The Bayh-Dole Act, A Lion without Claws

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In 1980, Senator Birch Bayh (D-IN) and Robert Dole (R-KS) sponsored the University and Small Business Patent Procedures Act that is commonly known by their names—the Bayh-Dole Act.¹ The intent of the Act was to facilitate the ability of universities to control the patents that emanated from Federally funded research. With control of the patents, universities could then either license their technology to

pharmaceutical or medical device companies or create and spin-out biotechnology start-ups utilizing the intellectual property and technology covered by the patents. To some, the aim of the Bayh-Dole Act was to stimulate economic growth at a time when the U.S. economy was somewhat stagnant.² In fact, in 2002, the *Economist* described the Act as “possibly the most inspired piece of legislation to be enacted in America over the past half century” as it “helped to reverse America’s precipitous slide into industrial irrelevance.” For others, however, the underlying hypothesis of the Bayh-Dole Act was that by allowing both scientists and universities to profit from discoveries made as a result of Federal funding, there would be strong incentive for investigators to disclose patentable technology and for universities to create technology transfer offices and algorithms that would allow both parties to share in any profits.

That the sponsors of the Act were precinct was evidenced by the fact that between 1980 and 2009, the number of patents awarded to U.S. universities increased from 380 to 3088 and the university-based research-licensing agreements contributed substantially to the gross domestic product.^{2,3} Furthermore, since 1971, the FDA has approved 153 new drugs that arose from Federally funded research—the majority of which were originally patented after the passage of the Bayh-Dole Act with a greater part focused on the treatment or prevention of cancer or infectious diseases.⁴

The Bayh-Dole act has not been without its detractors. Patient groups have questioned whether it is appropriate for pharmaceutical companies to profit from drugs that were created with taxpayer dollars. This is of particular concern when Federally funded research results in the development of costly pharmacologic and biologic therapies such as imatinib (Gleevec), paclitaxel (Taxol) and erythropoietin alpha (Epogen). Additional concerns have focused on conflicts of interest that arise when university investigators study drugs or devices that are manufactured by companies in which they hold equity and when “good business practices” preclude investigators from sharing new ideas and technology with the broader scientific community because of fears that disclosures will affect patent rights.

Prior to the Bayh-Dole Act, the government owned all intellectual property that arose from Federally funded research and granted licenses to the technology; however, the licenses were nonexclusive. As a result, industry had little interest in

in-licensing Federal intellectual property because there was little protection from competition.⁵ The Bayh-Dole Act changed the intellectual property landscape by allowing universities to forge exclusive licenses with industry; however, it also provided so-called “march-in-rights” that allowed the NIH to “claw back” a license if the licensee did not use the licensed technology for the public good. The Act provided four circumstances in which the march-in-rights could be invoked thereby providing the opportunity for the funding agency (eg. the NIH) to require the initial licensee to grant a nonexclusive, partially exclusive or exclusive license to a second party or for the government to grant a license themselves in the following circumstances: 1) the original licensee did not apply the invention to a field of use in a reasonable period of time; 2) the licensee did not use the intellectual property to improve the health or safety of the population; 3) there is a public safety need that is not being met; or, 4) the licensee breached the original licensing agreement.

As reported by Aaron Kesselheim and his colleagues, there have been only four times when public interest groups or policy makers have tried to use the march-in-rights of the Bayh-Dole Act.⁶ Each attempt was met with rejection. In 1997, CellPro, a start-up company that had licensed technology for separating undifferentiated stem cells from the Fred Hutchinson Cancer Center, sought to gain cross-licensing from Baxter. Baxter had an earlier patent that they had out-licensed from the Johns Hopkins University that was found to supersede the patent application of CellPro. The NIH was unwilling to intervene—arguing that the march-in-rights outlined in the Bayh-Dole Act were not intended to influence the marketplace for the benefit of a single company.⁷ In 2004, petitions were submitted regarding a human immunodeficiency virus protease inhibitor developed by Abbott Laboratories and a glaucoma drug developed by Columbia University. The petitioners sought a license to manufacture the drugs based on the argument that the price of the drugs in the U.S. was substantially higher than the price of the two drugs in other developed countries.⁸ The NIH rejected the petition arguing that march-in-rights were not established for the purpose of price control. Finally, patients with Fabry disease requested that the NIH use their march-in-rights to provide them with an open license for Fabry enzyme replacement therapy that was developed at Mount Sinai School of Medicine and licensed to Genzyme. Their argument was that Genzyme had not produced enough of the enzyme to meet the demands of U.S. patients. The patient group also provided data to the NIH showing that Genzyme had diverted the drug to Europe to compete with a comparable European product. Here, the NIH rejected the petition arguing that the patient group was not capable of manufacturing the product.⁶ Recently, our research group petitioned the NIH to use their march-in-rights for a very different purpose. Research from our laboratory identified a cardiac receptor as a target for pharmacologic therapy in the 1.5 million patients hospitalized each year for an acute exacerbation of heart failure.^{9–12} After filing a “for use” patient, we identified a biotechnology company that had

used Federal funds to develop two receptor antagonists targeted to the specific receptor. The company had evaluated both compounds in phase I studies, but was planning on using only one of the two compounds in subsequent studies that were focused on a non-cardiovascular indication. When the company was unwilling to out-license either of their two compounds for evaluation in patients with heart failure, we petitioned the NIH to use their march-in-rights. Our argument was that with heart failure accounting for over 1.5 million hospital admissions each year and costing the U.S. economy over \$60 billion in health care costs, our request met the intent of the march-in provision. Like all those who came before us, we too were unsuccessful because during the review by the NIH, the company had listed both compounds on clinicaltrials.gov. While this action might have met the language of the march-in clause of the Bayh-Dole act, we do not believe it met the spirit of the clause, that is, to insure that each patent has full and optimized use to better the health of the nation.

Based on our experience and those outlined by Kesselheim and his colleagues, it seems unlikely that the NIH or other Federal agencies will optimize the use of march-in-rights to ensure that discoveries that are made with Federal funds are used across the widest breadth possible. In our case, the unwillingness of the biotechnology company to out-license one of their compounds for evaluation in patients with heart failure might have been attributed to: 1) their concern that the process of out-licensing would have been costly and time-consuming for a small company; 2) a broad license for their product might make them more attractive to a potential buyer; and 3) their fear that a negative outcome in a heart failure trial would adversely affect the regulatory climate for the drug in a noncardiovascular indication. Although each of these concerns is valid, it could be argued that when opportunities arise to treat a disease for which there is no cure or to substantially decrease health care costs, we need to find some solution that would protect the interests of the patent holder while at the same time furthering the common good. Several paths remain open to investigators and public interest groups. First, Congress can give permission to other companies to produce and sell a patented product when there is an overwhelming societal need such as during an epidemic. Second, universities should consider issuing nonexclusive rather than exclusive licenses. Although non-exclusive licenses are less attractive to investors and to companies, Congress should consider mandating the use of nonexclusive licenses in the case where a single company can only develop a patent for a single disease target or intends to only develop a patent for a single indication. Congress should base their decisions on whether the multiple licensing of a drug or product is likely to lower health care costs, improve disease outcomes, enhance patient access or spur research growth.

Congress passed the Bayh-Dole Act in order to facilitate the translation of basic science discoveries to the development of new

cures for human disease. Senator Russell Long (D-LA) actually opposed the bill because he believed that neither companies nor individuals should accrue wealth from discoveries that were funded by Federal taxpayer dollars. It is unlikely that a socialistic approach to regulating technology developed through Federal funding would speed the progress of discoveries along the translational highway and in fact, would likely become just one more impediment. Nonetheless, thirty years after the passage of the Bayh-Dole Act, it is time for Congress to modernize the law based on the collective experiences of investigators and universities, the current fiscal economic environment, the high cost of developing new types of therapeutics including biologics and gene therapies, and the continued disparities in health care across the various socio-economic strata. No single individual or single company should have the exclusive rights to intellectual property when the discovery was funded by taxpayer dollars unless they can optimize its across all applicable diseases.

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