELECTRONIC J. BIOTECHNOLOGY 30, 31 (2000).

short two-sentence rider of less than 120 words attached to the federal appropriations act for fiscal year 1996.¹⁰⁸

The Amendment's first sentence barred the use of any fiscal 1996 federal appropriations for

- (1) the creation of a human embryo or embryos for research purposes;
- or (2) research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 [C.F.R. §] 46.208(a)(2) and 42 U.S.C. [§] 289g(b).¹⁰⁹

The Amendment's second sentence defined "human embryo or embryos" to "include any organism, not protected as a human subject under 45 [C.F.R. §] 46 as of the date of enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes."¹¹⁰ The word "organism" here was not specifically defined, an omission of significance, as discussed below, for the proponents of research with hESCs.

With the references to 45 C.F.R. § 46 and 42 U.S.C. § 289(g), two conclusions could be unmistakably drawn from the Dickey Amendment: first, Congress was according the same type of protection to human embryos, as defined therein, as that accorded to fetuses—in fact, fetuses in utero intended to be carried to term; and second, by extending to not only all of the then known procedures by which human embryos could potentially be created, but also to "any other means from one or more human gametes," Congress was aiming broadly at present and future embryonic stem cell research techniques, well beyond the scope of the December 2, 1994 presidential directive.¹¹¹

108. Balanced Budget Downpayment Act, I, Pub. L. 104-99, § 128, 110 Stat. 26, 34 (1996).

109. *Id.* Clause (1) of the Dickey Amendment statutorily codified the December 2, 1994 presidential directive that federal funds could not be used for in vitro creation of embryos for research. Clause (2) went beyond the December 2, 1994 presidential directive by statutorily prohibiting federally-funded research with excess IVF embryos. *Id.*

110. *Id.* Later enactments of the Dickey Amendment added terms to this definition. *See, e.g.*, Consolidated Appropriations Act of 2001, Pub. L. 106-554, § 510, 114 Stat. 2763, 2763A-71 (2000) (defining "human embryo or embryos" to include "any organism, not protected as a human subject under 45 [C.F.R. §] 46 as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells").

111. *See generally* Gerald D. Fischbach & Ruth L. Fischbach, *Stem Cells: Science, Policy, and Ethics*, 114 J. CLINICAL INVESTIGATION 1364, 1367 (2004) ("The Dickey Amendment includes 'research in which a human embryo is destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero.' Thus, preimplantation blastulae are included in the Dickey Amendment.") It is also important to note how the term "embryo" has been expanded. *See supra* note 110 and accompanying text.

As a rider to an appropriations bill, the original Dickey Amendment had a one-year period of effectiveness.¹¹² But with some modification (for example, inclusion of the term “diploid cells” as a proscribed source of organisms),¹¹³ it has been included in federal appropriations laws every year since its original adoption in 1995, thus making it a *de facto* law without termination.

4. HHS General Counsel Opinion and the NIH Draft Guidelines

With the announcements in November 1998 from the Gearhart and Thomson labs described below, debate flared on whether the NIH could fund research on pluripotent stem cell lines derived from hESCs. Those who sought to limit application of the Dickey Amendment argued that its scope did not apply to federal funding of research with hESC-derived cell lines so long as federal funds were not used to create those lines. In January 1999, the Office of the General Counsel of HHS gave support to this position by opining that human pluripotent stem cells do not comprise an “embryo” as defined in the Dickey Amendment.¹¹⁴ This opinion turned on the view that such cells are not an “organism”—an undefined term used in the Dickey Amendment to define the term “embryo.”¹¹⁵

112. Balanced Budget Downpayment Act, I, Pub. L. 104-99, § 106, 110 Stat. 26, 27 (“Unless otherwise provided for in this title of this Act or in the applicable appropriations Act, appropriations and funds made available and authority granted pursuant to this title of this Act shall be available until (a) enactment into law of an appropriation for any project or activity provided for in this title of this Act, or (b) the enactment into law of the applicable appropriations Act without any provision for such project or activity, or (c) March 15, 1996, whichever first occurs.”).

113. Exec. Order No. 13,435, 72 Fed. Reg. 34,592 (June 22, 2007) (“[T]he term ‘human embryo’ shall mean any organism, not protected as a human subject under 45 [C.F.R. §] 46 as of the date of this order, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells.”).

114. JUDITH A. JOHNSON & BRIAN A. JACKSON, CONG. RESEARCH SERV., STEM CELL RESEARCH 3 (1990).

Following the November 1998 announcement on the derivation of human embryonic stem cells, NIH requested a legal opinion from HHS on whether federal funds could be used to support research on human stem cells derived from embryos or fetal tissue. The January 15, 1999, response from HHS General Counsel Harriet Rabb found that current law prohibiting the use of HHS appropriations for human embryo research [the Dickey Amendment] would not apply to research using human stem cells “because such cells are not a human embryo within the statutory definition.” The finding was based, in part, on HHS’s determination that the statutory ban on human embryo research defines an embryo as an *organism*. Human pluripotent stem cells are not and cannot develop into an organism; they lack the capacity to become organisms even if they are transferred to a uterus. As a result, HHS maintained that NIH could support research which uses stem cells but could not support research which derives stem cells from embryos.

Id.

115. See *supra* notes 110-11.

To Dickey Amendment proponents, the HHS General Counsel's opinion made no sense. How could federal funds be used for research with pluripotent stem cell lines from human blastocysts when the Amendment flatly prohibited the use of federal funds to create those lines? They argued that research using such cells was clearly within the intended scope of the Dickey Amendment and that the HHS General Counsel opinion reflected a "legalism" that violated it.¹¹⁶

This argument notwithstanding, armed with the HHS General Counsel opinion, the NIH could continue its efforts to compose and begin conducting a federally-funded stem cell research program. In this pursuit, on August 25, 2000, after processing "approximately 50,000 comments from members of Congress, patient advocacy groups, scientific societies, religious organizations, and private citizens," the NIH published its final guidelines for research involving human pluripotent stem cells.¹¹⁷ While the NIH altered some wording from that proposed in its original draft guidelines, the thrust of the draft guidelines remained intact, falling into three categories: (1) assurance that the human embryos from which pluripotent stem cell lines would be derived were "in excess of clinical need"; (2) the elements of the informed consent required from donors of human embryos; and (3) the documentation to be provided with research applications or proposals on the provenance of the human embryos to be used.¹¹⁸

5. 2001 Fact Sheet and NIH Response

Unlike the actions of the Carter Administration in 1980, which had made it easy for the Reagan Administration to continue the *de facto* moratorium on embryology research, the HHS General Counsel opinion and NIH stem cell research guidelines from the Clinton Administration presented the Bush Administration with a significant challenge. And more significantly, whereas stem cell science was, at best, itself at an embryonic stage in the early 1980s, by 2001, advances in stem cell

116. See Fischbach & Fischbach, *supra* note 111, at 1367-68 ("[Raab's] opinion was adopted by Harold Varmus, . . . but it caused an uproar in Congress . . .").

117. National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells, 65 Fed. Reg. 51,976, 51,976 (Aug. 25, 2000). The authors speculate that many of these comments were probably thoughtful statements from both sides of the deep rift separating the proponents and opponents of research with hPSCs derived from hESCs, but that a large number may have been short, polysyllabic messages of opposition of the sort heard in the bleachers at a baseball game more so than comments designed to further the deliberative process of rule-making.

118. *Id.* For example, in the final guidelines, the word "early" was dropped from the originally-proposed term "early human embryos," and the phrase "infertility treatment" was changed to "fertility treatment." Compare Draft National Institutes of Health Guidelines for Research Involving Human Pluripotent Stem Cells, 64 Fed. Reg. 67,576, 67,577 (Dec. 2, 1999), with National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells, 65 Fed. Reg. at 51,976-97.

science were sufficiently significant to be suggestive of the potential for using stem cells to create cures for various diseases and conditions.¹¹⁹ On August 9, 2001, after months of wrestling with senior advisors' differences of opinion, the Bush Administration offered a Solomonic solution¹²⁰ in the form of a one-page "Fact Sheet," opening with a quote from President Bush: "As a result of private research, more than 60 genetically diverse stem cell lines already exist [and enable the conclusion] . . . that we should allow federal funds to be used for research on these existing stem cell lines 'where the life and death decision has already been made.'"¹²¹ The Fact Sheet noted that three principal types of protection (the requirement for informed consent of donors; the limitation of funding for cell lines derived from excess embryos created solely for reproductive purposes; and the prohibition of any financial inducements to the donors of such excess embryos) would continue in effect for permitted research with such existing stem cell lines.¹²²

6. Congress Tries to Overcome the Fact Sheet and the Presidential Directive on Pluripotency

From its pronouncement to the writing of this Article, the policy adopted in the 2001 Fact Sheet has met with ineffective opposition in

119. See, e.g., William B. Huber, Letter to the Editor, *The Stem Cell Decision: No End to the Debate*, N.Y. TIMES, Aug. 11, 2001, at A14.

120. See, e.g., Robert Pear, *Bush Administration Is Split Over Stem Cell Research*, N.Y. TIMES, June 13, 2001, at A29 ("On one side are officials . . . who emphasize that experiments with embryonic stem cells could lead to new treatments and cures for illnesses like diabetes and Parkinson's disease. On the other side are some top presidential advisers . . . who worry that federal support for such research will alienate conservative voters, anti-abortion groups and the hierarchy of the Roman Catholic Church. . . . Accordingly, administration officials said, they are seeking a compromise that would take account of moral objections to the research without forfeiting its potential benefits . . .").

121. Press Release, *supra* note 82. For reasons that go beyond this Article, as of August 22, 2008, there were twenty-one hESC cell lines meeting the federal funding eligibility criteria set forth in the 2001 Fact Sheet. See Nat'l Insts. of Health, Eligibility Criteria for NIH Funding of Human Embryonic Stem Cell Research, <http://stemcells.nih.gov/research/registry/eligibilityCriteria.asp> (last visited Mar. 8, 2009).

122. Nat'l Insts. of Health, *supra* note 121. Following the release of the White House Fact Sheet, the NIH announced the withdrawal of those sections of the previously issued NIH Guidelines for Research Using Human Pluripotent Stem Cells pertaining to research involving "human pluripotent stem cells derived: (1) From human fetal tissue; or (2) from human embryos that are the result of *in vitro* fertilization, are in excess of clinical need, and have not reached the stage at which the mesoderm is formed." National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells 65 Fed. Reg. 51,976, 51,979 (Aug. 25, 2000); see also National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells; Correction, 65 Fed. Reg. 69,951, 69,951 (Nov. 21, 2000). Further stating that "NIH funds may not be used to derive human pluripotent stem cells from human embryos. These Guidelines also designate certain areas of human pluripotent stem cell research as ineligible for NIH funding." *Id.*

Congress. With the Democratic victory in the 2004 election, Congress succeeded in passing the Stem Cell Research Enhancement Act of 2005 (“SCREA 2005,” also known as the “Castle-DeGette Bill”).¹²³ SCREA 2005 would have required HHS to conduct and support hESC research in accordance with specified ethical requirements and guidelines to be established in consultation with the NIH and “regardless of the date on which the stem cells were derived from a human embryo.”¹²⁴ President Bush vetoed SCREA 2005—the first veto of his administration—and the House of Representatives could not override it.¹²⁵ In 2007, a similar act of Congress (“SCREA 2007”) was again vetoed; and again the House was unable to override the veto.¹²⁶ Legal commentators have been critical of both the assumptions and the internal logic of both the executive and legislative branches with respect to SCREA 2005 and 2007, finding that neither “constitutes a logically coherent . . . policy.”¹²⁷

At the June 2007 White House press conference for the announcement of the veto of SCREA 2007, President Bush noted several technological substitutes for the use of excess preimplantation embryos to create pluripotent stem cells, including, for example, iPSCs (which at that point had not been successfully demonstrated with human cells) and cells extracted from amniotic fluid and placentas.¹²⁸ To increase federal support for these efforts, President Bush, simultaneously with the veto of SCREA 2007, issued Executive Order 13435.¹²⁹ This Order expanded the NIH stem cell line registry to include the new human pluripotent stem cell lines that would result from these embryo-free methods.¹³⁰ In addition, the Order renamed the “Embryonic Stem Cell Registry” to the “Pluripotent Stem Cell Registry,” with the President explaining in his

123. Stem Cell Research Enhancement Act of 2005, H.R. 810, 109th Cong. (2005).

124. *Id.* § 2.

125. Press Release, President George W. Bush, Office of the Press Sec’y, President Bush Discusses Stem Cell Veto and Executive Order (June 20, 2007) (on file with the Hofstra Law Review).

126. *Id.* (“Last year, Congress passed a similar bill—I kept my promise by vetoing it. And today I’m keeping my word again: I am vetoing the bill that Congress has sent.”).

127. Russell Korobkin, *Embryonic Histrionics: A Critical Evaluation of the Bush Stem Cell Funding Policy and the Congressional Alternative*, 47 JURIMETRICS 1, 2 (2006).

128. Press Release, *supra* note 125. In describing iPSCs and cells extracted from amniotic and placental matter, President Bush acknowledged the power of embryonic cells when he stated that these alternative sources for pluripotent stem cell lines “could also provide stem cells that seem to do what embryonic cells can.” *Id.* However, at that date, iPSCs created with human cells had not yet been announced.

129. Exec. Order No. 13,435, 72 Fed. Reg. 34,591 (June 20, 2007).

130. *Id.*

news conference that this “reflects what stem cells can do, instead of where they come from.”¹³¹

B. The Normative Dimension at the Federal Level

At the federal level, as we will show below, the normative debate storm clouds over stem cell research had been forming well before the time George W. Bush was elected. These clouds had been present at least as early as Bill Clinton’s reaction to the announcement in 1997 of the first mammal—Dolly, the sheep—produced through SCNT. But the 2001 Fact Sheet was still a crack of lightning heard around the globe. The Bush Administration would allow continued federal funding of hESC research only “on existing stem cell lines derived in accordance with [specified] criteria,” but would prohibit the use of federal funds for creating new hESC lines, creating human embryos for research purposes, and cloning of human embryos for any purpose.¹³² Simultaneous with setting this policy, the Administration created a new President’s Council on Bioethics “to study the human and moral ramifications of developments in biomedical and behavioral science and technology.”¹³³ These developments included “embryo and stem cell research, assisted reproduction, *cloning*, genetic screening, gene therapy, euthanasia, psychoactive drugs, and brain implants.”¹³⁴

While the word “cloning” has a rich history in the annals of biotechnology,¹³⁵ in this sentence that defines the mission of the

131. Press Release, *supra* note 125. On March 9, 2009, subsequent to the submission of this Article, President Barack Obama issued an Executive Order revoking the policy set forth in the August 9, 2001 Fact Sheet and Executive Order 13435. *See* Exec. Order No. 13,505, 74 Fed. Reg. 10,667 (Mar. 9, 2009). In addition, the March 9 Executive Order directed the NIH to draw guidelines for conducting NIH-funded research with both hESCs and iPSCs “to the extent permitted by law.” *Id.* Without explicit mention of the Dickey Amendment, this six-word limitation in the Executive Order clearly points to it and its potential to continue to limit federally funded research with cell lines derived from hESCs.

132. Press Release, *supra* note 82.

133. *Id.*

134. *Id.* (emphasis added).

135. Among scientists, the term “cloning” was first used in the early 1970s to describe the process by which DNA molecules replicate; then in the late 1970s, the term “clones” was used to describe the cells comprising monoclonal antibody-producing hybridoma lines; and finally in the 1990s the term cloning came to be used as short-hand for the SCNT process. *See, e.g.*, Process for Producing Biologically Functional Molecular Chimeras, U.S. Patent No. 4,237,224 (filed Jan. 4, 1979) (issued Dec. 2, 1980); Method of Producing Tumor Antibodies, U.S. Patent No. 4,172,124 (filed Apr. 28, 1978) (issued Oct. 23, 1979); Cloning Using Donor Nuclei from a Non-Quiescent Somatic Cells, U.S. Patent No. 6,215,041 (filed Jan. 8, 1998) (issued Apr. 10, 2001).

The importance of SCNT in the sixteen year period 1980-95 is reflected in the accelerated rate of publication of related scientific articles during that period. As measured by the search “stem cell nuclear transfer” on PubMed, there were seven such articles before 1980, with the first article

Council, the word is meant using the SCNT technique. The sentence, however, did not distinguish between the two different endpoints of SCNT: creating a “clone” of an organism, as exemplified by Dolly, by implanting the blastocyst resulting from SCNT into the uterus of an adult organism; or creating a blastocyst from which pluripotent stem cell lines could be derived. This distinction seemed to be missed or confused among policymakers. As an example, consider the following interchange of questions and answers related to cloning from a press conference held on March 28, 2001 by then White House Press Secretary Ari Fleischer:

MR. FLEISCHER: Well, you know the President’s position on stem cells.

Q: No, I know his position on embryonic stem cells. I don’t know his position on cloning.

MR. FLEISCHER: But that’s not a cloning issue. You just heard the President’s position on cloning of humans. That’s the President’s position.

Q: What about cloning human cells?

MR. FLEISCHER: I’m not aware of the distinction between the issue of cloning human beings and cloning human cells.¹³⁶

This series of questions and answers and the longer interchange in which it occurred illustrates three points: First, the conflation of the debates over embryonic stem cell research and SCNT cloning; second, the failure of stakeholders after at least thirty years to have educated themselves and decisionmakers about SCNT cloning, particularly the difference between the use of the technique for research purposes and reproductive purposes; and third, and most importantly, a deep-seated, widely-held view on all sides of the political and religious aisle that to create humans in ways other than by coitus or IVF for treating infertility is taboo.

1. Birth Announcement: Dolly, the SCNT-cloned Sheep

The cloning issue had burst onto the scene following the February 1997 announcement that a team led by Ian Wilmut at the Roslin Institute in Scotland had seven months earlier successfully produced Dolly, the

appearing in 1972. PubMed, <http://www.ncbi.nlm.nih.gov/pubmed/> (last visited Mar. 31, 2009) (follow the “Advanced Search” hyperlink; then enter “stem cell nuclear transfer”; then enter pertinent dates). From 1980 through 1989, there were 28 such articles, or 2.8 per year. *Id.* For the four-year period 1990-93, there were 27 such articles, or 6.75 articles per year. *Id.* Finally, between 1994 and June 30, 1995, there were 18 articles, or one every 30 days. *Id.*

136. Ari Fleischer, White House Press Sec’y, Press Briefing by Ari Fleischer (Mar. 28, 2001) (on file with the Hofstra Law Review).

first SCNT-cloned mammal.¹³⁷ Dolly's press coverage contributed mightily to public perceptions of SCNT and cloning—perceptions that varied as a function of the political, economic, religious, and intellectual filters through which those perceptions formed and the variance of which is reflected in the state-by-state patchwork of stem cell research and medicine law and regulation currently in place in the United States.¹³⁸ The reactions to Dolly's birth announcement also illustrated the innate entanglement between SCNT cloning used for research purposes and SCNT used for reproductive purposes, an entanglement reflected in the excerpt above from the March 28, 2001 White House press briefing and exacerbated by the lack of reliable, comprehensive federal regulation in these overlapping areas of science and medicine.¹³⁹

2. White House Reaction to Dolly

The Clinton Administration reacted swiftly to the news of Dolly's existence. On February 24, 1997, President Clinton asked the National Bioethics Advisory Commission ("NBAC")—a panel that he had formed three years earlier to address the ethical questions posed by the use of excess IVF embryos to create stem cell lines¹⁴⁰—to review the ethical and legal issues associated with the use of cloning technology. Without waiting for a response, on March 4, 1997, President Clinton sent a memorandum to the heads of all executive departments and agencies—not just to HHS—making it “absolutely clear that no Federal funds will be used for human cloning.”¹⁴¹ “Clinton also urged the private

137. Ian Wilmut et al., *Viable Offspring Derived from Fetal and Adult Mammalian Cells*, 385 NATURE 810, 812 (1997).

138. Gina Kolata, *First Mammal Clone Dies; Dolly Made Science History*, N.Y. TIMES, Feb. 15, 2003, at A4. On February 14, 2003, Dolly was euthanized after having developed a lung infection. Prior to the lung infection, she suffered from arthritis (reported to be common in middle-aged sheep) and was prone to obesity (although her weight was kept under control). *Id.* Four years before her euthanization, the team led by Dr. Wilmut had reported, subject to further confirmation, that the telomeres at the ends of Dolly's chromosomes were about twenty percent shorter than those of non-cloned sheep of a similar age. See Gina Kolata, *Cloned Sheep Showing Signs of Old Cells, Report Says*, N.Y. TIMES, May 27, 1999, at A19. While there was some belief that the nucleus from the somatic cell used in the SCNT procedure gave rise to Dolly, there was also skepticism about this. *Id.*

139. See, e.g., AD HOC GROUP OF CONSULTANTS TO THE ADVISORY COMM. TO THE DIR., *supra* note 104, at x (“In the continued absence of Federal funding and regulation in this area, preimplantation human embryo research that has been and is being conducted without Federal funding and regulation would continue, without consistent ethical and scientific review. It is in the public interest that the availability of Federal funding and regulation should provide consistent ethical and scientific review for this area of research.”).

140. Clinton, *supra* note 106.

141. William J. Clinton, President, Memorandum for the Heads of Executive Departments and Agencies: Prohibition on Federal Funding for Cloning of Human Beings (Mar. 4, 1997) (on file with the Hofstra Law Review).

sector to adopt a voluntary ban on the cloning of human beings.”¹⁴² In addition, bills were introduced in the Senate and the House of Representatives banning not only federally supported human cloning research but also human cloning.¹⁴³ After NBAC reported its findings and recommendations in June 1997,¹⁴⁴ the Clinton Administration sent to Congress the proposed Cloning and Prohibition Act of 1997, and within months, six additional cloning prohibition bills were introduced.¹⁴⁵

Concerned about the potential for someone, somewhere, to create a human through SCNT-cloning, the Food and Drug Administration (“FDA”) sent letters to the research community stating that such an act would be subject to FDA regulation under the Public Health Service Act and the Food, Drug, and Cosmetic Act and noting that such research could only occur under an active investigational new drug application (“IND”).¹⁴⁶ Some legal scholars believe that the FDA had no legal basis to assert regulatory power over cloning, finding “little evidence to support” the FDA’s position that “cloned human embryos are ‘drugs’”;¹⁴⁷ while the opposite view was taken by the biotechnology industry and the American Society for Reproductive Medicine, which noted that FDA regulation of cloning would be “preferred to any new action by Congress.”¹⁴⁸

The press coverage afforded Dolly did much to create the widespread public perception that cloning meant the use of scientific techniques to create identical copies of an animal. Scientists, on the other hand, were also using the term cloning in the narrow sense to mean using SCNT to create blastocysts for deriving pluripotent stem cell lines. Of course, for those who wanted to ban the use of excess IVF embryos to produce human pluripotent stem cell lines, so too did they want to ban

142. JOHNSON, *supra* note 97, at 5.

143. IRENE STITH-COLEMAN, CLONING: WHERE DO WE GO FROM HERE?, CONG. RESEARCH SERV. 2 (1998) (noting the bills introduced in Congress).

144. The NBAC recommendations included “a continuation of the moratorium on the use of federal funding in the support of any attempt to create a child by SCNT, and an immediate request to all non-federally funded investigators to comply voluntarily with the intent of the federal moratorium.” JOHNSON, *supra* note 97, at 3. NBAC further recommended the enactment of federal legislation “with a 3- to 5-year sunset clause, to prohibit anyone from attempting to create a child through the use of SCNT in a research or clinical setting.” *Id.*

145. STITH-COLEMAN, *supra* note 143, at 2.

146. Letter from Stuart L. Nightingale, Assoc. Comm’r of the Food & Drug Admin. (Oct. 26, 1998), available at <http://www.fda.gov/oc/ohrt/irbs/irbletr.html>.

147. Rick Weiss, *Legal Barriers to Human Cloning May Not Hold Up*, WASH. POST, May 23, 2001, at A1. For a discussion of the problems of overlapping definitions in United States drug law, see PETER BARTON HUTT ET AL., FOOD AND DRUG LAW 39-49 (3d ed. 2007).

148. JOHNSON, *supra* note 97, at 5-6.

SCNT for creating these cell lines. The failure to distinguish between these two very different uses of SCNT worked to the advantage of the opponents of SCNT.¹⁴⁹

3. The Creation of HESCs and ACT's Proposed Test

On November 6, 1998,¹⁵⁰ Professor John Gearhart of Johns Hopkins University announced the development of a procedure for creating and sustaining a line of pluripotent stem cells from human fetal gamete cells,¹⁵¹ and Professor James Thomson of the University of Wisconsin announced the development of a procedure for creating and sustaining a line of embryonic stem cells from human blastocysts.¹⁵² Six days later, a small company in Worcester, Massachusetts, Advanced Cell Technology ("ACT"), announced that it had used SCNT with cow egg cells and nuclei from human somatic cells to create a culture of embryonic stem cells.¹⁵³ The *New York Times* reported on its front page that the company said that it had accomplished this "feat" in 1996 and was announcing it "to test its public acceptability."¹⁵⁴

ACT's claims met with significant skepticism within the scientific community, but the Clinton Administration took the claims quite seriously. Expressing concern about "mingling of human and nonhuman species" and stressing the ethical concerns raised by ACT's announcement, the President requested of NBAC a "thorough review, balancing all ethical and medical considerations" of embryonic stem cell research in general, including the hESCs reported by the Gearhart and Thomson labs.¹⁵⁵

In September 1999, NBAC, in a two-volume report, noted that:

149. A 2007 report issued by the United Nations University's Institute of Advanced Studies called for an urgent global ban on human cloning. See generally UNITED NATIONS UNIV., INST. OF ADVANCED STUDIES, *IS HUMAN REPRODUCTIVE CLONING INEVITABLE: FUTURE OPTIONS FOR UN GOVERNANCE* (2007), available at http://www.ias.unu.edu/resource_centre/Cloning_9.20B.pdf. However, the report did not call for a ban on therapeutic cloning. *Id.* at 27-29. See also generally Nigel M. de S. Cameron & Anna V. Henderson, *Brave New World at the General Assembly: The United Nations Declaration on Human Cloning*, 9 MINN. J. L. SCI. & TECH. 145, 147 (2008).

150. Nicholas Wade, *Scientists Cultivate Cells at Root of Human Life*, N.Y. TIMES, Nov. 6, 1998, at A1.

151. *Id.*; see also Michael J. Shamblott et al., *Derivation of Pluripotent Stem Cells from Cultured Human Primordial Germ Cells*, 95 PROC. NAT'L ACAD. SCI. 13726, 13726 (1998).

152. Wade, *supra* note 150, at A1; see also James A. Thomson et al., *Embryonic Stem Cell Lines Derived from Human Blastocysts*, 282 SCIENCE 1145, 1145 (1998).

153. Nicholas Wade, *Researchers Claim Embryonic Cell Mix of Human and Cow*, N.Y. TIMES, Nov. 12, 1998, at A1.

154. *Id.*

155. Wade, *supra* note 81, at 31 (noting that President Clinton was more positive about the all-human embryonic stem cell research and stating that it "may have real potential for treating such devastating illnesses as cancer, heart disease, diabetes and Parkinson's disease").

Although wide agreement exists that human embryos deserve respect as a form of human life, there is disagreement both on the form such respect should take and on the level of protection owed at different stages of embryonic development. Moreover, it was clear from the outset that no public policy or set of recommendations could fully bridge these disagreements and satisfy all the thoughtful moral perspectives that are held by members of the American public.¹⁵⁶

Among the thirteen proposed recommendations proposed by NBAC,

[p]erhaps the most important recommendations reflect[ed] the Commission's view that federal sponsorship of research that involves the derivation and use of human embryonic stem (ES) cells and human embryonic germ (EG) cells should be limited in two ways. First, such research should be limited to using only two of the current sources of such cells; namely, cadaveric fetal material and embryos remaining after infertility treatments. Second, that such sponsorship be contingent on an appropriate and open system of national oversight and review.¹⁵⁷

4. Congress Takes the ACT Test: House Passes Bill, Senate Does Not

In November 2001, three years after posing its first test with SCNT using cow eggs and human somatic cell nuclei, ACT returned with a second test.¹⁵⁸ The fact pattern presented in this new test began with ACT's announcement that it had created the world's first cloned human embryos and that these had survived only for a few hours.¹⁵⁹ ACT's expressed intent was to use embryos of this type to derive stem cells for therapeutic purposes.¹⁶⁰

ACT's second test came several months after the introduction of several bills in Congress, one of which was passed by the House of Representatives on July 31, 2001 and which if enacted into law prior to ACT's announced work, would have potentially criminalized ACT's activities.¹⁶¹ This Bill, H.R. 2505, called the "Human Cloning Prohibition Act of 2001" and which passed in the House by a vote of

156. Letter from Harold T. Shapiro, Chair, Nat'l Bioethics Advisory Comm'n to President William Clinton (Sep. 7, 1999), in NAT'L BIOETHICS ADVISORY COMM'N, ETHICAL ISSUES IN STEM CELL RESEARCH (1999).

157. *Id.*

158. Gina Kolata, *Company Says It Produced Embryo Clones*, N.Y. TIMES, Nov. 26, 2001, at A14.

159. *Id.*

160. *Id.*

161. H.R. 2505, 107th Cong. § 302 (1st Sess. 2001).

265 to 162, banned any use of SCNT with human cells, without regard as to its purpose for either reproductive or research cloning, and the importation of any product derived from a cloning-derived human embryo.¹⁶²

In addition to the introduction of H.R. 2505 during the summer months prior to the 2001 Fact Sheet, Representative Greenwood had introduced H.R. 2608, a bill that would have banned human cell SCNT only for the purpose of reproductive cloning.¹⁶³ Supporters of H.R. 2505 “argued that a partial ban on human cloning, such as H.R. 2608, would be impossible to enforce”; while “critics of H.R. 2505 argued that SCNT creates a ‘clump of cells’ rather than an embryo, and that [H.R. 2505] would curtail medical research and prevent Americans from receiving life-saving treatments created overseas.”¹⁶⁴ Before the vote on H.R. 2505, a substitute amendment for it, that was identical to H.R. 2608, failed with a vote of 178 to 249.¹⁶⁵ With 2001 coming to a close, the Senate considered a bill like H.R. 2505 that would have imposed a six-month moratorium on all human cloning research, but the amendment failed.¹⁶⁶

Some commentators have addressed the constitutionality of a federal ban on SCNT with human cells. In commenting on these comments, Judith A. Johnson, a Specialist in Life Sciences in the Domestic Social Policy Division of the Congressional Research Service, thoughtfully observed:

Some legal scholars believe a ban on human cloning may be unconstitutional because it would infringe upon the right to make reproductive decisions which is “protected under the constitutional right to privacy and the constitutional right to liberty.” Other scholars do not believe that noncoital, asexual reproduction, such as cloning, would be considered a fundamental right by the Supreme Court. However, in decisions involving IVF, which is noncoital but not asexual because both parents are required, the justices have suggested that reproduction by IVF is a fundamental right, but the issue is unresolved. A ban on human cloning research raises other

162. See JOHNSON, *supra* note 97, at 6. It is interesting to note that H.R. 2505, also referred to as the “Weldon Bill,” arose from the House Judiciary Subcommittee on Crime. *Id.* Like the Dickey Amendment, the Weldon Amendment prohibits any federal funds from being “used to issue patents on claims directed to or encompassing a human organism.” NAT’L RIGHT TO LIFE COMM., CONGRESS BANS PATENTS ON HUMAN EMBRYOS: NRLC-BACKED WELDON AMENDMENT SURVIVES BIO ATTACKS (2004), http://www.nrlc.org/Killing_embryos/Human_Patenting/WeldonAmendmentEnacted.pdf.

163. See Cloning Prohibition Act of 2001, H.R. 2608 107th Cong. § 2(a) (1st Sess. 2001).

164. See JOHNSON, *supra* note 97, at 6.

165. *Id.*

166. *Id.*

constitutional issues: scientists' right to personal liberty and free speech. In the opinion of some legal scholars, any government limits on the use of cloning in scientific inquiry or human reproduction would have to be "narrowly tailored to further a compelling state interest."¹⁶⁷

C. The State Level

Believing that advancements with iPSCs or directly programmed cells can resolve the political and religious differences that have stymied hESC and SCNT with human cells, a significant issue in the coming years will be how to harmonize, entrain, and coordinate the divergent array of stem cell laws that have arisen since August 2001 between and among the federal and state governments in the United States. For example, as further described in Part IV of this Article, the differences between Bayh-Dole and CIRM with respect to intellectual property licensing terms have at least the potential to remain long after possible resolution of the hESC controversy with the help of iPSC or directly programmed cell technology.

The *de facto* blockade on NIH's pursuit of a leadership position in hESC and human-based SCNT research created a vacuum. Arguably, the blockade began in September 1980 with disbanding of the EAB, but may not have become apparent until the issuance of the 2001 Fact Sheet.¹⁶⁸ As vacuums rarely remain empty, this one was filled by the states, academic institutions, charitable foundations, hospitals and companies. Within a relatively short time following the release of the 2001 Fact Sheet, several state legislatures had passed, or were considering, bills relating to various aspects of stem cell research.¹⁶⁹ These bills and laws filled holes in both the funding and normative policy-making dimensions.

1. The Funding Dimension at the State Level

After President Bush in August 2001 had drawn a line in the sand on federal funding of certain kinds of research, a range of stakeholders including academic institutions, philanthropists, and certain states began filling the vacuum. The paradox here is that by attempting to limit such

167. *Id.* (footnotes omitted) (quoting Lori B. Andrew, *Is There a Right to Clone? Constitutional Challenges to Bans on Human Cloning*, 11 HARV. J. L. & TECH. 643, 664, 667 (1998)).

168. See Pérez-Peña, *supra* note 83, at 20 (describing state and private efforts to counteract the 2001 presidential order limiting federal funding for embryonic stem cell research).

169. *Id.* States where legislation authorizing embryonic stem cell research was introduced included New York, Maryland, Rhode Island, Tennessee, Washington, and Massachusetts. *Id.*

funding, the Bush policy may have encouraged more of it. Moreover, Richard M. Doerflinger of the United States Conference of Catholic Bishops is reported to have said, “[t]he proliferation of these various efforts points to a need for an honest debate” on the issue of stem cell research and medicine.¹⁷⁰ While iPSCs may prove in the long run to make this debate much less relevant, in the short run many scientists believe that work with hESCs must continue, if not only to validate the value of iPSCs¹⁷¹—thus making such “honest debate” still relevant, particularly in the context of a new federal executive administration after the 2008 presidential election.

The hESC funding vacuum at the federal level was especially noticeable in those states that had over the course of the 1980s and 1990s created sizeable tax and other incentives for the biotechnology industry to locate facilities in those states.¹⁷² The R&D in these facilities would continue on projects started in nearby academic laboratories funded, in part, by NIH grants under the Bayh-Dole regime as well as under the Small Business Innovative Research (“SBIR”) funding program.¹⁷³ With a dearth of federal funds for hESC research and recognizing the enablement potential, it was natural for these states to step into this funding vacuum.¹⁷⁴ Among the efforts to counter the ban on federal funding of new pluripotent stem cell lines, nine states adopted programs to fund such work. These nine include: California, Connecticut, Illinois, Maryland, Massachusetts, New Jersey, New York, Rhode Island, and Wisconsin.¹⁷⁵ These programs range in size from \$10 million in Illinois to the \$3 billion CIRM program in California.¹⁷⁶

170. *Id.*

171. See, e.g., Lief E. Fenno et al., *Human Embryonic Stem Cells: Emerging Technologies and Practical Applications*, 18 CURRENT OPINION IN GENETICS & DEV. 324, 327-28 (2008).

172. See, e.g., Biotechnology Indus. Org., Solutions for Health—Economic Growth, <http://www.bio.org/speeches/pubs/biotech/econgrowth.asp> (last visited Feb. 26, 2009); see also N.C. BIOTECHNOLOGY CTR. & N.C. DEP’T OF COMMERCE, NORTH CAROLINA: THE STATE OF MINDS 11-13, www.ncbiotech.org/biotechnology_in_nc/stateofmindsfinal.pdf.

173. See, e.g., N.J. Comm’n on Sci. & Tech., SBIR/STTR Assistance and Training, <http://www.state.nj.us/scitech/entassist/sbirsstr> (last visited Feb. 26, 2009).

174. National Institutes of Health, Estimates of Funding for Various Diseases, Conditions, and Research Areas, available at <http://report.nih.gov/rcdc/categories/> (providing data as of Jan. 15, 2009). Between fiscal year 2005 and fiscal year 2008, the NIH expended \$3.815 billion on stem cell research, of which \$282 million, or 7.39% of the total, was expended on hESC research. *Id.*

175. Interstate Alliance on Stem Cell Research, State Stem Cell Programs, www.iascr.org/states.shtml (last visited Feb. 25, 2009).

176. See JUDITH A. JOHNSON & ERIN D. WILLIAMS, CONG. RESEARCH SERV., STEM CELL RESEARCH: STATE INITIATIVES 6 (2006) (discussing an Executive Order signed by Governor Blagojevich, “authorizing \$10 million in funding for adult, cord blood, and embryonic stem cell research”); Dean E. Murphy, *Defying Bush Administration, Voters in California Approve \$3 Billion for Stem Cell Research*, N.Y. TIMES, Nov. 4, 2004, at P10 (stating that California’s voters approved Proposition 71 with fifty-nine percent of the votes cast, thereby authorizing the establishment of

Soon after these programs were adopted, the administrators responsible for their implementation and operation recognized the need for coordination and discussion between and among them.¹⁷⁷ To address this need they formed the Interstate Alliance for Stem Cell Research (“IASCR”).¹⁷⁸ IASCR’s mission statement highlights that “[s]tem cell research programs vary considerably in scope and [in] the regulatory requirements that underpin them” and notes that such “diversity . . . could impede collaboration and the sharing of research materials or raise overall costs.”¹⁷⁹ To counteract this, IASCR “provides a forum for information exchange and collaborative planning in an attempt to facilitate the sharing of data, resources, and cell lines across state borders to ensure the efficient development of research programs.”¹⁸⁰

2. The Normative Dimension at the State Level—A Complex Manifold

Following the release of the 2001 Fact Sheet, numerous bills relating to stem cell research and medicine have been introduced, and in some cases enacted into law, in many states.¹⁸¹ While several states permit research with human embryos and cells derived from those embryos, many other states significantly restrict such research.¹⁸² A preponderance of states have passed laws that prohibit the shipment, transfer, or receipt for any purpose of embryos produced through SCNT.¹⁸³ The resulting manifold of divergent state laws presents a series of practical questions as to how, where, and what research can occur—questions that are particularly important to R&D collaborations and for follow-on use of the results of such R&D. In addition, these laws can

CIRM and its funding through the issuance of \$3 billion of general obligation bonds at a then-estimated cost of \$6 billion payable over the next thirty years).

177. See Interstate Alliance on Stem Cell Research, Welcome, <http://www.iascr.org> (last visited Feb. 26, 2009).

178. *Id.* (“(IASCR) is a voluntary body whose mission is to advance stem cell research (human embryonic, adult, and other) by fostering effective interstate collaboration, by assisting states in developing research programs, and by promoting efficient and responsible use of public funds.”).

179. *Id.*

180. *Id.*

181. The National Conference of State Legislatures maintains an extensive Genetics Legislation Database at <http://www.ncsl.org/programs/health/genetics/geneticsDB.cfm> that “contains information on genetics bills considered in state legislatures from 2004 to present.” The primary topic areas covered in this database relevant to stem cell research and medicine include: ART/Frozen embryos; genetic privacy; genetics professional issues; human cloning; laboratory and testing standards; and research issues.

182. See *id.*; see also *supra* notes 175-76 and accompanying text.

183. A list of state laws and pending bills maintained by the National Conference of State Legislatures is referenced *supra* note 181.

also conflict with applicable federal laws. Part IV of this Article illustrates this federal versus state conflict in the context of CIRM's regulations, particularly CIRM's intellectual property regulations.¹⁸⁴

Beyond the state-by-state and federal versus state variation in laws relating to hESC research and medicine, there is also intra-state variation in the normative and funding dimensions. For example, consider the case of the State of Louisiana funding a stem cell and gene therapy initiative as part of the New Orleans Bioinnovation Research Center and LSU Health Sciences Center,¹⁸⁵ at the same time that Louisiana state law prohibits research on fetuses and embryos in utero and IVF embryos¹⁸⁶ and the State legislature is considering laws even more restrictive than the current federal policy on hESC research and SCNT with human cells.¹⁸⁷ Another example of this phenomenon is state laws that limit the extent of such research such as those that prohibit or severely restrict payments to oocyte donors.¹⁸⁸ Since human eggs are a necessary starting material for many of the strands of work in this field of research, the states in question appear to be giving with one hand and taking with the other, or at least have not fully reconciled the policy and regulatory elements of their various laws.

D. *Re-engagement of the NIH*

The diversity in current and proposed state law on stem cell research and medicine to which IASCR's mission points is not limited to state funding programs. This need will become more apparent now that President Obama has directed the NIH, "to the extent permitted by law," to come back onto the stage to conduct and fund research with cell lines derived from hESCs and therapeutic SCNT with human cells.¹⁸⁹ To the extent that the NIH is permitted by law to do this, a central question arises as to how it will seek to achieve the position of leadership it may have had it not been estopped from this research in August 2001, after over twenty years of trying to do so. Using the master clock metaphor, will a renewed NIH research program of this type be able to entrain similarly focused programs in the states? In this respect, how likely is it that states, having assumed jurisdiction over this type of research and

184. *See infra* Part IV.

185. Welcome to the Gene Therapy Program at LSU Health Sciences Center, www.medschool.lsuhschool.edu/genetherapy/ (last visited Feb. 18, 2009).

186. LA. REV. STAT. ANN. § 14:87.2 (2004); *see also* Nat'l Conference of State Legislatures, *supra* note 7.

187. *See* Nat'l Conference of State Legislatures, *supra* note 7.

188. *See, e.g.*, MASS. GEN. LAWS ANN. ch. 111L, § 8(c) (West 2003).

189. *See* Exec. Order No. 13,505, 74 Fed. Reg. 10,667 (Mar. 9, 2009).

established regulatory and funding programs to pursue it, will abandon them, at least in advance of the NIH having “walked the walk” through years or even decades of proven leadership?

Whether or not iPSCs created with somatic cells or directly reprogrammed somatic cells that tunnel through cell differentiation barriers ultimately displace pluripotent stem cell lines derived from the use of excess preimplantation embryos from IVF or SCNT procedures using human cells, the question will persist as to whether the regulatory system will be stuck in a suboptimal trajectory. The next Part of this Article discusses this possibility, by examining the intellectual property regulations adopted by CIRM, and contrasting the policies underlying that approach with those at the federal level underlying the Bayh-Dole Act. From whatever technology the inventions from CIRM-funded research arise—hESCs, human cell-based SCNT, iPSCs, direct reprogramming of somatic cells, or any other—if the invention owes at least in part to NIH and CIRM funding, there will exist tension over how it is to be used and who should profit from it. Beyond the limits of this Article are other examples of the possibility for suboptimal trajectories, such as in the field of informed consent rules and, again whether to limit research at this time to hESCs from excess preimplantation embryos, human cell-based SCNT, iPSCs, direct reprogrammed cells, or any other technology with similar application.¹⁹⁰

IV. LICENSING OF GOVERNMENT-FUNDED STEM CELL PATENTS

The epigraph to this Article comes from Hannah Arendt, and highlights how discoveries become absorbed into our daily life. That zone of absorption, where ideas are engineered into robust technologies of wide application, is one which stem cells have entered. It is a zone of profound interest to regulators, who can apply their skills to the problem and opportunity with a light touch or a heavy one. The pressure of their touch may be a function of the technology itself, any moral or social issues that are embedded in it, the legislative and political history that grow up around it, and also the intended scope of the regulation. There is also the confounding factor that regulators, of their own volition or due to political forces, or both, may assume the role of helmsman, attempting *a priori* to steer science to avoid or achieve very specific outcomes. (This point is exemplified by the September 1980 decision, discussed above in Part III, in which the Secretary of HEW allowed the

190. See, e.g., Baker, *supra* note 75, at 556 (“Now, ethics oversight committees at universities across the United States are questioning which lines should be permissible for research—and hoping that another agency, such as the NIH or a state government, will make the decision for them.”).

disbanding of the EAB through which key NIH funding decisions were to have been reviewed.)

A regulator, who wanted to enable technological innovation of all types, would tend to adopt general and neutral wording that aimed to permit, but not prescribe, private action within an acceptable range, by defining the limits of that range so that those within the limits could act with confidence and those who strayed would be checked. That light regulatory touch is illustrated with the Bayh-Dole Act, described above in Part II. If instead a regulator is asked to address a specific area of science to encourage its production of specific social benefits, the regulatory touch might be heavier, with agenda-driven goals imposed on every actor within the permitted range of action. That approach would transform the Bayh-Dole model into something that might superficially resemble it but in fact would operate very differently.

The Bayh-Dole Act has defined, and empowered, technology transfer in the United States for a generation. Its light regulatory touch aims to give grantee inventors and those with whom they contract, a reasonable degree of certainty.¹⁹¹ CIRM is clearly modeled on Bayh-Dole but deliberately departs from it in many important respects. The following discussion compares and contrasts key provisions of the Bayh-Dole Act and CIRM, and ultimately proposes that CIRM's ability to achieve its legislative mandate may ultimately be better enabled by moving away from the regulatory approach it has adopted so far, and toward the regulatory approach followed in the Bayh-Dole Act.

A. Similarities to the Bayh-Dole Act

CIRM has deliberately adopted the Bayh-Dole model in two main areas. One is the right of the funding agency to be kept apprised of progress in utilizing funded inventions, and the other is its right under certain circumstances to march-in on patents claiming the funded work. But even when CIRM emulates Bayh Dole deliberately (even down to using the same phrasing for invention reporting), its regulatory architecture produces divergence.¹⁹² CIRM asks a non-profit grantee to

191. See *supra* notes 45-67 and accompanying text.

192. CIRM, through its Independent Citizen's Oversight Committee ("ICOC") has adopted two intellectual property policies, one for non-profit grantees and the other for for-profit ones. Each policy has undergone the administrative law process and (apart from minor proposed changes for which the comment period recently ended) each policy now has the force of law. See CAL. CODE REGS. tit. 17, §§ 100300, 100400 (2008). The non-profit grantee regulations are found at sections 100300-310 and those for for-profit grantees are found at sections 100400-410. *Id.* §§ 100300-10, 100400-10. In adopting a dual regulatory regime, comprised of elements that are often nearly identical but that sometimes diverge greatly, CIRM has generated some technical difficulties. First,

report inventions using the very words of Bayh-Dole,¹⁹³ but its for-profit counterparts need not report inventions themselves but only any efforts it makes to patent them.¹⁹⁴ In that report, the for-profit grantee must state the “percentage of support provided by CIRM and by all other sources of funding that contributed in whole or in part to the discovery” of the CIRM-funded invention.¹⁹⁵ The non-profit grantee need not do so.

it leads to a proliferation of terms and provisions, all of which must be mastered by those working in the field. Second, because the words chosen for the two regimes are often similar but not identical, readers will wonder if the differences are meaningful. The textual similarities and differences may become fertile ground for arguments in any litigation or administrative proceeding. Third, the dual regime implies that the two classes of grantee deserve different treatment and occupy different spheres; but this may not be true and, in a commercial context, it could lead to problems. The entities funded by CIRM, whether for-profit or not, may contribute multiple inputs to the many diverse and complementary technologies needed by commercial firms, and those “end user” firms will have to harmonize the CIRM regimes in practice. Ambiguity imperils their ability to do so.

On December 19, 2008, CIRM issued a Notice of Proposed Regulation Adoption and Repeal, which proposed to adopt Chapter 6 of Title 17 of the *California Code of Regulations* and sections 100600-11 thereunder, and to repeal Chapter 3 (sections 100300-10) and Chapter 4 (Sections 100400-10). CAL. INST. FOR REGENERATIVE MED., NOTICE OF PROPOSED REGULATION ADOPTION AND REPEAL, Dec. 19, 2008, available at http://www.cirm.ca.gov/reg/pdf/Oal_notice_consolidated_IPregs.pdf [hereinafter CIRM, NOTICE]. The text of the proposed regulation is also available at CIRM’s website. CAL. INST. FOR REGENERATIVE MED., http://www.cirm.ca.gov/reg/pdf/consolidated_regulations_OAL_notice.pdf (last visited May 14, 2009) [hereinafter CIRM, PROPOSED REGULATIONS]. The comment period closed February 2, 2009. CIRM, NOTICE, *supra*. CIRM currently plans to issue final regulations by late August. Telephone Interview by Owen C.B. Hughes with Scott Tocher, Counsel to the Chair of the Indep. Citizens Oversight Comm., in San Francisco, Cal. (May 19, 2009).

As CIRM states in the Notice, the primary purpose of the proposed change is to “consolidate the existing regulatory framework that consists of different schemes for non-profit versus for-profit grantees” into what may be a “more user-friendly” set of regulations that will “better provide greater definition to the scope and application of the policies themselves.” CIRM, NOTICE, *supra*. The Notice reiterates that “the core principles of the CIRM intellectual property regulations . . . are unchanged” including mandatory programs for access by uninsured Californians to therapies resulting from funded work, mandatory sharing of biomaterials resulting from funded work that is the subject of publication, and the right of CIRM to march-in on patents covering funded work. *Id.* The proposed change would not be merely technical, however: The trigger events for march-in would no longer include a failure to satisfy a “public use” requirement. *See* CIRM, PROPOSED REGULATIONS, *supra*, § 100610(b). And the “due process” protections to grantees in a march-in would be somewhat better developed. *Id.* § 100610(e).

If adopted, Chapter 6 would alleviate some of the technical and drafting concerns expressed in Part IV of this Article, and would also reduce somewhat the lack of procedural protections for grantees facing an assertion of march-in rights. But the main substantive concerns described in Part IV would remain. *See infra* Part VI.B. Indeed, in terms of the compliance burden and the potential for collaborators and affiliates to find their own activities unexpectedly and disproportionately affected by CIRM’s regulatory regime, the proposed changes would not be an obvious improvement.

193. Compare 37 C.F.R. § 401.14(c)(1) (2008), with CAL. CODE REGS. tit. 17, § 100302.

194. CAL. CODE REGS. tit. 17, § 100402.

195. *Id.* § 100402; *see also id.* § 100302. Perhaps the non-profit grantee should volunteer such information to mitigate or avoid future disputes over prorating any amount otherwise due to California under the revenue-sharing provisions of section 100308. *See supra* notes 45-67.

As with Bayh-Dole, all CIRM grantees will file annual reports on how any inventions are utilized¹⁹⁶ but the reports are different. A non-profit grantee must use an “Invention Utilization Report”¹⁹⁷ that closely tracks the requirements of Bayh-Dole,¹⁹⁸ but a for-profit grantee is given no form, and is simply told to report annually “all patenting and Licensing Activities relating to CIRM-funded research.”¹⁹⁹ A for-profit grantee must file such reports during the term of the funded work and for fifteen years thereafter²⁰⁰ but non-profit grantees must do so indefinitely.²⁰¹

CIRM also follows Bayh-Dole in a second main area, by giving the funding agency the right to march-in on intellectual property that derives from the funded work. But as discussed below, this similarity is more apparent than real; it seems likely that the practical impact of the CIRM march-in right will be very different from that of Bayh-Dole.

B. *Going Beyond Bayh-Dole*

These drafting variations between CIRM’s two regimes, and the extent to which they mirror concepts found in Bayh-Dole, are of more than passing interest to the practitioner, but they hardly compare in importance with the numerous substantive departures that CIRM has deliberately chosen that go well beyond the Bayh-Dole model. Those departures include mandatory sharing of biomedical materials;²⁰² mandatory revenue sharing;²⁰³ mandatory access to, and discounts for, products resulting from funded work;²⁰⁴ detailed diligence requirements for grantees who propose to license any funded inventions;²⁰⁵ and the manner in which the march-in rights may be exercised.²⁰⁶ Each of these features—mandatory sharing of materials, mandatory sharing of revenues, mandatory concessions from exclusive licensees, and the

196. Compare 35 C.F.R. § 401.14(a), with CAL. CODE REGS. tit. 17, § 100302(e). See *supra* 55-56 and accompanying text.

197. CAL. CODE REGS. tit. 17, § 100302(e).

198. 37 C.F.R. § 401.14(h).

199. CAL. CODE REGS. tit. 17, § 100402.

200. *Id.*

201. See *id.* § 100302(e).

202. *Id.* §§ 100304, 100404.

203. *Id.* §§ 100308, 100408.

204. *Id.* § 100407.

205. See *id.* §§ 100306(b), 100406(c)(5) (describing diligence requirements for non-profits and for-profits, respectively).

206. See *id.* §§ 100310, 100410 (describing how march-in rights may be exercised for non-profits and for-profits, respectively).

manner in which the march-in rights may be exercised—deserves further attention.

1. Mandatory Sharing of Biomedical Materials and Methods

The CIRM requirement states that if a grantee creates “biomedical materials” in the course of funded work, and describes them in a publication,²⁰⁷ they must be shared with anyone else who asks to use them “for research purposes in California.”²⁰⁸ All requests must be honored within sixty days, at no cost or, in any case, for no more than the grantee’s cost.²⁰⁹

This could be criticized as unfair to the grantee or to the research community, or both. The grantee is being made to issue what are implicitly if not actually research licenses to whatever it creates at no more than its direct cost. If this impairs its enterprise, that would undermine CIRM’s larger objective. If the grantee were to avoid the sharing requirement by not publishing, that too would tend to undermine CIRM’s mission. As for the research community, the sharing requirement arbitrarily divides it into haves and have-nots: those who may invoke the provision, and their unlucky colleagues across the state line who cannot.²¹⁰

But quite apart from those concerns, the sharing requirements rest on the assumption that biomedical materials, once made, can be made again in bulk and then shipped to strangers, all easily, safely, and cheaply. But this assumption may not be well-founded at all. Stem cell science and technology are intimately concerned with the transformative power of specific materials. One cell line is not like another. One growth factor or vector or culture medium may produce results, while others cannot. This means that a stem cell researcher may be extraordinarily interested in gaining access to exactly the same material that another has

207. *Id.* § 100304, 100404(a) (explaining obligations for non-profits and for-profits, respectively). For a definition of “Biomedical Materials” see section 100301(d). For a definition of “Publication-related Biomedical Materials” as used for for-profits see section 100401(r).

208. *Id.* § 100304(a) (non-profit grantees). For-profit grantees face a similar requirement, “for bona fide purposes of research in California.” *Id.* § 100404(a). This adjective invites the supposition that non-profit grantees cannot resist even bad-faith research requests, but more seriously it leaves the for-profit grantee and its requesting parties the question of how *bona fides* are to be established.

209. CAL. INST. FOR REGENERATIVE MED., INITIAL STATEMENT OF REASONS FOR THE PROPOSED AMENDMENT OF INTELLECTUAL PROPERTY REGULATIONS FOR NON-PROFIT ORGANIZATIONS – SECTIONS 100304, 100306 AND 100308, available at http://www.cirm.ca.gov/reg/pdf/IP_ISR_non-prof.pdf (last visited Mar. 30, 2009).

210. The regulation could also be criticized for making compulsory what is, in the research community, a practice that is widely followed voluntarily. “Mandated generosity” is an oxymoron and generates no moral currency or sense of reciprocal obligation. Arguably this will do nothing to strengthen the culture of the research community.

used to achieve a result, so as to replicate or extend that result. But while it is easy to ask, the one asked may find it hard to deliver. Sometimes this stems from reluctance to help a rival or undercut a business model for which the material is an important asset. But more often the problem is simply that the material is novel or rare, and cannot be replicated easily. There may be no well-defined and validated methods for making it, for measuring what is made, or for controlling its variability from batch to batch. The material may have made in tiny quantities by heroic and ingenious methods after much expensive trial and error. Often it is a cell line, which is a fragile and dynamic entity, hard or impossible to keep stable over time or across space, particularly if it is to be shipped and re-established in a new setting.²¹¹ Thus, the materials covered by the CIRM requirement are the farthest thing from “catalog materials” offered by commercial vendors; yet no sooner will they have come into existence through the ingenuity and effort of a CIRM grantee, who then begins to characterize them and develop safe and efficient methods to make and handle them, than they may be demanded, at cost, by anyone seeking them for research—in California.²¹² The grantee, who may have little money and less expertise to produce batches of standardized material, may find this obligation to be burdensome indeed. Presumably it could ask for the money beforehand from CIRM, but it cannot charge the requesting party more than direct cost, for example, “without an allocation of costs for overhead, research, discovery or other non-direct costs of providing the material[s].”²¹³

CIRM may grant exceptions to non-profit grantees “[u]nder special circumstances”²¹⁴ or to for-profit grantees if they can show financial hardship, direct conflict with their business, or risk to public safety or health.²¹⁵ Alternatively, the requests may be satisfied not with physical

211. E-mail from John McNeish, Executive Director, Pfizer Regenerative Medicine, to Owen Hughes (Apr. 3, 2009, 13:46 EST) (on file with the Hofstra Law Review).

212. The definition of “biomedical materials” encompasses:

Entities of biomedical relevance first produced as a consequence of CIRM-funded scientific research including but not limited to unique research resources such as synthetic compounds, organisms, cell lines, viruses, cell products, cloned DNA, as well as DNA sequences, mapping information, crystallographic coordinates, and spectroscopic data. Specific examples include specialized and/or genetically defined cells, including normal and diseased human cells, monoclonal antibodies, hybridoma cell lines, microbial cells and products, viruses and viral products, recombinant nucleic acid molecules, DNA probes, nucleic acid and protein sequences, certain types of animals including transgenic mice and other property such as computer programs.

CAL. CODE REGS. tit. 17, § 100301(d).

213. *See id.* §§ 100304, 100404(a).

214. *Id.* § 100304.

215. *Id.* § 100404(e)(1)-(4).

material but with information; non-profit grantees must supply “information on how to reconstruct or obtain the material”²¹⁶ while for-profit grantees may furnish “information necessary to reconstruct or obtain *identical* material.”²¹⁷ This partially alleviates the concern but hardly answers it. Grantees may find themselves engaged in long-distance support efforts for dozens of frustrated researchers attempting to apply the experimental protocol needed to re-create the desired material.

2. Revenue Sharing

CIRM expects California to be able to recoup a portion of the revenue stream of any grantee, but this regulatory expectation will be part of the marketplace’s calculus when it tries to price any technology or product offered by a CIRM grantee. If CIRM’s policy imposes terms written in language that the market knows, such as royalty rates, the market can find a price for the affected property. But insofar as the terms are not easily priced—for example, because they appear to impose claims that cannot be quantified or that “reach through” to goods or services beyond those that are typically understood to be burdened by such claims—then the affected property may be slow or impossible to trade. As discussed below, it is possible that CIRM’s revenue-sharing provisions may present just such a pricing problem.

At its core, CIRM’s revenue-sharing model is very simple: California wants twenty-five percent of any net revenues resulting from funded work. But this simple notion immediately attracts qualifiers. Grantees may keep all of a “threshold amount” (\$500,000, adjusted for inflation)²¹⁸ and California will share in the excess. And the actual inventor may have a share (the “inventor’s share”)²¹⁹ which is deducted

216. *Id.* § 100304.

217. *Id.* § 100404(d) (emphasis added). As discussed in the text, the phrase “identical material” suggests an assumption that (1) there are standard methods available to both the supplier of the material and the person requesting it that will enable the original material (the “source material”) and the material to be re-created or obtained (the “target material”) to be characterized on all dimensions of interest and (2) the results for both source and target material to be compared so as to ensure that they are “identical.” The phrase “identical material” may beg the question, because the source material is novel and may not be well-understood, and the necessary analytical and synthetic technologies may not exist or, in any case, may not have been validated.

218. The inflation adjustment is based on February 2006 for non-profit grantees, but on December 2007 if the grantee is a for-profit. This difference could be explained by different dates of adoption for the two CIRM regimes, or by a lack of editorial coordination, or both. *Compare id.* § 100308(b), with *id.* § 100408(a)(1).

219. *Id.* § 100308(a).

before the threshold amount, and any remainder is split twenty-five percent to California and the balance to the grantee.²²⁰

Then the complexities begin to mount. Some come from the architecture of the CIRM policies which, as noted earlier, create a dual regime for regulating non-profit and for-profit grantees separately. For example, after a non-profit grantee shares with its inventors and with California, its net revenues are to be applied to the “support of scientific research or education.”²²¹ For-profit grantees need not reinvest their net revenues, but unlike non-profit grantees²²² they must share with California some of their revenues from direct commercial sales (“Net Commercial Revenue”)²²³ as well as from licensing of CIRM-funded work agreements (“Net Licensing Revenue”).²²⁴

For both types of grantees, California’s share is ratably reduced if parties other than CIRM were involved in the funded work. But the scope of the offset is differently expressed. A non-profit grantee may offset ratably only if others’ funds were “used in the creation of” the relevant patented invention²²⁵ but a for-profit grantee can do so whenever such funds “contributed to the development of” the invention.²²⁶

The growing complexity of CIRM’s idea that revenues are to be shared, is seen also in the way that California seeks to share in any Net

220. *Id.* § 100308(b).

221. *Id.* § 100308(d).

222. Non-profit grantees must share with California their “net revenues” from licensing, but it is not clear whether CIRM expects such grantees to derive any revenues from other, direct commercial activity such as future contract or collaboration work. *Id.* § 100308(a). Such work is at least possible. And the text is inconsistent in its usage. Subsection (a) speaks of “[n]et revenues” while subsection (b) says “net revenues received under a license agreement or agreements of any CIRM-funded patented inventions[.]” but subsection (c) uses “resultant revenues” from a “CIRM-funded patented invention[.]” and subsection (d) says “any revenues earned as a result of a CIRM-funded patented inventions.” *Id.* § 100308(a)-(d).

223. *Id.* § 100408(b). There is no analog to Net Commercial Revenues in the provision requiring non-profit grantees to share their revenues with California. *See supra* note 222.

224. CAL. CODE REGS. tit. 17, § 100408(a).

225. *Id.* § 100308(c). As noted above, *supra* note 222, the non-profit grantee apparently need not have included in its annual reporting to CIRM any notice of such additional funding sources. This could make for difficulties if the State were to challenge a proration of its twenty-five percent share, forcing the grantee to produce evidence long after the time when the additional funding sources had participated in the project that ultimately produced the contested revenue stream.

226. *Id.* § 100408(a)(2). The for-profit grantee must have reported the percentage of the various funding sources when it files its patent application. *Id.* § 100402(c). But again the scope of proration is expressed differently as “all other sources of funding that contributed in whole or in part to the discovery of the CIRM-funded invention.” *Id.* “Discovery” is not “development,” and in fact the latter is likely to continue well beyond the date when a patent application is filed. This discrepancy may produce serious disagreements over what kind of proration is permitted to for-profit grantees in practice.

Commercial Revenues of for-profit grantees. Initially the grantee will pay California a royalty between two and five percent, with the exact rate to be negotiated with CIRM. Once this royalty stream²²⁷ returns to California an amount equal to three times its funding, the grantee's payment obligations stop—unless and until its Net Commercial Revenues thereafter exceed \$250 million in any year, which triggers a “milestone” to California equal to another three times its funding.²²⁸ Then, again, the grantee's payment obligations cease—unless and until its revenues exceed \$500 million in any year, whereupon the same treble recoupment occurs, and (provided only CIRM has funded grants totaling at least \$5 million for research “contributing to the creation of Net Commercial Revenue”).²²⁹ California will thereafter also receive a one percent royalty on all Net Commercial Revenues “in excess of \$500 million for the life of the patent.”²³⁰

In short, for blockbuster products, California taxpayers will receive a nine hundred percent return on their investment as well as a continuing one percent royalty on the grantee's net revenues for the life of any patented invention to whose development they contributed more than \$5 million in the aggregate. That is the kind of return on capital, and the kind of broad claim to downstream revenues, that a venture capitalist would be happy to see. It represents the “true cost of funds” to potential grantees and their investors, and they will weigh this cost when they assess the grant opportunity.

A critical part of the potential grantee's assessment will be whether and under what circumstances it would ever be able to resist CIRM's claim to a portion of any revenues the grantee receives from any of its work. This is the “tracing” problem that faces all licensors and licensees who seek to establish a rational (and empirically ascertainable)

227. This revenue stream appears to be treated independently of licensing revenues. Thus, the grantee will not receive any “credit” toward its payment obligations under section 100408(b) for any amounts that California has received under subsection (a).

228. *Id.* § 100408(b)(2).

229. Net Commercial Revenue is defined as “[i]ncome from commercial sales of a product(s) resulting from CIRM-funded Research.” *Id.* § 100401(n). This definition would appear to exclude revenue from contract services which CIRM-funded research enabled the grantee to provide.

230. *Id.* § 100408(b)(3). The reference to “the life of the patent” seems to assume that there is a single patent, presumably the patent claiming the CIRM-funded invention, and that the relevant Net Commercial Revenues are those from products or services which would be infringed by the claims of that patent. This linkage is not explicitly stated, however; and since Net Commercial Revenue is defined at section 100401(n) as “[i]ncome from commercial sales of a product(s) resulting from CIRM-funded Research,” it does not seem to depend upon the presence of patents at all. Nor does it appear to cover services. Thus, a for-profit grantee might not have to share revenues derived from services at all, nor (after the expiry of any CIRM-funded patents) from products, even though they continued to be protected by other patents.

connection between what is licensed and what is sold. But in the case of CIRM recoupment claims, the problem is exacerbated because CIRM can trace its contribution not only on products that would infringe a patented invention arising from the CIRM-funded work, but also on any products “resulting” (whether patents emerge or not) from “research”²³¹ to which CIRM has contributed anything at all. A licensee in an ordinary commercial negotiation would reject or strongly resist such a formulation. Here it is mandatory.

The wording’s breadth also needs to be read against the likely facts. The applicants for CIRM funding are probably small, new businesses. By definition, the work that CIRM funds with them will be foundational. For example, its output will become input for their other and subsequent work. Further, being small, such grantees will have only a few projects. Their mission and budget will be directed toward original R&D work, not toward the creation of administrative processes to partition the work and document the effectiveness of the partitions, so as to improve their defense, many years later, against a claim by CIRM that its funding “resulted” in the product that finally enters the market. Thus the grantee and its investors, if prudent, will probably assume that CIRM will assert an interest in any commercial revenues arising from any product that colorably relates to the work funded by CIRM.

In light of these factors, it will be interesting to see how many for-profit entities accept CIRM funding²³² and how the CIRM revenue-sharing provisions are applied in practice to this research.²³³

3. Mandatory Concessions by Exclusive Licensees

Typically it takes a biopharmaceutical company over a decade, and often as many as fifteen years, to translate thousands of good ideas into one approvable product, in the course of which it will spend many hundreds of millions of dollars. Much of that money will be used to

231. It is not impossible that CIRM could claim a series of milestones and royalties if it were to fund separate elements of research, each of which became a distinct contributor to the resulting product. The regulations do not explicitly exclude this “stacking” scenario.

232. As of March 2009, CIRM had awarded 279 grants for research and facilities aggregating over \$693 million. Cal. Inst. for Regenerative Med., Approved CIRM Grants, <http://www.cirm.ca.gov/info/grants.asp> (last visited Mar. 9, 2009). Stanford University ranked first with thirty-five grants worth over \$101 million. *Id.* The majority of the recipients appear to be academic or other non-profit organizations, with for-profit entities as well, such as Novocell, Inc., which was awarded two grants for approximately \$876,000. *Id.*

233. Research is defined as “a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of these regulations, whether or not they are conducted or supported under a program which is considered research for other purposes.” CAL. CODE REGS. tit. 17, § 100020(i).

build or gain access to thousands of tools, reagents, and other resources that are needed along the development path.²³⁴ Such a complex path can only be negotiated by following a simple strategy: that the product be kept as free as possible of encumbrances. The simplest form of encumbrance is a royalty or other revenue sharing agreement. More onerous and complex encumbrances can include mandatory participations or exclusions, performance minima, and other obligations. All of these burden the product opportunity and affect the developer's willingness and ability to pursue it.

CIRM's regulations support a specific policy agenda which will impose additional encumbrances on products where CIRM funds any part of their development. As noted above, revenues from those products will be shared with California,²³⁵ but the producers must do more than share their winnings; they must also make the product or service available on favorable terms to certain classes of Californians, namely its uninsured, and those participating in the California Discount Prescription Drug Program (the "Program").²³⁶

The access plan requirements are set out at section 100407(a), which requires a for-profit grantee (or its exclusive licensee),²³⁷ before commercializing any "Drug"²³⁸ whose "development . . . was *in whole*

234. In the case of a biopharmaceutical, such tools and technologies will include assays to identify and select a substance with adequate activity against the putative target (a receptor, enzyme, or other site of action); assays to determine toxicity of the substance (acute toxicity in key organs and tissues, mutagenicity, carcinogenicity, reproductive toxicity and the like); tools and materials to improve the pharmacokinetics and pharmacodynamics of the substance so that it can be delivered to the target tissue in a safe and effective dose; biomarkers to measure where the substance goes and what it does; methods to isolate, purify and make the substance in a safe, efficient, reproducible manner; methods to administer the substance in a final dosage form that is safe, sterile, convenient and cost-effective; and many other tools, materials and methods. *See, e.g.*, BIOTECHNOLOGY INDUS. ORG., *supra* note 69, at 42-44 (outlining the rigorous product development process for biotech products).

235. *See supra* notes 218-33 and accompanying text.

236. *See* CAL. INST. FOR REGENERATIVE MED., INITIAL STATEMENT OF REASONS FOR THE PROPOSED AMENDMENTS OF INTELLECTUAL PROPERTY REGULATIONS FOR FOR-PROFIT ORGANIZATIONS – SECTIONS 100407 AND 1004078, http://www.cirm.ca.gov/reg/pdf/IP_ISR.pdf (last visited Apr. 20, 2009) (describing the purpose of the amendments as making these drugs more accessible to the uninsured).

237. Licensees may face claims under section 100407, whether the licensor is a for-profit or a non-profit grantee. CAL. CODE REGS. tit. 17, § 100407(b). Section 100306(d) requires licensees from non-profit grantees to abide by the requirements of Section 100407. *Id.* § 100306(d). Note that California Senate Bill 771 (sponsored by Senators Kuehl and Runner) would extend this obligation to any licensee, exclusive or not. *See* S.B. 771, Sen., 2007-2008 Sess. (Cal. 2007).

238. "Drug" is defined in section 100401 as:

(1) An article recognized in the official United States Pharmacopoeia, Homoeopathic Pharmacopoeia of the United States, or National Formulary, or any supplement to any of them; (2) an article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; or, (3) an article intended for use as a

or in part the result of CIRM-funded Research,”²³⁹ to submit a plan to afford uninsured Californians “access” to the drug. Under subsection (b) it must also provide the drug under the Program; then, under subsection (c), for any purchases of the drug under the Program that are made with California public funds, it cannot charge more for the drug than “any benchmark price” described in the Program.²⁴⁰

The Law of Unintended Consequences²⁴¹ is always in force, and particularly when broad definitions are used to drive important actions. Section 100407 uses an extremely broad definition of drug, so that it includes essentially any product or service (such as a diagnostic procedure) that is, or is incorporated into, a measure to care for the health of humans and animals.²⁴² That definition is then combined with an equally sweeping definition of “research” which even partly resulted in the drug’s “development.”²⁴³ Anything that falls within this scope will be susceptible to regulatory claims that the seller must provide access and discounts on its product or service.

As noted above, biopharmaceutical product development relies on many research tools and ancillary technologies that contribute to, but do not comprise, the product that is finally marketed.²⁴⁴ Quite apart from the potential of stem cells and materials derived from them to become therapeutic agents in themselves, it is hoped that these materials and the knowledge gleaned from working with them will contribute greatly to the development of “classic” drugs.²⁴⁵ But if a developer of such drugs were to seek an exclusive license to use research tools derived in any way from work funded by CIRM, it may face claims under section

component of any article specified in subdivision (1) or (2). This term includes therapeutic products such as blood, blood products, cells and cell therapies.

CAL. CODE REGS. tit. 17, § 100401(e) (emphasis added).

239. *Id.* § 100407(a) (emphasis added).

240. *Id.* § 100407(b)-(c). It may be asked how much incremental value these provisions deliver to California consumers of healthcare. Between Federal benefit programs, the Program, and a variety of other California programs, drugs are already available on the same or similar price terms as those mandated here. And because “Drug” is defined in such broad terms, the “best price” provisions of section 100407 would extend to products or services for which there is no pricing benchmark under the Program. *See id.* § 100401(e).

241. *See generally* Rob Norton, *Unintended Consequences*, in THE CONCISE ENCYCLOPEDIA OF ECONOMICS, <http://www.econlib.org/library/Enc/UnintendedConsequences.html> (providing a definition of the commonly used term).

242. CAL. CODE REGS. tit. 17, § 100407(a) (using definition of “Drug” provided in section 100401(e)).

243. *Id.* § 100407(a); *see also id.* § 100401(c) (defining CIRM-funded research as “Research that has been funded in whole or in part by a CIRM grant”); *supra* note 232 (highlighting the many tools and technologies required in “development”). A CIRM-funded invention could therefore “touch” a product at any of many points.

244. *See supra* note 233.

245. *See* BIOTECHNOLOGY INDUS. ORG., *supra* note 69, at 42.

100407.²⁴⁶ The strength of the claims will not depend on whether its licensor is a for-profit or a non-profit grantee,²⁴⁷ nor on how directly or materially the tool contributed to the product's design, development, and success.²⁴⁸ In many cases, exclusivity is neither relevant nor essential to the licensing of inputs needed to develop the product.²⁴⁹ But any exclusive licensee will need to ask itself whether any of the licensed subject matter²⁵⁰ was funded, even partially, by CIRM.²⁵¹

C. *March-In Rights*

If revenue-sharing is a way to share in the “upside” of private gain from public support, march-in rights are the complementary mechanism to avoid the “downside” of private actors failing to deliver what taxpayer money had begun. But, as discussed above, the march-in right is so strong that any exercise will overthrow the expectations not only of those whose funded work is at issue, but all current and prospective market actors.²⁵² Thus, even though the general idea of march-in is simple enough, much depends on how it is actually expressed. Every actor and all opportunities will be affected by ambiguities over what property is subject to the march-in right, what events might trigger its exercise, and exactly what follows from its exercise. Collectively, such ambiguities could fully devalue the opportunities that CIRM's funding was meant to support.

246. See CAL. CODE REGS. tit. 17, § 100407(b)-(c) (providing that exclusive licensees are subject to the same requirements as grantees).

247. See *supra* note 232.

248. CAL. CODE REGS. tit. 17, § 100308(d) (providing for sharing of revenues earned from any CIRM-funded patented invention). If California Senate Bill 771 were to pass, it would no longer depend on exclusivity. See S.B. 771, Sen., 2007-2008 Sess. (Cal. 2007).

249. Indeed the thrust of the CIRM policies and regulations is to discourage exclusive licensing. See CAL. CODE REGS. tit. 17, §§ 100306(b), 100406(b).

250. This inquiry may need to extend beyond the direct subject matter of the exclusive license and into the chain of title of all items used to develop it. See *id.* § 100401(e) (providing a broad definition of the term “drug”); see also *id.* § 100407(a) (requiring exclusive licensees to submit a plan to provide access to a drug if any part of its development was in part the result of CIRM-funded research).

251. One indication of how the biotech community perceives the bargain offered by CIRM is a 2006 survey taken by the California Health Institute (“CHI”), a nonprofit advocacy organization for California's biomedical R&D community. Over eighty percent of the CHI members who responded to the survey on the then-proposed CIRM policies concerning mandated access and pricing said 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.” E-mail from Dr. David L. Gollaher, President & CEO, Cal. Healthcare Inst., to C. Scott Tocher, Interim Counsel, Cal. Inst. Regenerative Med. (Dec. 4, 2006), available at http://www.chi.org/uploadedFiles/Legislative_Action/State_Issues/IPPNPO%205th%20set%20comments.pdf.

252. See *supra* text accompanying footnotes 58-73.

This concern relates to the march-in right itself and also to any ambiguity or silence on the procedures that surround its application. May the owner of property exposed to march-in expect many, or indeed any, due process protections? These are what the Takings Clause of the Fifth Amendment²⁵³ would seem to suggest are available.²⁵⁴ And no less important than the owner's ability to cure a taking before it occurs, or to seek compensation afterward: Can the owner put the moving party to its proof, for example by challenging the party seeking march-in in a well-regulated process of fact-finding and adjudication? If there is such a process, is it overseen by an independent tribunal, whether judicial or administrative? Will the decision be stayed pending any appeal? Even if these rights are styled as "ancillary" to the central property right itself, in practice they matter just as much.

1. Analysis of CIRM's March-in Scheme

A march-in right consists of a definition of the subject property, a description of the conditions that will trigger the right's exercise, and a description of what will befall the subject property if the right is exercised. As with other concepts embodied in the CIRM regulations, the idea seems to be stated in simple form but closer inspection reveals a number of complications and questions. In part, these arise because of CIRM's dual regime and its use of different words. But the more serious questions come not from the words that are used, but from what is not stated at all.

Subject Property: CIRM's march-in regulations define the subject property to include what would be covered by Bayh-Dole march-in, for

253. The Fifth Amendment states, in relevant part, "nor shall private property be taken for public use, without just compensation." U.S. CONST. amend. V. This protection is binding on the States through the Fourteenth Amendment and typically a governmental taking of private property would trigger an eminent domain proceeding. *See, e.g., Kelo v. City of New London*, 545 U.S. 469, 480-83 (2005). It may be, however, that California would argue that title to the affected property had never vested fully in the nominal owner (the CIRM grantee or its exclusive licensee). For example, it could be argued that the nominal owners took their rights subject to the march-in. This might be challenged insofar as the effect of the taking was to destroy or reduce the value of other property, owned outright by the grantee or its licensee, which it had created in reliance on quiet title in the patent being subjected to the march-in. Each argument might have merit; what is interesting here is not whether one side or the other might prevail in a proceeding, but that CIRM's regulations make no provision for any proceeding at all.

254. But even these protections can differ greatly in their practical value. To avoid a taking altogether is generally preferable to being paid later for what was taken. Thus, while a property owner would take some comfort from the right, after the fact, to demand that an independent arbiter use established methods to assess and award "just compensation" or otherwise to recognize the value of what was taken, the owner typically would prefer the right, before the fact, to be given notice of impending exercise of the march-in right, and an opportunity to cure or challenge the alleged deficiency.

example, subject patents,²⁵⁵ non-profit grantees,²⁵⁶ or its exclusive licensees face march-in rights on a “CIRM-funded invention.” For-profit grantees may lose control of those patents and also of “data generated in CIRM-funded Research.”²⁵⁷ This goes far beyond Bayh-Dole. It would put for-profit grantees at risk of having to share data, such as clinical data used to support regulatory filings, over which they and their investors had expected to maintain exclusive control. It is not at all clear how this would work. March-in rights pertain to the licensing of intellectual property, typically a patent. A patent is public and a march-in can be achieved by granting to others the right to practice its claims. However, patent claims typically do not cover “data” per se; and how a party awarded a right to use data under a march-in would actually do so, is far from obvious.²⁵⁸ The data may be of many kinds; it may be reliable, suspect, complete, partial; it may be public or secret; it may be owned by the CIRM grantee alone or with others and perhaps commingled with others’ data. Would the exercise of a march-in on a proprietary database enable CIRM to enter the grantee’s premises to access the database? Would the grantee be required to maintain the database “live” in its customary user environment? What if the database or other repository is not in California? Has the owner consented to CIRM’s jurisdiction? The CIRM decision to expand the march-in beyond patents is pregnant with such practical questions.

Trigger Conditions: CIRM’s four trigger conditions, like its definition of subject property, are similar to Bayh-Dole, but go much farther. Three of them resemble, to a degree, the Bayh-Dole trigger conditions: that the grantee achieve practical application of the funded invention; that “public use” of the invention is being made; and that march-in is not needed for reasons of “public health and safety.”²⁵⁹ The

255. CAL. CODE REGS. tit. 17, §§ 100310, 100410.

256. The same is true of for-profit grantees. *Id.* § 100410. For the sake of brevity, in the following the discussion, “grantee” includes “exclusive licensee” unless otherwise specified.

257. *See id.* § 100410(a). *But see also id.* § 100410(b)(1), (b)(4) (stating the property is not “data generated in CIRM-funded Research” but “CIRM-funded Research data”). Presumably this is a distinction without a difference. “CIRM-funded Research” is defined as “[r]esearch that has been funded in whole or in part by a CIRM Grant.” *Id.* § 100401(c).

258. *See id.* § 100410.

259. The second trigger condition, “requirements for public use,” is broader than its Bayh-Dole counterpart, which limits such requirements to those “specified by Federal regulations and such requirements are not reasonably satisfied by the contractor . . .” 37 C.F.R. § 401.14(j)(3) (2008). For non-profit grantees, CIRM simply references “requirements for public use and the requirements have not been satisfied by the grantee.” CAL. CODE REGS. tit. 17, § 100310(a)(3). A for-profit grantee is given a slightly different standard: “Fail[ure] to satisfy requirements for public use, including broad availability in California (for reasons other than price) in accordance with Title 17, California Code of Regulations, section 100407.” *Id.* § 100410(b)(3). This suggests that “public use” means something much more extensive than simply making the drug available to Californians

first condition is expressed in wording identical to that of Bayh-Dole, while the second and third use more expansive wording.²⁶⁰ The fourth condition has no Bayh-Dole analog and exposes the grantee to march-in if it fails to give uninsured Californians “access to resultant therapies and diagnostics” or “Drug[s].”²⁶¹

To avoid violating the trigger conditions, grantees will look for guidance; insofar as the conditions resemble those of Bayh-Dole, grantees may assume that CIRM will take account of the “common law” of Bayh-Dole policy and practice.²⁶² This strategy will be of limited value for the first three conditions,²⁶³ and of no value for the fourth condition, as grantees attempt to create and act on a plan to make the product accessible to uninsured Californians. Obviously, the grantee’s plan, and how well it adheres to it, will be vital to its continued control of patents covering the CIRM-funded invention. Equally obvious, its plan and its adherence to the plan will be in the public eye, and will invite scrutiny and comment from every quarter, however ill-informed or intemperate. Thus, of the four trigger conditions, this might be the one most likely to attract the attention of a regulatory body. If that body were

(as required by the fourth trigger condition, discussed below), but the reader is not given any sense of where the boundary of the required “public use” might be.

The third trigger condition is based on the Bayh-Dole concept of “public health and safety needs” but, where the Federal requirement is that march-in is “necessary to alleviate” such needs because they are not being “reasonably satisfied” by the contractor, CIRM rewrites the condition for each of its two regimes. *See id.* § 100310(a)(4) (governing non-profits); *id.* § 100410(b)(4) (governing for-profits). A non-profit grantee faces the Bayh-Dole criterion (adding before “health and safety needs” the qualifier “public,” and after the phrase the qualifier “which needs constitute a public health emergency”) but a for-profit grantee is tested by whether or not it “has unreasonably failed to use a CIRM-funded Patented Invention or CIRM-funded Research data to alleviate public health or safety needs” that “constitute a public health emergency as declared by the Governor.” *Id.* § 100410(b)(4).

Regarding the fourth trigger condition: Requiring an “access plan,” a non-profit grantee cannot “fail[] to adhere to the agreed-upon plan for access to resultant therapies” for access by California’s uninsured. *Id.* § 100310(b)(2). But a for-profit grantee will be exposed to march-in if it “has failed to provide or comply with a plan for access to a Drug.” *Id.* § 100410(b)(2). Given the broad definition of “Drug,” it will include measures to diagnose and prevent disease, as well as “resultant therapies” which is what the access plans of non-profit grantees are required to provide. *See id.* § 100401(e).

260. *Id.* §§ 100310(a)(2)-(a)(4), 100410(b)(1), (b)(3)-(b)(4).

261. *See id.* §§ 100407(a), 100306(d).

262. Of course, CIRM is not bound by the text of the federal law or regulations or by the decisions or guidance of federal agencies acting under them. Thus, even for terms that are facially the same as those used in Bayh-Dole, such as “practical application” of an invention, and which are defined in the Bayh-Dole implementing regulations at 37 C.F.R. § 401.2 but for which CIRM’s regulations offer no definition, CIRM may ignore the federal wording and impose its own. This reinforces the need for grantees to tread warily and, where possible, to ask CIRM for specific guidance.

263. *See supra* note 259-60.

ever to become vulnerable to political pressures, this is the trigger condition most likely to generate calls that CIRM exercise its right to march-in.

Of the four conditions, failure to give uninsured Californians access, is the one where CIRM's regulations give a grantee the least textual assurance that what it is doing is "right enough." The regulations do not say how the grantee will know whether the design of its access plan is acceptable and whether its performance of the plan is adequate.²⁶⁴ This vulnerability will encourage the prudent grantee to maintain close and regular contact with CIRM regarding the design and implementation of the plan, and to establish a record to ward off an arbitrary or capricious exercise of march-in rights. But while the grantee may seek that dialogue with CIRM, CIRM may not want to reciprocate. It has no jurisdiction over the programs through which healthcare is actually delivered to Californians, insured or otherwise. It may not have the expertise, the resources, or the institutional appetite to help grantees in this work. If CIRM does assume the role of guide or overseer of access plans, and if grantees relied on its advice or actions, there is nothing in the CIRM regulations to suggest whether California would in fact be bound by that advice and those actions, so as to give the relying grantee a defense against a march-in based on estoppel or administrative procedure.²⁶⁵

Having defined the subject property and trigger conditions, the CIRM regulations then describe how a march-in will be exercised. Again, its dual regime adds complexity, treating non-profit grantees differently from for-profit ones.²⁶⁶ But a grantee's more important

264. See CAL. CODE REGS. tit. 17, § 100407.

265. Under section 100407(a)(2), "[t]he access plan must be consistent with industry standards at the time of commercialization accounting for the size of the market for the Drug and the resources of the Grantee or its exclusive licensee." *Id.* This seems to assume that there will be "industry standards" that can be ascertained and applied to all access plans. Under section 100407(a)(3) the plan will be "review[ed]" by CIRM and CIRM "may make it available for review by the ICOC and the public." *Id.* CIRM is not required to offer an opinion of the plan, or to approve it. If it should make the plan available for review by the ICOC and the public, and receives comments from them, CIRM is not required to act on them. Apart from this lack of guidance on access plans, the CIRM regimes differ subtly on the wording for the trigger conditions. To achieve "practical application" of the invention a non-profit grantee must "ma[ke] responsible efforts in a reasonable time." *Id.* § 100310(a)(1). However, for-profit grantees must use "commercially reasonable efforts." *Id.* § 100410(b)(1).

266. For a non-profit grantee, CIRM may exercise the right directly if it "determines" that any of the predicate conditions exists. *Id.* § 100310(a). In contrast, if CIRM intends to exercise the march-in right against a for-profit grantee, it will first ask the grantee to grant the desired march-in license, with respect to either a "CIRM-funded Patented Invention and/or data generated in CIRM-funded Research." *Id.* § 100410(a). Only if the grantee refuses to do so will CIRM then exercise the march-in by granting the license "on behalf of" the recalcitrant grantee or exclusive licensee. *Id.*

concern is how much due process protection it will be given. CIRM's regulations do address this concern to a degree; CIRM must notify the grantee of the default and its intention to act, and, for most kinds of default, it will give the grantee a chance to cure the default.²⁶⁷ This outlines a notice process, while failing to help the grantee engage practically with CIRM. It does not tell either party how CIRM would explain how it arrived at its determination to march in, or how the grantee could offer evidence or arguments to CIRM that could correct factual errors or misunderstandings in whatever record CIRM had used to make the determination.²⁶⁸ In this important respect, then, the CIRM regulations fall short of those under Bayh-Dole, whose regulations give to a grantee such protections as informal notice and opportunity to comment; formal fact-finding with notice and the opportunity to put in evidence and cross-examine and otherwise challenge the evidence against the grantee, written records of the proceedings and the decision, a right to appeal an adverse result to the United States Court of Claims, and suspension of march-in until a final determination.²⁶⁹

In light of the drastic result of a march-in determination, and the silence of the CIRM regulations on how grantees might engage with CIRM to correct errors or otherwise defend their position if a march-in determination is made, the prudent grantee may try to avoid a march-in crisis through preemptive discussions with CIRM. As discussed above, with respect to access plans, a grantee could find that such "self-help" is difficult, expensive, time-consuming, and dependent on CIRM's ability and willingness to engage in such discussions.

If, despite a grantee's best efforts, CIRM determines to exercise its march-in right, the grantee has only two other procedural protections: to attempt a cure and, possibly, to appeal to the ICOC.

The cure provisions state that CIRM will suspend the exercise of the march-in rights for up to a year if the grantee or its exclusive licensee "promptly takes action to cure the deficiency."²⁷⁰ These provisions implicitly assume that the deficiency is not contested by the grantee or its exclusive licensee; that they and CIRM agree on a cure; and that the cure includes objective and reliable measures of whether it succeeded or

§ 100410(b). The phrase "on behalf of" suggests that CIRM may want to preserve an argument that it holds an agency power coupled with an interest to enter into contracts binding upon the grantee as the notional "principal." Given the probability that any exercise of the power would be to the grantee's immediate and severe detriment, such an argument seems problematic.

267. *Id.* §§ 100310(4)(b), 100410(c)-(d).

268. *See id.* §§ 100310, 100410.

269. *See supra* notes 59-60 and accompanying text.

270. CAL. CODE REGS. tit. 17, § 100410(d); *see also id.* § 100310(b) (stating that a non-profit grantee must take "diligent" action to cure the deficiency).

not. In light of the extremely general wording of the four trigger conditions for march-in, those assumptions do not seem well-founded. As a result, what may occur, throughout the cure process, is a great deal of ad hoc oversight by CIRM over parties who will lack any practical or legal power to object to the terms of such oversight.

A for-profit grantee has one last line of procedural defense against CIRM's arbitrary exercise of the march-in right, and that is the appeals process.²⁷¹ Such a grantee may appeal a march-in decision to the ICOC, by "notifying the President of the CIRM in writing within 30 days of the next regularly scheduled meeting of the ICOC" and "[t]he ICOC may reverse the decision . . . for any reason."²⁷² The regulation says nothing, however, of how (or even whether) the grantee may appear and be heard by ICOC, whether it may submit evidence and, if so, what evidence and how; whether ICOC's deliberations will be public; whether a full record of the deliberations will exist and who may see it; how and when the results of the deliberations will issue; whether an appeal will lie from that result, and if so in what tribunal.²⁷³

In summary, and in marked contrast to the considerable due process protections given to grantees of federal funding under Bayh-Dole, CIRM's regulations afford its grantees and their licensees almost no practical protection against the arbitrary and capricious exercise of a march-in right that could strip them of the intellectual property interests on which their commercial success and survival may directly depend.

2. CIRM March-In: A Hypothetical Collision

Because CIRM's march-in operates independently of that available to a funding agency under Bayh-Dole, the possibility exists that an invention may result from work in which both CIRM and Bayh-Dole funding is present.²⁷⁴ If so, a dual march-in scenario could arise. It is not clear how, or even if, that scenario would be stable or how it would

271. There is no analogous right of appeal for non-profit grantees. Why they should lack this right is unclear.

272. CAL. CODE REGS. tit. 17, § 100410(e).

273. *Id.*

274. It may be objected that CIRM and NIH funding are unlikely to coexist in the same project because CIRM's funding arose to fill a "vacuum" in funding by the NIH when the 2001 Fact Sheet was issued. It remains to be seen whether the new stance of President Obama will enable such funding overlaps. Whether or not that should occur, the march-in right pertains to products and services that are (or should be) in the stream of commerce, for example, they have arisen from the use of many different technological inputs. Some of those inputs may have been funded by CIRM, others by NIH. Given the extreme breadth of CIRM's wording over what its march-in rights may cover, or by what they may be triggered (for example, access to a "Drug" where any CIRM funding contributed "in part" to its development), the possibility of competing march-in rights deserves consideration.

resolve. If either CIRM or the Bayh-Dole funding agency were to act, the other might feel obliged to act as well. For instance, if CIRM were to march-in on a patented drug and award a license to a generic maker²⁷⁵ (“*A*”), the Bayh-Dole funding agency may consider *A* to be less qualified than another generic maker (“*B*”) and accordingly march-in and award a license to *B*. At this point, *A*, having agreed to the CIRM license in the expectation of a certain minimum demand for its output, may decide that *B*’s presence will make the project uneconomic. *B* will face the same concerns. There may also be issues with product confusion, diversion, regulatory acceptance, and the like.

It may be objected that a “march-in duel” is unlikely based on the Bayh-Dole experience: in nearly three decades, that statute has resulted in initiation of only three march-in proceedings, all by the NIH, and in each case the NIH determined not to invoke the march-in right.²⁷⁶ This suggests that for most grantees, march-in is highly unlikely to be a strategy-shaping concern. But this argument comes from a regime in which there has been only a single funding agency with the right to protect its investment through exercise of the march-in right. If the “game” becomes one with two or more players—as it may in cases where research is funded by the NIH, CIRM, and other state or non-United States government agencies—it may become unstable, and devolve into a classic “Prisoner’s Dilemma” game.²⁷⁷ In this multi-party funding context, the chance of a march-in may increase in a nonlinear catastrophic way.

Thus, unless all those who can march-in on a given product agree to coordinate their action, they may frustrate each other’s exercise of the right. It would seem that CIRM will want to negotiate a compact—a “memorandum of understanding” (“MOU”)—with all other funding agencies²⁷⁸ that may have march-in rights over products where CIRM believes it can assert the right. In this respect, we note that CIRM has

275. CIRM, as part of the California State government, would enjoy immunity from patent infringement claims under the Eleventh Amendment. *See, e.g.*, Nicholas Dernik, *State Sovereign Immunity: States Use the Federal Patent Law System as Both a Shield and a Sword*, 8 J. MARSHALL REV. INTELL. PROP. L. 134, 136 (2008); *see also* U.S. CONST. amend. XI. But its licensee might be more exposed. If so, it might require CIRM to indemnify it from any claims. But if a patent holder could enjoin the licensee from practicing the claims of the patent on which CIRM had asserted a march-in right, there might be a *de facto* stalemate; neither CIRM’s sovereign immunity nor its indemnity agreement would enable the licensee to ignore the injunction.

276. *See supra* note 60.

277. *See* WILLIAM POUNDSTONE, PRISONER’S DILEMMA 8-9 (1992).

278. The agencies with which such an agreement might be sought could include other states, if they have enacted laws that impose conditions on future use of material or intellectual property created in their territory or with their funding. The coordination problem could become quite unwieldy.

entered into a MOU with both the State of Victoria in Australia and the Cancer Stem Cell Consortium of Canada relating to research collaborations.²⁷⁹ Specific questions as to whether and how either of these MOUs addresses the question of dual march-in rights and general questions as to the constitutionality and operational aspects of MOU provisions relating to march-in rights or other statutorily- or regulatory-required components of government-funding programs lie beyond the scope of this Article.

V. CONCLUSION

During the second half of the twentieth century, Congress acted on three important insights about innovation: *first*, government support for innovation is worthwhile, and may be critical, to enable academic and not-for-profit research institutions to advance their work in fields of economic, societal, and ethical significance; *second*, such government-funded research can be part of a larger process of technological translation that turns an innovative idea into a product or service ready for general use; and *third*, to allow that process to so translate the innovations resulting from government-funded research, there must be a regime for fair and orderly licensing of the intellectual property rights in those results to the entities best prepared to undertake that translational process, whether those entities are organized for profit or not. These three insights, against a back-drop of a decade of nationwide economic duress, spurred Congress to establish such a regime through the Bayh-Dole Act of 1980.

Bayh-Dole reflects a general approach, and its rules and processes can apply to any area of discovery and invention, but Bayh-Dole does not take account of political, cultural, and ethical considerations that may place certain kinds of work, otherwise scientifically meritorious, outside the reach of federal funding. Where such exceptions arise, as has happened with hESC research, the work may well continue, but in a way that is less efficient and orderly. As the NIH's Human Embryo Research Panel noted in its 1994 report, "[i]n the continued absence of Federal funding and regulation in this area, preimplantation human embryo research that has been and is being conducted without Federal funding and regulation would continue, without consistent ethical and scientific

279. See Press Release, Cal. Inst. for Regenerative Med., Victoria and California Announce International Collaboration to Advance Stem Cell Research toward Cures (June 18, 2008), available at <http://www.cirm.ca.gov/press/pdf/2008/06-18-08.pdf>; Press Release, Cal. Inst. for Regenerative Med., Minister Clement, Governor Schwarzenegger Join Forces to Fight Cancer Through Stem Cell Research (June 18, 2008), available at http://www.cirm.ca.gov/press/pdf/2008/06-18-08_b.pdf.

review.”²⁸⁰ The emergence since 2001 of state-based funding and regulatory regimes for human stem cell research and medicine illustrates the accuracy of this prediction.

Diversity is often good. It can enable systems to find novel and breakthrough solutions, and it can add to their value and robustness. In this respect, governmental philosophies that nurture hundreds of flowers to bloom on multiple jurisdictional levels in the field of stem cell research and medicine may generally be a good thing. But this diversity may also come at a price. The potential conflict between the intellectual property licensing regime under Bayh-Dole and that under the CIRM regulations illustrates this concern. We believe that this concern will only become more acute if technology such as that underlying iPSCs and other emerging approaches to harness changes in cell fate, reduce or eliminate the current ethical concerns that have, to date, limited federal funding for stem cell research. The effect of such advances will be to create a larger zone in which multiple government stakeholders, federal and state in the United States, as well as those in other nations, may participate through funding and other work. If those stakeholders do not follow common rules, conflict seems likely. While it is beyond the scope of this Article to present the details of potential solutions along these lines, we believe that the problem is best addressed proactively, and we encourage all stakeholders, on a global basis, to work in that direction.

280. AD HOC GROUP OF CONSULTANTS TO THE ADVISORY COMM. TO THE DIR., *supra* note 104, at x.