Reforming the Business of Pharmaceutical Innovation

Advising research, policy, and practice
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Executive summary

Workshop #5 - Beyond Bayh Dole; policy reforms to maximize the return of public value from federally funded science

The Bayh-Dole Act of 1980 institutionalized the transfer of federally funded scientific advances from the public sector to industry where commercial development would produce public value in the form of innovative products, economic growth, and US-based jobs. The role of basic science in drug discovery and development, as well as the scale of federal funding for this research, have changed significantly over the past 40 years, and evidence suggests that only a small fraction of the research that enables drug discovery is captured by the Act. There have also been dramatic changes in the concept of the corporation, tax structures, and social circumstances that may affect the public return from the Act. This workshop will explore how the success of the Bayh-Dole Act may be extended in response to these changes to ensure the maximum public return from federal investments in science.

The goal of this workshop is to explore legislative approaches for reforming Bayh-Dole to promote and protect the public return on government investments in basic and applied science.

Background

Basic biomedical research in academic institutions, which is funded primarily by government, plays an essential role in pharmaceutical innovation, identifying fundamental mechanisms of health and disease and biological targets for drug discovery. Drug development, however, occurs overwhelmingly in the biopharmaceutical industry. There are several mechanisms by which basic, academic research informs applied research and development in industry including the dissemination of academic research through publications and presentations, educating students for the workforce, and consulting by academic faculty. The formal transfer of subject inventions or patents arising from government funding is governed by the “Patent and

Trademark Law Amendments Act" of 1980[1], known as the Bayh-Dole Act , whose stated purpose is to promote *"… the utilization of inventions arising from federally supported research or development…,"* specifically the *"…the commercialization and public availability of inventions made in the United States by United States industry and labor…"*. In doing so, the Act sought to promote and protect the public's interest in the innovative products enabled by federally funded research. There is increasing recognition of the critical role played by federally funded research in technological innovation, ranging from information and space technologies to medical devices and pharmaceuticals. From 1996–2017, total federal investment in non-defense R&D spending across technology sectors totaled $1.5 trillion (2020 $). An economic impact assessment conducted for the Association of University Technology Managers and the Biotechnology Industry Organization estimates that from 1996–2017, the licensing of government-funded research generated $723 billion–$1.7 trillion in gross industry output or $374–$865 billion in GDP[2] (2012 $).

Putting aside historical debates over the direct impact of the Bayh-Dole Act, it provides the operational structure for transfer of federally funded technologies to industry and the only significant policy aimed at promoting and protecting the public interest. Questions about the adequacy of the Act have been arisen from concern about the affordability and availability of many medicines, the scale of public sector investment underlying new products, the prioritization of shareholder value and cash distributions to shareholders by an increasingly financialized biopharmaceutical sector, the offshoring of jobs, aggressive tax avoidance strategies by companies, and the continuing lack of industry focus on public health issues such as antibiotics and vaccines.

In the last administration, the National Institute of Standards and Technology proposed changes to the language of the Bayh-Dole Act along with a request for comment.

Our work

A focus of our work has been on characterizing the relationship between the efficiency of drug development and the maturity of the underlying basic science. Building on the principle of systems engineering that the maturation, or readiness, of technologies is an important factor in product success, we developed an analytical model for the maturation of science and demonstrated an association between the maturation of basic research on a drug target or

[1] CFR (2010) Code of Federal Regulations, Title 37 Part 401 RIGHTS TO INVENTIONS MADE BY NONPROFIT ORGANIZATIONS AND SMALL BUSINESS FIRMS UNDER GOVERNMENT GRANTS, CONTRACTS, AND COOPERATIVE AGREEMENTS in Code of Federal Regulations.

[2] Pressman, Lori and Planting, Mark A. and Bond, Jennifer and Yuskavage, Robert and Moylan, Carol E., The Economic Contribution of University/Nonprofit Inventions in the United States: 1996 – 2017 (June 2, 2019). Available at SSRN: https://ssrn.com/abstract=3777218

chemistry and the efficiency of drug development.[3] We also characterized the public sector investment in the research that enabled new drug approvals from 2010-2019.[4] Recently, we completed studies looking at the economic returns on licenses of biotechnologies from academic institutions[5] and the fraction of the NIH investment in research associated with drug approvals over the past decade captured by patents included in the Orange Book.[6] Specifically:

- Using an analytical model for the advance of basic research, we have shown that few targeted therapeutics are successfully developed before research on the drug target or therapeutic modality (i.e. monoclonal antibody, gene therapy, nucleotides, RNAi) reaches an analytically described *established* point, and that the timeline for drug development is 3 years longer if clinical development commences before this point. The *established* point is commonly reached 20-25 years after the *initiation* of research in that area.
- The NIH contributed funding for published research related to every one of the 356 NMEs approved by the FDA from 2010-2019 or their 219 biological targets.
- This body of literature comprised >2 million scientific publications, of which 424K cited funding from the NIH. NIH funding for this research comprised 390K fiscal years of support and $186 billion in costs, with >80% of these costs associated with basic research publications.
- We examined the economic returns on licenses of biotechnologies from academic institutions to those of comparable licenses between for-profit corporations[7]. Academic licenses had lower median EFR (3% versus 8%, p<.001), deal size ($0.9M versus $31.0M, p<.001), and precommercial payments ($1.1M versus $25.4M, p<.001) than corporate licenses.
- Differences in the nature of the licensee (large pharma versus biotech), the development phase of licensed technologies (discovery through approved products) and deal terms (exclusivity, equity, R&D, or co-development) accounted for only a fraction of the differential in economic returns.

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[3] McNamee, L.M., Walsh, M.J., Ledley, F.D. (2017) Timelines of translational science: From technology initiation to FDA approval. *PLOS ONE*. 12.5 e0177371. journals.plos.org/plosone/article?id=10.1371/journal.pone.0177371

[4] Cleary, E.G., Beierlein, J.M., Khanukja, N., McNamee, L.M., Ledley, F.D. (2018) Contribution of NIH funding to new drug approvals 2010-2016. *Proceedings of the National Academies of Science.* 115(10), pp.2329-2334. www.pnas.org/content/early/2018/02/06/1715368115

Cleary, E.G., Jackson, M.J., Ledley, F.D. (2020) Government as the first investor in biopharmaceutical innovation; evidence from new drug approvals 2010–2019. (Working Paper Series No. 133) www.ineteconomics.org/uploads/papers/WP_133-Cleary-et-al-Govt-innovation.pdf

[5] Shah et al., Licenses of biotechnologies provide lower economic returns to academic institutions than biopharmaceutical companies. (in preparation).

6 Ledley et al., Public contribution to pharmaceutical innovation is not captured by Orange Book patents. (in preparation).

[7] This research made use of a dataset from Bioscience Advisors, provided by Mark Edwards and benefited from his expert advice. Note: the academic reports to government agencies detailing disclosed Subject Inventions, Patents, and Licenses related to Bayh-Dole are archived in iEdison but are explicitly not available to the public under the terms of Bayh-Dole.

- The NIH funded Projects identified in searching for drugs approved 2010-2019 or their biological targets were associated with 22K patents in RePORTER. Of these, 119 were associated with these drugs in Orange Book.[8]
- Of the 313 drugs in this dataset represented in Orange Book, 34 (10.8%) had a government funded patent cited in this database.
- The NIH contributed $163 billion to research related to these 313 drugs or their biological targets. The Orange Book patents were associated with 0.34% of this funding including 0.83% of funding for research directly related to the drug (applied research) and 0.09% of research related only to the target (basic research).

Questions raised by this work

Our interest in the Bayh-Dole Act does not relate explicitly to drug pricing or "march in" rights, and we hope this workshop will steer away from those temporal concerns to address the larger issues raised by changes in science and society over the past 40 years. To start the discussion:

- From the 1970s, pharmaceutical innovation came to be increasingly based on basic science and targeted drug discovery. Our work has demonstrated the importance of a critical mass of basic science in this process, including not only seminal discoveries/inventions, but also the research that confirms these discoveries, refutes inaccuracies, refines essential details, and validates its applicability to therapeutic strategies. Despite the essential nature of this research in pharmaceutical innovation, much of this work does not meet the legal definition of an "invention," and is not covered by Bayh-Dole. Can a greater fraction of federally funded biomedical research be captured by the Act?
- The concept that the purpose of the corporation was to maximize shareholder value also emerged in the late 1970s, and was furthered by changes in law and investment through the 1980s. The public value created by the Act was predicated on the assumption that commercialization of advances arising from federally funded research would make new products available to the public, create new (US-based) jobs in the development and manufacturing of these products, create economic growth, and increase the tax base. How is this value proposition impacted by increased globalization and offshoring of jobs, the increasing financialization of the industry, with its focus on maximizing shareholder value and cash returns to shareholders, and tax avoidance schemes that have seen many large companies domicile overseas? Can the original intent of the Act be strengthened to account for these changes?

[8] This research made use of a dataset from DrugPatentWatch provided by Yali Friedman, which represents an expanded version of Orange Book.

- How do trends in academic research, including the increasing adoption of "open innovation" models, increasing research funding by universities themselves (and their donors), the growth of public-private partnerships (even before COVID), and an increasing emphasis on downstream translational science in academic institutions impact the ability of the Bayh-Dole Act to promote and protect the public interest?

Discussants

- **Lita Nelsen, MBA**, *formerly* Massachusetts Institute of Technology
- **Bhaven Sampat, PhD**, Columbia University
- **Mark Edwards, MBA**, BioScience Advisors
- **Lori Pressman, MSEE**, Independent Consultant
- **Jim Glasheen, PhD**, *formerly,* University of Massachusetts Medical School; Technology Partners Venture Capital
- **Joe Allen**, Joseph Allen & Associates

Workshop plan

The session will begin with an informal introduction to the theme of this workshop, followed by 5-8 minute comments from each discussant describing their perspectives based on their work and experience. We hope these introductory comments will provide an opportunity for an open discussion between the discussants and other participants in the workshop.

If you wish to ask a question during the session, please indicate yourself or directly post the question in the Zoom Chat box. A member of our team will be monitoring this and will invite you to ask your question at an appropriate time.

For more information, please email SciIndustry@bentley.edu.