Compiled Written Public Comments

NIH Workshop on *Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer*

June 28, 2023 – August 19, 2023

Public Comments:

1. Fred Reinhart
2. Josh Sarnoff, DePaul University College of Law
3. John Fraser, Burnside Development and Associates
4. Sarah Kaminer Bourland, Patients for Affordable Drugs
5. Andrew Schlafly, Eagle Forum Education and Legal Defense Fund
6. Frank Cullen, Council for Innovation Promotion
7. James Edwards, Conservatives for Property Rights
8. Joseph P. Allen, Bayh-Dole Coalition
9. Walter Copan
10. Stephen Heinig, Association of American Medical Colleges
11. Adam Mossoff, George Mason University
12. Brian O'Shaughnessy, Licensing Executives Society (USA & Canada), Inc.
13. Lizbet Boroughs, Association for American Universities & COGR
14. Robert Taylor, Alliance of US Startups and Inventors for Jobs
15. Cassidy Parshall, Public Citizen
16. Stephen Susalka, AUTM
17. Fred Ledley, Paula Chaves da Silva, & Edward Zhou, Bentley University
18. Alex Moss, Public Interest Patent Law Institute
19. Jocelyn Ulrich, Pharmaceutical Research and Manufacturers of America
20. Hans Sauer, Biotechnology Innovation Organization
21. Mark Emalfarb
22. Atul Varadhachary, Fannin
23. James Love, Knowledge Ecology International
24. Katharine Ku, Wilson Sonsini Goodrich & Rosati
25. Peter Pitts, Center for Medicine in the Public Interest
26. Robert Pavey, Pavey Family Investments
27. Karen Kerrigan, Small Business & Entrepreneurship Council
28. Gerard Scimeca, Consumer Action for a Strong Economy
29. Patricia Kelmar, U.S. Public Interest Research Group
30. Jon Soderstrom, Wilson Sonsini Goodrich & Rosati
31. Justin Mendoza, Universities Allied for Essential Medicines
32. Kevin Walters, Wisconsin Alumni Research Foundation
33. Tom Giovanetti, Institute for Policy Innovation
34. Adam Mossoff, Hudson Institute
35. Stephen Ezell, The Information Technology & Innovation Foundation
36. Michael Mohr-Ramirez, Taxpayers Protection Alliance
37. Emily Michiko Morris, The University of Akron School of Law
38. Lori Pressman
39. Ashlyn Roberts, Incubate
40. Drew Johnson
41. Claire Cassedy, Knowledge Ecology International
42. James Love, Knowledge Ecology International

43. Charles Sauer, Market Institute
44. Jennifer Burke, Partnership to Fight Chronic Disease

Submission Date: 6/29/2023

Name: Fred Reinhart

Name of Organization: Not Provided

Comment:

As a 38-year veteran of academic technology transfer and Past President of AUTM, I would like to comment on the upcoming workshop.

The role of NIH, including its internal research and funding of extramural research is at the heart of America's successful medical, biomedical and pharmaceutical sectors. Americans benefit from access to a wide range of leading-edge diagnostics, vaccines and therapeutics. It is no secret that the U.S. is the leading innovator in these fields. One factor that supports these outcomes is the model that draws public and private stakeholders into cooperative partnerships in which each can contribute based on their strengths and resources.

NIH is the world's leader in medical research and awards funding to both research institutions and companies. Academia performs basic and applied research, identifies, protects and licenses promising inventions to new and existing companies. Industry does developmental and applied research and supplies the majority of funding to carry new Dx, Rx , vaccine and other innovations through the developmental and regulatory phases and into the commercial realm.

With respect to inventions derived from research in academia and teaching hospitals, over 300 important vaccines and therapeutics have reached the public as a result of academic licenses to industry. It would be foolish and counterproductive to undermine such an effective model yet several groups (specifically KEI and UAEM) are trying to do just that. They are doing so by making one blatantly false claim: that drugs like Xtandi, a prostate cancer drug, were developed with government money. They weren't. The federal government provided several million dollars to UCLA which resulted in early results that two companies built upon and brought to market after investing over $900,000,000. Thus, to say Xtandi was developed by the government and its price should be regulated by the government is simply not true. Such claims conveniently ignore the realities of the U.S. drug development model in which industry invests the majority of time and money that creates a new therapeutic.

The critics mentioned and others also have chosen to creatively and deliberately misinterpret Bayh-Dole law to claim that its "march-in" provision can be used to set prices. It cannot and the reasons have been widely detailed already. Yes, we need to ensure affordability and wide access to all new Dx, Rx and vaccines. We need to find ways to do that without undoing the remarkably effective system already in place.

Fred Reinhart
Plymouth, MI

Additional Comment (attachment): None

Submission Date: 7/8/2023

Name: Josh Sarnoff

Name of Organization: DePaul University College of Law

Comment:

Request to comment at the 7/31 workshop on transforming discoveries into products. FWIW, some of what I will say is included in the attached, discussing the ability of NIH to compel trade secrecy sharing should it develop the political will to do so.

Thanks.

Josh Sarnoff

Joshua D. Sarnoff (he, him, his)
Professor of Law
DePaul University College of Law
Center for Intellectual Property Law and Information Technology

Additional Comment (attachment): Available at https://hastingslawjournal.org/wp-content/uploads/1-Levine-final.pdf

Submission Date: 7/15/2023

Name: John Fraser

Name of Organization: Burnside Development and Associates

Comment:

Written submission as I am unavailable during the scheduled time of the July Workshop.

regards

John A. Fraser, RTTP, CLP
President
Burnside Development and Associates
Past President, AUTM

Additional Comment (attachment):

One more example of Tax Payers' Dollars at work though the National Labs, the Stevenson Wydler Act and the Bayh-Dole Act.

My name is John Fraser, a former President and Chair of AUTM. I have headed 4 academic technology commercialization offices – 2 in the US, 2 in Canada of which 2 were for-profit, 2 were not-for-profit.

I am unavailable during the schedule Workshop time, so I want to point out one more example of a very high profile drug and how research at a National laboratory and an academic center lead to the new, now widely known drug (**Ozempic and Wegovy**).

This occurred in the environment supportive of innovation provided by both the Stevenson-Wydler Technology Innovation Act of 1980 and the Bayh-Dole Act of the same year.

The following is verbatim from an article in the Wall Street Journal June 23, 2023

Monster Diet Drugs Like Ozempic Started With Actual Monsters

By Rolfe Winkler and Ben Cohen June 23, 2023 7:53 am ET

Before there was Ozempic or Mounjaro, there were fish guts and Gila monsters.

The blockbuster diabetes drugs that have revolutionized obesity treatment seem to have come out of nowhere, turning the diet industry upside down in just the past year. But they didn't arrive suddenly. They are the unlikely result of two separate bodies of science that date back decades and began with the study of two unsightly creatures: a carnivorous fish and a poisonous lizard.

In 1980, researchers at **Massachusetts General Hospital** wanted to use new technology to find the gene that encodes a hormone called glucagon. The team decided to study Anglerfish, which have special organs that make the hormone, simplifying the task of gathering samples of pure tissue.

They hired a Cape Cod fisherman to find the slimy bottom-feeders known for their sharp teeth and lightbulb-like lure. The fisherman tossed his catch on the dock, where two young scientists dissected “the ugliest fish you could ever imagine,” said Dick Goodman, one of those postdocs.

After plucking out organs the size of Lima beans with scalpels, they dropped them into liquid nitrogen and drove back to Boston. Then they determined the genetic sequence of glucagon, which is how they learned that the same gene encodes related hormones known as peptides. One of them was a key discovery that would soon be found in humans, too.

It was called glucagon-like peptide-1 and its nickname was GLP-1.

After they found GLP-1, others would determine its significance. Scientists in Massachusetts and Europe learned that it encourages insulin release and lowers blood sugar. That held out hope that it could help treat diabetes. Later they discovered that GLP-1 makes people feel fuller faster and slows down emptying of food from the stomach.

But there was a problem: GLP-1 vanishes from the human body nearly as fast as it is secreted, chewed up by enzymes and washed away by the kidneys in minutes. That meant there was little chance of developing the magic peptide into a drug.

To investigate whether it helped diabetics, scientists had to infuse GLP-1 intravenously. Studies showed it worked, lowering blood sugar. But some also foreshadowed the main side effect that plagues today’s GLP-1-mimicking drugs: nausea.

The early research that led to GLP-1 drugs included an experiment on Anglerfish.

David Nathan, a **MassGen** physician scientist who led a 1991 study, still remembers what happened when they increased the dose: “One person leaned over the side of his chair and threw up on my shoes.”

The key to the first drug would come from a serendipitous discovery inside another odd-looking animal.

Around the time Goodman was cutting open fish, Jean-Pierre Raufman was studying insect and animal venoms to see if they stimulated digestive enzymes in mammals. “We got a tremendous response from Gila monster venom,” he recalled.

It was a small discovery that could have been forgotten, but for a lucky break nearly a decade later when Raufman gave a lecture on that work at the **Bronx Veterans Administration**. John Eng, an expert in identifying peptides, was intrigued. The pair had collaborated on unrelated work a few years before. Eng proposed they study Gila monsters.

Gila monsters are poisonous lizards with powerful jaws and beaded skin.

Native to the U.S. southwest, Gila monsters (pronounced: HEE-luh) are poisonous lizards measuring 20 inches with powerful jaws and black-and-orange beaded skin. Adults eat four

meals per year, and live most of their lives below ground, slowly digesting energy stored in their tails.

Eng and Raufman studied powdered Gila monster venom ordered from the Miami Serpentarium, whose owner survived 172 snake bites over the years as he produced venom for research.

Eng isolated a small peptide that he called Exendin-4, which they found was similar to human GLP-1.

Eng then tested his new peptide on diabetic mice and found something intriguing: It not only reduced blood glucose, it did so for hours. If the same effect were to be observed in humans, it could be the key to turning GLP-1 into a meaningful advance in diabetes treatment, not just a seasickness simulator in an IV bag. Hoping that he could sell it to a pharmaceutical company that would develop it into a drug, Eng filed for a patent in 1993.

Jens Juul Holst, a pioneering GLP-1 researcher, remembers standing in an exhibit hall at a European conference next to Eng. The two had put up posters that displayed their work, hoping top researchers would stop by to discuss it. But other scientists were skeptical that anything derived from a lizard would work in humans.

"He was extremely frustrated," recalled Holst. "Nobody was interested in his work. None of the important people. It was too strange for people to accept."

After three years, tens of thousands of dollars in patent-related fees and thousands of miles traveled, Eng found himself standing with his poster in San Francisco. This time, he caught the attention of Andrew Young, an executive from a small pharmaceutical company named **Amylin.**

"I saw the results in the mice and realized this could be druggable," Young said.

When an Eli Lilly executive leaned over his shoulder to look at Eng's work, Young worried he might miss his chance. Not long after, Amylin licensed the patent.

They worked to develop Exendin-4 into a drug by synthesizing the Gila monster peptide. They weren't sure what would happen in humans. "We couldn't predict weight loss or weight gain with these drugs," recalled Young. "They enhance insulin secretion. Usually that increases body weight." But the effect on slowing the stomach's processing of food was more pronounced and Young's team found as they tested their new drug that it caused weight loss.

To get a better understanding of Exendin-4, Young consulted with Mark Seward, a dentist raising more than 100 Gila monsters in his Colorado Springs, Colo., basement. The lizard enthusiast's task was to feed them and draw blood. One took exception to the needle in its tail, slipped its restraint and snapped its teeth on Seward's palm—the only time he's been bitten in the decades he's raised the animals. "It's like a wasp sting," he said, "but much worse."

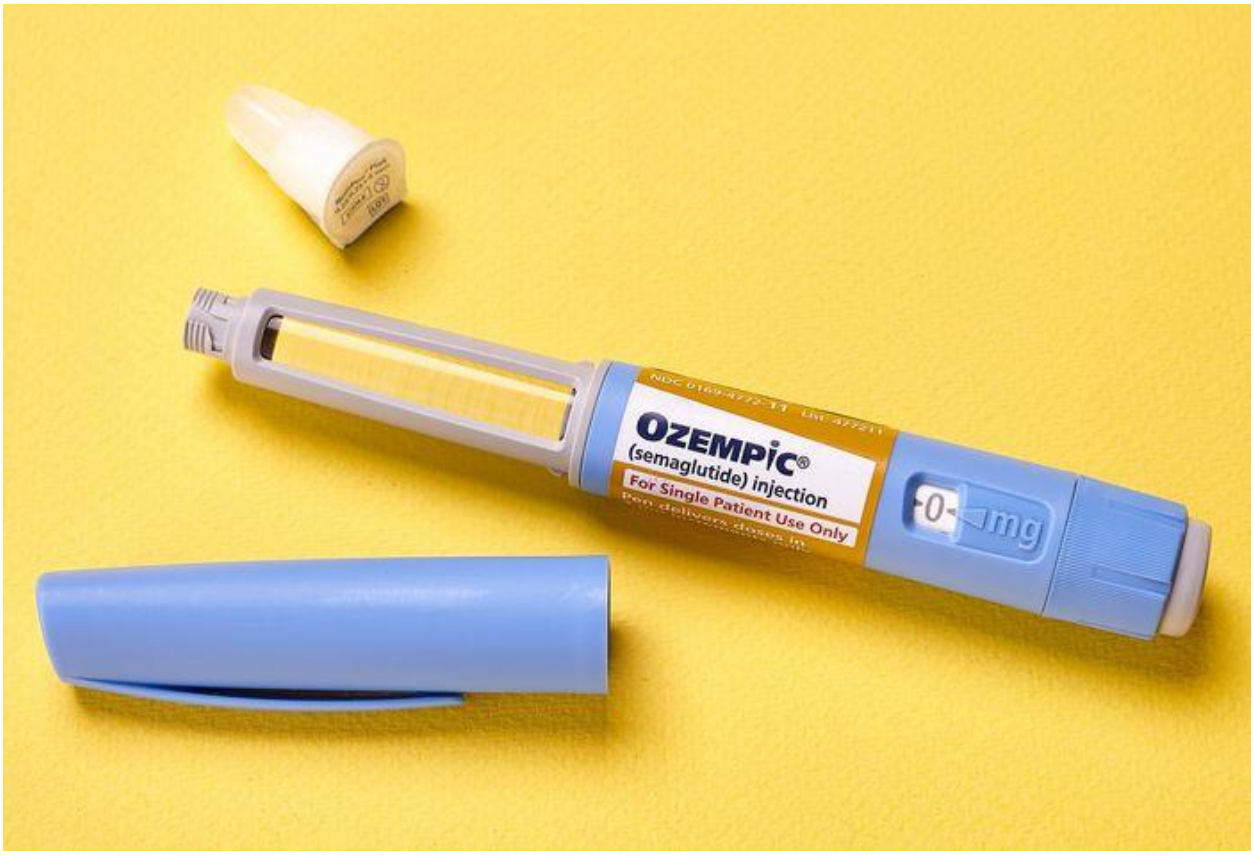
Nine years after the chance San Francisco meeting between Eng and Young, **the Food and Drug Administration approved the first GLP-1-based treatment in 2005.**

The twice-daily injection remained in the bloodstream for hours, helping patients manage Type 2 diabetes. Eng would be paid royalties as high as $6.7 million per year for the drug, according to federal government data available after 2015. “It was a long journey,” said Eng.

The proof of concept pushed other pharmaceutical companies to make more-effective and longer-lasting GLP-1 drugs.

At first, **Novo Nordisk** executives had little interest in GLP-1 drugs. They gave priority to Novo’s main business of selling insulin. “A lot of people didn’t believe in it,” says Jens Larsen, international medical director for the Danish company. He stopped his own mid-1990s study of IV-infused GLP-1 when patients on a higher dose started vomiting. The research was shelved until 2001.

The Gila monster-derived drug gave them a push, said Larsen: “It made companies more aware that this could be a serious competitor and we had to step up and put more people on it.”



An Ozempic pen by Novo Nordisk. PHOTO CREDIT: F. Martin Ramin/The Wall Street Journal
Photo: F. Martin Ramin/The Wall Street Journal

Novo kept at it, working on its own drug that more closely resembled the human peptide. With some clever chemistry it bumped up this drug’s time in the body to a day. Its first GLP-1 drug, the once-daily shot liraglutide, would receive FDA approval in 2010.

Seven years later came its longer-lasting diabetes drug, the once-weekly shot semaglutide. As it turned out, it was also the best of the drugs for weight loss, making it the first blockbuster in the category. A higher dose was approved in 2021 to treat obesity.

Those two approved doses are better known today by their brand names: Ozempic and Wegovy.

Submission Date: 7/24/2023

Name: Sarah Kaminer Bourland

Name of Organization: Patients for Affordable Drugs

Comment:

Hello,

Attached are comments from Patients for Affordable Drugs for the upcoming workshop on “Maximizing NIH’s Levers to Catalyze Technology Transfer.” We were unable to sign up in time to share oral comments, so please keep our organization in mind if any slots become available.

Thank you,

Sarah Kaminer Bourland Legislative & Policy Director (she/her)
Patients For Affordable Drugs, Patients For Affordable Drugs NOW

Additional Comment (attachment):

PATIENTS FOR AFFORDABLE DRUGS™

Patients For Affordable Drugs Comments on
Transforming Discoveries into Products:
Maximizing NIH's Levers to Catalyze Technology Transfer
July 24, 2023

Thank you for inviting comments ahead of the Workshop on *Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer*. Patients For Affordable Drugs (P4AD) is the only national patient advocacy organization focused exclusively on policies to lower prescription drug prices. We are bipartisan, independent, and do not accept funding from any organizations that profit from the development or distribution of prescription drugs.

It is critical that the National Institutes of Health (NIH) is convening stakeholders to discuss policies relating to biomedical innovation and policies to maximize NIH's levers to catalyze technology transfer. In our view, however, the discussion is limited given that it does not invite an explicit discussion of access and affordability. Drugs don't work if people can't afford them, and if NIH maximizes tech transfer but the products it invents are overpriced and do not reach patients, it will have failed in its mission to "seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability". That is why, since P4AD was launched in 2017, our organization has advocated for fair pricing for all NIH and taxpayer-funded drugs, including by working with and supporting members of Congress to introduce legislation to ensure fair pricing and maximization of public health.

Many United States government agencies — especially the NIH — are engines of innovation, driving research and development (R&D) leading to medicines with meaningful public health impact. Indeed the NIH is the largest public funder of biomedical research in the world. But too often, the very taxpayers who fund the riskiest research into these life-saving inventions are themselves denied access due to the exorbitantly high launch prices when eventually commercialized. The NIH and its critical role in biomedical R&D have been at the center of this debate since 1995, when the agency chose to remove the requirement for reasonable pricing in contracts with external entities. At that time, the average monthly price for a drug was $50. Since then, the NIH has continued to fuel innovation in the field, but has also contributed to exorbitant and unjustified pricing and profits for drug corporations. The current system socializes the research and development while privatizing the gain. One study estimates that each dollar in NIH investment can result in up to $2.13 in pharmaceutical sales. Now, nearly 30 years after

removing the reasonable pricing clause, the median annual price of a new drug is $222,000 and three in ten adults in the United States are forced to ration medication due to price. People of color are disproportionately harmed by high drug prices, which contribute to the fact that uninsured Latinos and Black Americans use 10-40% fewer medications than their White counterparts. **The NIH's approach to ensuring taxpayer-funded inventions are available on reasonable terms for all who need them is long overdue for change.**

We are also very disappointed at the orientation of the meeting; the agenda for the meeting betrays a perspective that is not at all patient-focused. **While purporting to be a convening of stakeholders this workshop does not include a single representative of the most important stakeholder for NIH-developed technologies: the patient.** This is completely unacceptable. There is still time to include patient voices, and this workshop will have much greater credibility with those whose lives and communities you seek to impact if you include patients in this discussion.

Background

Pharmaceutical companies argue high drug prices are required to attract investment and reward the industry for the financial and scientific risk they take on during research and development. In reality, the U.S. government takes on most of those early risks, undermining the industry's argument for high prices.

The government's involvement in COVID-19 vaccine development illuminates this point with crystal clarity. For years, drug companies were unwilling to invest their own money in emerging vaccine technologies they considered too risky. Instead, the U.S. government stepped up and made investments into the technologies that led to mRNA-based COVID-19 vaccines. We now know the unprecedented and rapid development of vaccines was driven by more than $300 million in public investments in mRNA technology prior to COVID-19 and $31.6 billion more to support the development and manufacturing of COVID-19 vaccines. Vaccine manufacturers have made record-breaking profits off products that were de-risked by the U.S. government:

- Pfizer sales of the vaccine reached $37.8 billion in 2022, making it the best-selling drug in history.
- The COVID-19 pandemic created more than 40 new pharmaceutical billionaires, including four from Moderna, a company that had never marketed a product prior to the federal government standing up Moderna's manufacturing capability and providing advance purchase agreements for COVID-19.
- According to nonprofit Oxfam, "Pharmaceutical giants are making over $1,000 a second in profit from vaccines alone and they are charging governments up to 24 times more than it would cost to produce vaccines on a generic basis."

While the COVID-19 case study involves numerous agencies, the NIH is no stranger to this phenomenon. A recent study of R&D expenditures revealed that the NIH's spending on R&D matches that of the biopharmaceutical industry. In fact, between 2010 and 2019, the NIH spent $187 billion for basic or applied research related to 354 of the 356 drugs approved by the Food and Drug Administration (FDA), which was at least as much or more than investment by the pharmaceutical industry when considering basic research contributions. A recent HELP Committee report highlighted the government's key role in basic research, invention of new medicines, clinical trials, and even manufacturing. The report found that the median "price of new treatments that NIH scientists helped invent over the past twenty years is $111,000." As an agency dedicated to "the application of that knowledge to enhance health, lengthen life, and reduce illness and disability," the NIH can no longer turn a blind eye when its investments are turned into blockbuster profits at the expense of patients and public health.

Striking the right balance between technology transfer to commercialize innovation and affordable access is possible and should be the driving force behind NIH policy changes. At minimum, P4AD recommends the following:

- **Address price at the point of technology transfer:** The NIH should implement a new reasonable pricing requirement in cooperative research agreements and licensing agreements or establish a multi-disciplinary entity for negotiation terms of technology transfer that would be required to consider the public health implications of inventions, especially if they were to be priced unaffordably for patients, taxpayers, and society as a whole. NIH grantees should be required to address access and affordability as a requirement for funding; for example, NIH grants to research institutions, medical schools and universities could require the inclusion of concrete and transparent strategies and policies to ensure equitable access to health technologies as a primary purpose of technology transfer.

- **NIH Grantees must be required to disclose funding in patent applications:** A May 2023 GAO study found that NIH awardees "did not consistently disclose NIH support in patents arising from research funded by the agency" and among those that did, the funding was inaccurately or incorrectly reported. This lack of disclosure contributes to ambiguity over intellectual property rights and makes it difficult to quantify taxpayer contributions to biomedical inventions. Without data on taxpayer contribution to commercialized inventions, it is difficult to quantify the public's stake in affordable pricing. In addition to requiring disclosure of all taxpayer funding in patent applications, the NIH and other agencies—including the U.S. Patent and Trademark Office—should have enforcement mechanisms at their disposal for violations of these disclosures.

Submission Date: 7/25/2023

Name: Andrew Schlafly

Name of Organization: Eagle Forum Education and Legal Defense Fund

Comment:

To whom it may concern:

Eagle Forum Education and Legal Defense Fund, a nonprofit organization founded by Phyllis Schlafly in 1981, is pleased to comment on the National Institutes of Health's (NIH) invitation to comment regarding the “Workshop on Transforming Discoveries into Products: Maximizing NIH’s Levers to Catalyze Technology Transfer.”

Please accept our comments, which are attached as a pdf file.

Thank you!

Andrew L. Schlafly
Counsel for Eagle Forum Education and Legal Defense Fund

Additional Comment (attachment):

July 25, 2023

National Institutes of Health
VIA EMAIL: SciencePolicy@od.nih.gov

RE: Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer

To whom it may concern:

Eagle Forum Education and Legal Defense Fund, a nonprofit organization founded by Phyllis Schlafly[1] in 1981, is pleased to comment on the National Institutes of Health's (NIH) invitation to comment regarding the "Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer."

Our organization's decades of work on patent policy, including the Bayh-Dole Act, provides perspective on the topic at hand. Fundamentally, secure, reliable intellectual property (IP) rights are the foundation for transforming discoveries into products. Since the Bayh-Dole Act became law in 1980, the NIH has generally played an important part in technology transfer, primarily as a funder of research at universities and other nongovernmental research institutions. Those entities own the discoveries, determine the appropriate IP protection, decide the best terms and partners for specific technology transfer efforts, and transfer technology as they deem appropriate, without interference from Washington. This model has worked extraordinarily well and successfully. Thus, the goal of NIH's present initiative should be "First, do no harm."

Bayh-Dole is intended to move taxpayer-funded discoveries from concept to commercial use. This law employs the certainty of IP rights in the resulting inventions to foster practical benefit from federally funded basic research. Each technology, license, and licensee face specific circumstances that affect the pace of commercialization and progress in achieving milestones. It is crucial to understand that royalties are the principal payment for the licensee to use the technology. As is widely recognized, the beauty of Bayh-Dole is that it puts incentives such as royalties in the right place, where these payments reward inventors and researchers and fund additional research. Such patent-centered, democratized decisionmaking directly bears

[1] Phyllis Schlafly was an outspoken advocate of the rights of inventors, emphasizing the importance of their traditional rights to our national prosperity and security. She wrote often about this topic. A compilation of her writings on this subject is *Phyllis Schlafly Speaks, Vol. 4, Patents & Inventions*. Skellig America, 2018 (Ed Martin, Editor).

upon technology transfer, translation, and resulting commercialization—and, therefore, end products.

March-In Rights

The Bayh-Dole Act includes a "march-in rights" provision. Its purpose is of an "in case of fire, break glass" nature. March-in is authorized, pursuant to statute, for very few, very narrow grounds. If initiated, patent holders whose inventions were derived from federally funded research and development (R&D) would have to issue a license for the IP to another. The specified grounds for such "march-in" licensing are when the patentee has failed to pursue timely commercialization of the invention, has not reasonably satisfied public health or safety needs, has failed to ensure the invention is substantially made in the United States, or can't meet or hasn't met specified federal requirements for public use. There is no legal authority under the Bayh-Dole Act for march-in to be used on the basis of a resulting product's price.

Counterproductively, activists seek to force unlawful application of this emergency-only measure for extra-statutory purposes. Their efforts risk injecting uncertainties and threaten to disrupt technology transfer and commercialization. We applaud NIH for consistently declining to misuse Bayh-Dole's march-in provision, as sought in several rejected product-price-based petitions over the decades. Yet, activists continue to play on people's emotions and gain unwarranted sympathy.

That Bayh-Dole omits price of products from the few grounds for march-in is intentional. The law's authors, Senators Birch Bayh and Robert Dole, affirmed this fact in the Washington Post, where they rebutted the preposterous notion of march-in over product price that was first asserted in a law review article:

> Bayh-Dole did not intend that government set prices on resulting products. The law makes no reference to a reasonable price that should be dictated by the government. . . . The [law reviewers'] article also mischaracterizes the rights retained by the government under Bayh-Dole. The ability of the government to revoke a license granted under the act is not contingent on the pricing of the resulting product or tied to the profitability of a company that has commercialized a product that results in part from government-funded research. The law instructs the government to revoke such licenses only when the private industry collaborator has not successfully commercialized the invention as a product.[2]

[2] Birch Bayh and Robert Dole, "Our Law Helps Patients Get New Drugs Sooner," Washington Post, April 11, 2002, p. A28.

The futility of price-based march-in is displayed in the fact that a march-in license recipient would have to expend enormous resources to set up manufacturing, supply, distribution, and marketing channels—duplicating the patent owner's commercialization. The recipient of such a license would have to meet all applicable regulatory requirements. All that would come at great cost and time. It is questionable, therefore, whether such expense would achieve activists' product price aims.

NIH's CRADA Disaster

NIH briefly bowed to political pressure in 1989, when it required a "reasonable pricing" provision in its Cooperative Research and Development Agreements (CRADAs). This condition for an exclusive license to NIH-developed inventions inserted uncertainty, deterring interest by those who otherwise might license the IP. The price-control requirement resulted in NIH CRADAs dropping off from 42 in 1989 to 32 on average per year. The pricing clause's discouragement of industry partnerships eventually caused NIH to drop the CRADA requirement. Thereafter, NIH saw CRADAs increase to about 90 agreements in 1996 and more than 160 in 1997.

In removing the contract language, then-NIH Director Harold Varmus noted "the pricing clause has driven industry away from potentially beneficial scientific collaborations with [NIH] scientists without providing an offsetting benefit to the public. . . . Eliminating the clause will promote research that can enhance the health of the American people."[3]

Director Varmus further observed, "The [product pricing] clause attempts to address the rare breakthrough product at the expense of a more open research environment and more vigorous scientific collaborations. One has to have a product to price before one can worry about how to price it, and this clause is a restraint on the new product development that the public identified as an important return on their research investment."

This important lesson should not be lost on NIH, especially given the agency's 2021 confirmation of the chilling effect of its product-pricing requirement.[4]

Constructive Alternatives

NIH could take multiple steps to facilitate technology transfer and practical commercial benefit, thereby fostering more products from more patents. One, NIH should ensure

[3] NIH news release, April 11, 1995. Available at https://bayhdolecoalition.org/wp-content/uploads/2023/05/NIH-Notice-Rescinding-Reasonable-Pricing-Clause.pdf

[4] NIH, "The NIH Experience with the Reasonable Pricing Clause in CRADAs FY1990-1995," Nov. 15, 2021. Available at https://bayhdolecoalition.org/wp-content/uploads/2023/06/CRADA-QA-Nov-2021-FINAL.pdf

the ability of IP owners and licensees to rely on the IP exclusivity that is critical to achieving commercial success and that incentivizes private investors to assume the risk involved in bringing an invention to market. This means vigilantly making certain that march-in is never to be twisted into a means of enacting government price controls.

NIH could enact guidance or a rule warning that future march-in petitions on essentially the same grounds (i.e., product price) will be treated as a nuisance. Petitioners who assert the rejected basis could be barred from having similar, future petitions considered. Also, such nuisance petitioners could be charged the costs the petition had imposed on government resources, i.e., tapping taxpayers' money.

Two, partnering vehicles, such as CRADAs and SBIRs/STTRs, could permit a portion of the R&D funding to be used to secure IP protection. This would help more IP-centered startups gain commercial traction and more early-stage firms become going concerns faster. Such faster growth would expedite product and market development.

Three, NIH could adopt or strengthen a confidentiality duty that would require the agency and agency personnel not to disclose confidential, privileged, or proprietary information through the Freedom of Information Act (FOIA) or by other means. This policy would help assure contractors that the confidential business information in their submissions will remain secure and protected.

In conclusion, Bayh-Dole's march-in provision has never been invoked in the law's more than 40 years. Further, officials of both Democratic and Republican administrations have uniformly refused to base march-in on price. Bipartisan prudence rejecting this power's use on the basis of a product's price over four decades is strong evidence of the illegitimacy of activist petitioners' assertions to the contrary. Those public servants have found no basis in the law; that should be good enough.

Sincerely,

/s/ Ed Martin

Ed Martin
President

/s/ Andrew L. Schlafly

Andrew L. Schlafly
Counsel
939 Old Chester Rd.
Far Hills, NJ 07931
(908) 719-8608

/s/ James Edwards

James Edwards
Patent Policy Advisor

Submission Date: 7/26/2023

Name: Frank Cullen

Name of Organization: Council for Innovation Promotion

Comment:

Dear Director Jorgenson,

I hope you're doing well. I've attached comments from the Council for Innovation Promotion -- a bipartisan coalition dedicated to promoting strong and effective intellectual property rights that drive innovation, boost economic competitiveness, and improve lives everywhere -- on the 7/31 Office of Science Policy technology transfer workshop.

The Council for Innovation Promotion appreciates your attention to these important issues, and also the opportunity to share our views. Please contact me should you have any questions or require additional information.

Sincerely,
Frank Cullen

--

Frank Cullen
Executive Director, Council for Innovation Promotion

Additional Comment (attachment):

July 26, 2023

Lyric Jorgenson, PhD.
Office of Science Policy
6705 Rockledge Drive, Suite 630,
Bethesda, MD 20892

Dear Director Jorgenson,

C4IP is a bipartisan coalition dedicated to promoting strong and effective intellectual property rights that drive innovation, boost economic competitiveness, and improve lives everywhere. C4IP appreciates the opportunity to offer comments on the importance of strong intellectual property protections in leveraging the power of NIH-backed research to improve health outcomes and advance U.S. interests in other areas, such as national security.

C4IP stands second to none in our appreciation for the work scientists at the NIH do in advancing basic research. The knowledge gained through this work provides the foundation for partnerships with private-sector enterprises able to bring forth breakthrough medical advances from the research lab all the way to patients.

The work done at NIH is essential. But NIH itself has neither the charter nor the expertise to develop its work into commercial products such as FDA-approved life-saving medications. It is only through licensing arrangements with private companies possessing such experience and expertise that NIH research ultimately reaches the public in the form of new medical treatments and other useful products.

Through purchase agreements between the NIH and the private sector, for example, scientists at Pfizer and BioNTech were able to bring their breakthrough mRNA Covid vaccine to patients in record time. Treatments for HIV/AIDS, the hepatitis vaccine, and countless other products also trace their roots to NIH-licensed research.

But these roots do not mature and bear fruit on their own. They require careful nurturing. Intellectual property protection is the key to the continued success of this system.

Without secure patents and other IP protections, investors and private sector innovators will have insufficient incentive to pursue these risky and expensive research projects. These protections include the ability to sell the ultimate product developed out of patented technology at a price agreed to between the patent holder/developer and any buyer for as long as the patent is in effect.

Any restriction on this ability diminishes the value of a patent -- and, therefore, the willingness of any potential developer to license it and invest in it given the uncertain nature of any returns on the investment at all. Unfortunately, it is the case that many products will fail in the later stages of research and development. Indeed, approximately 90% of drugs don't make it through clinical trials to receive full approval.

Yet discounting that risk and undermining investment incentives is just what some advocates have in mind when they call for the inclusion of a "fair pricing" clause in licenses of NIH research for development. The ability of an outside party, in this case, the government, to decide whether the price of a developed consumer product is "fair" will not lead to less expensive consumer products but to an end to the willingness of private companies to license NIH or other government research discoveries for development (to say nothing over the likely and costly litigation over what is “fair and reasonable”). Government research will sit on shelves gathering dust, to the benefit of no one.

This is not a speculative conclusion but one borne out by the historical record. Past attempts at the NIH and elsewhere in government to institute similar "fair pricing" policies were ultimately repealed because they chilled private sector investment without "providing an offsetting benefit to the public."

Conversely, when policymakers act to preserve and strengthen our IP system, Americans reap the benefits in the form of new medical treatments and stronger national security, economic growth, and job creation. Fully 50% of yearly GDP growth in the United States comes from expanded innovation.

The partnerships forged between the NIH and the private sector transform valuable research findings into new medical treatments and commercial products. These partnerships are prime examples of the power of intellectual property to advance public health and encourage commercialization that benefits all Americans.

The system as currently constituted works well, not least because of its stability and predictability. NIH should not leave the door open to ongoing uncertainty through further consideration of "fair pricing" or other measures that would undermine intellectual property protection. On the contrary, NIH should close that door firmly to ensure Americans continue to enjoy the fruit of government research through private-sector development.

The Council for Innovation Promotion appreciates your attention to these important issues, and also the opportunity to share our views. Please contact me should you have any questions or require additional information.

Sincerely,

Frank Cullen
Executive Director
Council for Innovation Promotion

Submission Date: 7/26/2023

Name: James Edwards

Name of Organization: Conservatives for Property Rights

Comment:

Attached please find comments from the coalition Conservatives for Property Rights (CPR) regarding the National Institutes of Health's (NIH) July 31 "Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer."

Kindest regards,

James Edwards

Additional Comment (attachment):

Conservatives
for
Property Rights

July 26, 2023

National Institutes of Health
VIA EMAIL: SciencePolicy@od.nih.gov

RE: Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer

To whom it may concern:

Conservatives for Property Rights (CPR), a coalition of policy organizations representing thousands of Americans, writes in response to the National Institutes of Health's (NIH) request for comments in connection with the "Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer."

CPR acknowledges NIH's taking stock of "policies and practices that shape biomedical innovation and promote access to NIH-funded discoveries." We recognize that NIH has a "role in the broader biomedical research enterprise in promoting the application of knowledge to enhance human health." In NIH's consideration of "how NIH, as a research institution, approaches the patenting and licensing of biomedical inventions," CPR cautions the agency to consider what is working and keep in mind how shifts away from what is working are likely to be steps backward, causing unintended consequences. Failing to proceed with caution in this exercise would have serious, counterproductive effects that harm patients, weaken our economy, and even give adversarial competitors such as China an advantage in technological leadership.

NIH's Sweet Spot

NIH has an important role in biomedical research as a funder of basic research. NIH grants and its in-house biomedical research advance understanding of scientific and biomedical concepts and relationships. While some may be patentable, these initial discoveries are typically not readily translatable and certainly not ready for commercialization. Rather, NIH's or NIH-funded discoveries require orders of magnitude greater funding in applied research and development (R&D) to have a prospect for a commercial product.

The latter stages appropriately rely on private investment because the failure rate is approximately 9 out of 10. One study reported it "underscore[d] that the development of basic discoveries requires substantial additional investments, partnerships, and the shouldering of financial risk by the private sector if therapies are to materialize as FDA-

approved medicine."[1] For NIH to assume the enormous risk of failure that comes with development of the basic research discoveries, where its investment is more fertile, would be the height of misuse of taxpayer money.

NIH should stay in its lane underwriting basic research. This is NIH's most effective, efficient means of transforming discoveries into products. NIH's core competency (grantmaking) seeds basic scientific discoveries, which in turn hold promise for more technology, whose patents and intellectual property (IP) are held by grantees (universities and research institutions), to transfer. More embryonic technologies actively being commercialized means more products and more competition. More consumer choice and competition constrain product price increases, even before patent expiration. This indirect role on NIH's part in product and market development make the best use of taxpayer dollars and produce the best prospects of technology transfer and commercialization efforts succeeding.

IP and Bayh-Dole

IP ownership and having more IP-protected technology incentivize institutions to transfer inventions to willing entities capable of attempting commercialization. The key to this success is secure, reliable IP rights.

The 40-plus year experience of the Bayh-Dole Act of 1980 bears recounting. Bayh-Dole solved the problem of wasted expenditure of taxpayer money. Prior to Bayh-Dole, federally funded research led to many discoveries. The U.S. government owned 28,000 patents from research it funded. But only 5 percent were commercialized. Taxpayers received no practical benefit from all the research for which their taxes paid.

Pre-Bayh-Dole, the government tightly controlled the IP from its funded research in Washington, D.C. Some 26 agencies' rules controlled commercial use of federally owned IP. Grantees often were not allowed to take title of their discoveries. The government only gave nonexclusive licenses to patents. Thus, very little new knowledge was ever transformed into products.

This success-story law changed all that failure. It has facilitated commercialization by providing reliable property rights. Bayh-Dole has unleashed thousands of inventions that otherwise would have never moved to commercial application.

---

[1] Duane Schulthess, Harry P. Bowen, Robert Popovian, Daniel Gassull, Augustine Zhang, and Joe Hammang, "The Relative Contributions of NIH and Private Sector Funding to the Approval of New Biopharmaceuticals," Therapeutic Innovation & Regulatory Science, January 2023; 57(1):160-169.

For instance, university inventions bring about more than two new products and two jobs every single day.[2] Bayh-Dole made possible the creation of the biotech industry. Its decentralized tech transfer has contributed $1 trillion to U.S. GDP from 1996-2020. Its patent licensing is responsible for about $2 trillion of industry gross output and supports 6.5 million jobs.[3] In the 1970s, most medicines Americans used were developed in Europe; since Bayh-Dole, the United States leads the world in drug discovery, R&D, commercialization, and the development of new innovative medicines.[4]

The stark contrast between the pre-Bayh-Dole barriers and central command-and-control policies, resulting in radically stunted benefits from the millions and millions of taxpayer dollars poured into research over four decades, and the post-Bayh-Dole democratization of ownership and IP decisionmaking by grant recipients over the fruits of their labors, must not be missed. The difference is night and day. Bayh-Dole spurs widespread invention; efficient, smart technology transfer and commercialization; and the outpouring of new products, startup companies, new jobs, invigorated innovation ecosystems across the country, and even new industries.

The Bayh-Dole Act provides the government "march-in" rights in certain narrow, extraordinary circumstances. March-in would require the patent owner or exclusive licensee to issue a license to the patented invention. The statute specifies the grounds for such march-in licensing: when the contractor has failed timely to pursue commercialization of the invention, has not reasonably satisfied public health or safety needs, has failed to ensure the invention is substantially made in the United States, or can't meet or hasn't met specified federal requirements for public use. None of these extremely limited exceptions for "march-in" relates to product prices. In more than 40 years, march-in has never been exercised despite a number of petitions requesting it. In denying march-in petitions, NIH has always acted appropriately and in accord with the statute. NIH has repeatedly, consistently declined the requested misuse of march-in. CPR commends this fidelity to the spirit and letter of this important law. We urge NIH to resolve to continue doing the right thing as the agency has heretofore done.

Catalyzing Technology Transfer

Again, NIH has far less involvement in technology transfer, where decisionmaking was revolutionized when Bayh-Dole democratized technology transfer decisionmaking to the grantee institutional level and away from Washington. Because

---

[2] Eagle Forum Education & Legal Defense Fund, summary of remarks by Joseph P. Allen, "Benefiting from Federal Research Funding: Technology Transfer, the Bayh-Dole Act, Patent Rights, and Society," Proceedings of Capitol Hill Briefing, Oct. 18, 2018, p. 5.

[3] AUTM and BIO, "The Economic Contribution of University/Nonprofit Inventions in the United States: 1996-2020," June 14, 2022.

[4] Stephen Ezell, "The Bayh-Dole Act's Vital Importance to the U.S. Life-Sciences Innovation System," Information Technology & Innovation Foundation, March 4, 2019.

of the localized prerogative to decide whether to obtain IP protection and how best to license it, this now properly locates and brings about the most effective, informed commercialization decisions.

As discussed, the benefits of the Bayh-Dole regime could hardly be clearer. Thus, NIH's (or any other federal government agency's) interference in or imposition of inadvisable conditions on IP, technology transfer, or commercialization would cause tremendous damage to the turning of discoveries into products and beyond.

NIH's policy levers to catalyze tech transfer include licensing commercially promising discoveries made by NIH researchers. This should be done efficiently, with minimized red tape, in keeping with Bayh-Dole's framework. In that context, NIH could seek to ensure that its policies and practices are user-friendly, "speed-of-business" for federal agency tech transfer processes and procedures. The agency should make certain that any such levers enable partnerships for translational R&D, technology maturation, and commercialization under existing partnership mechanisms (e.g., SBIR/STTR, CRADA).

With respect to CRADAs and other licensing vehicles and in light of the vast majority of public participants given speaking slots at the workshop, it is imperative that NIH remember and not forget the lesson of its Cooperative Research and Development Agreement (CRADA) experience in the 1990s. In 1989, NIH began requiring a "reasonable pricing" provision in its CRADAs as a condition for an exclusive license to NIH-developed technologies. That price-control clause injected uncertainty, diminished intellectual property value, and undermined property rights over eventual products.

The "reasonable pricing" requirement caused a significant drop in NIH CRADAs, which fell from 42 in 1989 to an average of 32 the next six years. This dramatic fall-off led NIH to eliminate the provision. CRADAs with NIH immediately rose to about 90 agreements in 1996 and more than 160 in 1997. The agency confirmed this lesson in 2021.[5]

When the government price control was removed, NIH Director Harold Varmus said "the pricing clause has driven industry away from potentially beneficial scientific collaborations with [NIH] scientists without providing an offsetting benefit to the public. . . . Eliminating the clause will promote research that can enhance the health of the American people." New price controls today would do the same harm. Instead of catalyzing tech transfer or turning discoveries into products, NIH would repeat the failures of the past and radically diminish the stated aim of this exercise.

In closing, CPR applauds the successes NIH has had in technology transfer, particularly by funding research at research institutions and universities and respecting the

---

[5] NIH, "The NIH Experience with the Reasonable Pricing Clause in CRADAs FY1990-1995," Nov. 15, 2021. https://www.techtransfer.nih.gov/sites/default/files/CRADA Q&A Nov 2021 FINAL.pdf

boundaries of Bayh-Dole. We urge NIH to stay true to its lane and abide by the law. We urge rejection of the siren song of government price controls, "reasonable pricing," abuse of march-in, and any other scheme that would violate the provisions of the Bayh-Dole statute and ignore the clear lessons of secure IP held by grantee institutions, inventors, or licensees.

Sincerely,

James Edwards, Ph.D.
Executive Director
Conservatives for Property Rights

Kevin L. Kearns
President
U.S. Business & Industry Council

James L. Martin
Founder/Chairman
60 Plus Association

Saulius "Saul" Anuzis
President
60 Plus Association

George Landrith
President
Frontiers of Freedom

Gerard Scimeca
Chairman
Consumer Action for a Strong Economy

Dick Patten
President
American Business Defense Council

Ashley Baker
Director of Public Policy
The Committee for Justice

Richard Manning
President
Americans for Limited Government
Americans for Limited Government Foundation

Submission Date: 7/26/2023

Name: Joseph P. Allen

Name of Organization: Bayh-Dole Coalition

Comment:

Dear Director Jorgenson,

My name is Joseph P. Allen, and I serve as executive director of the Bayh-Dole Coalition. The Bayh-Dole Coalition is a diverse group of research and innovation-oriented individuals and organizations committed to preserving the Bayh-Dole law, and informing policymakers and the public of its many benefits.

I am submitting the attached comments on behalf of the Bayh-Dole Coalition to the NIH ahead of their workshop: "Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer." Please let me know if you need any additional information and I look forward to the upcoming workshop.

Best,
Joseph P. Allen

--

Joseph P. Allen
Executive Director

Additional Comment (attachment):

July 26, 2023

Lyric Jorgenson, Ph.D.
NIH Office of Science Policy
6705 Rockledge Dr #750
Bethesda, MD, 20817

Dear Director Jorgenson,

The Bayh-Dole Coalition appreciates the opportunity to submit comments to the National Institutes of Health (NIH) in advance of the agency's workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer on July 31, 2023.

Perhaps the easiest way for the NIH to continue promoting successful technology transfer is to uphold the agency's longstanding commitment and respect for the Bayh-Dole Act of 1980. Partnerships under Bayh-Dole have made the U.S. the unquestioned leader in the life sciences. When the Covid-19 pandemic hit, the world looked to us for a solution, and we didn't let them down. NIH should be very proud of your role in that achievement.

As you are aware, NIH advances America's scientific progress and well-being not only by conducting research in its own labs, but also by funding R&D at universities and nonprofits across the country. For over 40 years, resulting discoveries have been turned into breakthrough therapies thanks to the Bayh-Dole Act. The law gives universities, small companies, and federal laboratories the ability to retain the patents on their discoveries and license them for their development and commercialization. That process is extremely risky and expensive. Most times even the best efforts fail. When they do, companies take the hit. But under our system, taxpayers receive a tremendous return on their investment in public research in the form of life-saving and life-improving technologies, medical devices, and drugs, benefitting people here and around the world.

We should keep in mind the critical factor in our success—finding private sector companies, primarily small businesses, which are willing to assume the risk and expense of turning NIH-supported inventions into useful therapies. As you know all too well, many times it is very difficult to attract even one company as a potential licensee because most of the resulting discoveries are at such an early stage. It was to help bridge this gap that NIH created your newest institute, the National Center for Advancing Translational Sciences, which states the realities you all face very well: "A novel drug can take 10 to 15 years and more than $2 billion to develop, and failure rates occur in about 95 percent of human studies." (https://ncats.nih.gov/about). Many academic institutions have created programs to move their technologies further down the R&D pipeline, reducing the risk of development for their industrial partners. Finding effective means to lessen the risk of developing new therapies would be the most significant improvement we could make to increase the impact of NIH-funded R&D.

More times than not, the companies who take on the burden of commercializing NIH-funded inventions are entrepreneurial start-ups, which risk everything to get a product to market. These are also the entities which should be consulted about how NIH is performing and where improvements can be made.

As you consider today's recommendations, it would be well to keep in mind this criteria for evaluating the comments you are receiving -- does this make it easier or harder to find industry partners which drive our innovation system?

It might also be well to keep in mind why the Bayh-Dole Act has worked day in and out for 43 years. When we were creating the law, we didn't go to people with theories, we went to people with decades of hands-on experience funding and managing federally-funded inventions. Indeed, the experience we particularly drew upon was that of NIH. Two of the principal architects were Norman Latker, NIH's patent counsel, and Howard Bremer of the Wisconsin Alumni Research Foundation, one of the creators of the profession of academic technology management. Both Latker and Bremer knew from personal experience why the pre Bayh-Dole era failed to commercialize NIH-funded inventions and how to create the authorities and incentives to correct the problem. The resulting success of the Bayh-Dole Act and its extension to the federal laboratories through the Federal Technology Transfer Act (which Latker wrote) speaks for itself.

Thus, you would do well to put the recommendations you are receiving into two buckets -- one for those with theoretical knowledge and another for those who have actually licensed, managed, and most importantly, commercialized federally funded inventions. Hopefully, it goes without saying which bucket deserves greater weight.

More than any other agency, NIH should be commended for preserving Bayh-Dole. NIH has consistently rejected attempts to undermine the law through the misuse of "march-in" rights by opponents who claim it allows the government to set prices on successfully developed products. As someone who was in the room when Bayh-Dole was conceived, who staffed the bill for Senator Birch Bayh, putting together the hearings of the Senate Judiciary Committee, writing the Committee's report on the legislation, and later overseeing its implementation at the Department of Commerce, I can say with some authority that is not how the law works. But you don't have to take my word for it. Every Administration which has received petitions to "march in" for price controls has rejected them as not sanctioned under the statute. The Biden Administration is only the latest to confirm that view.

NIH deserves considerable credit for your steadfast commitment to the rule of law, even though incredible political pressures have been applied against you. Some of you have even been attacked personally for not giving in to those who seek to overturn Bayh-Dole. At a time when many have lost faith in our institutions, your conduct illustrates what public service is all about.

Now those who oppose Bayh-Dole have disinterred a failed policy last seen in the 1990s. Then bowing to political pressures, NIH inserted "reasonable pricing clauses" stipulating how resulting products would be priced if they were based on inventions arising from its Cooperative R&D Agreements (CRADAs) or exclusive licenses. Contrary to the predictions of its proponents, this provision didn't lower drug costs -- it collapsed industry partnerships.

Realizing the disaster unfolding before its eyes, NIH scrapped this policy in 1995 declaring "the pricing clause has driven industry away from potentially beneficial scientific collaborations with PHS [public health service] scientists without providing an offsetting benefit to the public." The number of CRADAs increased fourfold in the years following that repeal. NIH knows firsthand that "reasonable pricing" provisions are

counter-productive. They will only deny the public access to new discoveries protecting the public health.

Our system works. It deserves to be preserved and defended. Hopefully, today's exercise will help make NIH commercialization even more effective. The Bayh-Dole Coalition stands ready to help achieve that goal in any way that we can.

Again, thank you for all that you have done -- and continue to do -- to protect and defend public health.

Thank you,

Joseph P. Allen
Executive Director
Bayh-Dole Coalition

Submission Date: 7/27/2023

Name: Walter Copan

Name of Organization: N/A

Comment:

Dear Director Jorgenson:

Thank you for the opportunity to submit comments regarding the National Institutes of Health's forthcoming workshop, Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer.

These are attached. Best wishes for a productive workshop. Please fee free to reach out if I can provide additional support.

Kind regards,
Walt

Walter G. Copan, PhD
Vice President for Research and Technology Transfer

COLORADOSCHOOLOFMINES | https://research.mines.edu/

Additional Comment (attachment):

Walter G. Copan, Ph.D.
Vice President for Research and Technology Transfer
Colorado School of Mines
1500 Illinois Street, Golden, CO 80401

July 25, 2023

Lyric Jorgenson, Ph.D.
Acting Associate Director for Science Policy
National Institutes of Health Office of Science Policy
6705 Rockledge Dr #750
Bethesda, MD 20817

Dear Director Jorgenson:

Thank you for the opportunity to submit comments regarding the National Institutes of Health's forthcoming workshop, *Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer*.

I currently serve as the vice president for research and technology transfer at Colorado School of Mines. I am also the co-founder of the Renewing American Innovation Project at the Center for Strategic and International Studies, where I serve as a senior adviser.

From 2017 to 2021, I served as Under Secretary of Commerce for Standards and Technology and 16th Director of the National Institute of Standards and Technology (NIST), a position to which I was confirmed unanimously by the Senate.

I write to you in my personal capacity. The comments below do not necessarily reflect the views of my current or former employers or any organization with which I am affiliated.

For much of its history, the United States has been the most innovative country in the world. Our leadership is no accident. It is the direct result of a carefully constructed set of policies -- dating back to the nation's founding -- that protect intellectual property (IP) rights and incentivize the inventiveness of our citizens to push the boundaries of what is considered possible.

One of the most influential of these policies is the Bayh-Dole Act. Prior to Bayh-Dole's passage in 1980, U.S. scientists were making many important discoveries at universities and research laboratories with the help of federal research investments, including funding provided by NIH.

However, the government retained the patent rights to those discoveries -- and, for the most part, these inventions added no direct benefit to the people of America nor to the Nation’s economy. Of the 30,000 patents the government held as of 1980, only about 5% were licensed to innovative

companies that would ultimately turn them into products.[1] Further, due to the government's practice to principally grant non-exclusive licenses to federal inventions, firms were reluctant to take the risk to invest their capital for development, and entrepreneurs were unable to secure financing for their new companies, knowing that others could also readily access the same technology.

The Bayh-Dole Act of 1980 changed all of that. For the first time, the law allowed universities and research institutions to retain the rights to their federally funded discoveries -- and to have the opportunity to exclusively license these rights to private companies with the necessary expertise to bring them to market.

Bayh-Dole launched an entire era of U.S. global innovation and industrial competitiveness, catalyzing collaborations and technology transfer between public and private sector partners. This framework has been a driving force behind the nation's most innovative breakthroughs ever since. Between 1996 and 2021, exclusive licensing partnerships between academic institutions and private companies were responsible for launching 15,000 new startups and contributing $1 trillion to the U.S. GDP. Technology partnerships arising from federally funded inventions brought more than 200 new life-changing medicines to patients.[2]

The Bayh-Dole law works because it establishes key incentives for innovation and for private sector investment through reliable access to intellectual property rights. Without secure access to the necessary IP, investors simply will not take the high risk of investing in a firm or a technology lacking a protectable IP position. Most notably, the Bayh-Dole system incentivizes firms to enter into exclusive licensing agreements with academic and research institutions for early-stage inventions arising from federally funded research by allowing the institutions to own the patents on their inventions. This crucial incentive grants companies the opportunity to achieve a return on investment for successfully commercialized products stemming from the license, and from investing in related development collaborations.

It's imperative that agencies like the NIH, which is the single largest government funder of biomedical research in the world, uphold these incentives and the integrity of the Bayh-Dole Act.[3] Critically, the NIH must continue to resist pressure from the well-meaning but ultimately ill-informed parties and lawmakers, who do not understand the balanced workings of the U.S. innovation system, of the consequences of misusing Bayh-Dole to impose price controls on prescription drugs and other products that resulted, in part, from research supported by federal dollars. The Bayh-Dole Act allows federal officials to "march-in" and relicense patents in only an extremely limited set of circumstances, where the original licensee fails to diligently invest and turn the government-funded discovery into a real-world product available in the marketplace. But

[1] https://techtransfer.syr.edu/abouThe Bayh-Dole Act - Office of Technology Transfert/bayh-dole/
[2] https://bayhdolecoalition.org/wp-content/uploads/2023/04/Driving-the-Innovation-Economy-Academic-Technology-Transfer-in-Numbers-2021.pdf pg. 1
[3] https://www.nih.gov/about-nih/what-we-do/impact-nih-research/serving-society/direct-economic-contributions

certain individuals claim that even if a discovery has been developed into a successful product, and widely available, march-in is still justified if the price of that product is considered too high.

This premise is entirely false. The Bayh-Dole Act was never intended to be a mechanism for government price control, as the Act's authors made crystal clear.[4] The law's narrowly tailored march-in provision was meant to ensure that society benefited from discoveries made with the help of taxpayer dollars -- not to negate current exclusive licenses nor to empower the government to create a controlled economy.

Granting such misguided requests would severely damage confidence in U.S. intellectual property rights and our stock markets, and in the Bayh-Dole Act's protections that have sparked the creation of so many technological breakthroughs. Few companies would license inventions that came from even a penny of federal funding contribution if the government could simply nullify their exclusive license if the price of the resulting product is deemed by some party as unsatisfactory. Misusing march-in rights in this manner would undermine the successful public-private innovation pipeline that Bayh-Dole generated, and that the NIH and other agencies are striving to expand. The provisions of the Bayh-Dole Act enable American entrepreneurs and existing companies to create value for the people of the U.S. and contribute to our economic development and vitality. The consistent voice of NIH for U.S. innovation is important to be maintained at this time because the integrity of Bayh-Dole Act is not just an NIH and healthcare cost issue. The Bayh-Dole Act applies to all products, in all markets, from all U.S. federal science and technology investments. The inventions and national economic benefits arising from each federal agency's research funding would ultimately be affected by misuse of the Bayh-Dole Act, including the innovations arising from NIST, the agency I had recently led.

Fortunately, the NIH has consistently refused to go down the path to undermine the Bayh-Dole Act, and NIH has appropriately denied all march-in petitions that have come across its desk. NIH must remain resolute in upholding the Bayh-Dole Act to achieve its mission for the public good. March-in advocates have continued to call for this misuse of the law, and further recently called for the NIH to re-implement a "reasonable pricing" clause in NIH agreements, not just for Cooperative Research and Development Agreements (CRADAs) but "in all future collaboration, funding, and licensing agreements for biomedical research."[5] Any requests of this nature must also be denied -- or risk disastrous consequences for American innovation. At a crucial time for U.S. innovation and competitiveness, the Bayh-Dole Act bedrock of our innovation system must not be undermined.

This is not just a hypothetical concern. In 1989, the NIH inserted a "reasonable pricing clause" in the required language of its CRADAs and certain exclusive licenses.[6] The clause required companies engaged in CRADAs or exclusive licenses to set "reasonable prices" for any resulting commercial products.

[4] Birch Bayh and Robert Dole, "*Our Law Helps Patients Get New Drugs Sooner,"* Washington Post, April 11, 2002, p. A28.
[5] https://www.sanders.senate.gov/in-the-news/sanders-vows-to-oppose-nih-nominee-until-biden-produces-drug-pricing-plan/
[6] https://itif.org/publications/2019/03/04/bayh-dole-acts-vital-importance-us-life-sciences-innovation-system/

The well-intentioned "reasonable pricing" clause backfired miserably. Under the policy -- which created ongoing uncertainties of government intervention in the outcomes of high-risk R&D -- undermined the economic incentive of exclusive licensing. The result was an immediate dramatic decline of private sector partnerships with NIH research. The data was clear that public-private partnerships collapsed due to the risks of investment uncertainty. The private sector no longer saw that NIH research partnerships were worth the inevitable commercial risks. Just six years after it came into effect, NIH Director Harold Varmus declared that NIH had to scrap the "reasonable pricing" clause. In 1996, a year after the provision was repealed, the number of private sector CRADAs with NIH once again surged.

The U.S. has run this experiment – and I trust we have learned an important lesson about the underpinnings of our innovation system. The delicate balance between the early-stage federally funded research conducted by universities and research institutions and conditions for high risk late-stage development undertaken by the private sector relies heavily on the predictability of rules for IP rights provided in exclusive licensing. Without this essential component, the entire technology transfer framework unravels to the detriment of the American public. The U.S. otherwise steps onto a downward slope for government intervention and control in all markets, as the Bayh-Dole Act applies to funding from all federal agencies.

Indeed, during my time at the NIST, the agency published a roadmap for "Unleashing American Innovation" in the NIST Green Paper that had resulted from the nation's most comprehensive review ever of the U.S. innovation system. We concluded that federal officials must, among other things, better engage with the private sector, strengthen IP protections, incentivize technology transfer, and maintain the integrity of the Bayh-Dole Act.[7] Today, my recommendations for the NIH and for all federal science and technology agencies remain consistent. We must remember the vision of Vannevar Bush on the importance of national investment in *"Science: The Endless Frontier,"* and that of Senators Birch Bayh and Bob Dole, who saw the important incentive of reliable intellectual property rights as essential to America gaining a return on federal science investments for our people and for our economic prosperity.

I appreciate the opportunity to provide comments in support of these important discussions. I would be pleased to provide any further assistance and data in supporting your considerations.

Sincerely yours,

/ S / Walter G. Copan, Ph.D.

[7] https://nvlpubs.nist.gov/nistpubs/SpecialPublications/NIST.SP.1234.pdf pg. 5

Submission Date: 7/27/2023

Name: Stephen Heinig

Name of Organization: Association of American Medical Colleges

Comment:

Attached, please find written comments of the Association of American Medical Colleges for consideration at the NIH's July 31 workshop and for inclusion in the record.
Please let us know directly if further information would be helpful, or if there is any difficulty in transmission.
Thank you.

Stephen Heinig
Director, Science Policy
Association of American Medical Colleges

Additional Comment (attachment):

Association of
American Medical Colleges
655 K Street, N.W., Suite 100, Washington, D.C. 20001-2399
T 202 828 0400 F 202 828 1125
www.aamc.org

July 27, 2023

Lyric Jorgenson, PhD
Acting Associate Director for Science Policy
Office of Science Policy
National Institutes of Health
Bethesda, MD

Re: Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer

Submitted electronically to SciencePolicy@od.nih.gov

The Association of American Medical Colleges (AAMC) appreciates the opportunity to provide feedback to the National Institutes of Health (NIH) for the workshop, *Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer*.

The AAMC is a nonprofit association dedicated to improving the health of people everywhere through medical education, health care, medical research, and community collaborations. Its members are all 157 U.S. medical schools accredited by the Liaison Committee on Medical Education; 13 accredited Canadian medical schools; approximately 400 teaching hospitals and health systems, including Department of Veterans Affairs medical centers; and more than 70 academic societies. Through these institutions and organizations, the AAMC leads and serves America's medical schools and teaching hospitals and the millions of individuals across academic medicine, including more than 193,000 full-time faculty members, 96,000 medical students, 153,000 resident physicians, and 60,000 graduate students and postdoctoral researchers in the biomedical sciences. Following a 2022 merger, the Alliance of Academic Health Centers and the Alliance of Academic Health Centers International broadened the AAMC's U.S. membership and expanded its reach to international academic health centers.

The AAMC's member institutions perform more than half of the extramural research sponsored by the NIH, and the Association is mindful that the American people invest substantial resources in medical research, especially relative to other areas of science. While profound social and economic benefits accrue from scientific research generally, our advocacy in support of investment in the NIH emphasizes the potential for research discoveries to translate into new treatments and cures for disease. The topic of this workshop is therefore extremely important to fulfilling this promise, and to strengthening our shared, continuing commitment to the social contract supporting medical research. Our comments here focus on several points that we believe should frame productive discussions on catalyzing technology transfer:

I. While the workshop's deliberations necessarily focus on patenting and licensing practices, the most beneficial "product" of NIH research is the scientific knowledge generated and widely disseminated.

Once, a case needed to be made before the public for how laboratory basic research was relevant to advances in health and medicine, but now, after generations, there is a demonstrable track record – from virology to cancer to CRISPR – that discovery and shared understanding of fundamental biology has made nearly miraculous impacts on human health. Along with discovering new molecular entities and pathways that may become targets for pharmaceutical development, NIH-funded scientists have developed new research platforms, new techniques and methods, data resources, and insights into the mechanisms of health and disease. Behavioral and social science research have similar impacts on improvements to human health, although such advances may not typically be reflected in patentable inventions.

Another vitally important form of knowledge transfer are NIH-supported trainees and scientific personnel. Students and post-doctoral scientists at medical schools and universities, often with NIH funding, participate in the leading edge of scientific exploration, and carry this experience across to other economic sectors. Scientists and leaders in US industry and elsewhere are often the products of NIH support and provide the nation with an ample base of human capital to support medical innovation.

II. The current NIH innovation system has seen spectacular successes.

In a recent study, Stevens and colleagues identified 364 FDA-approved drugs and vaccines over more than 40 years to which specific intellectual property (IP) was held by public sector research institutions, including the NIH and US medical schools, universities, hospitals, and research institutions largely funded by NIH.[1] The tally does not include research platforms or similar resources developed by these institutions that enable drug discovery but were not identified with a particular approved drug. In comparing the relative success of the nation's drug development ecosystem, Stevens et al. noted:

> In the context of the global public sector landscape, the US dominates drug discovery, accounting for two-thirds of these drugs and many of the important, innovative vaccines introduced over the past 30 years. Contributions by Canada, UK, Germany, Belgium, Japan, and others each amount to 5.4% or less of the total.[2]

The persistence of disease and burden in so many areas, including orphan diseases, and in areas like addiction, depression, obesity, etc., challenge us to improve and catalyze the innovation process. But reforms should not undermine what has been shown to work well. The success during the pandemic of a public-private partnership building on decades of mRNA research to develop and deploy COVID-19 vaccines in record time, and avert potentially millions of deaths, should be an inspiration for future action.

---

[1] Stevens AJ, Benson DE, Dodson SE, Jensen JJ, Rohrbaugh ML. Role of global public sector research in discovering new drugs and vaccines. *Journal of Technology Transfer*, 2023, Apr 27, published ahead of print.
[2] Ibid, p. 1.

III. Intellectual property protections serve many uses, but an essential feature is that IP protections like patents make it possible for private capital to be used to develop a new pharmaceutical or device.

A promising new molecular entity or pathway discovered by academic researchers usually requires much more effort to be developed into an approved drug. Further R&D is required to assess the chemical properties of a drug candidate, to confirm its effectiveness, identify potential interactions and adverse events, and conduct the extensive preclinical and clinical testing necessary for FDA approval. It remains a notoriously expensive, time-consuming process that only a small percentage of promising drug candidates survive, and is therefore a very high-risk investment. Patent protection and exclusivity rights are necessary to attract the private investment that supports most drug development. Even philanthropic, non-profit organizations have used patents in this way; to simply put an entity in the public domain would likely ensure that it remains undeveloped, just as no contractor would build on a vacant city lot without clear title. That said, not every valuable entity or process needs to be patented; the AAMC has supported NIH positions on research tools, biological samples, genomic and other data sharing encouraging use of these resources with or without proprietary encumbrances as possible. The AAMC was also one of the original organizations drafting the Nine Points document on socially responsible licensing of university technology.[3]

The National Institute of Standards and Technology (NIST) within the Department of Commerce recently studied the entire federal system for promoting innovation, including looking at the implementation regulations for the Bayh-Dole and Stevenson-Wydler Acts, and other controlling authorities. The AAMC joined other organizations in this review, and we highly recommend the report for the NIH workshop deliberations.[4] Overall, we agree with the review that the Bayh-Dole Act has been highly effective in promoting tech transfer from sponsored, extramural research.

On the question of exercising Bayh-Dole's march-in authorities over pharmaceutical pricing, the AAMC has consistently supported the NIH and the Federal Government's interpretation of its authority, which we noted most recently in a joint letter with other higher education associations to Secretary Becerra last year.[5] The AAMC has three central concerns over the proposed use of march-in to influence drug pricing. First, the outcome from granting a march-in petition would be uncertain; any exercise over pricing would likely be challenged in the courts, given the legislative record and express statements by Senators Bayh and Dole that the Act's march-in provisions were not intended for inventions widely available on market. Moreover, march-in would not be a comprehensive solution to the problems of excessive drug prices, as it would apply only to the subset of drugs covered by university patents arising from NIH sponsored research, and to which no other significant IP applies. Price issues exist for many drugs that are not related to university patents, including many essential drugs that have been on the market for decades. Our third and most central concern is that the precedent of exercising march-in over market pricing would create disincentives for industry and private investors to license university inventions. In calculating potential risks and returns, private investors might favor non-university, non-NIH funded inventions, even if the target results are less

---

[3] https://autm.net/about-tech-transfer/principles-and-guidelines/nine-points-to-consider-when-licensing-university

[4] NIST. Return on Investment Initiative for Unleashing American Innovation. April 2019. https://nvlpubs.nist.gov/nistpubs/SpecialPublications/NIST.SP.1234.pdf

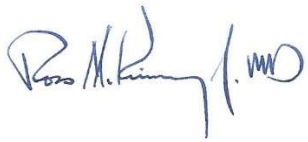
[5] https://www.aamc.org/media/61966/download?attachment

innovative. Rather than incentivizing tech transfer, the action would chill future licensing or industry collaboration, and undermine Bayh-Dole's intent.

In short, we are skeptical that pharmaceutical prices can or should be controlled from the laboratory and would look for alternative solutions to this problem. For example, the Inflation Reduction Act provides the Secretary of Health and Human Services the authority to negotiate drug prices under relevant sections of the Medicare program, and those negotiations are now in process. The USPTO and FDA are also looking at ways the patent system and approval process may be abused to indefinitely extend patent protections and impede the entry of generics to the market.

We are grateful for the opportunity to provide comments, and for continuing engagement with the research community. Please feel free to contact me or my colleagues Stephen Heinig, Director of Science Policy (sheinig@aamc.org) or Heather Pierce, JD, MPH, Senior Director of Science Policy and Regulatory Counsel (hpierce@aamc.org), with questions about these comments.

Sincerely,



Ross McKinney, Jr., MD
Chief Scientific Officer

cc: David J. Skorton, MD, AAMC President and Chief Executive Officer

Submission Date: 7/27/2023

Name: Adam Mossoff

Name of Organization: George Mason University

Comment:

Dear Director Jorgenson,

Please find attached my written comment for consideration by the NIH in its Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer.

If you have any questions, please feel free to contact me via email or by telephone at (703) 993-9577.

Best regards,

Adam Mossoff

Adam Mossoff
Professor of Law
Antonin Scalia Law School
George Mason University

Additional Comment (attachment):

GEORGE MASON UNIVERSITY
Antonin Scalia Law School
3301 Fairfax Drive, Arlington, Virginia 22201
Phone: 703-993-9577; Fax: 703-993-8088

Adam Mossoff
Professor of Law

July 27, 2023

Via Email Submission

Lyric Jorgenson, Ph.D.
Office of Science Policy
6705 Rockledge Drive, Suite 630
Bethesda, MD 20892

Re: Written Submission for Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer

Dear Director Jorgenson,

I respectfully submit this written comment to the National Institutes of Health (NIH) for consideration in the workshop, *Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer*. In support of evidence-based analysis and policymaking by the NIH, I have attached for consideration by the Office of Science Policy my article, *The False Promise of Breaking Patents to Lower Drug Prices*, ST. JOHN'S L. REV. (forthcoming 2023).[1]

My article explains why proposals for the NIH to use the Bayh-Dole Act or 28 U.S.C. § 1498 to impose price controls on patented therapeutics and diagnostics contradict the plain text and function of these two federal statutes. This is important for the NIH to consider in its workshop concerning tech transfer policies and licensing practices, because these "price-control theories of the Bayh-Dole Act and § 1498" have been asserted in numerous petitions to the NIH and in recent letters sent to the NIH by Senators Elizabeth Warren and Bernard Sanders.

Moreover, some speakers at the workshop, such as James Love, have incorrectly argued the price-control theories of the Bayh-Dole Act and § 1498 to the NIH and to other federal officials. Mr. Love has also mischaracterized federal contract regulations and provisions implementing § 1498, such as 48 C.F.R. § 52.227-1(a) (2020), as an alleged "compulsory licensing" mandate.[2] As I have

[1] This article is available for download at https://papers.ssrn.com/abstract=4348499.

[2] *See* In re COVID-19 Diagnostics and Therapeutics; Supply, Demand, and TRIPS Agreement Flexibilities, Investigation No. 332-596, at 62-63 (March 29, 2023) (Testimony of James Love).

explained in written testimony submitted to the International Trade Commission, this is incorrect.[3] Lastly, the mistaken view that Bayh-Dole or § 1498 authorize the NIH to enact regulations or engage in licensing practices to expand "access" through some form of price controls on patented therapeutics and diagnostics is proposed in a recent white paper, *Making Genetic Therapies Affordable and Accessible*, authored by many speakers at the workshop.[4]

To assist the NIH in evidence-based policymaking in implementing its specific powers granted under federal statutes and regulations in licensing patented therapeutics and diagnostics derived from upstream research supported in part by federal grants, I am submitting my article, *The False Promise of Breaking Patents to Lower Drug Prices*.

Thank you for your consideration. If you have any questions, please do not hesitate to reach out via email (amossoff@gmu.edu) or by telephone (703-993-9577).

Sincerely,

Adam Mossoff

/attachment

[3] *See* In re COVID-19 Diagnostics and Therapeutics; Supply, Demand, and TRIPS Agreement Flexibilities, Investigation No. 332-596 (May 5, 2023) (Final Written Submission of Adam Mossoff), https://edis.usitc.gov/external/attachment/795809-1992655.pdf.

[4] *See Making Genetic Therapies Affordable and Accessible* 42-43 (Innovative Genomics Institute, 2023), https://innovativegenomics.org/making-genetic-therapies-affordable-and-accessible/.

The False Promise of Breaking Patents to Lower Drug Prices

97 ST. JOHN'S LAW REVIEW __ (forthcoming 2023)

Adam Mossoff*

ABSTRACT

Congressional leaders, policy activists, and scholars contend that patents are a principal cause of rising drug prices. They argue that a solution exists in two federal statutes that allegedly authorize agencies to impose price controls on drug patents: 28 U.S.C. § 1498 and the Bayh-Dole Act. These "price-control theories of § 1498 and the Bayh-Dole Act" maintain that Congress has already endorsed the unprecedented and controversial policy of breaking patents to lower drug prices in private transactions in the healthcare market.

Neither § 1498 nor the Bayh-Dole Act authorize agencies to impose price controls, as confirmed by their plain text and by their interpretation by courts and agencies. Section 1498 is an eminent domain statute that applies only when a patent is used by and for the government, such for the military, the Post Office, or the Veterans Administration. The Bayh-Dole Act promotes commercialization of patented inventions derived from federal funding of upstream research; consistent with this commercialization function, this law specifies four delimited conditions when a federal agency may "march in" and license a patent when a patented product is not sold or available in the marketplace. Applying canons of statutory interpretation, the meaning of these two statutes is clear. Neither specifies that "price" triggers regulatory controls over private market transactions. Congress knows how to enact price-control laws, such as the Emergency Price Control Act of 1942 or when it specifies "reasonable price" as a goal of legislation. The price-control theories of § 1498 and the Bayh-Dole Act profess unprecedented agency powers lacking any authorization in existing statutes. Yet academic scholarship, as well as policy and legal work based on this scholarship, continue to promote the price-control theories of § 1498 and the Bayh-Dole Act. These are policy arguments masquerading as statutory construction.

* Professor of Law, Antonin Scalia Law School, George Mason University. Thank you to the participants at the 2022 Intellectual Property Scholars Conference at Stanford Law School for comments, and to attendees at many professional conferences and panel presentations over the past several years. Thank you also to Joseph Allen, Eric Claeys, and Joshua Sarnoff for comments on earlier drafts. A portion of this article is based on my comment submitted to the National Institute of Standards and Technology in April 2021 for its Notice of Proposed Rule Making for amending regulations implementing the march-in power in § 203 of the Bayh-Dole Act. Kent Hess, Peter Abernathy, Brandon Merrill, and Suzanne Johnson provided invaluable research assistance.

I. Introduction

The cost of medical care in the United States has long been debated in healthcare policy.[1] The causes of healthcare prices are complex and multi-varied, if only because the U.S. healthcare system is complex. The modern healthcare system comprises a myriad of legislative, administrative, and regulatory regimes enacted by the federal government and all fifty states, which are intertwined with equally complex commercial institutions built through private rights in property and contract.[2] In policy discussions about drug prices, though, some scholars and policymakers reduce this legal and institutional complexity to a single cause—patents.

The patent system is now at the center of policy debates and academic discussions about drug prices. Scholars blame patents for "rising drug prices."[3] Activists have filed at least ten petitions to federal agencies requesting that they break patents in order to lower drug prices in the healthcare market—petitioning the agencies to authorize through regulatory fiat a generic drug company to make and sell lower-priced drugs protected by patents owned by innovator drug companies.[4] These petitions have all been denied, with the most recent rejection on March 23, 2023 by the National Institutes of Health (NIH) in response to a petition seeking to impose price

[1] *See, e.g.*, *Consumer Group Decries Rise in Drug Prices*, LOS ANGELES TIMES (Mar. 16, 1995) ("Prices of the 20 top-selling prescription drugs are rising faster than inflation, despite drug company promises to slow the increases, a consumer group charged Wednesday."); *Uncertain Progress on Health Costs*, N.Y. TIMES, B20 (July 17, 1984) ("The Reagan Administration is declaring victory over 'the health care inflation monster' because medical costs are rising less feverishly. Any celebration, however, should wait until all the causes of the decline are better understood."); E. RICHARD BROWN, ROCKEFELLER MEDICINE MEN: MEDICINE AND CAPITALISM IN AMERICA 1 (1979) ("The crisis in today's health care system is deeply rooted in the interwoven history of modern medicine and corporate capitalism. The system's most obvious problems are cost, inflation, and inaccessibility of medical care in the United States.").

[2] *See* Douglas A. Hastings, *Foreword: The Changing Face of Law and Medicine in the New Millennium*, 26 AM. J.L. & MED. 135, 135 (2000) ("For over 200 years, our healthcare system has been, in effect, a mixed public and private system, essentially built on a private chassis with a great deal of public funding, regulating and prodding. It also has been a profoundly federalist system, generating fifty-one health regulatory schemes.").

[3] S. Sean Tu, *FDA Reexamination: Increased Communication Between the FDA and USPTO to Improve Patent Quality*, 60 HOUS. L. REV. (forthcoming 2022), at 2, https://papers.ssrn.com/abstract=4149718 ("Patients, doctors and insurers have all felt the distress of rising drug prices over the past decade. Underlying much of these cost increases are the exclusive rights granted by patents."); *see also* Hannah Brennan, Amy Kapczynski, Christine H. Monahan & Zain Rizvi, *A Prescription for Excessive Drug Pricing: Leveraging Government Patent Use for Health*, 18 YALE J. L. & TECH. 275, 277 (2016) ("Drug prices in the United States are among the highest in the world . . . . . [T]hey result from . . . our patent system . . . [and its] grant of a monopoly [that] allows a manufacturer to charge any price . . . ."); Amy Kapczynski & Aaron S. Kesselheim, *'Government Patent Use': A Legal Approach to Reducing Drug Spending*, 33 HEALTH AFFAIRS 791, 791 (2015) (claiming that "new medicines . . . are expensive not because they are expensive to manufacture but because they are protected by patents").

[4] *See Return on Investment Initiative for Unleashing American Innovation* 29 (NIST Special Publication 1234, April 2019) (identifying 10 petitions to break patents solely for the purpose of imposing price controls on drug patents).

controls on a patented drug that treats a prostate cancer.[56] A group of activists and academics also lobbied Congress to break patents in order to lower drug prices, arguing that drug prices "are high primarily because brand-name drug companies use government-granted exclusivities, such as patents, to prevent competition and charge high prices."[7]

These agency petitions and lobbying activities over several decades urging the federal government to break patents to lower drug prices assert that two federal statutes authorize this regulatory action. The first is a century-old statute that secures the right of patent owners to sue the federal government when it violates a patent right through its eminent domain power (28 U.S.C. § 1498).[8] Section 1498 requires the government to pay "reasonable and entire compensation" if a patented invention "is used or manufactured by or for the United States."[9] The second is the Bayh-Dole Act of 1980, a statute that declared definitively that inventors had a right to obtain patents if federal funding was used in the discovery or creation of their inventions.[10] To facilitate commercialization of new innovations, the Bayh-Dole Act affirmed that inventors whose research is funded even in part by the federal government may receive patents for their innovations.[11] In

[5] *See* Letter from Lawrence A. Tabak, Performing the Duties of the NIH Director, to Robert Sachs and Clare Love (Mar. 23, 2023), https://www.keionline.org/wp-content/uploads/NIH-rejection-Xtandi-marchin-12march2023.pdf (rejecting petition to impose price controls on Xtandi); *see also Return on Investment Initiative for Unleashing American Innovation*, *supra* note 4, at 29 ("NIH determined that the use of march-in to control drug prices was not within the scope and intent of its authority."); John R. Thomas, *March-In Rights Under the Bayh-Dole Act*, CONGRESSIONAL RESEARCH SERVICE 8-9 (Aug. 22, 2016), https://sgp.fas.org/crs/misc/R44597.pdf (As of 2016, "six petitions have been filed requesting that the NIH 'march in' with respect to a particular pharmaceutical. Each petition was denied. A common theme of each of the denials was the agency's views that concerns over drug pricing were not, by themselves, sufficient to provoke march-in rights.").

[6] *See* Letter from Clare Love & Robert Sachs to Xavier Becerra, Secretary of the Department of Health and Human Services 2 (Nov. 18, 2021), https://www.keionline.org/wp-content/uploads/Love-Sachs-HHS-Xtandi-Request-18Nov2021.pdf (proposing "a march-in request" for the drug, Xtandi, on the basis "that the price is demonstrably unreasonable"); Letter from Knowledge Ecology International and Union for Affordable Cancer Treatment to the National Institutes of Health, Department of Health and Human Services & Department of Defense 21 (Jan. 14, 2016), https://www.keionline.org/wp-content/uploads/Xtandi-March-In-Request-Letter-14Jan2016.pdf (making "march-in request" that "the federal government grant an open license to any generic drug manufacturer" due to "an excessive price" for Xtandi).

[7] Letter from Amy Kapczynski, Aaron S. Kesselheim, et al. to Senator Elizabeth Warren, at 1 (Apr. 20, 2022), https://tinyurl.com/yt62wt4t.

[8] *See* Decca Ltd. v. United States, 544 F.2d 1070, 1082 (Ct. Cl. 1976) ("It is [the government's] taking of a license, without compensation, that is, under an eminent domain theory, the basis for a suit under § 1498."); Carter-Wallace, Inc. v. United States, 449 F.2d 1374, 1390 (Ct. Cl. 1971) (Nichols, J., concurring) (stating that § 1498 authorizes a claim in court "to recover just compensation for a taking under the power of Eminent Domain"); Irving Air Chute Co. v. United States, 93 F. Supp. 633, 635 (Ct. Cl. 1950) (stating that § 1498 is "an eminent domain statute").

[9] 28 U.S.C. § 1498(a).

[10] *See* University and Small Business Patent Procedures Act of 1980, Pub. L. 96–517, 94 Stat. 3018 (Dec. 12, 1980) (codified in 35 U.S.C. §§ 200-212). This statute is popularly known as the "Bayh-Dole Act," as set forth in its Short Title. *See id.*, 94 Stat. at 3018.

[11] *See* 35 U.S.C. § 200 ("It is the policy and objective of the Congress to use the patent system to promote the utilization of inventions arising from federally supported research or development . . . to promote the commercialization and public availability of inventions made in the United States by United States industry and labor . . . .").

further promoting commercialization of patented inventions, the Bayh-Dole Act also authorizes federal agencies to "march in" and license a patent without authorization from the patent owner if the patented invention is not commercialized in the marketplace.[12]

Advocates for the price-control theories of § 1498 and the Bayh-Dole Act also make policy arguments, but these arguments are based on a core legal claim: the federal government has the existing statutory authority to lower drug prices by breaking patents on drugs.[13] In sum, the price-control theories of § 1498 and the Bayh-Dole Act maintain that Congress long ago resolved in the affirmative the debate over the highly controversial policy whether the federal government should impose price controls on drug patents. The only remaining policy question, its advocates contend, is whether federal agencies will act on their existing statutory authority.

This article addresses this purported *legal foundation* supporting the argument that breaking patents is the best governmental policy to lower drug prices. Contrary to claims of the price-control theories of § 1498 and the Bayh-Dole Act, these statutes do not authorize the federal government or any federal agencies to break patents solely for the purpose of lowering drug prices. This article derives this conclusion from the text of § 1498 and the Bayh-Dole Act and the consistent judicial and agency interpretations of these statutes. These statutory analyses are essential to the broader policy debates occurring in Congress and in agencies because these statutes define and delimit federal officials' authority to achieve policy goals. As the legal realists reminded us in the early twentieth century, policy arguments "empty without *objective description* of the causes and consequences of legal decisions."[14] They were speaking of court decisions, but this key insight applies equally to the objective description of the meaning of statutes.

In explaining why the price-control theories of § 1498 and the Bayh-Dole Act are a false promise to lower drug prices via price controls on patents, this article proceeds in three parts. First, it details the text and longstanding judicial interpretation of § 1498. Both its text and its interpretation by courts establish that § 1498 does not authorize the federal government to impose price controls on products manufactured and sold by private companies, such as drugs made by pharmaceutical companies and sold to patients in the healthcare market. This was confirmed by a district court's recent decision rejecting Moderna's attempt to use § 1498 as an affirmative defense from a patent infringement lawsuit brought against Moderna for its manufacture and use of its mRNA COVID-19 vaccine in the U.S. healthcare market.[15] Second, the article explicates the march-in provision of the Bayh-Dole Act, which is a more complex statute than § 1498, but the conclusion is the same: It does not authorize unprecedented agency actions to break drug patents

[12] *See* 35 U.S.C. § 203(a)(1)-(4).

[13] *See, e.g.*, Alfred B. Engelberg, Jerry Avorn, & Aaron Kesselheim, *A New Way to Contain Unaffordable Medication Costs – Exercising the Government's Existing Rights*, 386 N. ENGL. J. MED. 1104, 1104 (2022), https://www.nejm.org/doi/full/10.1056/NEJMp2117102 (stating that "existing laws" provide the government with the authority to lower drug prices and identifying § 1498 and the Bayh-Dole Act); Brennan, Kapczynski, et al., *supra* note 3, at 279 (claiming that "a legal remedy that has been hiding in plain sight" in § 1498 to lower drug prices).

[14] Felix S. Cohen, *Transcendental Nonsense and the Functional Approach*, 35 COLUM. L. REV. 809, 849 (1935) (emphasis added).

[15] *See* Arbutus Biopharma Corp. v. Moderna, Inc., No. CV 22-252, 2022 WL 16635341 (D. Del. Nov. 2, 2022).

to impose price controls on drugs manufactured and sold in the healthcare market. Similar to § 1498, the Bayh-Dole Act does not expressly authorize an agency to impose price controls on products produced and sold by private companies to private consumers in the marketplace, and it has never been used for this purpose. Such a power not only contradicts the commercialization function of the Bayh-Dole Act, it runs afoul of Supreme Court jurisprudence that unprecedented grants of power to an agency, such as imposing price controls on drug patents made and sold by private companies, must be expressly authorized by statute.[16] This construction of the march-in power in the Bayh-Dole Act is further confirmed by agency interpretations of this statutory provision over many decades, including the recent decision by the NIH not to invoke the march-in power on the patents covering Xtandi,[17] that have concluded that this statute does not authorize agencies like the NIH to impose price controls on drug patents.

II. As an Eminent Domain Statute, § 1498 Does Not Authorize Breaking Patents to Impose Price Controls on Private Transactions in the Marketplace

The price-control theory of § 1498 proposes to use this statute as an "important tool" to lower drug prices charged by private companies to private purchasers,[18] but § 1498 is not a price-control statute. It is an eminent domain statute based in nineteenth-century eminent domain cases in which the government directly used patented inventions without authorization of the patent owners. When the federal government did this, nineteenth-century courts responded by protecting patents as constitutional private property under the Takings Clause of the Fifth Amendment.[19] In one key case in 1876, the Supreme Court recognized that "[a]gents of the public have no more right to take such private property [in a patent] than other individuals" who may infringe a patent because the Constitution mandates that "[p]rivate property . . . shall not be taken for public use without just compensation."[20] In the early twentieth century, Congress enacted § 1498 to resolve confusion about the jurisdiction of courts to hear takings claims by patent owners, foreshadowing the enactment of the Bayh-Dole Act in 1980 to eliminate confusion about the patentability of inventions based in research supported by even a modicum of federal monies. The provenance of § 1498 is important, because it establishes that it is an eminent domain statute, as well established by court decisions, and thus its text precludes its use as a legal tool for imposing price controls on drug patents.

---

[16] *See* West Virginia v. Environmental Protection Agency, 142 S. Ct. 2587, 2609 (2022) ("[B]oth separation of powers principles and a practical understanding of legislative intent make us 'reluctant to read into ambiguous statutory text' the delegation claimed to be lurking there. . . . The agency instead must point to "clear congressional authorization" for the power it claims.") (citations omitted).

[17] *See supra* notes 5-6, and accompanying text.

[18] *See* Letter to Senator Elizabeth Warren from Amy Kapczynski, Aaron S. Kesselheim, et al., *supra* note 7, at 1.

[19] *See* U.S. CONST. amend. V ("[N]or shall private property be taken for public use, without just compensation."); Adam Mossoff, *Patents as Constitutional Private Property: The Historical Protection of Patents under the Takings Clause*, 87 B.U. L. REV. 689, 701-11 (2007) (discussing case law).

[20] Cammeyer v. Newton, 94 U.S. 225, 234-35 (1876).

A. Section 1498 is an Eminent Domain Statute

In the patent-takings cases in the nineteenth century, courts rejected numerous defenses by federal officials when called to account for their unauthorized uses of patented inventions. This included their arguments that patents are mere regulatory privileges that can be used by the government without authorization and that government officials are immune from lawsuits given sovereign immunity.[21] In rejecting a federal official's claim to sovereign immunity, one federal court held in 1879 that "[t]his property, like all other private property recognized by law, is exempt from being taken for public use without just compensation, by the supreme law of the land. Const. U. S. art. 5. . . . The property in a patented invention stands the same as other property, in this respect."[22] Unfortunately, the Supreme Court sowed confusion two decades later when the Court blithely stated in an 1894 decision that patent owners lacked a jurisdictional basis to sue the government for its unauthorized uses of their property.[23] Notably, the Court issued this decision without even acknowledging the existence of the earlier precedents in the lower courts and in its own decisions that patent owners had the right to sue the federal government for an unconstitutional taking of their property when officials used their patents without authorization.[24]

In 1910, Congress brought an end to this constitutional confusion by enacting § 1498 to reestablish the previously secure constitutional protection afforded to patents by the Supreme Court under the Takings Clause.[25] The House committee report for the bill that became § 1498 expressly stated that the federal government was using patents without authorization "in flat violation of [the Takings Clause] and the decisions of the Supreme Court."[26] During the congressional debates leading up to the enactment of § 1498, the bill's sponsor, Representative Currier, emphasized that the legislation "does not create any liability; it simply gives a remedy upon an existing liability."[27] (This is the same function of 42 U.S.C. § 1984 and 42 U.S.C. § 1988, which establish jurisdiction for a court to hear a constitutional claim and provide a remedy for a violation of a citizen's constitutional rights.) Throughout the debates in Congress in 1910, legislators repeatedly referenced the earlier Supreme Court decisions that had already secured to

[21] *See* Mossoff, *supra* note 19, at 701-11 (detailing the defenses against the takings or infringement claims).

[22] Campbell v. James, 4 F. Cas. 1168, 1172 (C.C.S.D.N.Y. 1879) (No. 2,361), *rev'd on other grounds*, James v. Campbell, 104 U.S. 356 (1881). Since the Supreme Court held on appeal that the patent is invalid, it did not reach the infringement or sovereign immunity issues as a matter of law. But the *James* Court still thought it important to state in dicta that the "exclusive property in the patented invention . . . cannot be appropriated or used by the government itself, without just compensation, any more than it can appropriate or use without compensation land." *James*, 104 U.S. at 358.

[23] *See* Schillinger v. United States, 155 U.S. 163 (1894).

[24] Justice Brewer's majority opinion and Justice Harlan's dissenting opinion in *Schillinger* clashed over the legal fiction of an "implied contract" that the Supreme Court had long employed to establish jurisdiction for courts to hear claims for unconstitutional takings of property in both real estate and patents under the enabling legislation that created the Court of Claims in 1855. But the majority opinion does neither acknowledges nor engages with any of the takings cases involving patents. *See* Mossoff, *supra* note 19, at 713 and n.130.

[25] *See* Act of June 26, 1910, ch. 423, 36 Stat. 851, 851-52 (1910) (codified as amended in 28 U.S.C. § 1498).

[26] H.R. REP. NO. 61-1288, at 3 (1910).

[27] Mossoff, *supra* note 19, at 712-13 (quoting 45 CONG. REC. 8755, 8756 (1910)).

patent owners their constitutional remedy under the Takings Clause.[28] In 1918, in the midst of federal procurement efforts with contractors, Congress amended § 1498 to provide jurisdiction to hear claims by patent owners for compensation when federal contractors infringe their patents.[29]

The text of § 1498 establishes that it is a jurisdiction-conferring statute for claims for compensation arising from exercises of the government's eminent domain power. Section 1498 states that a patent owner can sue the federal government in the Court of Claims (now-styled as the Court of Federal Claims) for "recovery of his reasonable and entire compensation" when a patented invention is "used or manufactured by or for the United States without license of the owner."[30] Judge Philip Nichols thus stated as a truism in a 1971 decision that § 1498 authorizes a court to hear a claim by a patent owner "to recover just compensation for a taking under the power of Eminent Domain."[31] A couple decades earlier, the Court of Claims succinctly stated in 1950 that § 1498 is "an eminent domain statute."[32]

B. Section 1498 Does Not Apply to Market Transactions Between Private Parties

As an eminent domain statute, the text of § 1498 provides that a patent owner may sue the federal government for "reasonable and entire compensation" when its patented "invention . . . is used or manufactured by or for the United States."[33] The nineteenth-century takings cases that underscored the enactment of this statute by Congress confirm that it applies to the classic case of an exercise of eminent domain by the federal government over a patented invention—the government acquires or uses a patented without authorization by the patent owner. Two such prominent nineteenth-century cases, for example, arose from the unauthorized use by the U.S. military of patented tents and patented cartridge (bullet) cases carried by soldiers.[34] The twentieth-century cases brought by patent owners under § 1498 are no different,[35] including a famous twentieth-century case arising from the U.S. military's unauthorized use of a patented battery during World War Two.[36] In sum, the plain text of § 1498 makes clear that it is not a grant of power to the federal government to impose price controls on products sold by private companies

[28] *See* Mossoff, *supra* 19, at 712 (citing H.R. REP. NO. 61-1288, at 1-4 (1910)).

[29] *See* Act of July 1, 1918, ch. 114, 40 Stat. 704, 705 (1918) (codified as amended in 28 U.S.C. § 1498).

[30] 28 U.S.C. § 1498(a).

[31] *Carter-Wallace, Inc.*. 449 F.2d at 1390 (Nichols, J., concurring).

[32] *Irving Air Chute Co.*, 93 F. Supp. at 635.

[33] *Id.*

[34] *See, e.g.*, United States v. Burns, 79 U.S. 246 (1870) (patented tents used during Civil War); McKever v. United States, 14 Ct. Cl. 396 (1878) (patented cartridge boxes).

[35] *See, e.g.*, *Hughes Aircraft Co. v. Messerschmitt-Boelkow-Blohm*, 625 F.2d 580 (5th Cir. 1980); *Hughes Aircraft Co. v. United States*, 534 F.2d 889 (Ct. Cl. 1976); *Croll-Reynolds Co. v. Perini-Leavell-Jones-Vinell*, 399 F.2d 913 (5th Cir. 1968), *cert. denied*, 393 U.S. 1050 (1969).

[36] *See* United States v. Adams, 383 U.S. 39 (1966). This is a famous patent case that is in many patent casebooks. *See, e.g.*, ROBERT P. MERGES & JOHN F. DUFFY, PATENT LAW AND POLICY: CASES AND MATERIALS 552-59 (7th ed. 2017).

to private consumers—it confers jurisdiction for a federal court to hear a lawsuit when a patented invention is "used or manufactured by or for the United States without license of the owner."

Despite this clear statutory text that a patented invention must be "used or manufactured" by the United States, a 2016 law journal article argued for a novel price-control theory of § 1498 as a solution to the problem of the "soaring cost" of drugs.[37] The scheme was both clever and simple: Congress enacts a law or a federal agency adopts a regulation that directs a private company to make and sell patented drugs at lower prices for private purchasers in competition with the owner of the drug patent. According to this argument, since the government authorizes the private company to sell the infringing drug at the lower price in the marketplace, the patent owner can only sue the federal government under § 1498 for compensation. It cannot sue the private company directly for patent infringement, because the federal government is the proximate cause of the patent infringement. In this lawsuit, a federal judge would set the "reasonable compensation" due to the owner of the drug patent that will be paid by the federal government. They argued that this "reasonable compensation" determined by a court would reflect a lower amount than the innovator would receive from sales of its patented drug, if only because it is a distinct remedy from the "lost profits" paid by infringing companies in run-of-the-mill patent infringement lawsuits between private companies. Thus, the federal government could impose price controls on drugs sold in the healthcare market with the price set at whatever federal judges think is "reasonable" compensation via a lawsuit against the government under § 1498.[38]

Perhaps recognizing that the government authorizing private parties to manufacture and sell products to private purchasers in the marketplace is not "used or manufactured by or for the United States," the proponents of the price-control theory of § 1498 also argue that federal agencies had done this before under § 1498 in the mid-twentieth century.[39] In an editorial, the *New York Times* repeated this claim that this has all happened before, and thus it can happen again, asserting that it was merely historical accident that the price-control theory of § 1498 "fell out of use."[40]

The problem with this "it's been done before" argument is two-fold. First, the text of § 1498 expressly authorizes lawsuits against the government only when an "invention . . . is used or manufactured by or for the United States."[41] In other words, the statute confers jurisdiction for lawsuits when the federal government exercises its eminent domain power, authorizing patent owners to receive "reasonable and entire compensation" for this unauthorized use—the patent law equivalent of the "just compensation" mandated by the Takings Clause. Even if federal agencies sporadically invoked § 1498 a few limited times during the initial decades of the nascent

[37] *See* Brennan, Kapczynski, et al., *supra* note 3, at 277.

[38] *Id.*; *see also* Joseph Adamczyk, Adrienne Lewis, Shivani Morrison, and Christopher Morton, *§ 1498: A Guide to Government Patent Use, a Path to Licensing and Distributing Generic Drugs* (Jan. 2021), https://dx.doi.org/10.2139/ssrn.3882823 (detailing similar proposal for the use of § 1498 to license generic drug companies to make and sell patented drugs at a lower price than that charged by the drug patent owner).

[39] *See* Brennan, Kapczynski, et al., *supra* note 3, at ___; Adamczyk, Lewis, et al., *supra* note 38, at ___.

[40] *How the Government Can Lower Drug Prices*, N.Y. TIMES (June 20, 2021), https://www.nytimes.com/2018/06/20/opinion/prescription-drug-costs-naloxone-opioids.html (repeating and endorsing the price-control theory proposed in the 2016 law journal article).

[41] *Id.*

administrative state and patent owners did not argue at the time that the agencies lacked authority under § 1498 to do this, these improper agency actions do not justify contradicting the plain statutory text today. As parents often remind their children: Two wrongs do not make a right.

Second, and perhaps more important, the claim by proponents of the price-control theory of § 1498 that the statute has been used in the past for this purpose is false. The federal government has not used § 1498 for the sole purpose of imposing price controls on *private companies* selling products to *private consumers* engaged in transactions in the marketplace. In a co-authored 2018 blog essay, we published the results of our own, independent review of the historical record on the use of this statute as alleged by the proponents of the price-control theory of § 1498.[42] The earlier agency actions that relied on § 1498 represented government procurement contracts, such as acquisition of medicines by the Veterans Health Administration of the U.S. Department of Veterans Affairs. This was not the scheme proposed by the price-control theory of § 1498 in which the federal government authorizes *private companies* to sell patented products or services solely to *private consumers* in the marketplace. In sum: "The historical record is absolutely clear that government agencies and courts have all applied § 1498 only to situations of government procurement and its own direct use. It has never been used to authorize private companies infringing patents for the sole purpose of selling the patented innovation to consumers in the free market."[43]

In a letter to Senator Elizabeth Warren in April 2022, advocates for the price-control theory of § 1498 broadened their argument that § 1498 should also apply to situations in which the use of the patented invention is merely for the general "benefit" of the government.[44] The letter derives this "benefit" language, not from the text of § 1498, but from a 2009 court opinion in *Advanced Software Design Corp. v. Federal Reserve Bank of St. Louis*, in which the court interpreted the phrase "by or for the United States" in § 1498.[45] In this case, the court held that regional Federal Reserve banks acted "for the government" when they used a process for detecting fraudulent Treasury checks that infringed a patent. The court concluded that "the benefits to the government of using the [patent-infringing fraud-detection] technology on Treasury checks are not incidental effects of private interests."[46] *Advanced Software* concluded that the patent owner had to proceed in its lawsuit against the federal government under § 1498, and not in a patent infringement lawsuit against the specific Federal Reserve bank. Given the formal relationship between the federal government and the Federal Reserve System in managing the official currency printed by the U.S.

---

[42] *See* Adam Mossoff, Sean O'Connor & Evan Moore, *Proposal for Drug Price Controls is Legally Unprecedented and Threatens Medical Innovation* (Nov. 5, 2018), https://cpip.gmu.edu/2018/11/05/proposal-for-drug-price-controls-is-legally-unprecedented-and-threatens-medical-innovation/.

[43] Adam Mossoff, Sean O'Connor & Evan Moore, *Proposal for Drug Price Controls is Legally Unprecedented and Threatens Medical Innovation* (Nov. 5, 2018), https://cpip.gmu.edu/2018/11/05/proposal-for-drug-price-controls-is-legally-unprecedented-and-threatens-medical-innovation/.

[44] *See* Letter from Amy Kapczynski, Aaron S. Kesselheim, et al to Senator Elizabeth Warren, *supra* note 7, at 37.

[45] *Advanced Software Design Corp. v. Fed. Reserve Bank of St. Louis*, 583 F.3d 1371, 1373-74 (Fed. Cir. 2009). Judge Braden and Joshua Kresh similarly describe *Advanced Software* and *Larson v. United States*, *see* Susan G. Braden & Joshua A. Kresh, *Section 1498(A) is Not a Rx to Reduce Drug Prices*, 77 FOOD & DRUG L.J. 274, 284-85 (2022).

[46] *Id.* at 1379.

Bureau of Engraving and Printing in the U.S. Department of Treasury, this decision makes sense, both legally and commonsensically.

The Federal Reserve System, however, is not the same legal or commercial entity as a private company that manufactures and sells a drug to other companies or patients in the marketplace. In fact, the *Advanced Software* court distinguished an earlier decision, *Larson v. United States*, whose facts are similar to the proposed scheme to lower drug prices under the price-control theory of § 1498.[47] In *Larson*, a patent owner sued a private medical company for infringing its patent on a medical device (a splint); the splints were paid through government programs such as Medicaid or Medicare, or at least the purchase price was reimbursed.[48] Given that "the government reimbursed the cost [of the infringing splint] through Medicare and other federal programs," the defendant argued that the patent owner's lawsuit must proceed against the government under § 1498.[49] The *Larson* court definitively rejected this argument, stating that "government reimbursement of medical care expenses did not constitute a *use* of a medical patent *for* government purposes," as required by the text of § 1498 in authorizing lawsuits against the federal government.[50] Seventeen years later, the *Advanced Software* court reaffirmed the holding in *Larson*, stating that "[t]he fact that the government has an interest in the [healthcare] program generally, or funds or reimburses all or part of its costs, is too remote to make the government the program's beneficiary for the purposes underlying § 1498."[51]

The interpretation of § 1498 by *Advanced Software* and *Larson* that it applies only to eminent-domain actions by the government in its own unauthorized use of patented technologies was confirmed in a recent decision in *Arbutus Biopharma Corp. v. Moderna*.[52] In this case, Arbutus sued Moderna for infringing Arbutus' patents covering mRNA technology when Moderna produced and sold its famous mRNA vaccine for COVID-19. Moderna filed a motion to dismiss on the basis of § 1498, arguing that the federal government purchased Moderna's mRNA vaccines in response to the COVID-19 pandemic through federal programs like Operation Warp Speed. Thus, Moderna argued that Arbutus was required to sue the federal government under § 1498 for its "entire and reasonable compensation," which precluded it from suing Moderna for patent infringement. In effect, Moderna argued that, since it "contracted with the Government for production and delivery of the vaccine for use in combatting the pandemic," it was immune from a patent lawsuit and Arbutus' real legal dispute was with the federal government, not Moderna.[53]

The *Arbutus* court rejected Moderna's argument because its production and sale of its mRNA vaccines was not "for the Government," as required by § 1498. Moderna's contract with the federal government did not provide that the advance purchases of vaccine doses was for the

[47] *See* Larson v. United States, 26 Cl. Ct. 365 (1992)

[48] *Id.* at 367-68.

[49] *Advanced Software*, 583 F.3d at 1379 (describing the defendant's argument in *Larson*).

[50] *Larson*, 26 Cl. Ct. at 369 (emphases added).

[51] *Id.* (quoting *Larson*, 26 Cl. Ct. at 369).

[52] *See* Arbutus Biopharma Corp. v. Moderna, Inc., No. CV 22-252, 2022 WL 16635341 (D. Del. Nov. 2, 2022).

[53] *Id.*, at *4.

benefit of and use by the government; rather, the purchase contract provided only that the government was making these advanced purchases of vaccines as part of a "whole of nation effort" in response to a "national emergency."[54] The *Arbutus* court concluded that Moderna's "development and sale of the vaccines was for the benefit of the vaccine's recipients," not for the benefit of the federal government.[55]At best, the court observed that "the U.S. Government was an *incidental beneficiary* who bore an interest in ensuring the safety of its citizens,"[56] not a *direct beneficiary* as required by § 1498 and the consistent interpretation of this statute by courts.[57] Several months later, the *Arbutus* court reaffirmed its interpretation of § 1498 in response to a surprise Statement of Interest filed by the Biden Administration in support of Moderna's earlier argument that § 1498(a) shielded it from a patent infringement lawsuit by Arbutus.[58]

In its first decision, the *Arbutus* court also recognized that "Moderna's argument . . . could mean that every government-funded product used to advance any policy goal articulated by the U.S. Government—such as IV needles to fight HIV to cancer drugs to fight the war on cancer—would be subject to a § 1498(a) defense."[59] Given the federal government's widespread funding and regulating of healthcare, Moderna's argument about the broad-based applicability of § 1498 would convert every patent infringement lawsuit arising from patents covering drugs or other healthcare treatments into a suit for compensation against the federal government for the exercise of its eminent domain power. This lack of any limiting principle in Moderna's interpretation of § 1498 is another key insight into the plain meaning of this statute: it does not apply when a drug is made by a private company for use by private citizens in the healthcare market.

In sum, *Larson*, *Advanced Software*, and *Arbutus* establish that general payment from the public fisc to a private party that infringes a patent is not sufficient by itself to qualify as a use of the patented invention "by or for the United States" under § 1498.[60] Given the extensive federal funding of a myriad of private activities far beyond biomedical research, a contrary decision would result in every private lawsuit being converted into a constitutional claim for compensation. It is not the function of § 1498 as an eminent domain statute to wipe out all private patent infringement

[54] *Id.*, at *5-*6 (quoting Moderna's contract with the federal government).

[55] *Id.*, at *7.

[56] *Id.*, at *7 (emphasis added).

[57] Since this was a ruling on a motion to dismiss, the *Arbutus* court was required to "accept as true the allegations of the Complaint," and this was an additional reason why the court ruled against Moderna's attempt to use § 1498 to dismiss the infringement complaint. *Id.*, at 7*. It is conceivable that additional facts might be introduced into evidence in the litigation that would lead the court to revise its analysis of whether the government is a direct beneficiary of the mRNA vaccine purchase contract, as opposed to an incidental beneficiary. Even if the court changed its decision, it would be on the basis of a key distinction between *direct* and *incidental* benefits to the government rooted in the text of § 1498 that it applies only to unauthorized uses of patents "for and by the United States," 28 U.S.C. § 1498, not uses for and by private companies selling to private consumers in the marketplace.

[58] *See* Arbutus Biopharma Corp. v. Moderna, Inc., No. CV 22-252, 2023 WL 2455979 (D. Del. Mar. 10, 2023).

[59] *Id.*

[60] *See Larson v. United States*, 26 Cl. Ct. at 368 & n.3. These judicial rulings are also consistent with agency guidance on government use of licensed rights in patented inventions under the Bayh-Dole Act, as discussed in Part Three below. *See, e.g.*, 32 C.F.R. § 37.860(b) (Bayh-Dole license does not include the right to practice the invention for commercial purposes).

lawsuits in which federal monies (or regulatory controls) create government interests in the private activities underlying the legal claims of patent infringement.

In conclusion, § 1498 does not apply to private commercial activities in which private companies manufacture and sell products for use by private parties in the marketplace. By its express terms, as confirmed by its interpretation and application by courts, § 1498 is an eminent domain statute that is limited to unauthorized uses of patented inventions by or for the federal government, such as use of patented inventions by the military or by federal agencies, such as the Veterans Administration. Even scholars who support more direct federal government regulation or control of the healthcare market have recognized this legal fact. In fact, one of the monographs relied on by those advocating for the price-control theory of § 1498 acknowledges that § 1498 must be "modified" if it is "to apply to governmental payment for drugs prescribed for beneficiaries of such federal health programs as Medicare and Medicaid."[61]

C. As an Eminent Domain Statute, § 1498 Mandates Full Compensation of the Market Value of a Patent that Vitiates Any Proposed Cost Savings

Even if the price-control theory of § 1498 did not contradict the text and judicial interpretation of this statute as implementing the constitutional limitations imposed on the eminent domain power of the federal government, the use of this statute to impose price controls on drug patents would likely create massive financial liabilities for the federal government. This follows logically from § 1498 as an eminent domain statute in which the government must pay "reasonable and entire compensation"—the patent law version of "just compensation" in the Takings Clause—when a patented invention is "used or manufactured by or for the United States without license of the owner."[62] In eminent domain law, courts have long construed the payment of "just compensation" as tantamount to payment of the *market value* of the property.[63] Similarly in patent law, the basic rule for the statutorily authorized payment of damages is to award *lost profits* to patent owner who is manufacturing and selling the patented invention.[64] Under the scheme proposed by the advocates of the price-control theory of § 1498, these remedies principles would direct courts to award patent owners their lost profits due to the lost sales of their drugs from the unauthorized manufacture and sale of the infringing drug.

---

[61] MILTON SILVERMAN & PHILIP R. LEE, PILLS, PROFITS, AND POLITICS 187 (1974). This monograph is cited in Letter to Senator Elizabeth Warren from Amy Kapczynski, Aaron S. Kesselheim, et al., *supra* note 7, at 2 n. 9.

[62] § 1498(a).

[63] *See* United States v. Miller, 317 U.S. 369, 374 (1943) ("In an effort . . . to find some practical standard [for awarding 'just compensation'], the courts early adopted, and have retained, the concept of market value.").

[64] *See* 35 U.S.C. § 284 (providing that "the court shall award the claimant damages adequate to compensate for the infringement"); General Motors Corp. v. Devex Corp., 461 U.S. 648, 654-55 (1983) ("Congress sought to ensure [in § 284] that the patent owner would in fact receive full compensation for 'any damages' he suffered as a result of the infringement."); Rite-Hite Corp. v. Kelley Co., 56 F.3d 1538, 1545 (Fed. Cir. 1995) (en banc) ("[T]he general rule for determining actual damages to a patentee that is itself producing the patented item is to determine the sales and profits lost to the patentee because of the infringement."); Del Mar Avionics, Inc. v. Quinton Instrument Co., 836 F.2d 1320, 1326 (Fed. Cir. 1987) ("The general rule for determining the actual damages to a patentee that is itself producing the patented item, is to determine the sales and profits lost to the patentee because of the infringement.").

The advocates for the price-control theory of § 1498 argue that lost profits for the market value of their property should not be the baseline for compensation, because they believe that courts should not award "monopoly" profits. Instead, they maintain that "reasonable and entire compensation" requires only the payment of a court-determined "reasonable royalty" that would reward drug innovators for their investments in creating the new medical treatment plus some additional compensation, such as reimbursement at marginal cost pricing.[65] This is incorrect for several reasons based in well-established, foundational remedies principles as implemented in patent law, in § 1498, and in Takings Clause jurisprudence.

First, as a matter of remedies doctrine in patent law, when a patent owner has not licensed its patent to others, awarding anything less than the patent owner's lost profits falls short of the statutorily mandated award of "damages adequate to compensate for the infringement."[66] In the foundational case on lost profits and reasonable royalties, *Panduit Corp. v. Stahlin Bros. Fibre Works*, the 6th Circuit held that it is improper for a court to set a reasonable royalty solely as "the equivalent of ordinary royalty negotiations among truly 'willing' patent owners and licensee," especially in the context of a patent owner that does not licensee its patents.[67] This would convert remedies doctrine into a tool for "competitors to impose a 'compulsory license' policy on every patent owner."[68] In such an approach, according to the *Panduit* court, "the infringer would be in a 'heads-I-win, tails-you-lose' position."[69] This contradicts the purpose of the remedies provision in the Patent Act and the general function of remedies law to make the plaintiff whole—to place the plaintiff in its rightful position *but for* the wrong committed by the violation of its rights.[70]

Second, as a matter of the "reasonable and entire compensation" requirement in § 1498, it courts will construe this as an award of lost profits in the scheme of the price-control theory of § 1498. In the last 38 years, the Federal Circuit has decided only four cases interpreting the compensation requirement in § 1498.[71] None of these cases arose from a situation in which an infringing product was sold in the marketplace by a private company competing directly with the patented product sold by the patent owner. (This reinforces the point from the prior section that § 1498 is applicable only to the use or manufacture of a patented invention for or by the federal government, and not for or by private companies.) If the government were to adopt the unprecedented price-control theory of § 1498, which would entail authorizing competing

[65] Brennan, Kapczynski, et al., *supra* note 3, at 307-18.

[66] 35 U.S.C. § 284.

[67] Panduit Corp. v. Stahlin Bros. Fibre Works, 575 F.2d 1152, 1158 (6th Cir. 1978).

[68] *Id.*

[69] *Id.*

[70] *See* Aro Mfg. Co. v. Convertible Top Replacement Co., 377 U.S. 476, 507 (1964) ("The question to be asked in determining damages is 'how much had the Patent Holder and Licensee suffered by the infringement. And that question (is) primarily: had the Infringer not infringed, what would Patent Holder-Licensee have made?'") (quoting Livesay Window Co. v. Livesay Industries, Inc., 251 F.2d 469, 471 (5th Cir. 1958)); *Rite-Hite Corp.*, 56 F.3d at 1545 ("To recover lost profits damages, the patentee must show a reasonable probability that, 'but for' the infringement, it would have made the sales that were made by the infringer.").

[71] *See* FastShip LLC v. United States, 892 F.3d 1298, 1310 (Fed. Cir. 2018); Paymaster Techs., Inc. v. United States, 180 F. App'x 942, 944–45 (Fed. Cir. 2006); Gargoyles, Inc. v. United States, 113 F.3d 1572, 1572 (Fed. Cir. 1997); Hughes Aircraft Co. v. United States, 140 F.3d 1470 (Fed. Cir. 1998).

commercial products sold by private companies in the marketplace, then a court would likely apply the same remedies doctrines as those they have applied for all other cases of patent infringement arising from the same commercial competition—applying the default rule of lost profits in construing "reasonable *and entire* compensation."[72] In fact, the Court of Claims has already acknowledged that "awarding lost profits" is a proper method for determining a reasonable royalty rate when a court must "appraise a patent license taken by the Government."[73]

Third, since § 1498 is an eminent domain statute,[74] courts may apply the remedies doctrines they have developed under the Takings Clause to the novel scenario in which the federal government instructs a private company to make and sell a drug without authorization from the patent owner. Takings Clause jurisprudence reflects the same remedies principles discussed above: the Supreme Court has held that a property owner should "be put in as good [a] position pecuniarily as he would have been if his property had not been taken."[75] In sum, property owners are constitutionally entitled to receive the market value of their property when it is taken from them by the government.[76] In the context of a drug patent, its market value is the profits earned by the company in selling the drug in the healthcare market, because a patent owner would not license a competitor without accounting for its lost profits from a new market competitor. Thus, an award of lost profits represents the market value that serves as the legal standard by courts in awarding "just compensation" under the Takings Clause in the Fifth Amendment.[77] As an eminent domain statute, it is reasonable for a court to look to the remedy principles applied under the Takings Clause in determining how to award the "reasonable and entire compensation" under § 1498 in the novel scenario of the federal government directing a private company to infringe a drug patent for its own profit through sales to private consumers in the healthcare market.[78]

In sum, the "reasonable and entire compensation" requirement in § 1498 would likely require compensating a patent owner for its lost profits in the novel legislative or regulatory scheme proposed by advocates of the price-control theory of § 1498. This would be in accord with the remedies principles already adopted by courts in patent law, in their interpretation of § 1498, and in the interpretation of the "just compensation" requirement under the Takings Clause—all of

[72] 35 U.S.C. § 284 (emphasis added).

[73] Decca Ltd. v. United States, 640 F.2d 1156, 1167 (Ct. Cl. 1980) (citing Imperial Mach. & Foundry Corp. v. United States, 69 Ct. Cl. 667 (1930)).

[74] *See supra* notes 8 and 25-32, and accompanying text.

[75] Seaboard Air Line Ry. Co. v. United States, 261 U.S. 299, 304 (1923) (citations omitted); *see also* United States v. 564.54 Acres of Land, 441 U.S. 506, 510 (1979).

[76] *See, e.g.*, United States v. 50 Acres of Land, 469 U.S. 24, 25 n.1 (1984); United States v. 564.54 Acres of Land, More or Less, Situated in Monroe & Pike Counties, Pa., 441 U.S. 506, 511 (1979).

[77] *See supra* note 63, and accompanying text.

[78] *See* Jones v. United States, 529 U.S. 848, 857 (2000); Almendarez-Torres v. United States, 523 U.S. 224, 237–38 (1998).

which seek to place a property owner in the rightful position it would have been but for the violation of its rights by awarding the owner the market value of its property.[79]

As a result, the price-control theory of § 1498 would not lead to a reduction in total drug costs—unless the federal government chose to massively subsidize the competing sales of drugs by paying the difference to the patent owner the profits it lost due to the unauthorized sales of the drugs. But such massive public subsidies would defeat the very purpose of the price-control theory of § 1498 in lowering drug prices. The legislative or regulatory scheme would become merely another cross-subsidy in which third parties would pay, through taxes or other means, the same costs of development of innovative, life-saving medicines as they had before the adoption of the scheme. In fact, it would be even more costly and inefficient, because now litigation costs would be an added transaction cost that did not exist before the price-control scheme.

D. The Price-Control Theory of § 1498 Creates Uncertainties, Additional Costs, and is Rife with Unintended Consequences

The potential for significant, additional costs in the scheme proposed by the price-control theory of § 1498 is worth highlighting as further evidence of how this policy proposal is not based in the plain meaning of the statute. As observed in the Introduction, the U.S. healthcare system is extremely complex given a myriad of legislative and regulatory regimes in both the federal and state govermments. The scheme to lower drug prices through the price-control theory of § 1498 is seemingly straightforward and surprisingly simple, at least as it is presented in hypothetical scenarios in academic articles, letters to Congress, or in the petitions to the NIH. But real-world legislation necessarily creates transaction costs in the institutional implementation of any new regulatory regime. In this respect, the price-control theory of § 1498 represents the "nirvana fallacy"—the comparison of a real-world institution with all its costs (real-world drug prices) with an idealized institutional arrangement that fails to acknowledge its own inherent transaction costs (the price-control theory of § 1498).[80]

The purpose of this section is to identify some of these legal and institutional complexities that necessarily create uncertainties, additional costs, and unintended consequences. It is not possible in a single section to identify all of the relevant legal and economic issues, but this is not necessary. The purpose is to identify how the price-control theory of § 1498, assuming for the sake of argument it is a legally authorized agency power, is not as simple and easy as it is portrayed by its advocates. Thus, it is sufficient to identify some institutional conflicts and accompanying costs in the panacea-sounding proposal to lower drug prices through the price-control theory of § 1498.

Unintended consequences and unacknowledged costs are well known in the patent system, especially given institutional changes in the patent system over the past several decades. One example is the Patent Trial & Appeal Board (PTAB), the new administrative tribunal to cancel

[79] *See* State Industries, Inc. v. Mor-Flo Indus., Inc., 883 F.2d 1573, 1577 (Fed. Cir. 1989) ("The measure of damages is an amount which will compensate the patent owner for the pecuniary loss sustained because of the infringement.").

[80] *See* Harold Demsetz, *Information and Efficiency: Another Viewpoint*, 12 J. L. & ECON. 1 (1969) (identifying and coining the "nirvana fallacy").

issued patents that was created in the America Invents Act of 2011.[81] Since the PTAB began operations in 2012, it has precipitated extensive legal and policy debate comprising regulatory disputes at the USPTO,[82] legislative bills proposed in Congress,[83] and six decisions by the Supreme Court in the PTAB's first decade of operation.[84] One would be hard pressed to identify a single administrative tribunal in the modern administrative state that has led to six separate Supreme Court decisions in a ten-year period. Another example is the institutional and legal regime for drug patents created by the Hatch-Waxman Act of 1984.[85] This law, which was enacted to lower drug prices, led to numerous, unforeseen legal disputes requiring resolution by the Supreme Court.[86] It also led to new regulatory actions by other agencies, such as the Federal Trade Commission.[87]

Given its direct function to promote faster generic drug entry into the healthcare market to lower drug prices, the Hatch-Waxman Act especially underscores the institutional and legal complexities that go unacknowledged in the price-control theory of § 1498. Congress enacted the Hatch-Waxman Act to reduce drug prices by creating a regulatory regime that results in faster entry into the healthcare market by generic drug companies competing with a drug innovator.[88] The Hatch-Waxman Act regime is a complex system of patent litigation, regulatory exclusivity, and approval of generic drugs by the Food and Drug Administration (FDA). It is too complex to describe succinctly, but a brief summary will suffice to establish its significance for this section.

Under the Hatch-Waxman Act, a generic company files an abbreviated new drug application (ANDA) with a "paragraph IV certification" at the FDA. An ANDA is filed while the

---

[81] *See* Leahy-Smith America Invents Act of 2011, Pub. L. 112-29, 125 Stat. 284 (2011) (codified in 35 U.S.C. § 6) (creating patent trial and review board).

[82] *See, e.g.*, Eileen McDermott, *General Counsels Ask Raimondo to Immediately Repeal* NHK-Fintiv *Framework*, IPWATCHDOG (Feb. 14, 2022), https://www.ipwatchdog.com/2022/02/15/general-counsels-ask-raimondo-immediately-repeal-nhk-fintiv/id=145968/; Britain Eakin, *Tech Giants Urge Fed. Circ. To Abolish 'Unlawful' Fintiv Rule*, LAW360 (Feb. 9, 2022), https://www.law360.com/articles/1463601/tech-giants-urge-fed-circ-to-abolish-unlawful-fintiv-rule; Ryan Davis, *Tech Cos. Back Apple High Court Bid to Ax PTAB's Fintiv Rule*, LAW360 (Aug. 31, 2021), https://www.law360.com/articles/1417615/tech-cos-back-apple-high-court-bid-to-ax-ptab-s-fintiv-rule.

[83] *See, e.g.*, Patent Trial and Appeal Board Reform Act of 2022, S. 4417, 117th Cong. (2022) (creating changes to the procedures at the PTAB); Restoring American Leadership in Innovation Act of 2021, H.R. 5874, 117th Congress (2021) (eliminating the PTAB); STRONGER Patents Act of 2019, S. 2082 & H.R. 3666, 116th Cong. (2019) (adopting numerous procedural and substantive reforms in the PTAB).

[84] *See* United States v. Arthrex, 141 S. Ct. 1970 (2021); Thryv v. Click-To-Call Technologies, 140 S. Ct. 1367 (2020); Return Mail v. USPS, 139 S. Ct. 1853 (2019); Oil States Energy Services, LLC v. Greene's Energy Group, LLC, 138 S. Ct. 1365 (2018); SAS Institute, Inc. v. Iancu, 138 S. Ct. 1348 (2018); Cuozzo Speed Techs., LLC v. Lee, 136 S. Ct. 2131 (2016).

[85] *See* Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984).

[86] *See, e.g.*, Federal Trade Commission v. Actavis, 570 U.S. 136 (2013); Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193 (2005); Eli Lilly & Co. v. Medtronic, Inc., 496 U.S. 661 (1990).

[87] *See* Federal Trade Commission v. Actavis, 570 U.S. 136 (2013).

[88] *See* Erika Lietzan, *The History and Political Economy of the Hatch-Waxman Amendments*, 49 SETON HALL L. REV. 53 (2018) (describing the enactment of the Hatch-Waxman Act and critiquing the conventional wisdom that this legislation was the result of Congress carefully balancing the interests of patent owners, generics, and the public).

drug patent is still in force and thus a specific function of the ANDA is to trigger patent infringement litigation between the drug innovator and the generic company. The lawsuit results in the usual patent infringement claims by the drug innovator and the panoply of affirmative defenses asserted by the generic company that the drug patent is invalid.[89] If the patent owner prevails in this litigation—demonstrating infringement by the generic drug company and defending the validity of its patent—the FDA then stays final approval of the ANDA until the patent expires. But the generic company may prepare its manufacturing facilities and ready commercialization of its generic version of the drug.[90] The generic company must also meet the FDA's safety and efficacy standards for generic drug approval. If it meets the FDA's safety and efficacy standards, once the patent expires, the generic company may immediately leap into the market and start selling the drug to patients and it is awarded with a period of "exclusivity" in which it will be the only generic company to compete with the drug innovator. This market exclusivity for the generic drug company is the reward for filing the first ANDA and traversing the costly patent litigation gauntlet. This Hatch-Waxman regime has been in place for four decades.

If an agency implemented the price-control theory of § 1498 in directing a generic drug company to sell a drug covered by a patent, it is unclear how this would function within the existing regulatory and litigation regime for drug innovators and generic companies under the Hatch-Waxman Act. The generic company submits an ANDA for approval to manufacture and sell a drug in competition with the drug innovator at the moment the patent expires, which is done for the purpose of lowering drug prices. The express goal of the Hatch-Waxman Act is the same goal as the price-control theory of § 1498: authorize a generic drug company to make and sell drugs to lower drug prices. If the price-control theory of § 1498 reflected the actual text and function of this statute, then a generic drug company would add an affirmative defense in its Hatch-Waxman litigation that the drug innovator cannot sue the generic company, because it must instead sue the federal government for "reasonable and entire compensation" under § 1498 (just as Moderna tried to argue that this is what Arbutus was required to do).[91]

How this new § 1498 defense would work within the overall Hatch-Waxman regime is unclear, creating significant uncertainty and extensive new litigation to resovle. These additional litigation costs would necessarily add to the costs of drug development and commercialization for drug innovators and to the costs of doing business by generic drug companies. These added costs would result in higher prices for medical care, including drugs.

The failure to account for the well-known Hatch-Waxman regime is just one example of how the price-control theory of § 1498 is no more based on a proper institutional assessment of the reality of drug patents and generic competition today than it is based in the text of § 1498 itself. These institutional and regulatory complexities should be acknowledged and accounted for with proper empirical studies. Without this proper institutional assessment of how the price-control theory of § 1498 would in fact be implemented within the existing institutions and laws governing

[89] 21 U.S.C. § 355(j)(5)(B)(iii).

[90] 35 U.S.C. § 271(e)(4)(A) ("[T]he court shall order the effective date of any approval of the drug or veterinary biological product involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed . . . ."); *see also* 21 U.S.C. § 355(j)(5)(B)(iii)(II)(bb).

[91] *See supra* notes 52-59, and accompanying text (describing Moderna's argument and the court's rejection of it).

drug patents, it has not proven that it will be cost effective compared to the "excessive drug pricing" by patent owners.[92] This is only one example of many institutions and laws implicated by the price-control theory of § 1498, demonstrating the extent to which this is truly a *theory*, not an evidence-based legislative or policy proposal.[93]

The price-control theory of § 1498 is a policy proposal lacking a basis in either the text or function of this eminent domain statute. It contradicts the express text of § 1498, it conflicts with the function of § 1498 in only conferring jurisdiction on the Court of Federal Claims to hear complaints by patent owners for compensation when an invention is used by or for the federal government in an exercise of the eminent domain power. Courts and agencies have consistently interpreted and applied § 1498 according to this plain text. Even if one assumes for the sake of argument that the price-control theory of § 1498 is legally viable, its advocates have not addressed the inherent institutional and legal complexities of their price-control scheme, such as how it would interrelate with the Hatch-Waxman Act and other legislative and regulatory regimes in the modern U.S. healthcare system. In sum, the price-control theory of § 1498 offers a false promise of breaking patents to lower drug prices.

III. The Bayh-Dole Act Does Not Authorize the Federal Government to Control Drug Prices

The search for legal authority authorizing the federal government to break patents to lower drug prices has led to the creation of a second price-control theory—the price-control theory of the Bayh-Dole Act of 1980. Similar to § 1498, the text of the Bayh-Dole Act and its consistent interpretation by federal officials militates against this price-control theory. In fact, the price-control theory of the Bayh-Dole Act was "unrecognized" from 1980 until two professors claimed to have discovered it more than two decades later in a law journal article in 2001.[94] Unlike § 1498, though, the Bayh-Dole Act is a more complicated statutory regime and thus it requires a more detailed exposition of its statutory function, the text that allegedly supports the price-control

[92] Brennan, Kapczynski, et al., *supra* note 3, at 275.

[93] Another statute that may be possibly implicated in the scheme to lower drug prices under the price-control theory of § 1498 is the Federal Acquisition Streamlining Act of 1994 (FARA). *See* Federal Acquisition Streamlining Act of 1994, Pub. L. No. 103-355, 108 Stat. 3243 (1994). This statute established a strong preference for federal acquisition of "commercial items" by the federal government "to the maximum extent practicable." 10 U.S.C. § 3453(a); *see also* 10 U.S.C. § 3454(b) ("The head of an agency shall ensure that procurement officials in that agency, to the maximum extent practicable . . . acquire . . . commercial products . . . to meet the needs of the agency . . . ."). A patented drug that is already available to the public would appear to meet the definition of a "commercial item" under the FARA. *See* 10 U.S.C. § 2376 (A "commercial item" is "any item other than real property, that is of a type customarily used by the general public or by nongovernmental entities for purposes other than governmental purposes, and that – (i) has been sold, leased, or licensed to the general public; or (ii) has been offered for sale, lease, or license to the general public."). If the scheme proposed by the price-control theory of § 1498 was deemed to be a means to avoid direct government purchases of drugs that are readily available as commercial items, then this would conflict with Congress's express policy in the FARA. As with the Hatch-Waxman regime, the price-control theory of § 1498 produces many unanswered legal and institutional questions, sowing extensive uncertainty and creating new, additional costs in litigation or in other legal processes.

[94] *See* Peter S. Arno & Michael H. Davis, *Why Don't We Enforce Existing Drug Price Controls? The Unrecognized and Unenforced Reasonable Pricing Requirements Imposed Upon Patients Deriving in Whole or in Part from Federally Funded Research*, 75 TULANE L. REV. 631 (2001).

theory, and the repeated agency interpretations of this statute that have consistently rejected the price-control theory.

A. The Function of the Bayh-Dole Act is to Promote Commercialization of Inventions

The Bayh-Dole Act was born of an unintended consequence of the federal government's decision to continue its funding programs for scientific research that it had first adopted during World War Two.[95] In fact, public funding of basic research by the government expanded in both breadth and scope in the post-war era.[96] As noted earlier, the creation of a new government policy can create unintended consequences both in commercial activities in the innovation economy and in the functioning of unrelated statutory or regulatory regimes.[97] The continuation and expansion of public funding of research in the second half of the twentieth century was no different in creating unintended consequences, whether positive or negative.[98]

One unintended consequence was the question of ownership of patented inventions derived from research funded—even if only in small part—by the government. This included funding of basic research in biochemistry and related fields that led to practical innovations, especially life-saving inventions in the modern pharmaceutical sector of the U.S. innovation economy. Beginning in the early to mid-twentieth century, the pharmaceutical sector arose from a business model of substantial investments in research and development to create new drugs that companies were able to commercialize through their property rights in these innovations—patents.[99] What happened

[95] *See* Daniel P. Gross & Bhaven N. Sampat, *America, Jump-Started: World War II R&D and the Takeoff of the U.S. Innovation System* (NBER Working Paper 27375, rev. Sep. 2022), https://www.nber.org/papers/w27375. Of course, the most famous research program was the Manhattan Project, which led to the invention of the first atomic bomb. *See* RICHARD RHODES, THE MAKING OF THE ATOMIC BOMB (1986). Another example is the research and development of radar, a ubiquitous technology today and the basis for consumer inventions like the microwave oven. *See* ROBERT BUDERI, THE INVENTION THAT CHANGED THE WORLD: HOW A SMALL GROUP OF RADAR PIONEERS WON THE SECOND WORLD WAR AND LAUNCHED A TECHNOLOGICAL REVOLUTION (1998).

[96] *See, e.g.*, BRUCE L. R. SMITH, AMERICAN SCIENCE POLICY SINCE WORLD WAR II (1990); Jeffrey K. Stine, *A History of Science Policy in the United States, 1940–1985*, Rep. for Task Force on Science Policy, Committee on Science & Technology, U.S. House of Representatives (1986) [copy on file with author].

[97] *See supra* Part I.D (identifying potential negative consequences of the price-control theory of § 1498 as a result of the "nirvana fallacy").

[98] *See* Gross & Sampat, *supra* note 95 (identifying positive aggregation externalities from federal funding of basic research in WWII).

[99] The modern biopharmaceutical sector and the drug patent were born twins in the nineteen thirties and forties. *See generally* BARRY WERTH, THE BILLION-DOLLAR MOLECULE 111-37 (1994) (discussing the early history of the pharmaceutical industry); THE COMPETITIVE STATUS OF THE U.S. PHARMACEUTICAL INDUSTRY 7-12 (1983) (same). The development and use of drugs existed prior to the nineteen thirties, but the rigorous research and development methods that are the hallmark of the biopharmaceutical sector did not begin until that time. *See* ALFRED D. CHANDLER, JR., SHAPING THE INDUSTRIAL CENTURY 177-211 (2005) (discussing the birth and evolution of many pharmaceutical companies, such as Merck and SmithKline, from the "therapeutic revolution" in the nineteen forties); JONATHAN LEIBENAU, MEDICAL SCIENCE AND MEDICAL INDUSTRY (1987) (surveying the pharmaceutical industry from the nineteenth century up through World War One). Werth writes:

> The birth of drug research in the 1930s had introduced a bristling new competitiveness as companies sought to protect their investments. Where patents were once reviled, they were now

(continued…)

when these drugs and other inventions were produced by research that was now funded several decades later by the federal government through the many post-WWII research programs? The federal government's initial answer to this question was that it owned the inventions no matter how small the contribution from the federal funding program.[100]

Government ownership of patents proved to stifle, rather than to promote distribution of new innovations. The Senate Judiciary Committee Report for the Bayh-Dole Act quoted approvingly an earlier policy report by the Carter Administration that "[e]xperience has shown that the Government . . . is not in a position to take advantage of its ownership of patents to promote enterprise."[101] Congress received evidence about extensive numbers of inventions that were lying fallow due to the government's inability to commercialize the patents it owned or due to costs associated with regulatory restrictions on commercialization created by government ownership of patents.[102] Drugs in particular went undeveloped as medical treatments for patients—not a single new drug had been commercialized from billions distributed by the National Institutes of Health (NIH) for biomedical research.[103]

In response to this problem, Congress enacted the Bayh-Dole Act in 1980.[104] The express function of the Bayh-Dole Act is to make clear that inventors making discoveries or creating inventions produced from research that was funded even in part by the public fisc may receive property rights in the fruits of their labors—patents. The statute expressly states that "[i]t is the policy and objective of the Congress to use the patent system to promote the utilization of

---

> pursued ruthlessly. Squibb, which had one patent in 1920, had more than 200 by 1940. In 1937 alone, Merck had filed forty-six domestic and foreign patent applications.
>
> WERTH, *supra*, at 122.

[100] *See* S. Rep. No. 480, 96th Cong., 1st Sess., at 21 (1979) (stating that "agencies can retain title to inventions arising from research which only received a small percentage of its funding from the Government").

[101] S. Rep. No. 480, 96th Cong., 1st Sess., at 18 (1979) (quoting Advisory Subcommittee on Patent and Information Policy of the Advisory Committee on Industrial Innovation (Dec. 20, 1978)).

[102] *See* S. Rep. No. 480, 96th Cong., 1st Sess., at 20 (1979) ("A GAO study conducted in 1968 found that [the NIH's] policy of retaining patent rights to inventions arising from its supported research programs resulted in an inability to obtain the cooperation of industry in developing potential new drugs."); S. Rep. No. 480, 96th Cong., 1st Sess., at 28 (1979) ("It is essentially a waste of public money to have good inventions gathering dust on agencies' shelves because of unattractiveness of nonexclusive licenses."); Jay Kesan, *Transferring Innovation*, 77 FORDHAM L. REV. 2169, 2175 (2009) ("Prior to the passage of the Bayh-Dole Act, the government agencies responsible for funding research did not have a uniform policy concerning the fate of the potential intellectual property rights in the fruits of government-funded research."); *see also* Dr. Wolfgang Klietmann, *Ivy League profs taking potshots at patents imperil innovation*, BOSTON HERALD (Dec. 5, 2022), https://www.bostonherald.com/2022/06/27/klietmann-ivy-league-profs-taking-potshots-at-patents-imperil-innovation/ ("Nearly 30,000 government-patented discoveries were sitting idle before Bayh-Dole. This meant that taxpayer money put towards scientific research wasn't actually benefiting taxpayers."); Joseph Allen, *Bayh-Dole Rocks While the Critics Play the Same False Note*, IPWatchdog (June 11, 2019), https://www.ipwatchdog.com/2019/06/11/bayh-dole-rocks-critics-play-false-note/id=110254/ (explaining that in "the pre-Bayh-Dole era . . . . federally funded inventions were micromanaged from Washington . . . . The result: less than 5% of 28,000 inventions were licensed" in the marketplace).

[103] *See* Allen, *supra* note 102 (explaining that in "the pre-Bayh-Dole era . . . . the Comptroller General found that not a single new drug had been developed . . . despite billions of taxpayer dollars invested in the National Institutes of Health (NIH)").

[104] Pub. L. No. 96-517, 94 Stat. 3015 (1980) (codified at 35 U.S.C. §§ 200–212).

inventions arising from federally supported research or development."[105] Accordingly, owners of patented inventions derived from federally funded research have the same basic rights as all other patent owners to commercialize their innovations, barring any limitations accepted by the inventor in the funding contract.[106] This includes obtaining venture capital financing to create startups,[107] licensing or engaging in other commercial transactions to create new innovation markets,[108] or transferring the patents to third parties who can more efficiently commercialize the innovation asset in the marketplace.[109]

The Bayh-Dole Act has been identified as one of the most significant acts of innovation policy adopted by Congress in the modern era,[110] but some scholars have critiqued the law on both empirical and policy grounds. Some academics have argued that it has not been successful given lack of evidence that university researchers are actually incentivized by patents to invent.[111] Others have argued that most universities do not on net benefit from patent licensing insofar as licensing revenue exceeds the operational expenses in running licensing programs, except for highly publicized albeit relatively rare "blockbuster" inventions.[112] Moreover, some academics critique

---

[105] 35 U.S.C. § 200.

[106] *See* 35 U.S.C. § 202(c) (specifying additional conditions agencies may adopt in research funding agreement).

[107] *See* Joan Farre-Mensa, Deepak Hegde & Alexander Ljungqvist, *What Is a Patent Worth? Evidence from the U.S. Patent "Lottery,"* 75 J. FINANCE 639 (2020) (identifying a causal link between a startup owning a patent and its increased chances of securing venture capital financing, and further demonstrating a causal link of these patent-based startups with higher rates of success as commercial enterprises in the marketplace).

[108] *See, e.g.*, JONATHAN M. BARNETT, INNOVATORS, FIRMS, AND MARKETS: THE ORGANIZATIONAL LOGIC OF INTELLECTUAL PROPERTY (2020) (detailing the historical and economic evidence of the commercialization function of patents as representing property rights in inventions); B. ZORINA KHAN, INVENTING IDEAS: PATENTS, PRIZES, AND THE KNOWLEDGE ECONOMY (2020) (detailing the historical and economic evidence of the comparative advantage of property rights (patents) over prizes as drivers of economic activity and economic growth); B. ZORINA KHAN, THE DEMOCRATIZATION OF INVENTION: PATENTS AND COPYRIGHTS IN AMERICAN ECONOMIC DEVELOPMENT, 1790–1920, at 9-10 (2005) ("[P]atents and . . . intellectual property rights facilitated market exchange, a process that assigned value, helped to mobilize capital, and improved the allocation of resources. . . . Extensive markets in patent rights allowed inventors to extract returns from their activities through licensing and assigning or selling their rights.").

[109] *See generally supra* note 108; *see also* Stephen Haber & Seth H. Werfel, *Patent Trolls as Financial Intermediaries? Experimental Evidence*, 149 ECON. LETTERS 64 (2016).

[110] *See Innovation's Golden Goose*, 365 ECONOMIST 3, 3 (2002) (calling the Bayh-Dole Act "[p]ossibly the most inspired piece of legislation to be enacted in America over the past half-century"); *see also* Jay P. Kesan, *Transferring Innovation*, 77 FORDHAM L. REV. 2169, 2174 (2009) ("From a patent standpoint, the Bayh-Dole Act was a very significant piece of legislation during the 1980s, because it led to an increase in nonprofit organizations' involvement in the patent system.").

[111] *See, e.g.*, Lisa Larrimore Oullette & Andrew Tutt, *How Do Patent Incentives Affect University Researchers?*, 61 INT'L REV. L. & ECON. (2020), https://doi.org/10.1016/j.irle.2019.105883.

[112] *See, e.g.*, David Orozco, *Assessing the Efficacy of the Bayh-Dole Act Through the Lens of University Technology Transfer Offices (TTOS)*, 21 N.C. J.L. & TECH. 115, 142 (2019) (observing that it is estimated that universities make annual aggregate royalties of $2.7 billion from approximately 8,000 patent licenses but that a "large portion of those royalties, however, are derived from a few sizeable inventions at a handful of academic institutions"); Jay P. Kesan, *Transferring Innovation*, 77 FORDHAM L. REV. 2169, 2179-81 (2009) (describing university licensing programs and the transaction costs and inefficiencies in these programs).

university patent licensing as conflicting with norms of open research or undermining incentives by university professors to engage in basic research.[113]

If these critiques are true, they are still too constricted in their accounting of the relevant variables, focusing solely on what occurs *inside* a university, such as on researcher incentives. There is no doubt that university researchers, especially full-time tenured professors, engage in research without the promise of patent protection. But the function of patents is not merely to incentivize invention; as property rights, patents function as all other property rights as a platform for commercialization of new products and services in the marketplace.[114] As stated by Congress, the purpose of the Bayh-Dole is to promote commercialization of new inventions just as all other innovations have been commercialized in the United States—through the longstanding mechanisms of property rights and contracts.[115]

Researchers have demonstrated that the Bayh-Dole Act has achieved its purpose in promoting commercialization in the marketplace by establishing a reliable legal platform on which to license and otherwise commercially deploy new products and services in the marketplace.[116] One recent study found that patent licensing facilitated by the Bayh-Dole Act contributed between $631 billion to $1.9 trillion to industry gross output between 1996-2020.[117] Walter Copan, the former Director of the National Institute for Standards and Technology, has stated that the Bayh-Dole Act has contributed to "more than 4.2 million jobs, and over 11,000 startup companies from the nation's universities."[118] It may be possible that these commercial and economic benefits are

---

[113] *See, e.g.*, Margo A. Bagley, *Academic Discourse and Proprietary Rights: Putting Patents in Their Proper Place*, 47 B.C. L. REV. 217, 251 (2006) (noting that a focus on patenting of university research can "be detrimental, leading in some cases to rancor, turf disputes, loss of collegiality, and more," and that "it may lead some academics to shift the focus of their research into areas more likely to generate proprietary, commercializable results"); Rebecca S. Eisenberg, *Public Research and Private Development: Patents and Technology Transfer in Government – Sponsored Research*, 82 VA. L. REV. 1663, 1667 (1996) (arguing that the Bayh-Dole's incentives to patent "threatens to impoverish the public domain of research science that has long been an important resource for researchers in both the public and private sectors")

[114] *See supra* notes 107-109, and accompanying text (describing briefly some of the commercial functions of patents as property rights).

[115] 35 U.S.C. § 200 ("It is the policy and objective of the Congress to use the patent system to promote the utilization of inventions arising from federally supported research or development . . . ."); *see also* Ian Ayres & Lisa Larrimore Ouellette, *A Market Test for Bayh-Dole Patents*, 102 CORNELL L. REV. 271 (2017) ("The commercialization argument takes on even more significance in the university context (where ex ante incentives are less important), and this focus is expressly stated in the text of the Bayh--Dole Act.").

[116] *See* Chester G. Moore, *Killing the Bayh-Dole Act's Golden Goose*, 8 TUL. J. TECH. & INTELL. PROP. 151, 155-57 (2006) (surveying evidence of economic success of Bayh-Dole Act in driving economic activity, spurring job growth, and growing the innovation economy).

[117] LORI PRESSMAN, MARK PLANTING, CAROL MOYLAN, & JENNIFER BOND, ECONOMIC CONTRIBUTIONS OF UNIVERSITY/NONPROFIT INVENTIONS IN THE UNITED STATES: 1996-2020, at 3 (2022), https://autm.net/AUTM/media/About-Tech-Transfer/Documents/BIO-AUTM-Economic-Contributions-of-University-Nonprofit-Inventions_14JUN2022.pdf.

[118] Walter Copan, *Reflections on the Impacts of the Bayh-Dole Act for U.S. Innovation, on the Occasion of the 40th Anniversary of this Landmark Legislation*, IPWATCHDOG (Nov. 2, 2020), https://ipwatchdog.com/2020/11/02/reflections-on-the-impacts-of-the-bayh-dole-act-for-u-s-innovation-on-the-occasion-of-the-40th-anniversary-of-this-landmark-legislation/id=126980/.

outweighed by the costs, but these trade-offs must be fully assessed in evaluating any legal institution, comparing all the benefits and the costs.[119] Thus far, critics of the Bayh-Dole Act have not fully compared and balanced both benefits and costs.[120]

B. The Price-Control Theory of the Bayh-Dole Act: The "March In" Power

Another indicator of the success of the Bayh-Dole Act is the price-control theory itself. Instead of critiquing the statute, advocates for the price-control theory now co-opt it for purposes other than to promote the licensing or other commercial uses of reliable and effective patents. Advocates for the price-control theory of the Bayh-Dole Act now argue that the statute authorizes the federal government (or, more specifically, a federal agency like the NIH) to license patents covered by the statute for the sole purpose of imposing price controls on drug patents. This is known as the "march-in power" or "march-in right," but neither the statutory text nor extra-statutory sources of legislative meaning state that *price controls* are authorized legal action under the prescribed march-in power. Before assessing the price-control theory of the Bayh-Dole Act, it is first necessary to describe the march-in power and the argument that this is an existing legal tool to lower drug prices in the healthcare market through the imposition of price controls.

1. The March-In Power in § 203 of the Bayh-Dole Act

Section 203 in the Patent Act, as enacted in the Bayh-Dole Act, creates the "march in right."[121] The provision authorizes a federal agency like the NIH that has funded research that resulted in a patented invention "to grant a nonexclusive, partially exclusive, or exclusive license" under four specified conditions.[122] Section 203 permits a federal agency to grant licenses "to a responsible applicant" without authorization from the patent owner in four specific, delimited circumstances: (1) if an assignee or licensee "has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use," (2) "to alleviate health or safety needs which are not reasonably satisfied," (3) "requirements for public use specified by Federal regulations . . . are not reasonably satisfied," or (4) "a licensee of the exclusive right to use or sell any subject invention in the United States is in breach of its agreement."[123]

All four conditions in § 203 authorize a federal agency to "march in" and license other companies to make and sell a patented product or service in specific circumstances in which a

[119] *Cf.* Brett Frischmann, *Innovation and Institutions: Rethinking the Economics of U.S Science and Technology Policy*, 24 VT. L. REV. 347 (2000) ("Weighing the costs and benefits of Bayh-Dole is a tremendous task that depends significantly on empirical research of, inter alia, the actual rates of foreign misappropriation of federally-funded research (not simply foreign competition) and a counterfactual measure of deadweight costs from under-utilization.").

[120] *See* Dov Greenbaum, *Academia to Industry Technology Transfer: An Alternative to the Bayh-Dole System for Both Developed and Developing Nations*, 19 FORDHAM INTELL. PROP. MEDIA & ENT. L.J. 311, 376 (2009) ("There is a dearth of hard data on the effect of Bayh-Dole on basic research, and much of what is available is contradictory.").

[121] *See* 35 U.S.C. § 203 (2011).

[122] § 203(a).

[123] § 203(a)(1)-(4).

patent owner or licensee is not commercializing the patented invention in the marketplace.[124] The first condition, for example, addresses circumstances in which a patent owner or licensee is figuratively sitting on its hands and not achieving the commercialization function that is the purpose of the Bayh-Dole Act. The second condition addresses a situation in which a patent owner or licensee lacks manufacturing capacity to fully respond to demand for health or safety needs. The third condition addresses the situation when regulatory mandates for public use are not met by a patent owner or licensee, such as a licensee being unable to produce enough water filters required for public drinking safety requirements set by the Environmental Protection Agency.[125] The fourth condition identifies the circumstances when a licensee is in breach of its agreement and thus is not commercializing the patented invention.

These are the four prerequisites, provided in the disjunctive, for a federal agency to exercise the march-in power in § 203(a)(1)-(4). Each sub-section in § 203(a) specifies necessary preconditions for the march-in power to be used by a federal agency or other official in the federal government. Notably, there is no mention of "price" in the four authorizing conditions for a federal official to invoke the march-in power to issue licenses without approval without approval from a patent owner.

Moreover, there is no catch-all march-in clause in § 203. This is significant for two reasons. First, Congress knows how to create broadly framed and explicitly expansive authorizations for agency action, if this is its purpose. For example, Congress has expressly created broadly-framed authorizations in other statutes, such as the well-known language in the Federal Communications Act of 1934 authorizing the Federal Communications Commission to grant radio transmission licenses according to whether the "public convenience, interest, or necessity will be served thereby."[126] Second, the canon of statutory construction of *expressio unius est exclusio alterius* establishes that, without a catch-all clause, the march-in power is delimited to only these four express "exemptions" from the longstanding rights of patent owners covered by the Bayh-Dole Act to freely assign or license their property in the marketplace.[127] In sum, Congress chose not to create an open-ended grant of authority in § 203 in listing only four specific march-in conditions

[124] *See* § 203(a)(1)-(4).

[125] Admittedly, § 203(a)(3) is not clear on its face, but this is the meaning attributed to this statutory language. *See* Joseph P. Allen, *Taking the Mystery Out of March-in Rights*, RealClearPolicy (Sep. 16, 2022), https://www.realclearpolicy.com/articles/2022/09/16/taking_the_mystery_out_of_march-in_rights_853859.html. Joseph Allen was a congressional staff member who worked for Senator Birch Bayh in the legislative process that led to the enactment of the Bayh-Dole Act and he was later appointed as the first Director of the new Office of Technology Commercialization in the U.S. Department of Commerce to develop the implementing regulations for the Bayh-Dole Act. More important, since § 203(a)(3) is not invoked as a relevant statutory provision in the price-control theory, whether this particular condition is clear is merely academic for the purpose of this Article.

[126] 47 U.S.C. § 307(a) ("The Commission, if public convenience, interest, or necessity will be served thereby, subject to the limitations of this Act, shall grant to any applicant therefor a station license provided for by this Act.").

[127] *See* Tennessee Valley Authority v. Hill, 437 U.S. 153, 188 (1976) ("In passing the Endangered Species Act of 1973, Congress was also aware of certain instances in which exceptions to the statute's broad sweep would be necessary. Thus, § 10, 16 U.S.C. § 1539 (1976 ed.), creates a number of limited 'hardship exemptions,' . . . . meaning that under the maxim *expressio unius est exclusio alterius*, we must presume that these were the only 'hardship cases' Congress intended to exempt."); *see also* 73 Am. Jur. 2d Statutes § 129 (2002) (describing the statutory canon of interpretation, *expressio unius est exclusio alterius*).

that strictly specify the narrow scope and application of the march-in power exemption in the Bayh-Dole Act.

2. The Price-Control Theory of § 203

As previously noted, the price-control theory of the Bayh-Dole Act was born of a law journal article published more than twenty years after the Bayh-Dole Act was enacted into law in 1980. In 2001, Professors Peter Arno and Michael Davis published their article, *Why Don't We Enforce Existing Drug Price Controls? The Unrecognized and Unenforced Reasonable Pricing Requirements Imposed Upon Patents Deriving in Whole or in Part from Federally Funded Research*.[128] As the title makes clear, they argued that the (previously unrealized) purpose of the march-in power in the Bayh-Dole Act is to impose price controls on the marketplace.

Professors Arno and Davis claim that, in enacting the Bayh-Dole Act, "Congress's concern with march-in rights focused exclusively on maintaining competitive conditions, controlling profits, and doing so through price control."[129] They specifically maintain that the legislative record confirms that Congress intended to the march-in power to be "focused exclusively on . . . price control." This is a surprising claim for a couple reasons.

First, there is a significant dearth of evidence for their claim that price controls was one of the expressly stated purposes of the Bayh-Dole Act. Professors Arno and Davis identify approximately seven references in the legislative record in which a few congresspersons and witnesses raised concerns about "prices," if one excludes their explicit decision to conflate references to the "public interest" in the legislative record as identical to "price control" references.[130] These few, scattered references to "prices" in the legislative record calls to mind the famous statement by Judge Harold Leventhal that the use of legislative history can be "the equivalent of entering a crowded cocktail party and looking over the heads of the guests for one's friends."[131] For example, other scholars have found statements in the legislative history emphasizing the commercialization function of patents as the primary goal of the Bayh-Dole Act—the "first-listed goal in the statute" according to two scholars.[132] In a 2004 statement to the NIH, former Senator Bayh further critiqued the price-control theory of the Bayh-Dole Act given the selective misreading of the legislative record by a march-in petition advancing "the same arguments" by Professors Arno and Davis.[133] In sum, in a lengthy legislative record pages

[128] *See* Arno & Davis, *supra* note 94.

[129] *Id.*, at 659.

[130] *See id*., at 656-67 (identifying a total of about seven statements in the entire legislative record to "price" or "pricing" of patented products as something that should be restricted or controlled).

[131] Conroy v. Aniskoff, 113 S. Ct. 1562, 1567 (1993) (Scalia, J., concurring).

[132] *See* Ayres & Oulette, *supra* note 145 (observing that commercialization is the "first-listed goal in the statute" and supporting this point about the function of Bayh-Dole from quotes from the legislative history).

[133] *See Statement of Senator Birch Bayh to the National Institutes of Health* 3-5 (May 25, 2004), https://bayhdolecoalition.org/wp-content/uploads/2023/05/2004-Bayh-Statement-to-NIH.pdf.

underlying the Bayh-Dole Act that is more than 1,000 pages in length,[134] Professors Arno and Davis found a few price-control friends to justify their conclusion that Congress "focused exclusively on . . . price control" in enacting § 203 as part of the Bayh-Dole Act.[135]

Second, as noted above, Professors Arno and Davis conflate "public interest" with "price control," which confirms that they are engaging in the scholarly equivalent of artistic license in reconstructing the legislative history of the Bayh-Dole Act. References to the public interest are not by themselves a confirmation of an "exclusive focus" on "price control." The commercialization of new innovations through patents is in the public interest; the inventions figuratively sitting on shelves unused by the public was the problem spurring the enactment of the Bayh-Dole Act to prompt commercialization of these inventions through patent rights. The Bayh-Dole Act reflects the longstanding policy that reliable and effective patents secured to innovators serve the public interest.[136] In the *Federalist No. 43*, James Madison justified the Patent and Copyright Clause on the basis that the "public good fully coincides in both [patents and copyrights] with the claims of individuals."[137]

Professors Arno and Davis' price-control theory of the Bayh-Dole Act was not based solely in their expansive reading of the legislative record. They did attempt to ground their price-control theory in the statute in a perfunctory section in their article,[138] but most of their article is devoted to critiquing the Bayh-Dole Act and to critiquing agencies and other stakeholders for failing to implement their price-control theory.[139] Nonetheless, their general interpretative approach is the statutory argument restated by advocates for the price-control theory of the Bayh-Dole Act to this day; in fact, perhaps sensing the weakness of their reliance on the legislative record, the statutory argument largely dominates the price-control arguments today.[140]

The statutory interpretation of the Bayh-Dole Act as a price-control statute proceeds in two steps. First, price-control theorists focus on the first march-in condition in § 203(a)(1), which

---

[134] *See* Act of December 12, 1980, 94 Stat. 3015, https://1.next.westlaw.com/Document/I71880d30a97e11e0b16e010000000000/View/FullText.html?VR=3.0&RS=cblt1.0&__lrTS=20230211221450846&transitionType=Default&contextData=(sc.Default)&firstPage=true&bhcp=1 (listing entire legislative record and identifying lengthy as approximately 1,073 pages).

[135] Arno & Davis, *supra* note 94, at 121.

[136] *See, e.g.*, Douglas Dynamics v. Buyers Products Co., 717 F.3d 1336, 1346 (Fed. Cir. 2013) (recognizing that "the public has a great[ ] interest in acquiring new technologies through the protection provided by the Patent Act"); Blanchard v. Sprague, 3 F. Cas. 648, 650 (C.C.D. Mass. 1839) (No. 1,518) (Story, Circuit Justice) ("Patents for inventions are now treated as a just reward to ingenious men, and as highly beneficial to the public."); Pilot Inc. v. Coolman Outdoor Corp., No. 18-CV-02286 (JAK) (SPX), 2019 WL 2620723, at *5 (C.D. Cal. Apr. 10, 2019) (observing that that "[u]nfair competition through patent infringement is contrary to the interests of the public"); Amazon.com Inc. v. Barnesandnoble.com Inc., 73 F.Supp.2d 1228, 1248-49 (W.D. Wash. 1999), *vacated on other grounds and remanded*, 239 F.3d 1343 (Fed. Cir. 2001) ("The public has a strong interest in the enforcement of intellectual property rights.").

[137] Federalist No. 43 (James Madison), in THE FEDERALIST PAPERS 272 (Clinton Rossiter ed., 1961).

[138] *See* Arno & Davis, *supra* note 94, at 649-53.

[139] *See id*., at 667-91.

[140] *See supra* notes 5-7 (citing sources).

covers a patent owner or licensee who "has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use."[141] Second, they look to the statutory definition in § 201(f) of the phrase "practical application," as this term is used in § 203(a)(1); there, "practical application" is defined to "mean manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized and that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms."[142] In this lengthy definition § 201(f), they focus on the phrase, "available to the public on reasonable terms."

The price-control theory is thus based a two-step interpretative process of combining § 203(a)(1) and § 201(f) in the Bayh-Dole Act. The phrase "available to the public on reasonable terms" in the final clause of the definition in § 201(f) is applied to the phrase "practical application" in § 203(a)(1) as a specific condition for authorizing the march-in power.[143] Advocates for the price-control theory argue that high prices prevent drugs from being made "available to the public on reasonable terms," and thus this means that high prices for drugs are not achieving "practical application of the subject invention in the field of use."[144] They conclude that high drug prices

[141] 35 U.S.C. § 203(a)(1). Some advocates for the price-control theory of the Bayh-Dole Act also invoke § 202, which specifies agency powers in imposing conditions in research funding agreements, including that the government may claim a royalty-free license for its own use of patents. *See* § 35 U.S.C. § 202(c)(4); Kapczynski, Kesselheim et al. *supra* note 7, at 5 ("In the Bayh-Dole Act, § 202 grants the government irrevocable, non-transferrable, royalty-free licenses to covered patents. . . . [T]he only requirement under § 202 is that the patent be used by, for, or on behalf of the government."). But whether one looks to § 202 or § 203 is a distinction without a difference. First, § 202 does not specify "price," "reasonable price," or "price controls" as conditions or limitations agencies may impose on inventors in research funding agreements. *See infra* Part III.C. Second, the royalty-free license authorized in § 202(c)(4) is expressly limited to use of a patent "for or on behalf of the United States." This is almost identical to § 1498, the eminent domain statute, which does not authorize agencies to impose price controls on private transactions in the marketplace. *See supra* Part II.B. Courts give similar statutory language similar effects, and thus the eminent domain provision in § 202(c)(4) does not authorize price controls. Third, § 202(c)(8) authorizes agencies to impose conditions in funding research agreements expressly incorporating the march-in conditions in § 203, and thus it incorporates by reference the same phrase "available to the public on reasonable terms" in § 203(a)(1) already invoked by price-control theorists. As explained, this phrase is not an authorization to impose price controls on private transactions in the marketplace. *See infra* Part III.C-F.

[142] 35 U.S.C. § 201(f).

[143] *See, e.g.*, Peter Arno, Robert Sachs & Kathryn Ardizzone, *Will the Biden administration use 'march-in' to protect prostate cancer patients from excessive drug prices?*, STATNEWS (Jan. 3, 2022), https://www.statnews.com/2022/01/03/march-in-rights-protect-prostate-cancer-patients-from-excessive-drug-prices/ (identifying "available to the public on reasonable terms" in § 203(a)(1) as "strong legal underpinnings" for using the march-in power to impose price controls to lower the price of Xtandi); Letter from Eric Sawyer to Xavier Becerra, Secretary of the Department of Health and Human Services (Dec. 13, 2021), at 1, https://www.keionline.org/wp-content/uploads/Eric-Sawyer-HHS-Xtandi-Request-13Dec2021.pdf (proposing march-in power be exercised on Xtandi given "price gouging" by the drug innovator (Astellas) and thus it "is not "making the benefits of the patented inventions 'available to the public on reasonable terms,' which is a requirement of bringing a product to 'practical application,' as defined in 35 USC 201(f)").

[144] *Id.*; *see also* Jeannie Baumann, *New Biomed Unit Under Pressure to Use Untried Drug Patent Grabs*, BLOOMBERG LAW (May 2, 2022), https://www.bloomberglaw.com/bloomberglawnews/pharma-and-life-sciences/XCKMFCBG000000?bna_news_filter=pharma-and-life-sciences#jcite (quoting Emory University law professor Liza Vertinsky that "If no one can afford it, that's not reasonably available"); Steven Seidenberg, *March-*
(continued…)

triggers an authorizing condition under § 203(a)(1) for a federal agency to march in and grant a license to another drug company to sell the patented drug at a lower price in the U.S. healthcare market. Thus, the price-control theory of the Bayh-Dole Act claims this statute empowers the federal government to impose price controls on drug patents by authorizing it to license these patents to generic drug companies directed by the federal government to charge lower prices.

C. The March-In Section in the Bayh-Dole Act is Not a Price-Control Provision

The price-control theory is based on an unduly narrow, out-of-context interpretation of two phrases within two sections of the Bayh-Dole Act. Although the price-control theory appears to be merely interpreting the text in these two statutory phrases, it does so at the expense of ignoring the plain text of both provisions in which these phrases are contained and ignoring the statute as a whole in which these provisions are contained as well. By myopically focusing on these two phrases, which are taken out of their grammatical and statutory context, the price-control theory violates longstanding canons of statutory construction and additional sources of statutory meaning that militate against this interpretation of § 203. This includes the consistent interpretation of § 203 by agencies over several decades that this section does not authorize price controls, among other extra-textual sources of meaning. This Section details this statutory analysis.

1. Section § 203 Does Not Authorize Price Controls in Its Express Text

The Supreme Court has stated that the "first step in interpreting a statute is to determine whether the language at issue has a plain and unambiguous meaning."[145] The first place all courts begin is the text of the statute, but the text is not read out of context as individual words. "The plainness or ambiguity of statutory language is determined by reference to the language itself, the specific context in which that language is used, and the broader context of the statute as a whole."[146]

In considering the meaning of the text in § 203(a)(1), and the definitional text in § 201(f), one fact stands out: none of these statutory provisions state that "price" or "reasonable price" is a trigger for the federal government to exercise the march-in power. As the United States Supreme Court has explained: "We have stated time and again that courts must presume that a legislature says in a statute what it means and means in a statute what it says there. When the words of a

in Rights: A Lost Opportunity To Lower US Drug Prices, IPWATCH (May 18, 2017), https://www.ip-watch.org/2017/05/18/march-rights-lost-opportunity-lower-us-drug-prices/ ("When inventions are priced exorbitantly – particularly in comparison to prices in other high-income industrialized countries – those inventions are not available to the public on reasonable terms. So march-in rights can, and should, be used to allow third parties to make and sell the invention at lower prices."); Jennifer Penman & Fran Quigley, *Better Late Than Never: How the U.S. Government Can and Should Use Bayh-Dole March-In Rights to Respond to the Medicines Access Crisis*, 53 WILLIAMETTE L. REV. 1, 2 (2017) (stating that "the current medicines pricing and access crisis . . . calls for the U.S. agencies to finally fulfill the terms of the [Bayh-Dole] Act").

[145] Robinson v. Shell Oil Co., 519 U.S. 337, 340 (1997) (citations omitted); *see also* Caminetti v. United States, 242 U.S. 470, 485 (1917) ("It is elementary that the meaning of a statute must, in the first instance, be sought in the language in which the act is framed, and if that is plain, . . . the sole function of the courts is to enforce it according to its terms.") (citations omitted).

[146] *Robinson*, 519 U.S. at 341 (1997) (citations omitted).

statute are unambiguous, then, this first canon is also the last: 'judicial inquiry is complete.'"[147] This is the "cardinal canon" that all courts apply "in interpreting a statute."[148]

This cardinal canon of statutory interpretation confirms that § 203 does not authorize a federal agency to "march in" to grant a license to a private company directed to charge lower prices to consumers through commercial transactions in the marketplace. If Congress intended to create a price-control power in § 203, it would have specified this as one of the statutory conditions, or at least specified this power in express language in one of the existing statutory conditions.

Congress would have expressly enacted text conferring a price-control power in § 203 if it intended this to be a price-control statute because it has enacted such text many times in past statutes.[149] The Emergency Price Control Act of 1942 is one such example.[150] Similarly, rate-regulation statutes enacted by the states according to their police powers expressly authorize legislators or regulators to set "prices" or determine "rates."[151] Contrary to these price-control or rate-regulation statutes, § 203(a) and § 201(f) are devoid of any archetypical pricing terms, such as "price," "prices charged by an assignee or licensee," "market price," or "reasonable price." According to the "the ordinary meaning of the words used" in § 203 and § 201(f) in the Bayh-Dole Act, the march-in power does not authorize licenses for the purpose of imposing price controls.[152]

Proponents for the price-control theory might still argue that the relevant statutory text is not plain and unambiguous in its meaning, leaving the door open for a federal agency to engage in a reasonable construction of its terms.[153] Accordingly, they would claim that § 203(a)(1) speaks of the lack of "practical application" and "use" of a patented invention as a triggering condition for the exercise of the march-in power by a federal agency, and § 201(f) speaks of the lack of

---

[147] Connecticut Nat'l Bank v. Germain, 503 U.S. 249, 253-54 (1992) (quoting Rubin v. United States, 449 U.S. 424, 430 (1981)) (internal citations omitted).

[148] *Connecticut Nat'l Bank*, 503 U.S. at 253.

[149] *See, e.g.*, Economic Stabilization Act of 1970, Pub. L. No. 91-379, § 202, 84 Stat. 799, 799-800 ("The President is authorized to issue such orders and regulations as he may deem appropriate to stabilize prices, rents, wages, and salaries at levels not less than those prevailing on May 25, 1970."); Housing and Rent Act of 1947, Pub. L. No. 129, 61 Stat. 193, 198 (imposing rent controls on existing structures set at levels permitted to be charged under the Economic Price Control Act of 1942).

[150] *See* Pub. L. No. 77-421, 56 Stat. 23 (1942).

[151] *See, e.g.*, Nebbia v. People of New York, 291 U.S. 502, 515 (1934) ("The Legislature of New York established by chapter 158 of the Laws of 1933, a Milk Control Board with power, among other things to 'fix minimum and maximum ... retail prices to be charged by ... stores to consumers for consumption off the premises where sold.'"); Stone v. Farmers' Loan & Trust Co., 116 U.S. 307, 308 (1886) (reviewing "the statute of Mississippi passed March 11, 1884, entitled 'An act to provide for the regulation of freight and passenger rates on railroads in this state, and to create a commission to supervise the same, and for other purposes'").

[152] INS v. Phinpathya, 464 U.S. 183, 189 (1984) (stating that "in all cases involving statutory construction, our starting point must be the language employed by Congress, . . . and we assume that the legislative purpose is expressed by the ordinary meaning of the words used") (quotations and citations omitted).

[153] *See* Chevron, U.S.A., Inc. v. Natural Resource Defense Council, Inc., 467 U.S. 837, 844 (1984) ("Sometimes the legislative delegation to an agency on a particular question is implicit rather than explicit. In such a case, a court may not substitute its own construction of a statutory provision for a reasonable interpretation made by the administrator of an agency.").

"reasonable terms" in licenses as one example of a failure of this "practical application." Rate-regulation regimes are often adopted for the purpose of ensuring *reasonable* prices or *reasonable* pricing terms.[154] Thus, the absence of "reasonable terms" in patent licenses, as a definitional element in § 201(f) for the march-in condition in § 203(a)(1) of a lack of "practical application" of a patented invention, could conceivably encompass high drug prices.

But this argument does not carry the day for the price-control theory. As noted above, statutory authorizations for imposing price controls or other forms of rate regulation expressly refer to reasonable *prices*, and not merely broadly framed "reasonable terms" of licenses or contracts.[155] In fact, statutes distinguish between "price" and "terms" by listing them separately.[156] This distinction is also consistent with past official usage of "practical application," which referred to the "successful development and terms of the license, not with a product's price."[157] For example, President John F. Kennedy issued a statement on patent policy in 1963 in which he expressly stated that government licensing may be required to achieve "practical application" of an invention to "guard against failure to practice the invention" by a government "contractor."[158] In enacting the Bayh-Dole Act in 1980, Congress could have included language referring to unreasonably high prices as a triggering condition for a march-in provision; this is the standard, undisputed "price" or price-related text that legislatures has long used in price-control or rate-regulation statutes. Congress chose not to include this language in the Bayh-Dole Act.

2. A Power to Impose Price Controls Conflicts with the Bayh-Dole Act as a Whole

It is not an accident that Congress did not include express text specifying high prices or unreasonable prices as a triggering condition for an agency to use its march-in power in § 203. In interpreting a statutory provision, courts inquire into "the specific context in which that language

[154] *See, e.g.*, 47 U.S.C. § 335(b)(3) ("A provider of direct broadcast satellite service shall meet the requirements of this subsection by making channel capacity available to national educational programming suppliers, upon *reasonable prices, terms, and conditions*, as determined by the Commission . . . .") (emphasis added).

[155] *Id.*

[156] *See id.*

[157] Joseph Allen, *New Study Shows Bayh-Dole is Working as Intended—and the Critics Howl*, IPWATCHDOG (March 12, 2019), https://www.ipwatchdog.com/2019/03/12/new-study-shows-bayh-dole-working-intended/id=107225/.

[158] Government Patent Policy, Memorandum of Oct. 10, 1963, Fed. Reg. 10943 (Oct. 12, 1963).

is used, and the broader context of the statute as a whole."[159] The Supreme Court has bluntly stated: "We do not . . . construe statutory phrases in isolation; we read statutes as a whole."[160]

As Justice Antonin Scalia put the point, "we do not really look for subjective legislative intent. We look for a sort of 'objectified' intent—the intent that a reasonable person would gather from the *text* of the law . . . ."[161] Unlike in some statutes, Congress expressly stated its "objectified intent" in the text of the Bayh-Dole Act: "It is the policy and objective of the Congress to use the patent system to promote the utilization of inventions arising from federally supported research or development." The march-in power is an *exemption* from the purpose of the Bayh-Dole Act to stimulate universities and other researchers receiving federal research funds to receive patents to license or otherwise commercialize their inventions into the marketplace. In fact, this exemption was included in the Bayh-Dole Act because it advanced its primary commercialization function: if a patented invention is not licensed or made available in the marketplace by its owner or licensees, then an agency is authorized to act to achieve this goal. Thus, § 203(a)(1)-(4) specifies four conditions in which the march-in power is justified, and, as explained above, these conditions identify situations in which inventions are not sold or commercialized in the marketplace.[162]

In construing § 203 within the Bayh-Dole Act as a whole, it becomes apparent that the price-control theory commits the interpretative vice of "wooden textualism." This is the interpretive vice in statutory analysis in which a court or agency focuses solely on the meaning of a word or phrase taken out of its context within the statute as a whole.[163] The price-control theory commits wooden textualism by deriving its statutory argument through a myopic focus on phrases in "isolated provisions" in the Bayh-Dole Act.[164] It invokes "reasonable terms" as a definitional element in § 201(f) without regard to the complete statutory condition set forth in § 203(a)(1) in which the defined phrase "practical application" appears. If "reasonable terms" as a definitional element for "practical application" is considered within the *full context* of the march-in condition

---

[159] *Robinson*, 519 U.S. at 340; *see also* Graham Cty. Soil & Water Conservation Dist. v. U.S. ex rel. Wilson, 559 U.S. 280, 290 (2010) ("Courts have a 'duty to construe statutes, not isolated provisions.'") (quoting Gustafson v. Alloyd Co., 513 U.S. 561, 568 (1995)); Gonzales v. Oregon, 546 U.S. 243, 273 (2006) (stating that "statutes 'should not be read as a series of unrelated and isolated provisions.'") (quoting Gustafson v. Alloyd Co., 513 U.S. 561, 570, (1995)); Food & Drug Admin. v. Brown & Williamson Tobacco Corp., 529 U.S. 120, 133 (2000) ("It is a 'fundamental canon of statutory construction that the words of a statute must be read in their context and with a view to their place in the overall statutory scheme.'") (quoting Davis v. Michigan Dept. of Treasury, 489 U.S. 803, 809 (1989)); Louisville & N.R. Co. v. Gaines, 3 F. 266, 276 (C.C.M.D. Tenn. 1880) ("Where the language [of a statute] is clear and explicit the court is bound . . . . It must be construed as a whole. The office of a good expositor, says My Lord Coke, 'is to make construction on all its parts together.'").

[160] Samantar v. Yousuf, 560 U.S. 305, 319 (2010) (quoting United States v. Morton, 467 U.S. 822, 828, (1984)).

[161] Antonin Scalia, *Common-Law Courts in a Civil Law System: The Role of the United States Federal Courts in Interpreting the Constitution and Law*, *in* A MATTER OF INTERPRETATION: FEDERAL COURTS AND THE LAW 17 (Amy Gutmann, ed., 1997) (emphasis added).

[162] *See supra* notes 121-127, and accompanying text.

[163] *Cf.* Scalia, *supra* note 161, at 23-24 (critiquing out-of-context linguistic construction of statutory terms because a "good textualist is not a literalist").

[164] Gonzales v. Oregon, 546 U.S. 243, 273 (2006) (stating that "statutes 'should not be read as a series of unrelated and isolated provisions.'") (quoting Gustafson v. Alloyd Co., 513 U.S. 561, 570, (1995)).

in § 203(a)(1) and of the Bayh-Dole Act broadly, then the conclusion seems ineluctable that § 203(a)(1) does not authorize a federal agency to impose price controls on drug patents.

The Bay-Dole Act addressed the policy and economic dilemma that innovations were not being commercialized in the marketplace given the government's inability to commercialize the patented inventions it owned as a result of even a modicum of federal funding of upstream research.[165] The Bayh-Dole Act has achieved its goal through a simple declaratory provision: any invention derived from research funded even in part by the federal government may be patented and the owner of this patent has the same rights as all other patent owners to commercialize its property in the marketplace.[166] The Bayh-Dole Act was enacted on the basis of the commercialization function of the U.S. patent system, and these new patent owners, such as universities, have since conveyed their property rights via assignments or licenses in the marketplace.[167]

Given this "broader context of the statute as a whole" of the Bayh-Dole Act,[168] § 203 lists four narrow, delimited circumstances in which federal officials or agencies can "march in" and license other companies when a patented invention is not being deployed in the marketplace pursuant to the commercialization function of this statute. The commercialization function of the Bayh-Dole Act animates all four march-in conditions in § 203, as each sub-section addresses a distinct set of circumstances in which a patented product or service is not available in the marketplace. For example, § 203(a)(4) would authorize a federal agency to march in and license another company if an exclusive licensee is in breach of its license agreement with the patent owner, the patent owner has not licensed another company, and thus the product or service is languishing commercially and not being sold in the marketplace to the benefit of consumers.

The march-in condition set forth in § 203(a)(1) provides that "effective steps" must be taken by a patent owner or licensee "to achieve practical application of the invention in its field of us." This march-in condition must be read in the same "context and with a view to [its] place in the overall statutory scheme" of the Bayh-Dole Act as the other three march-in conditions set forth in § 203.[169] To focus exclusively on a portion of the definition in § 201(f) of "practical application" as ensuring the invention is available on "reasonable terms" without regard to this statutory context

[165] *See supra* notes 99-110, and accompanying text. *See also* Stephen Ezell, *The Bayh-Dole Act's Vital Importance to the U.S. Life-Sciences Innovation System* 24-27 (ITIF, March 2019), https://itif.org/publications/2019/03/04/bayh-dole-acts-vital-importance-us-life-sciences-innovation-system?mc_cid=f1a53e317f&mc_eid=5c5d018a35 (detailing inability or lack of licensing of government of inventions developed from federally funded research).

[166] These rights are expressly secured in 35 U.S.C. § 261. *See also* Adam Mossoff, *Exclusion and Exclusive Use in Patent Law*, 22 Harv. J. L. & Tech. 321, 343-45 (2009) (discussing legislative history of § 261 and its function in codifying case law reaching back to 1790s securing rights of patent owners to convey their property).

[167] *See supra* notes 108-109, and accompanying text.

[168] *Robinson*, 519 U.S. at 340.

[169] *Davis*, 489 U.S. at 809.

violates the basic interpretative maxim not to engage in wooden textualism in construing the reasonable meaning of a statutory provision within the context of the statute as a whole.[170]

What is the reasonable meaning of a failure of "practical application" as a trigger for the march-in power in § 203(a)(1), especially as a distinct condition from the other three march-in provisions in § 203(a)(2)-(4)? This is the general provision in the march-in power section specifying a situation in which a patent owner or licensee fails to deploy through regular commercial means a product or process in the marketplace, what those commercial means may be. In the healthcare market, for example, § 203(a)(1) would apply when a drug is not manufactured or sold to patients, as distinguished from a licensee failing to make or sell drugs given its breach of a license agreement under § 203(a)(4) or the patent owner or licensee is unable to manufacture sufficient numbers of drugs to respond to a "health or safety" crisis under § 203(a)(2).[171] In sum, the phrase "reasonable terms" in § 201(f), as comprising part of the definition of "practical application" in § 203(a)(1), is not an open-ended authorization for a federal official or agency to impose price controls—it is part of a statutory regime whose function is to ensure that patented products or services are commercialized in the relevant marketplace.[172]

In construing § 203 within the context of the Bayh-Dole Act as a whole, it is evident why the price-control theory insists that agencies focus only on the isolated phrases "reasonable terms" in § 201(f) and "effective steps to achieve practical application" in § 203(a)(1). If the function of the Bayh-Dole Act is to promote commercialization of new inventions through patent licensing and other commercial activities in the marketplace, then the exemptions would authorize actions that would conflict with this only if the invention is not being commercialized as the statute intended. The exemptions would certainly not promote government actions that would undermine incentives to commercialize, such as an open-ended authorization to impose price controls whenever a federal official may deem a price to be too high or unreasonable.

D. Agency Interpretations of the March-In Power in § 203 Have Consistently Rejected the Price-Control Theory of the Bayh-Dole Act

The plain text of § 203 and its function within the Bayh-Dole Act as a whole explains why federal agencies—spanning bipartisan administrations over several decades—have repeatedly rejected numerous petitions to use the march-in power to impose price controls on drug patents.

---

[170] The same rule of construction applies to the use of the phrase "upon terms that reasonable for the circumstances" in the preamble of § 203 that sets forth what a federal agency may do in licensing the patented product or process through its march-in power. In sum, this is not an open-ended reference to or authorization for price controls, but rather it ensures the context-specific commercial conditions for differing innovations are recognized and respected by the agency in its licensing agreements.

[171] This provision could not have been invoked during the COVID-19 pandemic, because there was massive production of the COVID-19 vaccine doses. Approximately 12 billion doses had been manufactured by the end of 2021, almost double the global population. *See* Adam Mossoff & Amesh Adalja, *Patents as a Driver of the Unprecedented Biomedical Response to COVID-19*, 59 INQUIRY: THE JOURNAL OF HEALTH CARE ORGANIZATION, PROVISION, AND FINANCING (2022), https://journals.sagepub.com/doi/10.1177/00469580221124819. It is estimated that approximately 24 billion vaccine doses were produced in 2022. *Id.*

[172] Section 203(a)(3) also authorizes the march-in power when a patent owner or licensee fails to meet the statutory conditions of § 204 (a mandate of manufacturing the product in the U.S.).

In 2016, the Congressional Research Service identified six petitions submitted to the NIH requesting it to exercise its march-in power solely for the purpose of lowering prices of patented drugs sold in the healthcare market.[173] The NIH denied all six petitions on the grounds that § 203, as confirmed by the NIH's prior interpretation of this statutory, did not permit the march-in power to be used for the purpose of lowering drug prices.[174] By 2019, four more petitions had been filed with the NIH by policy organizations and activists, each requesting again that the NIH invoke the march-in power for the sole purpose of lowering drug prices.[175] As with the prior six petitions reaching back to the 1990s, the NIH rejected these petitions on the statutory ground that "the use of march-in to control drug prices was not within the scope and intent of its authority."[176]

In 1997, for example, the NIH was petitioned to invoke the march-in power for the Isolex 300, a patented medical device used in organ transplant procedures.[177] The NIH rejected the petition for failing to meet the burden of proof that any of the four distinction march-in conditions specified in § 203 had been triggered, authorizing the NIH to march in and license other companies to make and sell this medical device in the healthcare market. The NIH found that the Isolex 300 was being commercialized in the marketplace: the patent owner was actively licensing the patented device, seeking regulatory approval, and meeting research demands.[178] These facts precluded the triggering of the march-in power under the four authorizing conditions in § 203.

The NIH went further and explained why the price-control theory of the Bayh-Dole Act was not justified by the plain text of § 203 and the function of the Bayh-Dole Act in promoting the commercialization of patented inventions. The NIH stated that, even if the petitioner proved that there would be greater accessibility and *lower prices* given additional licenses from the NIH invoking the march-in power, this was by itself insufficient authorization under § 203.[179] The NIH stated emphatically that the march-in power in § 203 did not exist for the purpose of "forced attempts to influence the marketplace."[180] It acknowledged the inherent conflict between the function of the Bayh-Dole Act in promoting and commercializing new innovations and the adoption of the march-in power for the purpose of imposing price controls, observing that "such actions may have far-reaching repercussions on many companies' and investors' future willingness to invest in federally funded medical technologies."[181] This was not merely a freestanding policy assessment by the NIH of this petition; it derived this conclusion from the plain meaning of § 203 within the context of the Bayh-Dole Act and its commercialization function.

---

[173] *See* John R. Thomas, *March-In Rights Under the Bayh-Dole Act* 8-10 (Congressional Research Service, Aug. 22, 2016).

[174] *Id*.

[175] *See Return on Investment Initiative for Unleashing American Innovation*, *supra* note 4, at 29.

[176] *Id*.

[177] *See, e.g.*, NIH Office of the Director, *Determination in the Case of Petition of CellPro, Inc.* (Aug. 1, 1997), https://www.ott.nih.gov/sites/default/files/documents/policy/cellpro-marchin.pdf (rejecting petition in part to invoke march-in power given argument that company was too slow in bringing a medical device to market).

[178] *Id.*

[179] *Id.*

[180] *Id.* at 7.

[181] *Id.* at 7.

Another petition in 2004 again requested that the NIH invoke the march-in power in § 203 to license a patent specifically to lower the price for Norvir, a drug used to treat AIDS. Again, the NIH rejected the petition.[182] The NIH explained that "the extraordinary remedy of march-in is not an appropriate means of controlling prices," and that "[t]he issue of drug pricing has global implications and, thus, is appropriately left for Congress to address legislatively."[183]

Applying the classic rule, "if at first one does not succeed, try, try again," another petition was submitted to the NIH in 2013 asking it again to invoke the march-in power in § 203 for the purpose of lowering the price of Norvir sold by AbbVie to consumers in the healthcare market. The NIH again rejected the petition, stating that the imposition of price controls on drug patents was not a statutorily authorized march-in power in § 203 of the Bayh-Dole Act.[184] The NIH bluntly concluded: "As stated in previous march-in considerations the general issue of drug pricing is appropriately addressed through legislative and other remedies, not through the use of the NIH's march-in authorities."[185] The frustration by NIH officials with the serial petitions seeking to impose price controls on drug patents via the march-in provision in the Bayh-Dole Act is palpable.

Lastly, on March 21, 2023, the NIH rejected the latest petition (filed again) for this agency to invoke the march-in power solely to lower the price of Xtandi, a cancer drug covered by patent.[186] In its latest rejection of the price-control theory of the Bayh-Dole Act, the NIH reiterated that the "purpose of the Bayh-Dole Act is to promote commercialization and public availability of government-funded inventions."[187] With this statutory framework and purpose in mind, the NIH expressly "found Xtandi to be widely available to the public on the market" and "[t]herefore, the patent owner, the University of California, does not fail the requirement of bringing Xtandi to practical application."[188] The NIH further pointed out that this decision about Xtandi is consistent with its prior multiple rejections of march-in petitions also seeking to lower drug prices.[189] It also recognized that the administrative processes and delays, especially in light of Xtandi's remaining patent term, led it to conclude that "NIH does not believe that use of the march-in authority would be an effective means of lowering the price of the drug."[190]

---

[182] *See* NIH Office of the Director, *In the Case of Norvir Manufactured by Abbott Laboratories, Inc.* (July 29, 2004), http://www.ott.nih.gov/sites/default/files/documents/policy/March-In-Norvir.pdf.

[183] Dr. Elias A. Zerhouni, Nat'l Institute of Health, *Determination in the Case of Norvir I*, at 5-6 (July 2, 2004).

[184] NIH Office of the Director, *In the Case of Norvir Manufactured by AbbVie* (Nov. 1, 2013), https://www.ott.nih.gov/sites/default/files/documents/policy/March-In-Norvir2013.pdf.

[185] *Id.*

[186] *See* Letter from Lawrence A. Tabak, Performing the Duties of the NIH Director, to Robert Sachs and Clare Love, *supra* note 5.

[187] *Id.* at 2.

[188] *Id.*

[189] *Id.*

[190] *Id.*

The NIH's multiple decisions over several decades in interpreting the scope of the march-in power granted to it under § 203 is significant evidence that the price-control theory of the Bayh-Dole Act is without basis in the statute. The eleven or more decisions ranging from the 1990s through 2023 in which the NIH has consistently rejected march-in petitions requesting it impose price controls on drug patents under § 203 constitute "the well-reasoned views of the agenc[y] implementing a statute [that] 'constitute a body of experience and informed judgment to which courts and litigants may properly resort for guidance.'"[191] The Supreme Court has "long recognized that considerable weight should be accorded to an executive department's construction of a statutory scheme it is entrusted to administer."[192]

E. The Supreme Court Has Rejected Agencies' Claims to Unprecedented Powers Similar to the Price-Control Theory of the Bayh-Dole Act

The Supreme Court's 2022 decision in *West Virginia v. Environmental Protection Agency* confirms the significance of the NIH's repeated interpretation of § 203 over several decades.[193] As the NIH has repeatedly stated, the march-in power is an "extraordinary" act that is "not an appropriate means of controlling prices" and that proponents of price controls on drug patents must look to "Congress to address legislatively" the power to achieve this goal.[194] The power to impose price controls on drug patents is simply the delimited conditions set forth in § 203 of the Bayh-Dole Act. The price-control theory of the Bayh-Dole Act argues that federal agencies can take the extraordinary and unprecedented administration action in imposing price controls on drug patents solely on the basis of an inference of implied authority from generalized language in two distinct clauses construed in isolation within the entire statute. It would be unprecedented for a federal agency to impose price controls on drugs produced and sold by private companies to consumers and patients in the healthcare market solely on the basis of statutory text stating only that a lack of "reasonable terms" represents a failure of "practical application" of a drug patent.[195]

West Virginia closes the door on this broad-based argument for unprecedented agency power to impose price controls on drug patents absent explicit authorization in § 203.[196] This was not the first time the Supreme Court rejected an argument for discretionary administrative power based in generalized, out-of-context statutory phrases in the governing statute. In *Food & Drug Administration v. Brown & Williamson Tobacco Corporation,*[197] the Court assessed the FDA's broad-based construction of generalized, out-of-context phrases in its governing statute to justify its unprecedented assertion of power to regulate cigarettes. The *Brown & Williamson* Court rejected the FDA's "'expansive construction of the statute,' concluding that 'Congress could not

[191] *See* United States v. Mead Corp., 533 U.S. 218, 227 (2001) (quoting Bragdon v. Abbott, 524 U.S. 624, 642 (1998) (quoting Skidmore v. Swift & Co., 323 U.S. 134, 140 (1944)))

[192] *Chevron*, 467 U.S. at 844.

[193] *See* West Virginia v. Environmental Protection Agency, 142 S. Ct. 2587 (2022).

[194] *See supra* notes 183-185, and accompanying text.

[195] *See supra* note 138-141, and accompanying text (explaining the statutory interpretation set forth by the price-control theory of the Bayh-Dole Act).

[196] *See West Virginia*, 142 S. Ct. at 2609.

[197] Food & Drug Admin. v. Brown & Williamson Tobacco Corp., 529 U.S. 120 (2000).

have intended to delegate' such a sweeping and consequential authority 'in so cryptic a fashion.'"[198] This conclusion applies with equal force to the price-control theory of the Bayh-Dole Act, which engages in an "expansive construction of the statute" to justify a "sweeping and consequential authority" based entirely in generalized "cryptic" statutory language.[199]

F. The Price-Control Theory was Rejected by the Namesakes of the Bayh-Dole Act

The price-control theory of the Bayh-Doel Act was allegedly "discovered" by two professors more than two decades after the enactment of the Bayh-Dole Act,[200] which reconfirms the applicability of the fundamental principles of statutory interpretation and constitutional law that limit agency powers, as stated in *Brown & Williamson*, *West Virginia*, and in other cases.[201] The eponymous sponsors of the Bayh-Dole Act agree. Senator Birch Bayh and Senator Robert Dole expressly rejected the price-control theory of the Bayh-Dole Act.

Similar to the *New York Times* editorial in 2021 advocating for the price-control theory of § 1498, which was prompted by a 2016 law journal article,[202] Professors Arno and Davis published an op-ed in the *Washington Post* in 2002 restating their argument from their law journal article the year before that the Bayh-Dole Act mandates that patented inventions resulting from "federal funds will be made available to the public at a *reasonable price*."[203] Professors Arno and Davis' op-ed prompted a response from Senators Bayh and Dole, published as a letter to the editor in the *Washington Post* two weeks later:

> Bayh-Dole did not intend that government set prices on resulting products. The law makes no reference to a reasonable price that should be dictated by the government. . . . The [Arno and Davis] article also mischaracterizes the rights retained by the government under Bayh-Dole. The ability of the government to revoke a license granted under the act is not contingent on the pricing of the resulting product or tied to the profitability of a company that has commercialized a product that results in part from government-funded research. The law instructs the government to revoke such licenses only when the private industry collaborator has not successfully commercialized the invention as a product.[204]

---

[198] *See West Virginia* 142 S. Ct. at 2608 (quoting Food & Drug Admin. v. Brown & Williamson Tobacco Corp., 529 U.S. 120, 159 (2000)).

[199] *Brown & Williamson*, 529 U.S. at 159.

[200] *See supra* note 128, and accompanying text.

[201] *See* Alabama Ass'n of Realtors v. Dep't of Health and Human Services, 141 S. Ct. 2485, 2487 (2021) (rejecting the Center for Disease Control's moratorium on rental evictions given the "wafer-thin reed" of support in its organic statute's text and the "unprecedented" nature of the asserted regulatory power).

[202] *See supra* notes 37-40, and accompanying text.

[203] *See* Peter Arno & Michael Davis, *Paying Twice for the Same Drugs*, Washington Post (March 27, 2002), https://www.washingtonpost.com/archive/opinions/2002/03/27/paying-twice-for-the-same-drugs/c031aa41-caaf-450d-a95f-c072f6998931/ (emphasis added).

[204] Birch Bayh and Robert Dole, *Our Law Helps Patients Get New Drugs Sooner*, Wash. Post (Apr. 11, 2002), https://www.washingtonpost.com/archive/opinions/2002/04/11/our-law-helps-patients-get-new-drugs-sooner/d814d22a-6e63-4f06-8da3-d9698552fa24/.

In sum, there is no "clear congressional authorization" in § 203 that grants federal agencies power to impose price controls on patented products or services that are commercialized in the marketplace.[205] Beyond the plain text of § 203, the price-control theory of the Bayh-Dole Act contradicts the function of this statute in promoting the commercialization of inventions by patent owners in the marketplace.[206] The NIH has confirmed this lack of express statutory authorization in § 203 to impose price controls in its consistent, repeated rejections of numerous march-in petitions over several decades that have sought use of this power solely to lower drug prices. Although it does not have the same legal status as the canons of statutory interpretation and official interpretation and application of a statute, Senators Bayh and Dole make clear that the price-control theory of the Bayh-Dole Act proposes an unprecedented assertion of agency power to control prices in private market transactions between private parties given only generalized, out-of-context statutory phrases like "practical application" and "reasonable terms."

IV. Conclusion

For at least five decades, a significant policy debate over drug prices has waxed and waned in the U.S. Initially, this was principally a debate only in healthcare policy. In recent decades, the patent system has been drawn into this sometimes heated debate with scholars and activists arguing that drug patents are a primary cause of what they contend are unacceptably high drug prices.[207] They argue that the federal government can break patents and impose price controls on drug patents. They assert that two federal laws—§ 1498 and the Bayh-Dole Act—are an "important tool" authorizing federal agencies to achieve their policy goal of imposing price controls on drug patents.[208]

This is a false promise. The price-control theories of § 1498 and the Bayh-Dole Act represent policy arguments superimposed on two statutes by advocates seeking a quick-and-easy path to justifying an unprecedented regulatory policy—the imposition of price controls on drug patents. Since 1790, Congress has considered proposals for various forms of compulsory licensing of patents, and Congress has consistently rejected these proposals.[209] Perhaps recognizing this significant hurdle in proposing an unprecedented—and expressly rejected—policy proposal for

[205] *See supra* notes 145-157, and accompanying text (describing the text in § 203 and the lack of any express authorization to control or delimit prices).

[206] *See supra* notes 159-172, and accompanying text (applying the canon of statutory interpretation that § 203 must be construed within the entire context of the Bayh-Dole Act).

[207] *See supra* note 3, and accompanying text (detailing this policy argument).

[208] *See supra* note 18, and accompanying text.

[209] *See, e.g.*, BRUCE W. BUGBEE, GENESIS OF AMERICAN PATENT AND COPYRIGHT LAW 143-44 (1967) (discussing the rejection of a Senate proposal for a compulsory licensing requirement in the bill that eventually became the Patent Act of 1790); Kali Murray, *Constitutional Patent Law: Principles and Institutions*, 93 NEB. L. REV. 901, 935-37 (2015) (discussing a congressional bill in 1912 requiring compulsory licensing for patent owners not manufacturing a patented invention, which received twenty-seven days of hearings, but was not enacted into law).

price controls on drug patents, advocates attempt to bootstrap their policy arguments by arguing that Congress has already approved of a price-control policy in two existing federal statutes.

The price-control theories of § 1498 and the Bayh-Dole Act are profoundly mistaken. Neither § 1498 nor the Bayh-Dole Act authorize agencies to impose price controls on drug patents for the purpose of lowering drug prices. This is confirmed by their plain text, their consistent interpretation by courts and agencies, by principles of constitutional law, and by extra-textual sources of statutory meaning. Ultimately, the price control theories of § 1498 and the Bayh-Dole Act engage in interpretative acts of legerdemain that essentially pull a price-control rabbit out of statutory hat to proclaim, "Voila, lower drug prices through price controls on patents!"

This article has not addressed the policy arguments for or against price controls on drug patents, but only because advocates for price controls have chosen to advance as their primary argument a seemingly straightforward claim about statutory authorization—the price-control theories of § 1498 and the Bayh-Dole Act. This requires engaging in rigorous analysis of the meaning of these respective statutes as a necessary first step before engaging with the normative arguments based on the price-control theories of § 1498 and the Bayh-Dole Act. Ultimately, policy advocates should be careful not to replace rigorous normative justifications with statutory claims that are the equivalent of "law office history"—the practice by legal actors of using isolated, out-of-context historical facts in the service of modern policy arguments.[210] The price-control theories of the Bayh-Dole Act and § 1498 are policy arguments masquerading as statutory construction. It is time to lay these legal myths to rest and to have a forthright policy debate.

[210] Larry D. Kramer, *When Lawyers Do History*, 72 GEO. WASH. L. REV. 387, 389-94 (2003) (criticizing bad historiography of lawyers, who produce "law office history" intended only "to generate data and interpretations that are of use in resolving modern legal controversies" (citations omitted)).

Submission Date: 7/27/2023

Name: Brian O'Shaughnessy

Name of Organization: Licensing Executives Society (USA & Canada), Inc.

Comment:

Dear Colleagues:

The Licensing Executives Society (USA & Canada), Inc. appreciates the opportunity to submit comments for NIH consideration in relation to its "Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer." Our comments are attached.

Please feel free to contact me with any questions.

Respectfully submitted,

--Brian

Dinsmore

Brian P. O'Shaughnessy
Partner
Chair, IP Transactions and Licensing Group

Dinsmore & Shohl LLP • Legal Counsel

Sr. V.P., Public Policy
Past President (2016-2017)

Additional Comment (attachment):

July 27, 2023

Lyric Jorgenson, Ph.D.
Acting Associate Director for Science Policy
National Institutes of Health
Office of Science Policy
6705 Rockledge Dr. #750
Bethesda, MD 20817

Dear Director Jorgenson:

On behalf of the Licensing Executives Society (USA & Canada), Inc., we appreciate the opportunity to provide comments in advance of the National Institutes of Health's upcoming workshop, *Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer*.

LES is an independent, non-profit, non-partisan, professional association devoted to the commercialization of inventions and intellectual property through education, networking, standards development, and certification. We are the leading professional organization devoted to the industry of technology licensing -- that is, technology-related commercial transactions involving patents, trade secrets, know-how, trademarks, and copyrights. Our members come from across the innovation economy and include business executives, technology transfer professionals, IP experts, and entrepreneurs representing diverse industries, including life sciences.

We commend NIH for convening this workshop and engaging in an important discussion on efficient and effective development of federally funded discoveries. A fully functional innovation ecosystem requires an array of funding and market-based incentives to transform experiments into commercial products. Our members rely on the market-based incentives to justify the assumption of risk and investment inherent in commercially developing the basic research done at research centers like NIH. Absent those incentives, government funded discoveries will not be licensed by private enterprise for commercial development, and the public will derive no benefit from the federal funding of such basic research.

Such was the case less than a half-century ago. At that time, the federal government retained the patent rights in any invention made with the assistance of any federal funds, and often provided only non-exclusive licenses. As a result, private enterprise

was reluctant to invest in the transformation of such basic research into viable commercial products. Economists refer to it as the free-rider phenomenon. Innovators know that without some form of protection, imitators will enter the market, and, without the same costs of development, depress prices to the point only the imitator can bear, and drive the innovator out of the very market the innovator created.

As a result of such concerns, promising scientific discoveries from research centers like NIH were passed over and left undeveloped, wasting taxpayer dollars, and depriving us all of the benefits of products derived of those discoveries.

The Bayh-Dole Act and the Federal Technology Transfer Act (Stevenson-Wydler Act) addressed that problem, and opened up a new era of vibrant, productive public-private partnerships. These laws granted universities, small businesses, and federal labs proprietary rights to inventions made with any amount of federal funding, enabling them to exclusively license those discoveries to private enterprise for development, and ultimately commercialization. As a result of those licenses, universities, small companies, and federal labs earn royalties, providing the resources needed to fund additional research, reward inventors, and enter into cooperative research and development agreements (CRADAs).

These laws fostered fruitful collaboration combining the extensive theoretical knowledge of the country's leading academics and government scientists with the business acumen and resources of the private sector. In the years since, countless licensing deals and associated sponsored research has given the public the benefit of products developed from those discoveries. Technology transfer to the private sector from our universities alone led to nearly 800 new commercial products in 2021.[1] These products, and many more, have had profoundly beneficial effects on our quality of life.

As the NIH contemplates ways to further improve technology transfer, we urge the agency to uphold the original intent and structure of Bayh-Dole and the Federal Technology Transfer Act. Specifically, we urge NIH to reject initiatives that would seek to exploit these valuable relationships with industry to impose price controls.

Some of those initiatives would condition the development of those technologies on a commitment to make resulting products available at a "reasonable price." But since no one knows at such an early stage what the resulting products will be, how much time and effort is required to get to a commercial product, or who will decide what constitutes a reasonable price,

[1] https://autm.net/AUTM/media/Surveys-Tools/Documents/AUTM-Infographic-2021_1.pdf pg. 2

industry will not take the deal. As a result, groundbreaking technologies will be left undeveloped, doing no one any good.

Instead, NIH should do what it did most recently in March 2023 on the drug Xtandi. There the NIH rejected efforts to impute to NIH the role of a super-regulator of the pharmaceutical market. NIH had been petitioned, as it had in the past, to use the carefully defined, narrowly constructed "march-in" power to revoke carefully crafted agreements with private enterprise relating to Xtandi. The petitioner had argued that because the petitioner deemed the price of Xtandi to be excessive, NIH should distort the purpose of march-in to permit others to make and sell the drug at a lower price. But the march-in power was never meant to be a mechanism for price controls, and NIH lacks the expertise to second guess the pharmaceutical market. Thus, NIH again refused to invoke the march-in power for purposes of price controls.[2] Among other things, NIH seems to have recognized that federal labs should do what they do best - research, and let markets control prices. Indeed, the authors of the Bayh Dole Act themselves expressly rejected the proposition that the march-in power could be used for purposes of price controls.[3]

If NIH were to adopt the role of price regulator after the fact, whether through reasonable price provisions or march-in, private enterprise would be ever more reluctant to license federally funded discoveries for commercial development – undermining decades of successful collaboration between government, university, and private sector partners.

This is not mere speculation. We've run this experiment before, and the results are clear. In response to political pressure, in 1989 NIH began imposing reasonable pricing clauses in its CRADAs, licenses, and extramural research grants and contracts. This contractually bound licensees to set a reasonable price for any product that was developed under the license. However, after running this reasonable pricing experiment for six years, and after conducting an extensive study on its effect on potential licensees, the NIH Director eliminated the practice, stating that it had "driven industry away from potentially beneficial scientific collaborations with [NIH] scientists without providing an offsetting benefit to the public."[4]

---

[2] https://www.aamc.org/advocacy-policy/washington-highlights/nih-declines-march-cancer-drug-nist-releases-new-bayh-dole-regulations

[3] https://www.washingtonpost.com/archive/opinions/2002/04/11/our-law-helps-patients-get-new-drugs-sooner/d814d22a-6e63-4f06-8da3-d9698552fa24/?itid=lk_inline_manual_11

[4] https://bayhdolecoalition.org/wp-content/uploads/2023/06/CRADA-QA-Nov-2021-FINAL.pdf pg. 2

NIH should make every effort to avoid resurrecting failed price control policies and practices. The greatest potential for public benefit derived of federally funded discoveries resides in our patent system, and in reliable and durable license agreements under the Bayh-Dole Act and the Federal Technology Transfer Act. The prospect that those agreements will be unilaterally altered or revoked after the fact will only drive industry away and deprive the public of the benefits of that research. The choice is simple: either protect patent rights and associated licenses that promote technology transfer and product development, or resurrect failed practices that will stunt U.S. biomedical innovation for years to come.

Thank you for this opportunity to comment. LES looks forward to further engaging with NIH on this important matter both now and in the future.

Respectfully submitted,

Brian P. O'Shaughnessy

Sr. V.P., Public Policy
Licensing Executives Society (USA and Canada), Inc.

Submission Date: 7/27/2023

Name: Lizbet Boroughs

Name of Organization: Association for American Universities & COGR

Comment:

Dear Dr. Jorgenson,

On behalf of AAU and COGR, I am pleased to submit our joint comments for consideration during the NIH's upcoming workshop, "Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer. "

My best,

Lizbet Boroughs, MSPH
Associate Vice President for Federal Relations
Association for American Universities (AAU)

Additional Comment (attachment):

To: Lyric Jorgenson, PhD
Acting Director, Office of Science Policy, and Acting Associate Director for Science Policy
National Institutes of Health

From: Kate Hudson, JD, Associate Vice President and Counsel, AAU
Lizbet Boroughs, MSPH, Associate Vice President of Federal Relations, AAU
Robert Hardy, Director of Research Security & Intellectual Property Management, COGR

Date: July 27, 2023

Re: Comments on NIH's Workshop: Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer, July 31, 2023

The Association of American Universities (AAU) and COGR appreciate the opportunity to share input on the ongoing discussion regarding NIH's levers to catalyze technology transfer. AAU is an organization of 71 leading U.S. and Canadian research universities that transform lives through education, research, and innovation. COGR is an association of over 200 public and private U.S. research universities and affiliated academic medical centers and research institutes. COGR focuses on the impact of federal regulations, policies, and practices on the performance of research conducted at our member institutions, and we advocate for sound, efficient, and effective regulation that safeguards research and minimizes administrative and cost burdens.

Our combined member universities comprise the majority of competitively awarded federal funding for research that improves public health, seeks to address national challenges, and contributes significantly to our economic strength, while educating and training tomorrow's visionary leaders and innovators. Additionally, many of our member institutions operate hospitals and affiliated health systems throughout the U.S. and are themselves large-scale purchasers of drugs and therapies developed for patients by the commercial market. AAU and COGR member institutions represent multiple stakeholder positions in the NIH research and commercialization lifecycle.

As in all ecosystems, changes to one part of the ecosystem affect other parts as well. Disruptions to the current innovation ecosystem that are hastily designed and implemented will have ripple effects which will discourage research partnerships between federally funded researchers, industry, and other important players in the technology transfer pipeline. Such changes in policy and practice must be done in a deliberate manner to ensure the effectiveness and longevity of the technology transfer and U.S. innovation system. To do otherwise would jeopardize U.S. leadership in biomedical research and innovation, to the detriment of the American people and the world.

In addition to providing these written comments today, our associations echo the sentiments submitted to this solicitation by AUTM, the non-profit leader in efforts to educate, promote and inspire professionals to support the development of academic research that changes the world and drives innovation forward.

The American Innovation Ecosystem & the Role of the NIH

The United States leads the world in novel biomedical innovation, thanks in large part to strong and sustained government support for research, strong research universities, talented researchers, efficient drug approval processes, and a pricing system that enables companies to earn sufficient revenues to reinvest in future generations of innovation. [1] Indeed, the Bayh-Dole Act, combined with sustained government support for research at NIH, has helped to ensure U.S. competitiveness in biomedical research and technology. It remains critical that this existing policy apparatus and federal support be maintained and strengthened.

The pathway from discovery to commercialization is a years, often decades-long process. The average length of development is 10-15 years from identification of a biomarker to development of a medication through regulatory approval process to market distribution. The expected cost to develop a new drug—including capital costs and expenditures on drugs that fail to reach the market—has been estimated to range from slightly less than $1 billion to more than $3 billion, with many different factors that determine the necessary levels of investment. Detailed case studies reveal that public support has played at least some role in virtually all of the 26 most clinically and commercially significant drugs and drug classes approved over the past several decades.[2, 3]

NIH's investments in university-based basic research are a part of the innovation ecosystem, setting the stage for the industry-led applied research and development activity that leads to the commercialization of new medicines and treatments. Broad scientific endeavors such as the Framingham study, the Human Genome Project, and research on vaccine development have helped catalyze the identification of novel approaches to improve diagnostics and treatments.[4] The Framingham study led to the identification of cholesterol as a factor for cardiac disease and the development of medications to mitigate risks for strokes and heart attacks.[5] The Human Genome Project, among many other things, facilitated

[1] Ezell, S, The Bayh Dole Act's Vital Importance to U.S. Life-Sciences Innovation System, Information Technology & Innovation Foundation, 2019.
[2] Wouters, OJ, McKee, M, Luyten, J: Estimated Research and Development Investment Needed to Bring New Medicines to Market, 2009-2018. *JAMA*. 2020; 323 (9): 844-853.
[3] NASEM 2020 Workshop "The Role of NIH in Drug Development Innovation and its Impact on Patient Access" National Academies of Sciences, Engineering, and Medicine. 2020. The Role of NIH in Drug Development Innovation and Its Impact on Patient Access: Proceedings of a Workshop. Washington, DC: The National Academies Press. https://doi.org/10.17226/25591.
[4] Collins, Francis S., Opportunities for Research and NIH. *Science* 327,36-37(2010). DOI:10.1126/science.1185055
[5] Franklin, S. S., and Wong, N. D. (2013). Hypertension and cardiovascular disease: contributions of the Framingham heart study. *Global heart*, *8*(1), 49–57. https://doi.org/10.1016/j.gheart.2012.12.004

improvements in cancer diagnoses through the identification of genetic variants[6]. Decades-long research on vaccine efficacy helped catalyze mRNA approaches to vaccine development[7], which allowed Operation Warp Speed to develop, test, and bring to market revolutionary vaccines in response to COVID-19.

NIH's support for basic research related to the biological target, rather than the development of a specific drug, is consistent with its national service and public health mission to promote and facilitate pre-competitive research aimed at advancing the health and well-being of the American people. NIH has historically remained removed from the drug development and marketing process, which should be rightfully left up to private industry. This is why, of the 356 drugs approved and brought to market from 2010 to 2019, all were brought to market in the United States by a biopharmaceutical company, rather than by an academic, governmental, or non-governmental organization.[8]

Role of University-Industry Collaboration

Universities are hubs for research, discovery, and innovation. Very often, academic researchers identify a new idea or concept that has potential for development into a commercial product. University-industry collaborations and partnerships are critical for realizing the public benefits of federally funded research. Initial discovery is critical, but potential impact for the public requires proof that concepts work in humans and years of further investment and development by industry. The expertise, infrastructure, and capital required to bring a medication or technology to commercial market is most often a function of industry investment, which neither the federal government nor research universities are able to bear.

Technology transfer of NIH-funded research between universities and industry allows research to catalyze into the development of potential biomedical innovations. Technology transfer can be operationalized through a variety of mechanisms, such as licensing agreements, assignment of intellectual property rights, material transfer agreements, and collaborative research agreements. The most utilized technology transfer vehicle is licensing.

Examples of technology transfer success stories from universities to industry partnerships leading to biomedical innovation include:

- Emory's development of an HIV medication that disrupts viral DNA from replicating. Emory licensed its discovery in 1996 to a biotech company for further development. Emtriva™ was eventually brought to market in 2003 by Gilead pharmaceuticals.[9]

---

[6] Hood, L., Rowen, L. The Human Genome Project: big science transforms biology and medicine. *Genome Med* 5, 79 (2013). https://doi.org/10.1186/gm483

[7] Clin, J., Invest. 2021;131(19):e153721. https://doi.org/10.1172/JCI153721.

[8] Cleary, Ekaterina, Jackson, Matthew J. and Ledley, Fred, Government as the First Investor in Biopharmaceutical Innovation: Evidence From New Drug Approvals 2010–2019 (August 5, 2020). Institute for New Economic Thinking Working Paper Series No. 133 https://doi.org/10.36687/inetwp133

[9] Schinazi, R., & Liotta, D. (n.d.). *HIV Antiretrovirals*. Emory University Office of Technology Transfer. http://www.ott.emory.edu/about/success/hiv.html

- University of Wisconsin Madison researchers developed a synthetic form of Vitamin D to better control calcium imbalance in patients on kidney dialysis. Paricalcitol (sold commercially as Zemplar™) was brought to market by AbbVie Inc.[10]
- University of California, Berkeley researchers searched for ways to suppress the proliferation of melanoma cells by activating the patient's own immune response.[11] Researchers identified a checkpoint molecule (CTLA-4) that suppressed immune response to cancer cells. When CTLA-4 was targeted by monoclonal antibodies, immune cells could better attack cancer cells. Over a decade later following investments by four companies, Yervoy™ was approved by the FDA.[12]

Placing Arbitrary Pricing Constraints on Potential Commercial Products Will Disrupt Innovation

There is a long history of discussions to include "reasonable pricing" provisions by the NIH Patent Policy Board. In 1989, provisions were adopted to address the pricing of products licensed from federal health research agencies. Reasonable pricing clauses, as has been demonstrated previously by NIH policies from 1989-1996, create an untenable risk calculation to investors and collaborators which discourage them from tapping into federally supported research discoveries made at universities. Given the cost of developing and bringing a medication to market, companies have been and will continue to be reluctant to enter a "reasonable pricing" agreement with the NIH years before a medication has proven that it can be successfully commercialized.

As NIH is aware from other efforts to impose price controls on medications, there is a tradeoff between prices and innovation. The Congressional Budget Office estimated that a legislative proposal introduced by Rep. Nancy Pelosi (D-CA) The Lower Drug Costs Now Act of 2019 (H.R. 3), would reduce the number of drugs available for the market over the next 10 years.[13]

Current calls for Congressional scrutiny of potential levers to reduce the cost of medications, specifically challenges to provisions of the Bayh-Dole Act, will detrimentally disincentivize investment and collaboration as it relates to federally funded research and university-industry partnerships. Without economic incentives to further research, develop, and clinically test university discoveries through private investment, those discoveries will remain in the laboratory and not proceed to the commercial

[10] University of Wisconsin Madison. (2008). Synthetic vitamin D protects bone strength in kidney failure patients. Better World Project. https://autm.net/about-tech-transfer/better-world-project/bwp-stories/paricalcitol-zemplar%E2%84%A2

[11] Fernandes, M. P., Oliveira, C., Sousa, H., & Oliveira, J. (2023). New Approaches in Early-Stage NSCL Management: Potential Use of PARP Inhibitors and Immunotherapy Combination. *International journal of molecular sciences*, *24*(4), 4044. https://doi.org/10.3390/ijms24044044

[12] Hoos, A., Ibrahim, R., Korman, A., Abdallah, K., Berman, D., Shahabi, V., Chin, K., Canetta, R., & Humphrey, R. (2010). Development of ipilimumab: contribution to a new paradigm for cancer immunotherapy. *Seminars in oncology*, *37*(5), 533–546. https://doi.org/10.1053/j.seminoncol.2010.09.015

[13] Swagel, L. P. (2019, October 11). Effects of Drug Price Negotiation Stemming From Title 1 of H.R. 3, the Lower Drug Costs Now Act of 2019, on Spending and Revenues Related to Part D of Medicare. Washington, DC; Congressional Budget Office.

market. This will result in the creation and distribution of far fewer life-saving drugs and therapies for both the American people and the world.

In addition, these impacts will be concretely felt at the local and regional levels throughout the country, as university-industry collaborations would decline significantly. Because such collaborations attract capital and translate to a wide array of regional economic benefits at the campus level and beyond, the brunt of this impact will be felt not just in key metropolitan areas but in other more rural areas as well and will come at a time when catalysts for regional economic development in the innovation economy is a national economic priority and national security concern (i.e., regional innovation initiatives in the Inflation Reduction Act (IRA) and the CHIPS & Science Act via the National Science Foundation, and the Economic Development Administration (EDA) via the U.S. Department of Commerce).

NIH Levers to Catalyze Technology Transfer

NIH currently has additional levers at hand that may reduce costs in drug development and increase rates of commercialization success. Continued and increased support of these existing levers offers the optimal public policy solution for catalyzing technology transfer. These existing levers include:

- The NIH's National Center for Advancing Translational Sciences (NCATS) seeks to improve the "bench to bedside" translational process and utilizes a variety of tools such as streamlining enrollment in NIH-Funded clinical trials through the SMART IRB program and improved data collection.
- The development of additional artificial intelligence tools, approved by NIH, to help scientists analyze large data sets would improve identification of biomarkers that can be utilized by industry.
- Proposals to expand NCATS both in terms of personnel and role inside NIH would be effective in bringing greater knowledge and efficiency to biomedical translation.
- NIH's Centers for Accelerated Innovations (CAI) and its recently established REACH: Research Evaluation and Commercialization Hubs, which combine public-private expertise to evaluate and develop discoveries for commercialization has shown early promise in efforts to reduce the time period from discovery to therapeutic product.
- NIH's Small Business Innovation Research Program and Small Business Technology Transfer Program (SBIR/STTR) has expanded the provision of vital early-stage capital for technology transfer and commercialization efforts specifically in biomedical innovation. Additionally, recent enhancements to SBIR/STTR's guidance on partnership identification and business development have helped researchers in need of advice on how to better navigate the innovation pipeline.

Other federal agencies such as the Food and Drug Administration and the U.S. Patent and Trademark Office can work more closely with NIH stakeholders to enhance regulatory engagement during the drug development process. This could streamline and make the process of bringing a drug to market more efficient.

Conclusion

We strongly believe that building upon existing NIH programs, as well as cross-collaboration with other federal agencies to improve and streamline the research, regulatory, and approval processes, will bring the best outcomes in catalyzing technology transfer efforts by the NIH overall.

Thank you for the opportunity to engage with NIH regarding its role in the development pipeline. AAU and COGR look forward to future conversations on discovery, innovation and enhancing the health of the nation.

Submission Date: 7/27/2023

Name: Robert Taylor

Name of Organization: Alliance of US Startups and Inventors for Jobs

Comment:

Attached is my written statement for the NIH workshop entitled “Transforming Discoveries into Products: Maximizing NIH’s Levers to Catalyze Technology Transfer.”

I submitting this document as a signed version in PDF format, which includes a signature page and an Appendix. I also am submitting it in Word format without a signature or Appendix, should the agency need to alter the margins or pagination to incorporate into a larger document.

My contact information is below, if you have any questions.

Bob Taylor

PLEASE ACKNOWLEDGE RECIEPT

Robert P. Taylor
RPT Legal Strategies PC

Additional Comment (attachment):

ALLIANCE OF U.S. STARTUPS & INVENTORS FOR JOBS

Prepared Statement of Robert P. Taylor

General Counsel, Alliance of US Startups and Inventors for Jobs ("USIJ")
National Institutes of Health Workshop entitled
Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer

My name is Robert P. Taylor, General Counsel for Alliance of U.S. Startups and Inventors for Jobs ("USIJ"). I am pleased with the invitation to appear as a public speaker during the subject workshop to present the views of USIJ and its constituencies, which comprise individual inventors, entrepreneurs, startups, and the investors that fund these entities. Many of USIJ's members and supporters are engaged in developing health care related products such as new drugs, medical devices and health care management tools. USIJ was founded nearly a decade ago to help inform government officials, members of Congress, and the Federal Judiciary regarding the role that patents play in promoting investments, development and technology transfers of these and other products that incorporate new technologies. By ameliorating some of the competitive risks associated with investments in startups and small companies, patents should play a key role in enticing venture capitalists and other investors to fund such activities, particularly in the area of pharmaceuticals, biotechnology and medical devices.

This USIJ cohort is currently responsible for the majority of new health care therapies and products, sometimes in collaboration with a larger company and other times on their own.[1] This is not to suggest that larger healthcare companies do not create new products on their own as well, but the inherent risks associated with investing in such products before they have full FDA approval often make it more attractive to wait until a smaller company has been successful in proving the science and scalability of making a product before committing funds for obtaining full FDA approval. Moreover, for a startup focused on a single technology, the risk of failure is far more likely to be existential than for a larger more diversified company. The key point from our perspective is that entrepreneurs, startups and small companies are an extremely important part of the healthcare ecosystem and present their own need for special consideration.

---

[1] A study entitled "The US Ecosystem for Medicines: How new drug innovations get to patients," concludes that for the period 2011 to 2020, "55% of U.S. originated therapies were created by small biotech companies; 45% were created by large companies." https://vitaltransformation.com/2022/12/the-us-ecosystem-for-medicines-how-new-drug-innovations-get-to-patients.

Introduction.

NIH has long been at the forefront of American leadership in scientific research relating to the development of health-related products and services, and our citizens can be justifiably proud of the accomplishments of this agency. That is particularly so for the period since implementation of the bipartisan Bayh-Dole Act ("BDA") (35 U.S.C. §§ 200 – 209) in 1980, which unleashed a staggering amount of entrepreneurial zeal and creative energy. That outcome was entirely predictable because it is precisely the type of creative effort that – when properly incentivized – has driven American innovation since the founding of our republic. Prior to the implementation of the BDA, much of the scientific and technological research carried out by government agencies or developed pursuant to government grants to universities, research labs and others lay fallow in file drawers, notebooks and patents owned by either the government or the contractors that carried out the research. Although many if not most of the patents covering this government funded research were available for licensing, and a handful were in fact licensed, none of those licenses led to products that actually reached the market. This palpable lack of interest in commercializing products based on NIH research is informative – unless investors and private companies can actually own or control the technologies they bring to fruition, they are not likely to commit the time or money needed for this high risk undertaking. Simply put, what Congress learned after years of trying to interest private companies in using the inventions reflected by the patents on government funded research was that full ownership or exclusivity is an essential enticement without which there are far fewer takers, if any.

The BDA corrected this tragic waste of uncaptured value by allowing universities and research labs to own the patents that arise from their research efforts and to license those patents exclusively to private investors willing to provide the capital necessary to develop the manufacturing and delivery capabilities needed and to see the new products through the regulatory approval process.[2] As a result of these licensing relationships, the aftermath of the BDA has been the approval by FDA of hundreds of new drugs and medical devices, with many more in varying stages of completion.

To implement the objective of this workshop – "Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer" – I urge the agency to focus on those aspects of these public/private partnerships created under BDA that are most important in enticing companies to pour money and effort into moving beyond the science to create useful

---

[2] The BDA, in Section 202, provides for contractor ownership of patents developed using government research grants. Exclusive licenses, depending on their specific terms, can be tantamount to full ownership. The primary feature of such licenses is that the patent owner is not allowed to license other entities to practice the patent, either within a designated field of use or at all.

products. Most everyone understands that startups, small companies, entrepreneurs and their investors make a major contribution to our nation's development of new products based on research funded by NIH (and other agencies as well). As noted above, more than half of all new drugs come from this cohort. What are not as widely understood are the motivating factors that incentivize and disincentive these entities to start down the lengthy and risky path that leads to the new products. I encourage NIH to examine these factors from the perspective of the entrepreneurs and scientists who will devote the time and energy needed to create a marketable product from a partially proven idea, and the venture capitalists and other investors who must provide the funds necessary to make this process work.

Risk of Failure.

An overarching consideration in the mind of any startup entrepreneur or investor is the high probability at the outset that the enterprise will fail, usually ending in the complete loss of invested time and money by the founders. There are many types of risk that all startups and their investors must contend with – *e.g.*, the technology that works in the lab may not work at a scale feasible for commercial production; the executive team may fail to execute on the business plan; funding may be discontinued before the process is completed as some investors reassess the prospects for success; a newer and better technology may come along that nullifies some or all of the business assumptions; the ultimate cost of production may exceed the achievable selling price; etc.

A particularly daunting risk facing the developers of any new drug or medical device is the enormous and unpredictable cost associated with the need for regulatory approval. It is not unusual for any new drug to require years of experimentation and research before it can be proven to be both effective as a treatment and safe for humans and animals, during which time the developer receives little or no revenue from the product. Although overall costs can vary widely, a new drug can easily require ten or fifteen years of development work and $2B or more from inception to final FDA approval.[3] Even for those drugs that turn out to be successful, the time value of money makes this type of investment even more expensive, particularly for venture capital firms that must show returns on their investments to remain in business. It is also the case that only about 10% of the drugs on which work is initially commenced ever reach the point of market approval, meaning that close to 90% of the initial efforts at drug development fail for

---

[3] A report entitled "Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs," published in the Journal of Health Economics 47 (2016) describes a study of 106 new drugs developed by 10 different companies. The study estimates the average cost per drug at $1.4B without considering the time-value of the out-of-pocket investments. If a reasonable cost of funds is added, the total average cost is $2.8B per drug. https://pubmed.ncbi.nlm.nih.gov/26928437.

one of more of a variety of reasons, even after the science itself is proven and promising, because in clinical trials the product is either not safe or not effective or both.[4] Simply put, this is not an undertaking for the risk averse.

Price Controls Pose an Ongoing Existential Risk to Investing in Drug Development.

A foundational principle for investing in new drug development is that assumption of all the foregoing risks makes sense, if at all, only if the profitability of a successful venture is sufficiently attractive to cover the cost of the inevitable failures. Some critics of drug manufacturers are prone to look only at the product that successfully reaches the market and argue that the operating margin for the product is too high, leading to an uninformed insistence that NIH demand that products stemming from NIH funded research be sold at "reasonable prices." These arguments are wrong for a variety of reasons, most pointedly that bureaucrats have no idea as to what a reasonable price might be, because the actual cost of the risks assumed are not calculable. There are **theories** as to what might be a reasonable price for a specific drug, of course, but these calculations are not made by the people that, years earlier and during the development process, were willing to put up their own capital for funding the enterprise. The imposition of price controls after the fact is particularly damaging to investor confidence, because ownership or exclusive license rights to inventions are the primary basis for making the investments in the first place.[5] That is precisely why only a market-based system that allows the seller to price its product at a level of its own choosing can work effectively. Many startups go bankrupt trying to develop new products in areas dominated by established incumbents, and those that succeed must cover the cost of the failures or the investments will never be made in the first place.[6]

NIH's experience with the BDA actually confirms the difficulty in a governmental agency's efforts to inject itself into the arms-length bargaining that takes place in the real world.[7] NIH's

---

[4] The study referred to in the previous footnote puts the success rate for the drugs studied at 11.83%. *Id.* at p.23.

[5] Indeed, the seemingly perpetual demands for price controls is, in itself, a risk factor that must be accounted for in an investor's assessment of whether to accept a license from NIH or a government contractor to develop a new drug.

[6] This should not be controversial. Investing in drug development is somewhat akin to wildcat drilling for crude oil, which has been a common way of locating potential subterranean pools of oil since the early 20th century. The profit from a successful well has to cover the cost of all the dry ones or the entire business model makes no economic sense. Current figures put the success rate at about 10% for on shore drilling, which is roughly on a par with success rates for drug development. https://knowledge.energyinst.org/search/record?id=115186

[7] The provisions in the recently enacted Inflation Reduction Act that give CMS the power to dictate prices have yet to take effect. It seems clear enough already, however, that to whatever extent CMS engages in these "negotiations," it is likely to reduce the number of new drugs that are available for Medicare patients and cause a

effort in 1989 to add a "reasonable price" provision to the licenses that were offered under the BDA had the effect of reducing the number of private enterprises that were willing to assume the risks of developing products under these licenses. In 1995, the agency removed the pricing requirement, acknowledging that the effort had been a mistake.[8] Investor interest thereafter rebounded, but no one will ever know what possible drugs might have been missed for lack of funding during the decline. Nevertheless, the siren song of price controls continues to waft through governmental circles periodically, as it seems to be doing currently, and must be rejected as the bad idea it has always been.

Governmental Contributions to Drug Research Are Grossly Overstated by Proponents of Price Controls.

Because the research for many new drugs is often initiated, in part, through basic scientific research funded by NIH or other governmental agency, we often hear arguments that this contribution gives the government the right to control the price or access to the drug once it is proven. This bogus argument reflects either pure ignorance or ideological foolishness – in either case it is preposterous in light the actual reality. Of course, a seminal research contribution by NIH may be an important contributor, but its principal value is to assist the recipient in attracting the private capital necessary to perform the vast majority of developmental work, assume virtually all of the risk, and bear the bulk (or all) of the cost. The fact is that the NIH contribution is but a tiny fraction of the total investment required to bring a new drug to market, with the remainder coming from investors with a large appetite for risky investments.

A study published in September 2022, entitled "The Relative Contributions of NIH and Private Sector Funding to the Approval of New Biopharmaceuticals,"[9] showed that upwards of 95% of the total cost of developing a new drug to the point of clinical trials market is born by private investors, with the NIH contribution less than 5%. Moreover, for drugs that actually received FDA approval, the disparity is even more striking, with 98.5% of the total coming from private funding. For oncology drugs, the private contribution to cost is almost 99%. The study was based on NIH records covering the period between 1984 and 2021, during which NIH made 23,230 extramural grants for drug research, which in turn led to a total of 8126 patents that could be linked to discoveries funded by these grants. The study identified 41 therapies traceable to

---

significant loss of jobs in the biopharma industry. https://vitaltransformation.com/2023/06/the-impact-of-ira-policy-expansion-proposals-on-the-us-biopharma-ecosystem

[8] https://www.techtransfer.nih.gov/sites/default/files/CRADA%20Q%26A%20Nov%202021%20FINAL.pdf and https://ipwatchdog.com/2019/03/12/new-study-shows-bayh-dole-working-intended/id=107225

[9] Journal of Therapeutic Innovation & Regulatory Science (2023) Vol. 57:160 – 169. TIRS publishes peer-reviewed original research, review articles, commentaries, and letters to the editor on medical product discovery, development, regulation, access, and policy. https://www.springer.com/journal/43441

some portion of this universe of patents that reached the clinical trial stage successfully, and determined that 18 of the 41 received FDA approval. For the 41 therapies that underwent clinical trials, the aggregate contribution of NIH grants totaled $2.4B while the private contribution was $50.7B, or 95.5% of the total. This number did not include any post-approval contributions which make the disparity even greater. For drugs that actually received FDA approval, NIH funding accounted for $670M of the total cost while private sector investment totaled $44.3B or 98.5% of the total. Appendix A replicates Table 1 of the study listing all 41 therapies individually and showing the private versus public funding ratio for each.

The arguments favoring price controls – whether they come in the form of requests for the unlawful exercise of "march-in rights" that would distort the statutory language of 35 U.S.C. §203 or a request that NIH revert to the inclusion of a "reasonable price" requirement in its basic licenses to universities and other government contractors, as it did in 1989, are bereft of any proper basis in law or fact. Neither NIH nor any other government agency has any way of knowing or calculating what a "reasonable" risk-adjusted return should be, and the history of governmental efforts to control prices for the benefit of the public works out to have the opposite effect.[10] There is no more justification for NIH to try and control the price of drugs made under the BDA than there is for NIH or other government agency to argue that use of the federally funded interstate highway system entitles it to impose price restrictions on goods hauled to their destination that way; the suggestion is preposterous. This particularly so in light of the cost and risk factors discussed above and the need to attract new capital in order to have them at all.

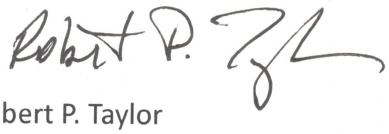
Conclusion.

Apart from the brief (and unsuccessful) experiment in the early 1990s, NIH has successfully resisted numerous invitations to reinterpret the intent of Congress as to "march-in rights" or to impose unmanageable price restrictions on the universities and research labs that develop new therapies. Contrary to the false premise that this will lower drug prices for the benefit of the American public, we do not believe that to be the case. Were either of those efforts to succeed, the most likely outcome is that investment in new drug development will decline, as it did in the early 1990s, to the detriment of those that might need the drugs that never are discovered or developed.

---

[10] The basic economic fallacy in attempts to control the price of goods or services is deftly explained by Robert L. Schuettinger in "Forty Centuries of Wage and Price Controls: How Not to Fight Inflation," published by Heritage Foundation (1979). https://cdn.mises.org/Forty%20Centuries%20of%20Wage%20and%20Price%20Controls%20How%20Not%20to%20Fight%20Inflation_2.pdf. The book recounts numerous historical examples of such efforts, dating back to the Code of Hammurabi, the Egyptian Pharaohs and continuing today, all notable failures.

Respectfully submitted,



Robert P. Taylor
General Counsel, USIJ
July 27, 2023

Table 1 Total Public (NIH) and Private Funding for Cohort of Forty-One Therapies.

Therapy	Total Public Funding ($ Mil)	Total Private Funding[a] ($ Mil)	Year Approved
IMMU-132 /(Trodelvy)	$0.850	$22,519.457	2020
Tysabri	$7.575	$8756.691	2004
Myalept	$8.332	$3179.600	2014
Nexavar	$5.305	$1384.030	2005
Stivarga	$5.072	$1384.030	2012
Bexxar	$6.616	$1093.400	2003
Zelboraf	$7.144	$1047.950	2011
Spinraza	$1.604	$965.400	2016
Emtriva/Genvoya	$6.407	$951.000	2003
RTA-408	$71.746	$850.000	–
Diamyd	$5.799	$639.000	–
Zarnestra	$16.380	$628.000	–
RcoPro	$104.354	$625.000	1995
CMX001	$4.151	$613.500	–
Surfaxin	$38.388	$558.140	2012
Ixinity	$3.598	$508.300	2015
DTX301	$124.321	$481.733	–
Obizur	$7.014	$400.000	2014
haNK	$5.143	$350.460	–
Neuradiab	$313.768	$326.600	–
Increlex	$1.172	$326.270	2005
Treg	$1.804	$325.000	–
Prochymal	$4.959	$279.250	–
Amdoxovir	$19.124	$245.000	–
Horizant	$453.074	$219.990	2011
PA-457	$10.773	$218.830	–
TNFerade	$197.250	$205.900	–
Daytrana	$4.151	$200.000	2006
V2006	$11.215	$184.270	–
Gencaro	$2.377	$174.955	–
ThermoDox	$79.250	$170.000	–
SR9025	$36.127	$160.000	–
Rintega	$314.546	$145.100	–
GI-5005	$2.788	$122.600	–
Tolsura	$5.401	$96.700	2018
RiVax	$1.717	$93.000	–
Levovir	$41.201	$73.500	–
AEOL 10,150	$64.835	$69.460	–
Combipatch/Vivelle-dot	$4.150	$65.000	1998
Oncoprex	$404.693	$34.120	–
MBX-400	$10.934	$0.000	–
Total	$2,415.108	$50,671.236	
Total (approved only)	$670.208	$44,280.958	

Private funding excludes post-FDA approval funding

Submission Date: 7/27/2023

Name: Cassidy Parshall

Name of Organization: Public Citizen

Comment:

Hello,

Please find attached comments from Public Citizen regarding the National Institutes of Health Office of Science Policy's July 31, 2023 workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer.

Thank you for the opportunity to provide written comments.

Sincerely,
Cassidy Parshall

Additional Comment (attachment):

PUBLICCITIZEN
1600 20th Street, NW • Washington, D.C. 20009 • 202/588-1000 • www.citizen.org

Public Citizen Comments to the National Institutes of Health re: Maximizing NIH's Levers to Catalyze Technology Transfer

July 27, 2023

Thank you for the opportunity to provide written comments regarding the National Institutes of Health (NIH) Office of Science Policy's July 31, 2023 workshop on policies and practices that shape biomedical innovation and promote access to NIH-funded discoveries.

Public Citizen is a nonprofit consumer advocacy organization with more than 500,000 members and supporters. Public Citizen's Access to Medicines Program works with partners across the United States and around the world to make medicines available for all through tools in policy and law.

Our comments will deliver two key messages:

- NIH has considerable power, and therefore responsibility, to improve affordable access to medicines in the United States and around the world.
- NIH's licensing policies, research and development (R&D) contract conditions, and rights under the Bayh-Dole Act are powerful tools to improve access to the medicines the agency helps develop.

NIH has considerable power, and therefore responsibility, to improve affordable access to medicines in the United States and around the world.

The United States government is the largest funder of biomedical research in the world, foremost through more than $40 billion dollars in annual funding of NIH, the vast majority of which supports extramural research at universities and other research

institutions.[1] Recent research found that NIH funding contributed to research associated with 354 out of 356 new drugs approved from 2010-2019, totaling $187 billion in public funding.[2] This extensive public investment in drug R&D gives the U.S. government and NIH significant power to condition the pricing and technology sharing behavior of manufacturers, and to facilitate access to publicly funded medicines.[3] In our view, the agency has underused these powers, with serious consequences for global health and costs to U.S. consumers. In a report released in June 2023 by the Majority Staff of the United States Senate Health, Education, Labor and Pensions (HELP) Committee, it was found that "the average (median) price of new treatments that NIH scientists helped invent over the past twenty years is $111,000."[4]

The federal government's early and robust investment in coronavirus research laid the foundation for the rapid development of many COVID-19 vaccine candidates.[5] In a 2020 report titled "Leading COVID-19 Vaccine Candidates Depend on NIH Technology," Public Citizen revealed that several first-generation candidates were using the 2P approach that was developed by NIH scientists.[6] Among these manufacturers, Moderna uniquely benefited from federal support. "We did the front end. They did the middle. And we did the back end," said Dr. Barney Graham, a former top NIH official, referring to the process for designing the spike protein sequence, manufacturing vaccines, and running clinical trials.[7]

---

[1] Public Citizen, Civil Society Organizations Call on the Department of Health and Human Services to Combat Excessive Drug Prices, https://www.citizen.org/wp-content/uploads/cso-letter-to-biden-re-nih-director.pdf; https://www.nih.gov/about-nih/what-we-do/budget

[2] Comparison of Research Spending on Ekaterina Galkina Cleary, PhD1,2,3; Matthew J. Jackson, PhD1,4; Edward W. Zhou, PharmD1,4; et al. New Drug Approvals by the National Institutes of Health vs the Pharmaceutical Industry, 2010-2019. https://jamanetwork.com/journals/jama-health-forum/fullarticle/2804378

[3] *See* Robert Weissman, Public Citizen, 'Preparing for the Next Public Health Emergency: Reauthorizing the Pandemic and All-Hazards Preparedness Act,' https://www.citizen.org/wp-content/uploads/Weissman-Senate-HELP-testimony-5.4.23.pdf

[4] Senate Health, Education, Labor, and Pensions Committee, Majority Staff, 'Public Investment, Private Greed,' https://www.sanders.senate.gov/wp-content/uploads/Sanders-Public-Medicines-Report.pdf

[5] Zain Rizvi, Public Citizen, 'Blind Spot: How the COVID-19 Outbreak Shows the Limits of Pharma's Monopoly Model,' https://www.citizen.org/article/blind-spot/

[6] Zain Rizvi, Public Citizen, 'Leading COVID-19 Vaccine Candidates Depend on NIH Technology,' https://www.citizen.org/article/leading-covid-19-vaccines-depend-on-nih-technology

[7] 'Rich Countries Signed Away a Chance to Vaccinate the World,' https://www.nytimes.com/2021/03/21/world/vaccine-patents-us-eu.html; Zain Rizvi, Public Citizen, 'Sharing the NIH-Moderna Vaccine Recipe,' https://www.citizen.org/article/sharing-the-nih-moderna-vaccine-recipe/

Despite significant taxpayer investment in the NIH-Moderna vaccine, the U.S. government failed to include safeguards for global access in its contracts with Moderna. The manufacturer went on to generate tens of billions in Covid vaccine sales while leaving the world with insufficient vaccine supply for more than a year. In a Public Citizen report, researchers showed that it was possible to manufacture enough vaccine for the world much more quickly – if the technology was shared by Moderna.[8]

Now Moderna is quadrupling the price of its Covid vaccines, which are expected to be needed annually.[9] This exceptional cost to U.S. consumers should have been avoidable. One approach would have been to include reasonable pricing provisions in the licenses NIH gave Moderna for use of government technology.

We appreciate the steps that the U.S. government and NIH have since taken to improve access to medicines globally. In 2022, President Biden announced licenses for 11 publicly owned medical technologies to the World Health Organization's (WHO) COVID-19 Technology Access Pool (C-TAP).[10] We commended this, noting that, "The announcement is a turn toward sharing not only doses, but knowledge, which is the difference between charity and justice. This path, if pursued with seriousness of purpose, can improve resilience to future pandemics and bring a measure of justice to a terribly unjust time." The collaborative research agreement between the National Institutes of Allergy and Infectious Diseases and South African manufacturer Afrigen is another positive step forward towards equitable access through sharing the latest science and technology.[11]

We call on NIH to shepherd global access and commit its full resources to this path of technology sharing by adopting licensing policies and R&D contract standards that proactively support medicines access. We believe it is both within NIH's power and responsibility to help ensure that taxpayers get a fair return on their investment while maximizing the impact of NIH's critical health technologies by making them available

---

[8] Public Citizen, 'How to Make Enough Vaccine for the World in One Year,' https://www.citizen.org/article/how-to-make-enough-vaccine-for-the-world-in-one-year/

[9] Robert Weissman, Public Citizen, 'Preparing for the Next Public Health Emergency: Reauthorizing the Pandemic and All-Hazards Preparedness Act,' https://www.citizen.org/wp-content/uploads/Weissman-Senate-HELP-testimony-5.4.23.pdf

[10] NIH Makes COVID-19 Technologies Available to Global Manufacturers Through WHO Program, https://www.techtransfer.nih.gov/policy/ctap; https://www.who.int/initiatives/covid-19-technology-access-pool/us-nih-licenses

[11] Public Citizen, 'NIH-Afrigen Agreement Will Help WHO's Fight Against Pandemics,' https://www.citizen.org/news/nih-afrigen-agreement-will-help-whos-fight-against-pandemics/

equitably and globally.[12]

In a June 2022 letter to President Biden, Public Citizen and 20 other civil society organizations called for the nomination of an NIH Director who will "prioritize patient access and public health in their role as the world's premier steward of biomedical research." We noted that, "the NIH Director is empowered to remedy price gouging and access constraints through licensing competition using march-in and worldwide royalty-free rights. The NIH can also proactively support access by adopting upstream policies that build transparency and reasonable pricing conditions into funding and cooperative research and development agreements."

NIH's licensing policies, research and development contract conditions, and rights under the Bayh-Dole Act are powerful tools to improve access to the medicines the agency helps develop.

Licensing NIH-owned inventions

NIH can increasingly use licensing agreements to support global and equitable access to NIH technologies, including through reasonable pricing provisions and non-exclusive licensing practices.

The Bayh-Dole Act requires NIH and other government agencies granting partially-exclusive or exclusive licenses to U.S. government-owned inventions to ensure that the scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application.[13] We urge NIH to take seriously this requirement and rigorously and transparently assess whether a license should be nonexclusive or have its exclusivity limited, for example, by omitting low- and middle-income countries from the geographic scope of exclusivity or by providing that a licensee will have its exclusivity curtailed or eliminated after certain revenue benchmarks have been achieved. Exclusive licenses grant corporations monopoly power, leading to high drug prices and in many cases rationing of essential medicines, where individuals or state programs cannot pay. As a result of monopoly pricing, Americans pay more than two-and-a-half times as much for prescription drugs than people in other countries.[14] One-in-

[12] Public Citizen, Letter to President Biden calling for a pro-access to medicines NIH Director, https://www.citizen.org/wp-content/uploads/cso-letter-to-biden-re-nih-director.pdf

[13] 35 U.S.C. § 209, Licensing Federally Owned Inventions. Knowledge Ecology International, Joint Comments by KEI, UACT, Social Security Watch and Health Gap on the proposed NIH Exclusive License in CAR Therapy to Lyell Immunopharma (Sept. 19 2019), https://www.keionline.org/31713.; Zain Rizvi, Public Citizen, 'Blind Spot: How the COVID-19 Outbreak Shows the Limits of Pharma's Monopoly Model,' https://www.citizen.org/article/blind-spot/

[14] RAND, Prescription Drug Prices in the United States Are 2.56 Times Those in Other Countries,

four Americans report they have been unable to afford their medicines.[15] Exclusivities can also throttle supply and allow companies to profiteer from taxpayer funded technologies.[16] If the government nonetheless grants an exclusive license, it should ensure that the exclusivity is appropriately limited as required under law.

Nonexclusive licenses should be the norm and leverage must be exercised at the outset to induce manufacturers to share technology, price reasonably, deliver transparently, and otherwise contribute to ensuring access. We appreciate NIH's nonexclusive licensing of the proline-substituted coronavirus spike protein. Nonetheless, NIH could have gone further to facilitate vaccine access, given its essential contribution. In a March 2021 letter to the Department of Health and Human Services and NIH, Public Citizen and other civil society organizations specified that the licensing agreement should "1. Empower the U.S. government to authorize manufacturing of mRNA-1273 – including by government-owned production facilities, 2. Require technology sharing with the World Health Organization to help ramp up global production, and 3. Include requirements for accessible pricing universally." These safeguards could have ensured that NIH technology maximized its impact on protecting public health in the United States and globally.

Additionally, NIH should work to identify qualified international licensees, and work closely on licensing and access strategies for key technologies with WHO and the Medicines Patent Pool. The Covid technologies recently licensed to WHO through C-TAP should set a precedent for NIH sharing technology globally. This would allow manufacturers from around the world to help scale-up production and prevent rationing.[17] The Medicines Patent Pool (MPP) aims to help solve the challenges faced by developing countries in accessing medical technologies by negotiating deals that are acceptable to both patent holders and generics firms. The U.S. licensed government-owned patents related to the HIV medicine darunavir to MPP in 2010, the first license

---

https://www.rand.org/news/press/2021/01/28.html; https://www.citizen.org/wp-content/uploads/Becerra-antimonopoly-letter-for-sign-on-1.pdf

[15] Gallup, Medication Insecurity by Race and Political Identity, https://news.gallup.com/poll/316052/large-racial-divide-covid- cost-concerns.aspx; https://www.citizen.org/wp-content/uploads/Becerra-antimonopoly-letter-for-sign-on-1.pdf

[16] Public Citizen, Letter to NIH Director Francis Collins: Ensure Access, Affordability and Open Science in COVID-19 Treatments and Vaccines, https://www.citizen.org/wp-content/uploads/Public-Citizen-letter-to-Francis-Collins-re-COVID-19-treatment-plans.pdf

[17] Zain Rizvi, 'The NIH Vaccine,' https://www.citizen.org/article/the-nih-vaccine/

granted to MPP.[18] This forward-looking contribution helped establish MPP and encourage subsequent licenses from the pharmaceutical industry. We hope NIH will build on this precedent and work increasingly closely with WHO and MPP.

Conditions in R&D funding agreements

Conditions in NIH research and development contracts are another powerful policy tool that NIH can use to support affordable access to the medicines and technologies that the agency helps fund. It should be a requirement that the corporations benefiting from public funding and public science act in the public interest.[19] This should include standard clauses ensuring federally funded inventions are priced reasonably. Reasonable pricing clauses were first introduced in 1989 and routinely used by the NIH in the early 1990s, and their reintroduction has been called for today by Senate HELP Committee Chair Bernie Sanders (I-VT).[20]

Most Favored Nations (MFN) clauses are one example of reasonable pricing that should be routine in any NIH R&D funding agreement. The Senate HELP Majority Staff recently found that "U.S. taxpayers virtually always pay more than people in other countries for treatments that NIH scientists helped invent."[21] At a bare minimum, Americans should not have to pay more than people in other rich countries for medicines our country helped to develop.[22] The MFN clause included in the United States' agreement for Pfizer's Paxlovid ensured that the U.S. received the lowest price for the drug among the G7 countries + Switzerland.[23]

Public Citizen's comments recently submitted to the Senate HELP Committee state: "[Operation Warp Speed] episodically used Most Favored Nations (MFN) clauses

---

[18] US National Institutes of Health (NIH) First to Share Patents with Medicines Patent Pool As it Opens for Business, https://medicinespatentpool.org/news-publications-post/us-national-institutes-of-health-nih-first-to-share-patents-with-medicines-patent-pool-as-it-opens-for-business

[19] Zain Rizvi, Public Citizen, 'Leading COVID-19 Vaccine Candidates Depend on NIH Technology,' https://www.citizen.org/article/leading-covid-19-vaccines-depend-on-nih-technology

[20] New Report Shows How Badly Big Pharma Is Ripping Off American People With Publicly Funded Medications, https://www.sanders.senate.gov/press-releases/news-new-report-shows-how-badly-big-pharma-is-ripping-off-american-people-with-publicly-funded-medications/

[21] Senate Health, Education, Labor, and Pensions Committee, Majority Staff, 'Public Investment, Private Greed,' https://www.sanders.senate.gov/wp-content/uploads/Sanders-Public-Medicines-Report.pdf

[22] Public Citizen Comments to the Senate HELP Committee re: Discussion Draft Legislation to Reauthorize the Pandemic and All-Hazards Preparedness Act, https://www.citizen.org/article/public-citizen-comments-to-the-senate-help-committee-on-the-pandemic-and-all-hazards-preparedness-act/

[23] Knowledge Ecology International, 'Pfizer Agrees to International Reference Pricing in US Government Contract for COVID-19 Therapeutic,' https://www.keionline.org/37294

allowing the government to purchase medicines at the lowest price available in 'covered nations.' When the government substantially subsidizes and de-risks R&D for a drug or vaccine, then a reasonable price should be substantially lower and reflect that public investment, rather than future supra-competitive profits, is the primary driver of innovation...Drug corporations and other opponents of reasonable pricing requirements often claim that when a version of reasonable pricing policy was in place in the early 1990s, that it chilled collaborations between the U.S. government and private collaborators, and that when the policy was lifted, that the number of cooperative agreements 'increased significantly and quickly.'[24] However, opponents' narrative of historical experience with reasonable pricing fails to withstand examination." Knowledge Ecology International's James Love has repeatedly debunked this argument before:[25,26]

> *This claim, made frequently by the technology transfer community, bears some scrutiny. KEI obtained data from the NIH on CRADAs under the Freedom of Information Act (FOIA), which is available here.[27] Until 1996, the NIH only reported what are now called "Standard" CRADAs. Beginning in 1996, the NIH added a new category, "Materials" CRADAs. All of the CRADAs involving the reasonable pricing clause were standard CRADAs.*
>
> *From 1990 to 1994, the calendar years when the reasonable pricing clause was used for the whole year, the average number of standard CRADAs executed was 33. There was also a significant biotech stock market crash in 1992 and 1993. From 1996 to 2000, the number of standard CRADAs increased, to an average of 46 per year. But a lot was happening that had nothing to do with the reasonable pricing clause.*
>
> *The average NIH budget was 55% higher in 1996 to 2000 than in 1990 to 1994. Probably more consequential, from year end 1992 to year end 1994, the NASDAQ*

---

[24] James Love. "Jamie Love Responds to Criticism of Knowledge Ecology International Letter," IP Watchdog, May 15, 2019. https://ipwatchdog.com/2019/05/15/jamie-love-responds-criticism-knowledge-ecology-international-letter/id=109239/

[25] KEI Comments on:
KEN23378 1T draft of the 2023 Reauthorization of the Pandemic and All-Hazards Preparedness Act (PAHPA), https://www.keionline.org/wp-content/uploads/KEI-comments-2023-pahpa.pdf

[26] Ibid.; James Love. "The number of standard and material CRADAs executed by the NIH from 1985 to 2020 and the relationship to NIH reasonable pricing clause," Knowledge Ecology International. April 5, 2021. https://www.keionline.org/wp- content/uploads/KEI-BN-2021-3.pdf

[27] "Cooperative Research and Development Agreements (CRADAs)," Drug Database. http://drugdatabase.info/cradas/

biotech index declined from 170.64 to 81.54, a decline of 48%, whereas from year end 1995 to year end 2000, the same index increased from 133.77 to 634.32, an increase of 374%.

More significantly, regarding the CRADA data, the number of standard CRADAs fell to 28 by 2005, and was relatively flat from 2000 to 2013, despite a massive 17-fold increase in the NASDAQ biotech index, and a 64% increase in the NIH budget. Are we supposed to conclude that increases in the NIH budget or rising share prices and new private investments aren't good for innovation because the number of CRADAs did not increase from 2000 to 2013?

March-in and paid-up rights under the Bayh-Dole Act

In addition to proactively establishing pro-access licensing policies and contract conditions, NIH should march-in and use its worldwide paid-up rights under Bayh-Dole to support access at home and abroad.[28] Publicly funded and publicly owned inventions developed through federal funding are governed through rules under the Bayh-Dole Act. These rules afford funding agencies, like NIH, certain rights over inventions developed with taxpayer funding to protect the public interest, including:

1) the right to "march-in" and license competition when a drug corporation is failing to make a medicine available on reasonable terms, or to alleviate health or safety needs not being met by the manufacturer;[29] and
2) a nontransferable, irrevocable, paid-up license to practice or have practiced the invention for or on behalf of the United States throughout the world.[30]

Patients and activists have long fought for the Department of Health and Human Services to use these rights to lower the price of the prostate cancer medicine enzalutamide (brand-name Xtandi), a medicine invented at University of California Los Angeles with NIH funding.[31] The Average Wholesale Price of Xtandi in the United States is six times the price of Xtandi in Japan.[32] More than 40 civil society organizations, in a letter to Secretary

[28] Public Citizen, Letter to President Biden calling for a pro-access to medicines NIH Director, https://www.citizen.org/wp-content/uploads/cso-letter-to-biden-re-nih-director.pdf
[29] 35 USC 203(a)(1) & (2)
[30] 35 USC 202(c)(4)
[31] Public Citizen & Partners Urge President Biden to Lower Price of Xtandi, https://www.citizen.org/wp-content/uploads/xtandi-march-in-request-cso-support-letter-2022.10_final-1.pdf
[32] Letter to Secretary Becerra and Acting Director Tabak on Xtandi March-in Petition and Most Favored Nation Clause in Pfizer Contract, Clare M. Love, Eric L. Sawyer, Robert Sachs, Universities Allied for

Becerra, have also called on the Department of Health and Human Services to use its march-in authority under the Bayh-Dole Act as a key policy option to combat excessive drug prices:

> *The federal government has the power under existing law to increase competition and lower drug prices...the Bayh–Dole Act allows the federal government to "march-in" on drug patents developed with federal funding, or to use such patents royalty-free on behalf of the United States.*[33] *These actions can help introduce additional producers. Generic competition, the Food and Drug Administration has found, can lead to price reductions of 95 percent.*[34]

We appreciate the opportunity to comment. Thank you.

Essential Medicines, February 3, 2022, https://www.keionline.org/wp-content/uploads/Love-Sachs-Sawyer-UAEM-Letter-Xtandi- PfizerContract-3Feb2022.pdf

[33] KEI, KEI Briefing Note 2017:1. Bayh-Dole Act and difference between March-In Rights and the world wide royalty free rights in patents, https://www.keionline.org/24132

[34] FDA, Generic Competition and Drug Prices: New Evidence Linking Greater Generic Competition and Lower Generic Drug Prices, https://tinyurl.com/uxdc9

Submission Date: 7/27/2023

Name: Stephen Susalka

Name of Organization: AUTM

Comment:

Dear Director Jorgenson,

Please find attached AUTM's written comments for the NIH's Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer.

Sincerely,
Steve

Stephen J. Susalka, PhD, CLP, RTTP (He/Him)
Chief Executive Officer

Additional Comment (attachment):

July 27, 2023

Lyric Jorgenson, PhD
Acting NIH Associate Director for Science Policy
National Institutes of Health
Office of Science Policy
6705 Rockledge Drive
Suite630
Bethesda, MD 20892
SciencePolicy@od.nih.gov

AUTM's Written Comments Regarding the Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer

Dear Director Jorgenson:

Thank you for the opportunity to provide written comments for the NIH Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer.

AUTM is the non-profit leader in efforts to educate, promote, and inspire professionals to support the further development of academic research that drives innovation and changes the world. Our community is comprised of more than 3,000 members who work in more than 800 universities, research centers, hospitals, businesses, and government organizations around the globe. AUTM's members are primarily from academic settings (67%). 15% are practicing attorneys; 5% are from industry; and 22% of our members are international.

AUTM members in academic settings are focused on advancing early-stage inventions and other technologies to the marketplace primarily through licensing to partners (i.e., implementers). Between 2012 and 2021 (the most recent decade for which we have data), our skilled professionals filed over 150,000 patents for academic inventors and over 16,000 in 2021 alone.

Between 2012 and 2021, our U.S. members negotiated over 60,000 intellectual property license agreements on behalf of U.S. universities and academic research institutions, and in 2021 alone over 8,000 such license agreements.

For these reasons, AUTM has valuable insights and an important voice regarding all aspects of technology transfer including the critical decisions about what to patent and what to license as well as how to do so in the most efficient manner.

Introduction

AUTM believes strongly in the importance of catalyzing technology transfer. Technology transfer has resulted in immeasurable societal benefits since 1980 when the Bayh-Dole Act ushered in the current technology transfer system. Studies have shown that since 1980, technology transfer has resulted in billions of dollars of private-sector investment, thousands of new companies formed, countless high-paying jobs, and the introduction of hundreds of new products and services that have improved the standard of living of Americans and contributed significantly to the growth of the American economy.

This history demonstrates the quantitative and qualitative benefits of increased technology transfer. AUTM believes that additional efforts to make technology transfer more efficient and more prevalent will lead to even more life-changing and economy-boosting innovations.

The good news is we know how to ensure the continued growth of technology transfer because we can look back and identify what has worked—namely, promoting innovation, ensuring strong and reliable property rights in inventions, allowing partnerships with industry for testing and development of such inventions, and access to the free market for the products that ultimately emerge from this process. The best way to promote these foundational elements of technology transfer is to provide as much predictability as possible in our currently balanced, yet fragile, innovation ecosystem. This includes supporting and defending strong patent rights and the Bayh-Dole Act while opposing the inclusion of reference price provisions in government funding, collaboration, and license agreements.

The Bayh-Dole Act (the "Act") has been in existence for more than 40 years now and, for most of those years, the Act has been faithfully executed, the United States has had the world's strongest patent system and, save for a 5-year period in the early 1990s, has promoted free market access by avoiding the imposition of reference price provisions.

As recommended below, efforts to weaken technology transfer should be rejected. The Act's march-in provisions were not designed to (and would not) lower drug prices. The same is true of efforts to weaken patents or burden technology licenses with provisions directed to reference pricing. Such efforts will harm innovation and will not have the desired effect of lowering drug prices.

Recommendations

AUTM recommends that the NIH's Office of Science Policy (OSP) take a leadership role on this issue to support strong patent rights, enable robust technology licensing rights, and oppose any policies or regulations that would weaken the American innovation ecosystem. This leadership will maximize NIH's own technology transfer, which would provide a significant carryover effect for all technology transfer. NIH OSP leadership will go a long way toward supporting the limitless benefits of technology transfer.

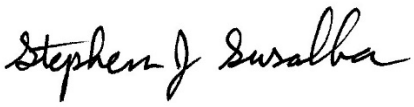
AUTM recommends that the NIH OSP support the NIH in (i) maintaining its consistent stance that the march-in provisions of the Bayh-Dole Act are not to be used as a mechanism to attempt to lower drug prices and (ii) continuing to reject all such petitions. Eliminating the threat of price-based march-in will remove a major obstacle to the partnerships that are necessary to further develop and commercialize the promising new technologies that come out of federally funded research laboratories.

AUTM also recommends that the NIH OSP insist on maintaining the ability of federally funded research organizations to grant licenses, including exclusive licenses, to their partners and the private sector. Exclusivity is sometimes an essential component of the commercialization process—without it, partners would be understandably leery of investing the time and resources necessary to develop a successful product. And without such investment, the technology stays in the lab and never becomes a product with the potential to benefit society.

Finally, AUTM recommends that the NIH OSP strongly oppose any inclusion of reference pricing language in government funding, collaboration, or license agreements. Including such language in any of those agreements will devastate university technology transfer as well as government technology transfer by impeding both universities and government research facilities from entering into the private-sector partnerships necessary to turn early-stage technologies into products and services. Such a result would cause great harm to the U.S. economy and, as just one example, to patients around the world who desperately await new treatments for devastating diseases—such as cancer, Alzheimer's Disease, heart, lung, and kidney disease—and for ever-evolving pathogens.

Thank you again for the opportunity to comment on this crucially important issue. AUTM looks forward to further engagement with the NIH both now and in the future.

Sincerely,



Stephen J. Susalka, Ph.D.
Chief Executive Officer

Submission Date: 7/27/2023

Name: Fred Ledley, Paula Chaves da Silva, & Edward Zhou

Name of Organization: Bentley University

Comment:

Please accept our written comments concerning the Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer

We are looking forward to joining this workshop on Monday.

Fred Ledley
Paula Chaves da Silva
Edward Zhou

Fred Ledley, M.D.
Professor, Departments of Natural and Applied Sciences, Management
Director, Center for Integration of Science and Industry
Bentley University

Additional Comment (attachment):

Written comments re:	**Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer**
Submission to:	**Office of Science Policy, National Institutes of Health SciencePolicy@od.nih.gov**
Event Date:	07/31/2023
Response to notice:	https://osp.od.nih.gov/events/workshop-on-transforming-discoveries-into-products-maximizing-nihs-levers-to-catalyze-technology-transfer/
Comments by:	Fred D. Ledley, M.D.[1] Director, Center for Integration of Science and Industry Professor, Departments of Natural & Applied Science, Management Bentley University, Waltham, MA Edward Zhou, Pharm. D. Center for Integration of Science and Industry Bentley University, Waltham, MA Paula Chaves da Silva, Ph.D. Center for Integration of Science and Industry Bentley University, Waltham, MA
Submitted:	July 27, 2023

[1] Contact information: Center for Integration of Science and Industry, Jennison 143, Bentley University, 175 Forest Street, Waltham, MA; email: fledley@bentley.edu; tel: +1.781.891.2046; web: www.bentley.edu/sciindustry

We are pleased to offer written comments to this workshop focused on "*… making federally funded inventions more accessible to the public…* ." These comments are informed by recent research from the Center for Integration of Science and Industry at Bentley University that has:

- Quantified the scope of NIH funding for basic or applied research, clinical development, or patents associated with drugs approved by the FDA 2010-2019. [2] This work identified $187 billion in NIH-funded research directly related to these drugs (applied research – 17%) or their biological targets (basic research – 83%),[3] representing a (discounted) investment comparable to reported levels of investment by industry, thus reducing the investment required by industry by approximately half.[4] These studies further show that less than 3.5% of this funding contributing to phased clinical trials[5] and <1% resulted in patents cited as providing market exclusivity and subject to the public interest protections of Bayh-Dole.[6]
- Compared the financial returns of biotechnology license from academic institutions with those between commercial firms.[7] This work demonstrated that the effective royalty rates and other payments associated with licenses of academic technologies under Bayh-Dole were less than half of those between commercial firms independent of the development stage of products anticipated under these Agreements or other intrinsic terms of the Agreements.
- A novel approach to quantify the "health value" or direct health benefit realized by individuals taking specific pharmaceutical products independent of impacts on economic activity or indirect, econometric inferences.[8]

Specifically, we would like to offer four comments:

1. The NIH makes investments in new drug approvals comparable to those of industry. While the NIH contributes primarily to early-stage, basic research, rather than applied research or development, evidence shows that this established foundation of basic science is requisite for successful product development. As such**, the public sector should expect normative returns on NIH investments in new drugs comparable to those of the biopharmaceutical industry.**
2. The restriction of the Bayh-Dole Act to "subject inventions" limits the Act's applicability to the results of basic research. **Effort should be directed at demonstrating the utility and enablement**

[2] Cleary, EG, Beierlein, JM, Khanuja, NS, McNamee, LM, & Ledley, FD (2018). Contribution of NIH funding to new drug approvals 2010–2016. Proceedings of the National Academy of Sciences, 115(10), 2329-2334. https://www.pnas.org/doi/abs/10.1073/pnas.1715368115; Cleary, EG, Jackson MJ, Zhou EW, Ledley FD. (2023) Comparison of Research Spending on New Drug Approvals by the National Institutes of Health vs the Pharmaceutical Industry, 2010-2019. JAMA Health Forum. 2023;4(4):e230511, https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0288447; Zhou, Edward W., Matthew J. Jackson, and Fred D. Ledley. "Spending on Phased Clinical Development of Approved Drugs by the US National Institutes of Health Compared With Industry." *JAMA Health Forum*. Vol. 4. No. 7. American Medical Association, 2023. https://jamanetwork.com/journals/jama-health-forum/fullarticle/2807184; Ledley and Cleary (2023) NIH funding for patents that contribute to market exclusivity of drugs approved 2010–2019 and the public interest protections of Bayh-Dole. PLOS ONE https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0288447; 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 Institute for New Economic Thinking, Working Paper No. 133, August 5th, 2020 (Revised July 19th , 2021) https://www.ineteconomics.org/uploads/papers/WP_133-Revised-2021.0719-Cleary-Jackson-Ledley.pdf

[3] Cleary et al., (2018) op cit; Cleary et al (2020) op cit; Cleary et al (2023), op cit.

[4] Cleary et al. (2023) op cit

[5] Zhou et al., (2023) op cit

[6] Ledley and Cleary (2023) op cit

[7] Shah, P., Vaughan G., Ledley, F.D. (2023) Comparing the economic terms of biotechnology licenses from academic institutions with those between commercial firms. PLOS ONE journals.plos.org/plosone/article?id=10.1371/journal.pone.0283887;

[8] Chaves da Silva, P. and Ledley, FD unpublished data

provided by NIH-funded basic science to ensure that the public interest provisions of the Act apply to a larger fraction of NIH-funded research.

3. Licenses of biotechnologies originating in academic institutions embody financial terms that are significantly less favorable than those of comparable licenses between commercial firms. **Additional effort needs to be made to establish that a "reasonable royalty rate" for academic licenses requires financial terms comparable to those of corporate licenses.**
4. **Impact indicators should be developed that measure the direct, measurable impacts of innovative pharmaceuticals on individuals and their health rather than indirect impacts on economic indicators or broad measures of population health.**

Background

The Bayh-Dole Act represents the only significant statutory instrument for promoting and protecting the public's interest in the health benefits arising from government-funded biomedical research and the products enabled by this research, direct economic returns from commercialization of these products, and indirect returns impacts on jobs, productivity, and economic growth. This is evident in the stated objectives of the Bayh-Dole Act to "*…promote the utilization of inventions arising from federally supported research or development…*," advance "*…the commercialization and public availability of inventions made in the United States by United States industry and labor…*," and protect the public "*…against nonuse or unreasonable use of inventions"*.[9]

By promoting commercialization of practical applications enabled by federally funded research, Bayh-Dole was designed to provide returns to the public sector in the form of commercial products to address unmet public needs, create jobs, stimulate economic growth, and expand the tax base.[10] Additionally, by ceding the revenues from technology licenses to non-profit institutions incorporated in the public interest,[11] Bayh-Dole positioned these institutions as proxies for the public sector in securing a direct return on public investment. To this end, Bayh-Dole further authorized these institutions to retain the proceeds from such licenses, providing that the proceeds are shared with the inventor and that institutional funds "*will be utilized for the support of scientific research or education*."[12]

Recent economic studies contextualize government's contributions to innovation as that of an "*early-stage investor*" and government funding for research as an "*investment.*" As such, these studies argue there should be an equitable balance of investment risk and return between the public and private sectors and frame the role of policy as shaping this balance[13] in which the public and private sectors both receive returns on investment commensurate with the risk of these investments.

---

[9] CFR. 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 Code of Federal Regulations 2010 [cited 2020 July 3, 2020]. Available from: https://www.govinfo.gov/content/pkg/CFR-2010-title37-vol1/pdf/CFR-2010-title37-vol1-part401.pdf.

[10] Sampat BN. Patenting and US academic research in the 20th century: The world before and after Bayh-Dole. Research Policy. 2006;35(6): p. 772–789; Federal Council for Science and Technology, Effects of Government Policy on Commercial Utilization and Business Competition, Government Patent Policy Study, final report. Federal Council for Science and Technology, 1968; Bray MJ, Lee JN. University revenues from technology transfer: Licensing fees vs. equity positions. J Bus Ventur. 2000;15(5-6): p. 385–392.

[11] Salamon LM. The new governance and the tools of public action: An introduction. Fordham Urb. LJ. 2000;28: p. 1611.

[12] Ouellette LL, Weires R. University Patenting: Is Private Law Serving Public Values? Michigan State Law Review. 2020;2019(5): p. 1328-1387.

[13] Mazzucato M, Li H. The entrepreneurial state: socializing both risks and rewards. Real-World Economics Review. 2018;84; Mazzucato M. An entrepreneurial society needs an entrepreneurial state. Harv Bus Rev. 2016:1-4; Lazonick W, Mazzucato M.

Based on our research, we offer three specific suggestions:

1. The public sector should expect normative returns on NIH investments in new drugs comparable to those of the biopharmaceutical industry.

Figure 1 shows a schematic of NIH funding for basic or applied research prior to first approval of drugs approved from 2010-2019.[14] NIH data includes NIH-funded projects related to: (i) the drug target (basic research) after accounting for spillover effects in which research on each drug target is associated with 2.85 approved products[15] (ii) the drug product (applied research) including phased clinical trials. Industry costs include the costs of phased clinical trials and "pre-human" studies. Statistical analysis demonstrates that the NIH spending on each new drug prior to first approval was not less than reported industry costs using different scenarios.[16] We call on the NIH to promote policies based on the expectation that the return on public investments in pharmaceutical innovation should not be less than the returns on private investment.

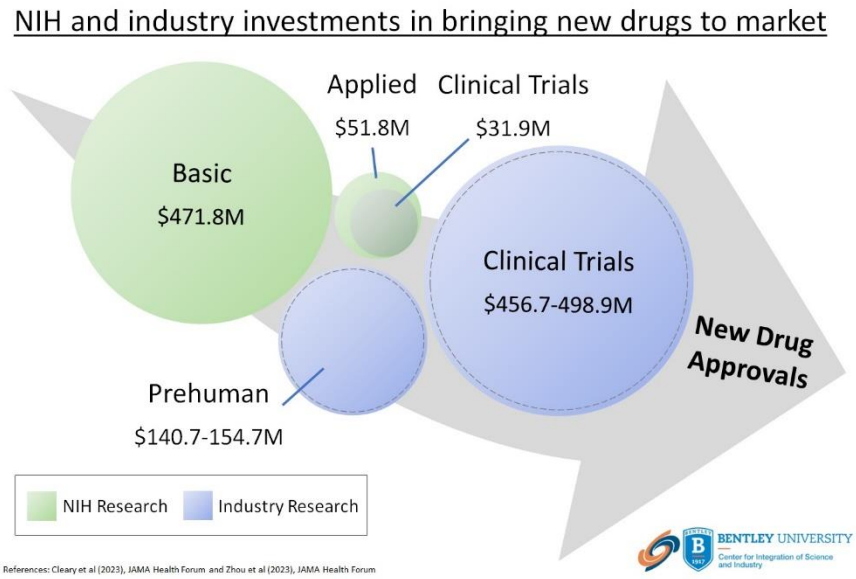


Figure 1. Average contributions of NIH and industry to first approval of novel pharmaceuticals 2010-2019. Data is based on NIH funding for basic research on drug targets, applied research on the drug (including clinical trials), and reported investments by industry from DiMasi et al (2016) or Wouters (2020).

The risk-reward nexus in the innovation-inequality relationship: who takes the risks? who gets the rewards? Industrial and Corporate Change. 2013;1093-1128; Laplane A, Mazzucato M. Socializing the risks and rewards of public investments: economic, policy, and legal issues. Research Policy. 2020;49: ; Cleary EG, et al (2023) op cit; Cleary EG, et al (2020) op cit G

[14] NIH data from Cleary et al., (2023) op cit; Zhou et al., (2023) op cit. Industry data from DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: new estimates of R&D costs. Journal of health economics. 2016 May 1;47:20-33. https://www.sciencedirect.com/science/article/abs/pii/S0167629616000291; Wouters OJ, McKee M, Luyten J. Estimated research and development investment needed to bring a new medicine to market, 2009-2018. Jama. 2020 Mar 3;323(9):844-53. https://jamanetwork.com/journals/jama/article-abstract/2762311

[15] The number of drug approvals/target was estimated from Santos R, Ursu O, Gaulton A, Bento AP, Donadi RS, Bologa CG, Karlsson A, Al-Lazikani B, Hersey A, Oprea TI, Overington JP. A comprehensive map of molecular drug targets. Nature reviews Drug discovery. 2017 Jan;16(1):19-34. https://www.nature.com/articles/nrd.2016.230%E2%80%B3

[16] Cleary et al. (2023) op cit.

2. Effort should be directed at demonstrating the utility and enablement provided by NIH-funded basic science to ensure that the public interest provisions of the Act apply to a larger fraction of NIH-funded research.

It is generally recognized that government plays a central role in funding the basic science that underlies innovation. Basic research is defined as "*…experimental or theoretical work undertaken primarily to acquire new knowledge of the underlying foundations of phenomena and observable facts, without any particular application or use in view,*"[17] though it may be "*use inspired.*"[18]

Table 1 shows the NIH-funded publications, project years of NIH funding, and costs associated with basic or applied research for drugs approved by the FDA from 2010-2019.[19] The method involves identifying publications in PubMed (PMID) related to the drug target (basic research) or the drugs (applied research), estimates the number of years of project funding related to that research (project years) and costs for those project years.[20] These data show that approximately 83% of the government-funded research related to these products represented basic research on the drug targets, rather than applied research on the drugs themselves.

Table 1. NIH funding for basic and applied research related to 356 NMEs approved by the FDA, 2010-

	DRUG Search[a]	TARGET Search[b]	Total
PubMed search results			
# Searches	356	217	
# Publications in PubMed (1985-2019)	229,401	1,911,507	2,017,408[c]
RePORT NIH-funded publications			
# Publications with NIH funding (1985-2019)	36,195	409,123	424,293[c]
% Publications with NIH funding	16%	21.4%	21%
Totals			
# Searches identifying publications with NIH funding	310	217	
% Searches identifying publications with NIH funding	87%	-100%	
RePORT Project Years and Costs	**Applied Research[d]**	**Basic Research[d]**	**Total**
# Project Years	42,549	317,354	359,903
Project Years costs ($ millions)	$30,954	$156,429	$187,383
% Total NIH funding	17%	83%	

[a]PubMed search performed with drug name and synonyms. [b]PubMed search performed with name of biological target. [c]Total is nonadditive due to publications identified in both drug and target searches. [d]Publications identified in a drug search are classified as applied research. Publications identified in a target search, but not a drug search, are classified as basic research.

While there is evidence that an established body of basic biomedical research on drug targets or technological components of a product is requisite for drug approval[21] basic research is not primarily

[17] NSF. Definitions of Research and Development: An Annotated Compilation of Official Sources. 2018.
[18] Stokes DE. Pasteur's quadrant: Basic science and technological innovation. Brookings Institution Press; 2011.
[19] Cleary E et al (2023) *op cit*; see also working paper Cleary et al., (2020) Institute for New Economic Thinking, *op cit*.
[20] The method is described in detail and available as a dashboard for public use at https://www.bentley.edu/centers/center-integration-science-and-industry/nih-funding-drug-innovation-dashboard

[21] McNamee LM, Ledley FD. (2017) Modeling timelines for translational science in cancer; the impact of technological maturity. PLOS ONE 12.3, e0174538, journals.plos.org/plosone/article?id=10.1371/journal.pone.0174538; McNamee LM, Walsh MJ, Ledley FD. (2017) Timelines of translational science: From technology initiation to FDA approval. PLOS ONE. 12.5 e0177371; Beierlein JM, McNamee LM, Walsh MJ, Kaitin KI, DiMasi JA, Ledley FD. (2017) Landscape of innovation for cardiovascular pharmaceuticals: from basic science to new molecular entities. Clinical Therapeutics. 39: 1409-1425 e20

concerned with applications and, thus, less like to generate a "subject invention"[22] than applied research and less likely to satisfy USPTO standards for patentability, which requires demonstration of utility and enablement in addition to novelty.[23]

This dynamic may be responsible for the observation that <1% of this NIH funding was represented in patents cited in DrugPatentWatch[24] (which includes the FDA Orange Book) and that these patents arose disproportionately from applied, rather than basic, research.[25] Our research identified NIH funding for basic or applied research related to each of the 313 drugs approved 2010-2019 with entries in DrugPatentWatch.[26] Table 2 shows that there were 6,344 patents in DrugPatentWatch associated with drugs approved 2010-2019. There were 22,409 patents identified as arising from NIH-funded projects that produced basic or applied research related to these products in RePORTER.[27] Only 104 of these

Table 2. Number of new drug approvals 2010–2019 associated with NIH-funded patents.

	# drugs
Drugs approved 2010-2019 with entry in FDA Orange Book or DrugPatentWatch[1]	313
…with at least one patent in FDA Orange Book or DrugPatentWatch	297
	# patents
…associated patents in FDA Orange Book or DrugPatentWatch	3,644
	Cleary dataset[2]
NIH-funded patents related to drugs approved 2010–2019	22,409
…number in FDA Orange Book or DrugPatentWatch (% associated patents)[3]	104 (2.9%)
	# drugs
Drugs with NIH-funded FDA Orange Book or DrugPatentWatch patents (% drugs)[4]	29 (9.3%)

[1] DrugPatentWatch includes all active and expired patents from the FDA Orange Book and certain additional patents on biological products identified by companies or patent search. [2] Cleary identified NIH-funded projects associated with drugs approved 2010–2019 or their targets as well as patents arising from these projects [2]. [3] Percentage of patents in FDA Orange Book or DrugPatentWatch associated with drugs approved 2010–2019. [4] Percentage of drugs approved 2010–2019 listed in FDA Orange Book or DrugPatentWatch. n/a – not applicable.

patents were cited in DrugPatentWatch in association with these products. Moreover, while NIH-funded research was associated with each of the 313 drugs approved 2010-2019 with citations in

[22] The Bayh-Dole Act defines a subject invention as "*…any invention of a contractor conceived or first actually reduced to practice in the performance of work under a funding agreement" and further requires that it must be "conceived or first actually reduced to practice in performance of the project.*" See: 27.Title 35 U.S. Code Chapter 18—Patent rights in inventions made with federal assistance, as amended Nov 1, 2000 (1980).

[23] USPTO. Manual of Patent Examining Procedure. Requirements for Specification Under 35 U.S.C. 112, First Paragraph 2020. https://mpep.uspto.gov/RDMS/MPEP/e8r9#/result/d0e213359.html?q=enablement&ccb=on&ncb=off&icb=off&fcb=off&ver=e8r9&syn=adj&results=compact&sort=relevance&cnt=10&index=1

[24] DrugPatentWatch is a registered trademark of thinkBiotech LLC available at www.drugpatentwatch.com. The dataset incorporates patents cited in the FDA Orange Book or cited in litigation regarding market exclusivity.

[25] Ledley and Cleary (2023) op cit

[26] This dataset for this project was somewhat smaller than the 356 drug approvals from 2010-2019 and $187 billion in NIH funding described in Cleary et al (2020) and Cleary et al (2023) due to the fact that not all approved products are covered by the Hatch-Waxman Act and included in the FDA Orange Book. While the DrugPatentWatch database expands on Orange Book dataset to include certain biological product, the current project restricted the dataset to the 313 products with at least one patent cited in this database.

[27] Note: The RePORTER database does not allow association of patents with specific project years of research funding. Thus, the 22,409 patents include research funded by the same project that contributed to basic or applied research on these drugs, but not necessary the publications directly related to these drugs or their targets. See Ledley and Cleary (2013) *op cit* for details.

DrugPatentWatch, only 29 (9.3%) had patents arising from this NIH-funded research. Overall, only 0.56% of NIH funding for research directly related to the drugs approved by the FDA from 2010-2019 was represented in patents cited in DrugPatentWatch, including only 0.38% of NIH funding for basic research on drug targets and 1.5% of NIH funding for applied research on the drugs themselves.

There is little publicly available data on the fraction of NIH-funded projects that produce disclosure of possible subject inventions or the fraction of such disclosures that lead to patent filing or licenses.[28] It is, thus, unclear whether the basic science research that enables drug approvals is not reported as a possible subject invention, is not pursued by technology transfer offices, or leads to patent applications that are rejected by the USPTO for inadequate demonstration of utility or enablement. In any case, the result is that little of the NIH-funded research that enables new drug approvals is subject to the public interest protections of Bayh-Dole designed to promote commercialization of products that represent practical applications of this research and the reasonable availability of these products to the public.

While the patent-centric design of the Bayh-Dole Act is beyond the scope of this research, we call on the NIH to support research on an experimental and theoretical basis for establishing that NIH-funded basic science, in fact, enables new drug discovery and development sufficient to satisfy the definition of a "subject invention" as well as USPTO standards of "utility," and "enablement." Information should also be collected and made public concerning the scope of disclosures under Bayh-Dole, the reasons universities or the NIH may choose not to pursue a provisional or full patent filing on subject inventions as well as the reasons that a patent application may be abandoned or rejected by the USPTO. Only by working to make NIH-funded basic research subject to the public interest provisions of Bayh-Dole can the technology transfer process operationalized by the Act ensure that the public interest in the fruits of this research is protected and the public receives an equitable return on their investment in pharmaceutical innovation.

3. Additional effort needs to be made to establish that a "reasonable royalty rate" for academic licenses requires financial terms comparable to those of corporate licenses.

Figure 2[29] shows the economic returns from academic licenses to commercial firms as well as those between commercial entities derived from BioSciDB[30] including the effective royalty rate on $500M in net sales, total reported deal size; and total precommercial payments. There were statistically significant differences between the returns to academic institutions from biotechnology licenses and those of licenses between commercial entities. Academic licenses had lower effective royalty rates (median 3% versus 8%, $p<0.001$), deal size (median $0.9M versus $31.0M, $p<0.001$), and precommercial payments (median $1.1M versus $25.4M, $p<0.001$) than corporate licenses. Controlling for the clinical phase of the most advanced product included in the license reduced the median difference in effective royalty rate between academic and corporate licenses from 5% (95% CI 4.3–5.7) to 3% (95% C.I. 2.4–3.6) but did not change the difference in deal size or precommercial payments. Excluding licenses for co-commercialization did not change the effective royalty rate but reduced the median difference in deal size from $15.8M (95% CI 14.9–16.6) to $11.4M (95% CI 10.4–12.3) and precommercial payments from

[28] While there is mandatory reporting of these events under Bayh-Dole, the Act also prohibits public disclosure of this information See: Rai AK, Sampat BN. Accountability in patenting of federally funded research. Nature biotechnology. 2012 Oct;30(10):953-6. https://www.nature.com/articles/nbt.2382

[29] From Shah et al.,(2023) *op cit*. Tables and portions of the text have been extracted from that publication.

[30] The BioScience database (now BioSciDB, part of Evaluate Ltd.) was provided courtesy of Mark Edwards.

$9.0M (95% CI 8.0–10.0) to $7.6M (95% CI 6.8–8.4). Controlling for deal terms including exclusivity, equity, or R&D in multivariable regression had no substantive effect on the difference in economic terms.

This research demonstrated that the economic returns to academic institutions from licenses of biotechnologies arising from federally funded research are substantially lower than those of comparable licenses between commercial firms. While the absolute value of the economic returns is influenced by the development stage of products, whether the licensee was a biotechnology or large pharmaceutical company, and whether the license agreement involved co-commercialization, the disparity between academic and corporate licenses is largely independent of these factors. There is currently no data resource available to systematically assess the returns to licenses granted pursuant to Bayh Dole[31] and whether or not these returns satisfy the legal standard of a "reasonable royalty rate."[32]

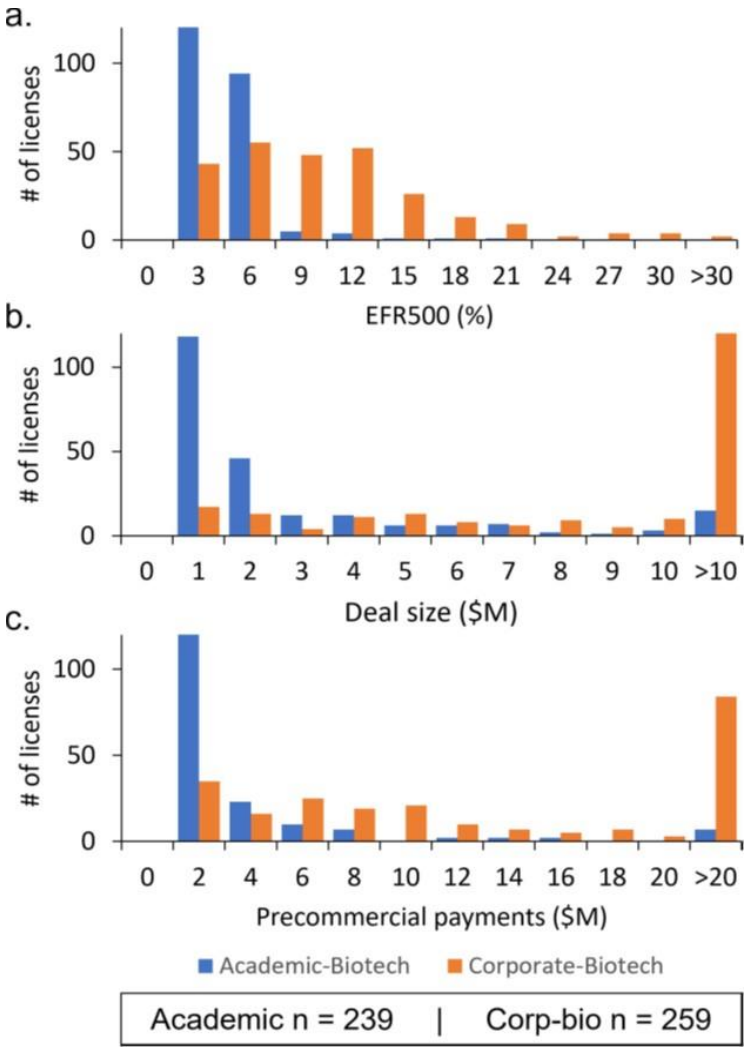


Figure 2. Histogram showing distribution of: (a) effective royalty rate; (b) deal size; and (c) precommercial payments associated with licenses from academic institutions to biotech or between commercial firms. Fom Shah et al (2023) op cit

We call on the NIH to engage in further research directed at establishing the principle that a "reasonable royalty rate" on academic licenses of

[31] Data in the BioScience database contains licenses agreements reported to the SEC obtained through FOIA petitions. The dataset is thus limited to licensed that a company considers "material" to their valuation. "Materiality" is legally defined as *"a substantial likelihood that the disclosure of the omitted fact would have been viewed by the reasonable investor as having significantly altered the 'total mix' of information*" and is assessed in relation to the significance of an item to users of a registrant's financial statements" (SEC, 1999). See: FASB, Amendments to Statement of Financial Accounting Concepts No. 8. Conceptual Framework for Financial Reporting Chapter 3, Qualitative Characteristics of Useful Financial Information. 2018, Financial Accounting Standards Board; Securities and Exchange Commission (SEC), SEC Staff Accounting Bulletin: No. 99–Materiality, August 1999; SCOTUS, MATRIXX INITIATIVES, INC., ET AL. v. SIRACUSANO ET AL. CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT No. 09–1156. SCOTUS 2011.

[32] A "reasonable royalty rate" is defined as "t*he amount which a prudent licensee who desired, as a business proposition, to obtain a license to manufacture and sell a particular article embodying the patented invention would have been willing to pay as a royalty and yet be able to make a reasonable profit and which amount would have been acceptable by a prudent patentee who was willing to grant a license.*" See Ouellette LL, Weires R. University Patenting: Is Private Law Serving Public Values? Michigan State Law Review. 2020;2019(5): p. 1328-1387; Jarosz JC, Chapman MJ. The Hypothetical Negotiation and Reasonable Royalty Damages: The Tail Wagging the Dog. Stan. Tech. L. Rev. 2012;16: p. 769; Seaman CB. Reconsidering the Georgia-Pacific standard for reasonable royalty patent damages. BYU L. Rev. 2010: p. 1661.

biotechnologies should not be lower than the rate associated with comparable corporate licenses. This requires greater attention to the reasons that technology transfer offices are not able to negotiate more equitable returns and addressing any systematic deficiencies in the research or licensing process that are identified.[33] It is also necessary to establish the legal principle that the reasonable royalty rate for academic licenses must be comparable to the rates of similar corporate licenses.

3. Impact indicators should be developed that measure the direct, measurable impacts of innovative pharmaceuticals on individuals and their health rather than indirect impacts on economic indicators or broad measures of population health.

Current methods for assessing the impact of technology transfer and the return on government investments in R&D are based largely on economic impact studies and impacts on metrics of employment, productivity, or economic growth. Such metrics, along with population measures of overall morbidity or mortality, do not measure the direct effects of new products on individuals, their state of health, or their wellbeing. Moreover, these methods cannot delineate the impact of individual products. A true measure of the impact of products licensed from academic or government institutions requires new methods that can delineate the impacts of individual products.

We are exploring methods for estimating the "health value" generated by development and dissemination of a specific pharmaceutical product. The method uses established measures of the quality of life gained (measured in Quality-adjusted life years [QALYs]) by use of a pharmaceutical product times the number of individuals using that product. The "value" of improved health is then calculated using a globally adjusted value for the "willingness to pay" (measured in WTP/QALY). Willingness to pay is classically recognized in marketing a mechanism for assessing the value ascribed to a product by an individual. An example of this analysis is shown in Table 3.

Table 3. Health value provided to CMS beneficiaries and US population by treatment with products to treat hepatitis C developed by Gilead Sciences.

		CMS beneficiares				*US population*			
Brand name	**QALY gained**	**individuals benefited**	**Health value**	**Drug spending**	**Residual Health Value**	**individuals benefited**	**Health Value**	**Drug spending**	**Residual Health Value**
Sovaldi	2.61	90,700	$12.1	$8.3	$3.8	156,655	$20.8	$13.1	$7.7
Harvoni	3.26	271,429	$44.5	$23.5	$20.9	388,105	$63.7	$33.4	$30.2
Epclusa	3.94	126,619	$24.0	$7.2	$16.8	176,332	$33.6	$9.0	$24.6
Total		*488,748*	$80.5	$39.1	$41.5	*721,093*	$118.0	$55.5	$62.4

All $ values in billion USD inflation adjusted to 2016. Health Value is calculated using a globally adjusted willingness to pay (WTP) of $52,619.4/QALY (Kouakou and Poder, 2022). Product names: Sovaldi (sofosbuvir); Harvoni (ledipasvir-sofosbuvir); Epclusa (sofosbuvir and velpatasvir). Data sources. QALY data represents average QALY gained compared to no antiviral treatment identified through literature review. Number of individuals benefited obtained from Market Information Data Analytics System (MIDAS) or Centers for Medicare & Medicaid Services (CMS). Reference: Chaves da Silva, P, Conti, R, Ledley FD (unpublished data).

This example estimates the "health value" generated by use of three drugs for treating hepatitis-C developed by Gilead Sciences. In this experiment, the number of QALY gained by an individual using the product is expressed relative to individuals not receiving antiviral drugs.

[33] Various postulated rationale are discussed in Shah et al (2023) op cit.

The results are expressed in two ways. First: total health value represents the number of QALY gained by taking the product times the number of individuals treated (benefiting) times a globally adjusted WTP of $52,619/QALY.[34] Second, the residual health value is calculated by subtracting the price paid for these drugs (i.e. retail price including Medicare out of pocket, or insurance). The results demonstrate the total health value realized by patients under Medicare Part D was >$80 billion with a residual health value of >$41 billion. Nationwide, the total health value realized through use of these products was >$118 billion with a residual health value of >$60 billion. While these studies are in their early stages, we would note that these results are not typical and reflect the value of drugs that cure a significant, endemic disease and have been made widely available through donations and emergence of generic products. These early results suggest it will be possible to directly measure the health value to individuals of novel pharmaceutical products in addition to the broad economic benefits to society. We encourage NIH to further support development of direct measures of pharmaceutical innovation on health.

Fred D. Ledley, M.D.
Paula Chaves da Silva, Ph.D.
Edward Zhou, Pharm.D.
July 27, 2023

[34] Kouakou CR, Poder TG. Willingness to pay for a quality-adjusted life year: a systematic review with meta-regression. The European Journal of Health Economics. 2022 Mar;23(2):277-99. https://link.springer.com/article/10.1007/s10198-021-01364-3

Submission Date: 7/27/2023

Name: Alex Moss

Name of Organization: Public Interest Patent Law Institute

Comment:

Please find attached the comments of the Public Interest Patent Law Institute regarding the upcoming NIH Workshop. Please let me know if there are any problems with the transmission.

Regards,
Alex Moss

_____
Executive Director
Public Interest Patent Law Institute

Additional Comment (attachment):

Public Interest
Patent Law Institute

COMMENTS OF THE PUBLIC INTEREST PATENT LAW INSTITUTE FOR WORKSHOP ON TRANSFORMING DISCOVERIES INTO PRODUCTS: MAXIMIZING NIH'S LEVERS TO CATALYZE TECHNOLOGY TRANSFER

The Public Interest Patent Law Institute ("PIPLI") is grateful for the opportunity to participate in and provide comments for the Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer ("Workshop").

PIPLI is a nonprofit, nonpartisan public interest organization dedicated to ensuring the patent system promotes innovation and access for the public's benefit. Because the lives and livelihoods of countless Americans depend on access to medical advances, their interests should be central to policy decisions affecting the advancement and accessibility of medical research, but members of the public rarely participate directly in the institutions responsible for these policies, such as the National Institutes of Health and U.S. Patent and Trademark Office.

PIPLI's mission is to enhance public participation and representation in institutions such as these that shape the nation's science and technology policies so that they promote the advancement and accessibility of scientific advances more effectively and equitably. In service of its mission, PIPLI conducts policy research; provides pro bono assistance to individuals and organizations on patent-related matters; advocates for greater transparency in courts and government agencies; and submits amicus briefs and policy comments to courts and government agencies.

I. OVERVIEW

The National Institutes of Health (NIH) plays a crucial role in advancing life-saving medical breakthrough, such as its contribution to the development of mRNA technology, which underlies highly effective COVID-19 vaccines is a remarkable achievement of great societal value. Given the significance of NIH research, it is essential to maximize its ability to facilitate the development and widespread access to medical technology.

In connection with these goals, we have identified three key areas where the NIH can further enhance public benefits from its work. First, NIH patents should be of the highest quality to ensure their effectiveness and integrity as well as to serve as models of patent quality for others to follow. Second, the NIH should carefully consider and develop guidelines for researchers deciding whether, when, and why to file patent applications. Third, the NIH should provide more information about its patent licenses for the benefit of licensees, policymakers, scholars, patients, and the overall efficiency of licensing markets.

We sincerely appreciate the opportunity to share our comments on these vital matters and commend the NIH for engaging in constructive discussions with scholars, policy advocates, and patients. We hope that this marks the beginning of a series of fruitful conversations leading to policies and practices that amplify the impact and benefits of the NIH's invaluable work on enhancing scientific progress, public health, and the nation's well-being moving forward.

II. COMMENTS

A. NIH Patents Should Be High Quality Patents.

Ensuring that the NIH patents are high quality patents is critical to the agency's mission of promoting research and development in the medical field, enhancing public health, and expanding the base of scientific knowledge. High quality patents can help drive innovation by clearly defining the subject of patent protection and thus of technology transactions for licensing partners and the NIH itself to determine whether and what kind of licenses are required. Patents that provide information that allows others to make and use the claimed invention fuel further research and ensure the public gets its full share of the patent bargain. And patents that claim genuinely novel and non-obvious inventions contribute to the stock of available knowledge, fulfilling the patent system's fundamental objective. Low quality patents, however, can have adverse effects. For example, they may provide excessive rights beyond their contributions; create uncertainty about space for research, development, and competition by others; and deprive the public of access to information required to make medical technology accessible on a wide scale.

While issuing high quality patents is the USPTO's top priority,[1] But given the USPTO's workload, their heavy workload makes it challenging to prevent low quality patents from being granted. At the beginning of 2023, the USPTO's approximately 8,000 examiners faced a backlog of 694,600 unexamined patent applications, expecting a similar number of new filings as the previous year (457,500).[2] Moreover, a Government Accountability Office report revealed that 69% of patent examiners handling biology and organic chemistry applications felt they had insufficient time for effective prior art searches.[3] This leads to a concerning situation where around 40% of granted patents are later found invalid when challenged.[4]

The NIH possesses a unique opportunity to aid the USPTO in ensuring and enhancing patent quality. Patents resulting from NIH-funded research can serve as examples of patent quality, alleviating the USPTO's burden and providing a model for grantees and other research entities, both public and private, to follow. Key characteristics of high-quality patents include well-defined and appropriately limited claims; comprehensive and understandable disclosures enabling others to make and use the invention; and claims meeting substantive patentability requirements of eligibility, novelty, and non-obviousness. Furthermore, by mandating that patent agents and

---

[1] *See, e.g.*, Remarks by USPTO Director Kathi Vidal to the Public Patent Advisory Committee, May 10, 2022, https://www.uspto.gov/about-us/news-updates/remarks-uspto-director-kathi-vidal-ppac-0 ("Today's discussion centers around patent quality. This is job number one. It is the most important aspect of our operations. We are constantly looking at ways to improve the examination of patent applications and the claims within them. We want our examiners to know how important their work is to the success of the patents they allow.").

[2] Statement of USPTO Director Kathi Vidal before the U.S. House of Representatives, April 27, 2023, https://www.uspto.gov/about-us/news-updates/statement-under-secretary-commerce-intellectual-property-and-director-united.

[3] Gov. Accountability Office, *Intellectual Property: Patent Office Should Strengthen Search Capabilities and Better Monitor Examiners' Work*, July 20, 2016, at 76, https://www.gao.gov/assets/gao-16-479.pdf.

[4] Josh Landau, *A Little More Than Forty Percent: Outcomes At The PTAB, District Court, and the EPO*, Patent Progress, May 1, 2018, https://www.patentprogress.org/2018/05/a-little-more-than-forty-percent/.

attorneys filing NIH patents adhere to patent quality guidelines, these practices will become ingrained in their approach and, over time, permeate the entire patent bar.

We respectfully urge the NIH to conduct additional workshops or public consultations to establish patent drafting guidelines for NIH researchers and grantees. This proactive step will lead to improvements in the quality of patents arising from NIH-funded research, helping to maximize the benefits they provide to the agency, licensing partners, researchers, and patients alike.

B. The NIH Should Carefully Consider Whether, When, and How to File Patent Applications.

Granted patents are not necessarily the sole or most optimal means of accomplishing the NIH's objectives of fostering scientific research. Therefore, we strongly encourage the NIH to proactively assess the advantages of patent protection in each case. Some situations may call instead for ensuring that advancements are openly available to all, without being subject to patent protection.

However, there is a potential risk that other entities may attempt to patent such advancements, which could hinder access for researchers and patients. In such scenarios, the NIH might consider seeking patent protection. Nonetheless, an alternative approach should also be considered: filing patent applications with comprehensive disclosures, ensuring they are published and thus become accessible prior art, without proceeding with the subsequent steps (or incurring related fees) necessary for them to mature into granted patents.

While printed publications are technically considered prior art references during patent examination, it is evident that patent documents are "[b]y a substantial majority, the principal references utilized by examiners."[5] This gives rise to significant problems, primarily because "patent literature is not likely to contain a complete description of technologies in new and emerging markets or markets that have not traditionally been characterized by heavy patenting activity, . . . yielding questionable patent grants in these fields that can easily be called into question by taking common sense and general knowledge into account."[6] Encouraging researchers to submit their work in the form of a patent application, even if they might not intend to obtain an issued patent, for the purpose of ensuring it is available to examiners (and potential patent challengers) as prior art would be a valuable measure to address these challenges.

Published applications are especially useful because they expand the base of available prior art without burdening the agency with the work and cost of obtaining and maintaining granted patents, increasing transaction costs for private entities, or imposing the costs of excessive exclusivity on the public.

---

[5] Jorge L. Contreras, *Common Knowledge and Non-Patent Literature in the Internet Age*, Berkeley Tech. L. J., Mar. 12, 2016, at 1, https://btlj.org/2016/03/common-knowledge-and-non-patent-literature-in-the-internet-age-2/#easy-footnote-bottom-1-4842 (citing John R. Allison & Mark A. Lemley, *Who's Patenting What? An Empirical Exploration of Patent Prosecution*, 53 Vand. L. Rev. 2099, 2130-32, 2158-60 tbl.13 (2000); Julie Callaert et al., *Traces of Prior Art: An Analysis of Non-Patent References Found in Patent Documents*, 69 Scientometrics 3, 7, tbl.1 (2006) (observing that 83% of USPTO references were patents); Christopher A. Cotropia, Mark A. Lemley & Bhaven Sampat, *Do Applicant Patent Citations Matter*?, 42 Research Policy 844, 847 (2013)).

[6] *Id.*

Evidence shows that patent applications are also uniquely valuable to patent examiners when compared to granted patents.[7] As one study explains:

> Patent examiners use abandoned published applications more often than issued patents when issuing anticipation rejections (concluding the applied-for invention is not novel—i.e., it has been done before) and obviousness rejections (concluding the applied-for invention is obvious—i.e., enough of a technical advance over what has been done before) in an office action. Beyond just rejections, our study finds that abandoned applications are more likely than issued patents to be cited as relevant by patent examiners during patent prosecution. The office actions require applicants to narrow and amend their claims or include specific arguments as to why the USPTO incorrectly determined that the claims are anticipated or obvious. Given our empirical findings that the USPTO rejected a large number of applications based on published yet abandoned art, a significant quantity of patent scope was narrowed because of abandoned applications. These abandoned published applications appear to be quite valuable disclosures, at least from the USPTO's perspective; yet, the applicants received no patent reward.[8]

In other words: patent examiners are more likely to cite published applications than granted patents when rejecting unpatentable applications. These rejections can prevent invalid patents from issuing or increase the quality of granted patents by leading applicants to clarify and/or narrow the scope of their claims.

Submitting patent applications with the intent of obtaining their publication as prior art references rather than pursuing their issuance as granted patents has great promise as a means of enhancing access to scientific knowledge. To facilitate this approach, we encourage the NIH to develop clear guidelines for determining when published applications would be more conducive to advancing technology development and transfer than obtaining granted patents. Furthermore, we recommend close collaboration with the USPTO to streamline the process, making it easier for applicants (within and outside the NIH) to submit such filings.

C. NIH Patent Licensing Information Must Be More Transparent to Policymakers, Scholars, and the Public.

The American public has a strong interest in accessing more information about NIH patent licenses than is currently available. Information about royalty rates and licensing revenue generated from these patents is essential for policymakers, scholars, and the public to understand and improve the effect that public policy and funding decisions have on the development and accessibility of medical advances.

---

[7] Christopher A. Cotropia & David L. Schwartz, *The Hidden Value of Abandoned Applications to the Patent System*, 61 B.C.L. Rev. 2809 (2020), https://scholarship.richmond.edu/cgi/viewcontent.cgi?article=2623&context=law-faculty-publications.

[8] *Id.* at 2812–13.

While some information may need to be kept confidential for a limited period, perpetual confidentiality is not warranted. Even data with national security implications must be disclosed after a reasonable time frame.[9] The importance of public access to information about government activities information must not be taken lightly: "Our democratic principles require that the American people be informed of the activities of their Government," and "our Nation's progress depends on the free flow of information both within the Government and to the American people."[10] Information about patent licensing is relevant to policy issues of paramount importance, such as the high drug prices in the U.S., shortages in drug manufacturing supply chains, and corporate tax avoidance strategies.

At the very least, the public should be able to access royalty rate information in a manner that incorporates confidentiality protections when appropriate—for example, through redactions of identifying information about licensees or regular reports of aggregated royalty and revenue data—as well as at times when such protections are no longer appropriate—for example, within a reasonable time after the expiration of a license or patent.

Recent reports indicate that the NIH is licensing at least some of its patents under highly generous yet undisclosed terms. For instance, the Senate HELP Committee found that one licensing agreement provided for royalty payments of approximately 1% on product sales without ensuring that product prices would be reasonable or limited in any respect.[11]

This information raises serious concerns about the extent to which the public is benefiting from publicly funded research. When the public takes on investment risks, it should receive a reasonable rate of return through licensing revenue, reduced market prices, or a combination of both. Given this context, we urge the NIH to consider reintroducing reasonable pricing clauses to its licenses and licensing requirements at least when licenses offer royalty rates that appear unreasonably low, such as rates of 5% or less. Additionally, the NIH should consider including such clauses when licensees utilize tax shelters, such as operating as subsidiaries of foreign corporations paying most of their taxes overseas.[12] It is economically and morally inappropriate for the American public to invest in research while other countries pay less for resulting products and receive more of the tax income generated.

That said, greater transparency might provide valuable context or provide other public benefits. For example, if the NIH regularly licenses patents at rates as low as 1%, the disclosure of this information could support generic drug manufacturers in obtaining similarly low rates during

---

[9] *See, e.g.,* Executive Order 13526—Classified National Security Information, Dec. 29, 2009, ("If the original classification authority cannot determine an earlier specific date or event for declassification, information shall be marked for declassification 10 years from the date of the original decision, unless the original classification authority otherwise determines that the sensitivity of the information requires that it be marked for declassification for up to 25 years from the date of the original decision.").

[10] *Id.*

[11] U.S. Senate HELP Committee, *Public Investment Private Greed*, June 12, 2003, at 2, https://www.sanders.senate.gov/wp-content/uploads/Public-Medicines-Report-updated.pdf.

[12] *See, e.g.*, Jesse Drucker, *Ireland central to alleged $1.4bn 'abusive' tax shelter by pharma giant: Accidental disclosure by IRS exposes $1bn tax fight with Bristol Myers Squibb*, Irish Times, April 3, 2021, https://www.irishtimes.com/business/health-pharma/ireland-central-to-alleged-1-4bn-abusive-tax-shelter-by-pharma-giant-1.4527583.

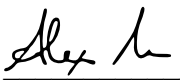
negotiations or litigation against private patent owners, which would lead to reduced production costs and market prices for generic medicines. In the long run, such transparency could also decrease transaction costs and prevent patent litigation by increasing the clarity and predictability of patent royalties and making licensing markets more efficient and symmetrical.

The potential value of patent licensing information is especially great because of the law governing damages for patent infringement. By law, patent owners are entitled to receive no more and no less than a "reasonable royalty" for patent infringement (35 U.S.C. § 284). Comparable licenses are often used as evidence of what constitutes a "reasonable" royalty. Therefore, providing information about government patent licenses can be invaluable evidence for generic drug manufacturers, particularly those without access to such data due to not being government licensees.

III. CONCLUSION

PIPLI appreciates the opportunity to provide comments on these important issues and commends the NIH for organizing this Workshop. We eagerly anticipate future opportunities for public consultation as well. Specifically, we strongly urge the NIH to conduct workshops or create other avenues for public feedback concerning guidelines on NIH patenting decisions, patent application drafting, and the transparency of patent license information. Progress in these areas is vital for maximizing the NIH's influence on technology transfer and public health outcomes.

Respectfully submitted,



Alex H. Moss
Executive Director
Public Interest Patent Law Institute
alex@piplius.org

July 27, 2023

Submission Date: 7/28/2023

Name: Jocelyn Ulrich

Name of Organization: Pharmaceutical Research and Manufacturers of America

Comment:

Dear Dr. Jorgenson,

Please find attached comments from PhRMA to inform the proceedings of NIH's Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer.

Sincerely,

Jocelyn

Jocelyn Ulrich, MPH
she/her/hers
P*h*RMA
Deputy Vice President
Policy, Research and Membership

Additional Comment (attachment):

July 27, 2023

SUBMITTED VIA EMAIL to sciencepolicy@od.nih.gov

RE: Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer

Dear Dr. Jorgenson,

The Pharmaceutical Research and Manufacturers of America (PhRMA) is pleased to submit comments to inform the proceedings of NIH's Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer. PhRMA believes that maximizing the timely transfer of federal investments in science and technology and attracting greater private sector investment to create innovative products, processes, and services as well as new businesses and industries, is critically important for America's patients, the U.S. economy, and our national security.

PhRMA represents the country's leading innovative biopharmaceutical research companies, which are devoted to researching and developing medicines that enable patients to live longer, healthier and more productive lives. Since 2000, PhRMA's member companies have invested more than $1.1 trillion in the search for new treatments and cures, including an estimated $102.3 billion in 2021 alone.[1]

The U.S. biopharmaceutical industry relies on a well-functioning, science-based regulatory system, strong and reliable intellectual property (IP) protections, and coverage and payment policies that support and encourage medical innovation to thrive. This framework, in addition to the collaborative biopharmaceutical research ecosystem that includes both the private and public sectors, yields more innovative medicines than any other country in the world. The American biopharmaceutical research ecosystem is among our country's greatest strengths – largely due to policies enacted by Congress to ensure that federally funded inventions can move from the laboratory to the marketplace for the public good.

Congress passed the Bayh-Dole Act in 1980 with bipartisan support to incentivize the private sector to transform discoveries resulting from government funded early-stage research into useful products. By allowing grant recipients such as universities to retain the title to the patents covering their inventions and enabling them to license the patents and the right to use those inventions to private sector partners, the Bayh-Dole Act facilitates the development of commercially available medical treatments. Prior to enactment of the Bayh-Dole Act, the government retained the patents on federally funded inventions – and only 5% of those patents

[1] 2022 PhRMA Annual Membership Survey, https://phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Refresh/Report-PDFs/P-R/PhRMA_membership-survey_2022_final.pdf

were ever licensed for use in the private sector.[2] Collaboration was further incentivized by The Federal Technology Transfer Act of 1986, which authorized Federal laboratories to enter into cooperative research and development agreements (CRADAs) with private businesses and other entities. These policies have proven critical to maximizing taxpayer benefit for government-funded research. Several studies have demonstrated that increases in NIH-funded basic research results in increased private R&D investment and innovation.[3] One study found that in the decade following an increase in NIH funding, private R&D spending grew by about eight times as much as the increase.[4] Another study found that each $10 million increase in NIH funding resulted in private sector investment yielding a net increase of 2.7 patents.[5]

Although many medical discoveries have their origin in the research laboratories at the NIH or federally funded academic medical centers, technology transfer is what allows these discoveries to be developed, reduced to practice and made available to improve public health through licensing and collaboration agreements with the private sector. According to the NIH Office of Technology Transfer, "technology transfer moves medical innovation from the benchtop through additional research and development, testing, regulatory approval, manufacturing, and finally to distribution as a medical product which will improve the health of everyone."[6] Partnership between the government and the private sector is critical because each plays a fundamentally different but complementary role in the biopharmaceutical R&D ecosystem. According to the Congressional Budget Office (CBO), "the complementary relationship between public and private R&D spending arises mainly because NIH funding focuses on basic research that leads to the discovery of new drugs and vaccines, whereas private spending focuses on applications of such research."[7] While NIH plays an important role in fostering basic research in genomics, molecular biology and other life sciences that have identified new disease mechanisms, these discoveries are far from fully developed therapies for patients. These discoveries only become fully developed therapies available to patients because of private industry contributions, both financial and technical.

The biopharmaceutical industry's unique role in the research ecosystem is to utilize its scientific and industrial expertise and invest at risk to build upon and further advance basic science research to determine if safe and effective treatments can be developed and made available to patients. The federal government cannot research, develop and manufacture vaccines and other new treatments without the resources, scientific expertise, R&D, manufacturing and

[2] Mittal, A. K. (2009). *Federal Research: Information on the Government's Right to Assert Ownership Control Over Federally Funded Inventions*. Available at: https://www.gao.gov/assets/gao-09-742.pdf

[3] Schacht, Wendy H. (2012). *Federal R&D, Drug Discovery, and Pricing: Insights From the NIH-University-Industry Relationship*, Congressional Research Service Report RL32324.

[4] Toole, Andrew A. (2007). *Does Public Scientific Research Complement Private Investment in R&D in the Pharmaceutical Industry?* Journal of Law & Economics, 50(1) 81–104, https://doi.org/10.1086/508314.

[5] Azoulay, Pierre et al. (2019*). Public R&D Investments and Private-Sector Patenting: Evidence From NIH Funding Rules*, Review of Economic Studies, 86(1)117–15. Available at: https://academic.oup.com/restud/article/86/1/117/5038510?login=true

[6] https://www.techtransfer.nih.gov/nih-and-its-role-technology-transfer

[7] https://www.cbo.gov/publication/57126

technological platforms and financial investment from private sector biopharmaceutical companies.

A rich body of research documented the nature of the complementary roles of the public and private sectors in advancing medical treatments. In 2001, the NIH concluded in a study for Congress that the biopharmaceutical industry was responsible for the discovery and development of 91 percent (43 out of 47) of all the top-selling marketed drugs in 1999.[8] A 2010 analysis of 252 drugs approved between 1998 and 2007 found that 76 percent originated in industry vs. 24 percent in academia.[9] A 2014 study of the most transformational drugs of the 25 prior years, as identified by over 200 physicians, found that the private sector was responsible for the vast majority of the work required to develop a therapy.[10] An analysis of the contribution of NIH funding to new drug approvals 2010 – 2016 found that although NIH funding contributed to published research associated with every one of the 210 new drugs approved by the FDA in those years, 90% of the NIH funding supported basic research related to the biological targets for drug action rather than the drugs themselves.[11] And an analysis of 23,230 NIH grants awarded in the year 2000 that were ultimately linked through the reported patent filings to 18 FDA-approved therapies showed that NIH funding totaled $0.670 billion, whereas private sector funding totaled $44.3 billion.[12] Accordingly, the private sector makes a substantial investment in research and development of biopharmaceuticals that far exceeds the contribution of the public sector.

The NIH has certain rights and procedures when it considers licensing a patented invention for further development by the private sector. Companies that want to obtain a license to develop an NIH invention must complete an application, and if the applicant has requested an exclusive or partially exclusive license the NIH will publish a notice in the Federal Register, as required by law, and after review and evaluation of public comments will make a final determination regarding the license.

NIH considers several factors when determining whether to grant a license, and what kind of license. The criteria for consideration as to exclusive licenses include whether an exclusive license serves the best interest of the public and whether it is a reasonable and necessary incentive to promote the investment of risk capital to bring the invention to practical application

[8] Department of Health and Human Services (DHHS), National Institutes of Health (NIH). (2001). *Report to the United States Congress, NIH Response to the Conference Report Request for a Plan to Ensure Taxpayers' Interests are Protected.* Available at: https://www.techtransfer.nih.gov/sites/default/files/documents/policy/wydenrpt.pdf
[9] Kneller, R. (2010). *The Importance of New Companies for Drug Discovery: Origins of a Decade of New Drugs*. Nature Reviews/Drug Discovery, 9, 867-82. Print.
[10] Chakravarthy R, Cotter K, DiMasi J, et al. (2016). *Public- and private-sector contributions to the research and development of the most transformational drugs in the past 25 years: from theory to therapy*. Ther Innov Regul Sci. 2016;50(6):759-768.
[11] Galkina Cleary, E., Beierlein, J. M., Khanuja, N. S., McNamee, L. M., & Ledley, F. D. (2018). *Contribution of NIH funding to new drug approvals 2010-2016*. Proceedings of the National Academy of Sciences of the United States of America, 115(10), 2329–2334. https://doi.org/10.1073/pnas.1715368115
[12] https://vitaltransformation.com/2022/09/the-relative-contributions-of-nih-and-private-sector-funding-to-the-approval-of-new-biopharmaceuticals/

by a licensee. NIH can negotiate to ensure that exclusive or partially exclusive license terms and conditions are not broader than necessary.[13,14]

Private companies often understandably prefer exclusive licenses that allow them to be the sole user of a patented invention for certain uses for a specified period of time in order to provide a measure of certainty and predictability during the highly risky, lengthy, and costly drug development process. The investment necessary to develop a new medicine can cost an average of several billion dollars and take 10-15 years, and only 12% of medicines entering clinical trials ever obtain an FDA approval.[15] NIH is also aware of these risks when making licensing decisions. As part of licensing agreements NIH receives royalties from the private sector which can be reinvested in research and potential new discoveries by the agency. GAO has found that NIH received up to $2 billion in royalties between 1991 and 2019.[16]

Given the high costs and length of time to research and develop new medicines and vaccines, as well as to invest in manufacturing facility enhancements and to invest in new facilities altogether, strong and reliable IP rights are critical for providing the potential for returns and spurring companies to make the needed investments needed to develop future medicines. Manufacturers seek the certainty and predictability provided by IP protections to make the decades long investments in new technologies, and in building and expanding upon state-of-the-art manufacturing facilities. Strong and reliable IP protections are also critical to fostering public-private partnerships and other forms of collaboration, including investment in emerging innovator companies.

Though the Bayh-Dole Act allows the federal government to "march-in" under a narrow set of circumstances, "march-in" was never intended to serve as a mechanism for regulating the pricing of any products, including prescription medicines. The provisions provide the right for the government to "march in" under a narrow set of circumstances and force patent holders to grant a license to a "responsible applicant" able to utilize the technology to address an unmet need. In the nearly four decades that the Bayh-Dole Act has been in place, NIH, after careful review, has rejected each of the seven march-in petitions based on pricing that have been submitted to the agency. In each case, NIH consistently concluded that the products subject to a march-in petition had reached practical application and met health or safety needs. Even in an instance where march-in was requested to respond to a manufacturing supply challenge, NIH concluded that the manufacturer was "working diligently to resolve its manufacturing difficulties"[17] and "no

[13] https://www.techtransfer.nih.gov/licensing
[14] See 37 CFR § 404.7
[15] DiMasi, J. A., Grabowski, H. G., & Hansen, R. W. (2016). Innovation in the pharmaceutical industry: new estimates of R&D costs. *Journal of health economics*, *47*, 20-33.
[16] https://www.gao.gov/products/gao-21-52
[17] Thomas, J. (2016). March-In Rights Under the Bayh-Dole Act. CRS. Available at: https://fas.org/sgp/crs/misc/R44597.pdf.

remedy that is available under the march-in provision would address the problems identified by the requestors."[18]

In an Op-Ed to the Washington Post, the bill's authors, Senators Birch Bayh and Bob Dole, stated: "The ability of the government to revoke a license granted under the act is not contingent on the pricing of a resulting product or tied to the profitability of a company that has commercialized a product that results in part from government-funded research. The law instructs the government to revoke such licenses only when the private industry collaborator has not successfully commercialized the invention as a product."[19] Similar provisions cover the licensing of NIH inventions, which empower the NIH to terminate the license in whole or in part if the agency determines that the licensee is not executing its commitment to achieve practical application of the invention, the licensee is in breach of an agreement, termination is necessary to meet requirements for public use, or the licensee has been found by a court to have violated Federal antitrust laws in connection with its performance under the license agreement.[20] Changing policy on these provisions to allow price to be considered as a factor for action on the part of NIH could chill the private sector's willingness to enter into contractual agreements and licenses with the agency.

PhRMA is also strongly opposed to any proposals to add "reasonable pricing" requirements to agreements between the NIH and private companies. Policy proposals to place pricing restrictions on the private sector as a condition of partnering with the government have been tried before with disastrous results for patients and taxpayers. In 1989, the NIH imposed "reasonable pricing" conditions in all Cooperative Research and Development Agreements (CRADAs) between federal labs and outside parties to conduct research or development. The policy was revoked in 1995 after public meetings were held with companies, patient advocates and researchers after which the agency concluded that these pricing conditions significantly chilled collaboration between the public and private sectors.[21] In his announcement of the decision, then Director of the NIH, Harold Varmus, M.D., said, "An extensive review of this matter over the past year indicated that the pricing clause has driven industry away from potentially beneficial scientific collaborations with PHS scientists without providing an offsetting benefit to the public." Dr. Varmus further said, "Eliminating the clause will promote research that can enhance

[18] National Institutes of Health (NIH). (2010). National Institutes of Health Office of the Director: Determination in the Case of Fabrazyme Manufactured by Genzyme Corporation. Available at: https://www.ott.nih.gov/sites/default/files/documents/policy/March-In-Fabrazyme.pdf.

[19] Bayh, B. and Dole, R. (2011). Our Law Helps Patients Get New Drugs Sooner. Washington Post op-ed. Available at: https://www.washingtonpost.com/archive/opinions/2002/04/11/our-law-helps-patients-get-new-drugs-sooner/d814d22a-6e63-4f06-8da3-d9698552fa24/?itid=sr_1

[20] https://www.techtransfer.nih.gov/licensing

[21] National Institutes of Health. (1994). Reports of the NIH Panels on Cooperative Research and Development Agreements: Perspectives, Outlook, and Policy Development. Available from: https://www.ott.nih.gov/sites/default/files/documents/pdfs/NIH_%20CRADA_Report_on_Reasonable-Pricing_Clause_1994.pdf

the health of the American people." [22] After the removal of the clause, there was a subsequent rebound in CRADAs.[23]

Policies enabling the government to determine the "reasonable price" of medicines developed with support from NIH also fail to recognize that reducing the incentives for the private sector to invest in the future development of medicines could have serious unintended consequences for our national security and ability to respond to public health emergencies. The NIH and BARDA routinely partner with biopharmaceutical companies to support medical countermeasure (MCM) development through funding, technical assistance, and core services like clinical trial site management and manufacturing scale-up. Several MCMs, such as monkeypox vaccines, smallpox antiviral drugs, H5N1 influenza vaccines and anthrax vaccines are maintained in the strategic national stockpile, where they can be made available in the face of a public health threat.[24] Pipeline products being explored have potential but there is no guarantee they will ultimately receive FDA approval or have more than limited commercial utilization, and thus seeking to inject further uncertainty by setting an arbitrary price at the outset may simply serve to further chill critical R&D investments and collaborations between the public and private sectors with the end-result leaving the United States unprepared to quickly respond to emerging health threats.

As NIH considers the feedback from this Workshop's proceedings, PhRMA suggests the agency can learn from other similar efforts from agencies such as NIST, who published a roadmap for "Unleashing American Innovation" in 2019 through its Return on Investment Initiative Green Paper.[25] Among other things, the authors of the report found that federal officials must better engage with the private sector, strengthen IP protections, and incentivize technology transfer.[26]

The biopharmaceutical industry is proud to be a key player in the U.S. biopharmaceutical research ecosystem. We rely on a well-funded and robust public research infrastructure to generate meaningful scientific exchange and partner with to advance science for the benefit of American patients. We look forward to ongoing dialogue on these issues. Please free to reach out to David Korn, Vice President, IP and Law at dkorn@phrma.org or me at julrich@phrma.org with any questions or for additional discussion.

Sincerely,

Jocelyn Ulrich, MPH
Deputy Vice President
Policy and Research
PhRMA

[22] Press Release, NIH News, April 11, 1995. Available from: https://www.ott.nih.gov/sites/default/files/documents/pdfs/NIH-Notice-Rescinding-Reasonable-Pricing-Clause.pdf
[23] https://www.techtransfer.nih.gov/sites/default/files/CRADA%20Q%26A%20Nov%202021%20FINAL.pdf
[24] https://aspr.hhs.gov/SNS/Pages/Requesting-SNS-Assets.aspx
[25] https://nvlpubs.nist.gov/nistpubs/SpecialPublications/NIST.SP.1234.pdf
[26] See page 5 at; https://nvlpubs.nist.gov/nistpubs/SpecialPublications/NIST.SP.1234.pdf

Submission Date: 7/28/2023

Name: Hans Sauer

Name of Organization: Biotechnology Innovation Organization

Comment:

Please find attached BIO's comment in preparation for the NIH upcoming technology transfer workshop. Thank you in advance for considering our comments; we look forward to the workshop on Monday.

Sincerely,
Hans Sauer

Hans Sauer, Ph.D., J.D.
Deputy General Counsel,
Vice President, Intellectual Property
—
Biotechnology Innovation Organization (BIO)
www.bio.org

Additional Comment (attachment):

Biotechnology Innovation Organization
1201 New York Ave., NW
Suite 1300
Washington, DC, 20005
202-962-9200

Comments of the Biotechnology Innovation Organization (BIO) to the July 31, 2023 NIH Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer

Vial email to SciencePolicy@od.nih.gov

July 27, 2023

On behalf of its member organizations, the Biotechnology Innovation Organization ("BIO") is pleased to submit this Comment in preparation for the NIH July 31 Workshop on Technology Transfer.[1] BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers, and related organizations across the United States and in more than 30 other nations. BIO members range from startup companies developing their first commercial products to multi-national Fortune 500 pharmaceutical corporations. BIO's members routinely collaborate and interact with researchers in NIH's intra- and extramural programs, and have long supported the NIH in its critically important role of funding and advancing biomedical science in the United States and throughout the world.

As an initial matter, we are pleased to participate in the NIH's upcoming workshop, and we look forward to learning more about any specific interests or concerns the NIH may have identified with how it currently "approaches the patenting and licensing of biomedical inventions," and with its role "in the broader biomedical research enterprise in promoting the application of knowledge to enhance human health." Articulating those interests or concerns will help enable informative and focused comments in ongoing dialogue between the NIH and its stakeholder community. We appreciate the NIH's outreach and look forward to learning more at the workshop.

Biomedical research productivity in the United States is the highest in the world, with 62% of new drugs first approved by the FDA having their origins in the U.S., more than the rest of the world combined.[2] This high biomedical research productivity depends on a fluid system of technology transfer, licensing, and partnering that was first perfected in the United States, and in which both the private and the public sector participate. For example, in a cohort of 223 new U.S. drug approvals from 2011-2020, thirty drugs (13.5%) originated in public sector institutions and all were licensed to biopharmaceutical firms for development and regulatory submission.[3] In another study of 248 small molecule drugs approved by the FDA between 2008-2017, thirty-five (14%) had evidence of U.S. academic or public research institution involvement in their creation (about half of which were specifically found to have a US government

[1] See https://osp.od.nih.gov/events/workshop-on-transforming-discoveries-into-products-maximizing-nihs-levers-to-catalyze-technology-transfer/

[2] The US Ecosystem for Medicines. How New Drug Innovations Get to Patients. White paper available at: https://vitaltransformation.com/2022/12/the-us-ecosystem-for-medicines-how-new-drug-innovations-get-to-patients/

[3] See id. Another 33 drugs (15%) were first conceived in large biopharmaceutical firms and transferred to small- or medium-sized firms during development; and 20 drugs (9%) were first conceived by small or medium-sized enterprises and transferred to large ones prior to FDA approval.

contribution);[4] and another 13 drugs (5%) involved inventive contributions from *foreign* public research institutions; all of which were licensed to the private sector for development and commercialization. These studies are consistent with earlier reports that found the U.S. public sector to have contributed *directly* to the invention of about 10-15% of new drugs over the past several decades.[5]

In addition to direct contributions to the invention of at least some new drugs, public sector research also plays an important enabling role by funding basic research and generating new insights into biology and disease. For example, NIH-supported published research was found to be relevant to each of 210 new medicines first approved by the FDA from 2010-2016. Over 90% of this research related to the underlying mechanism of disease and the drug targets (not the drugs themselves), and thus represents an indirect, but important, contribution to the generation of new therapies.[6] This in itself should be unsurprising, as all new drugs are built on a solid foundation of earlier research, which itself built on yet earlier research, much of which was publicly-funded.

In fact, our system is very effective in funding basic research that the private sector is not in a position to conduct. The results of this publicly-funded research in the vast majority of cases enters the public domain through scientific publications, scholarly exchange, generally-accessible databases and other mechanisms that are accessible to anyone. At times, publicly funded research also results in technology that is suitable for patenting (either by the government or by the academic institutions it funds), and is then offered for licensing to suitable private firms better able to translate those early discoveries into FDA approved therapies. This collaboration between the public and private sectors forms the foundation for US leadership in this field. In evaluating our tech transfer system, BIO urges NIH to examine what has made this partnership so successful so that we can build on that success.

Because taxpayers support a great amount of basic biomedical research, many people believe that the public pays twice for drugs; once by funding underlying research and once when payors and patients buy drugs for personal use. This has led to calls for measures that tie medicine prices to public science funding, such as an (renewed) implementation of “reasonable pricing clauses” in government research grants and contracts. Explicit in such proposals is a belief that taxpayers are being insufficiently rewarded for their contributions to the creation of new drugs and therapies.

U.S. investment from all sources in both basic and applied biomedical R&D in 2020 was estimated to amount to approximately $245 billion, of which $61.5 billion was attributable to the federal government; $16.8 billion to academic and research institutions; $3 billion to foundations, philanthropies, and professional societies; and $161.8 billion (66% of the total) to the private sector.[7]

---

[4] Nayak, Avorn, and Kesselheim, Public Sector Support for Late-Stage Discovery of New Drugs in the United States: Cohort Study, *BMJ* 2019;367:l5766; available at: https://doi.org/10.1136/bmj.l5766 . A US government contribution was defined as the drug originating in a federal laboratory, or a patent assignment to a federal agency, or a patent declaring US government funding of the invention.

[5] See, e.g. Sampat and Lichtenberg, What are the Respective Roles of the Public and Private Sectors in Pharmaceutical Innovation? Health Aff. 30 (2011), 332-339; Stevens et al., The Role of Public-Sector Research in the Discovery of Drugs and Vaccines, N. Engl. J. Med. 364 (2011) 535-541.

[6] Cleary et al., Contribution of NIH Funding to New Drug Approvals 2010-2016, Proc. Natl. Acad. Sci. USA 115 (2018) 2329-2334.

[7] Research!America, U.S. Investments in Medical and Health Research and Development 2016-2020; available at: https://www.researchamerica.org/wp-content/uploads/2022/09/ResearchAmerica-Investment-Report.Final_.January-2022-1.pdf

By this measure, the federal government does indeed contribute a significant chunk of the total national biomedical R&D spend – about 25% of the total. Great difficulties arise, however, when trying to quantify the public contribution to new drug development in the context of ongoing debates over drug prices. For example, in an effort to quantify the NIH contribution to the creation of remdesivir, one of the first COVID antiviral compounds, study authors added up decades of NIH-supported basic research publications in the general fields of nucleoside analogue chemistry (the drug molecule's chemical class) and RNA-dependent RNA polymerase (the enzyme on which remdesivir acts), to arrive at an eye-popping public contribution of $6.5 billion in basic research funding that, they propose, "led to" the drug and should be counted when considering its pricing.[8] A subsequent GAO study, however, found only a much smaller public contribution of $161 million to preclinical and clinical investigations of remdesivir itself (a 40-fold difference) and no inventive government contribution to the drug product at all. Meanwhile, the manufacturer of remdesivir estimates its financial outlays for the drug's preclinical and clinical development at approximately $1.3 billion.[9]

This example illustrates some of the many conceptual and practical problems with comparing the public funding of research in the field to which a drug pertains against the cost of subsequent R&D on the drug itself. Government funding makes vast and critical contributions to the advancement of medicine by furthering our understanding of human disease and pointing in promising directions for applied drug research, but the weight of the evidence shows that in most cases the private sector invents the drugs that are based on that research and assumes the cost and risk of translating new scientific insights into practical new products.[10]

It is true that direct returns to the government from licensing, in monetary terms, constitute only a small fraction of the NIH budget,[11] but criticisms of insufficient returns do not account for the vast indirect benefits and externalities that accrue to the public in the United States (and in foreign countries around the world) in the form of improved health outcomes, job creation, research productivity, education, economic development, and tax revenues. When the government's *direct* financial contribution to drug development is assessed (i.e. not counting basic research in the general field to which the drug pertains), the picture is quite different. For example, a prospective study of >23,000 NIH grants in FY 2000, representing $7.1 billion in public funding, showed that only a small fraction could be linked to only 18 new drug approvals over the subsequent two decades. And for these 18 drugs, the government's contribution to their creation constituted $640 million whereas the private sector firms that developed

---

[8] Cleary et at., Foundational Research and NIH Funding Enabling Emergency Use Authorization of Remdesivir for COVID-19, available at: https://www.bentley.edu/news/65-billion-nih-funding-foundational-research-enabled-emergency-use-authorization-remdesivir

[9] US Government Accountability Office Report GAO-21-272, Information on Federal Contributions to Remdesivir, available at: https://www.gao.gov/assets/gao-21-272.pdf

[10] Developing a new drug through clinical trials and regulatory approval has been estimated to consume about 10 years and require an investment ranging from 0.7-2.5 billion dollars at an approximately 90% chance of development failure. These risks and costs are borne almost entirely by the private sector.

[11] NIH Technology Transfer Report FY 2021, available at: https://www.techtransfer.nih.gov/sites/default/files/documents/pdfs/FY2021%20NIH%20Technology%20Transfer%20Annual%20Report.pdf . NIH licensing revenue for FY 2021 was reported at approximately $127 million.

these drugs to approval contributed $44.3 billion.[12] This study, as well as other accumulated evidence, indicates that the government's direct monetary returns may be small in relative terms, but generally commensurate with its proportionally small direct investment in drug development.

Conversely, the lion's share of public research funding does not go towards new product development, but towards advancing science and enriching the public domain with new knowledge, thus creating opportunity, and stimulating commercial risk-taking and vast amounts of private follow-on investment. Seen this way, most public research funding is properly viewed as an infrastructure investment where the resulting body of scientific knowledge becomes available to anyone, anywhere – it is non-excludable - and where one entity's use of that knowledge does not diminish another entity's ability to use it too – it is non-rivalrous. In this sense the NIH helps fund a public good whose importance cannot be overstated. If entrepreneurial businesses, inspired by scientific knowledge that was funded by the public and made available to anyone, decide to invest capital and take on business risk, they are doing exactly what the system intends. In addition to the direct public health benefits derived from the invention of new therapies, this private follow-on investment then generates even more jobs, and fuels economic development.

And in instances where publicly-funded institutions *do* make direct contributions to the invention and development of new products, direct benefits can flow back through profit sharing, royalty payments, repayment of the initial investment, or some other bargained-for mechanism. Indeed, publicly-funded institutions around the country routinely, in appropriate circumstances, acquire proprietary rights in their inventions which they use for partnering, licensing, or other valorization of their institutions' research, in keeping with federal technology transfer statutes and their institutions' policies.

Nonetheless, some members of Congress, advocacy groups, and opinion journalists persist in wanting to link public research spending to the price of downstream products, regardless of the investments made and risks taken by the biopharmaceutical businesses that develop these products. In instances where companies benefited from decades of prior basic research that has long been in the public domain, these companies are said, effectively, to owe a scientific debt to the public, and they should price their products accordingly. And in instances where companies licensed publicly-funded proprietary technology, met their due diligence obligations, and paid milestones and royalties, the licensing institution is nonetheless said to have struck a bad bargain and should have insisted on lower consumer prices of the licensed product. Either way, the narrative goes, taxpayers have generously funded biomedical research and are therefore "owed" more "reasonable" prices for medicines.

Such pseudo-transactional notions[13] - that the current system of public biomedical research funding justifies a form of drug price control – not only misstate the realities of our public-private R&D ecosystem; they are also profoundly infeasible. For example, if public research funding entitles taxpayers to a discounted price for a successful drug, how much of a discount would be justified? Should that price reduction be commensurate with how much public funding was involved, relative to how much private funding went into commercializing the drug? In the much-publicized march-in petition for Xtandi®, the US government's contribution has been stated as approx. $500,000 in the form of initial research funding,

[12] Schulthess *et al.* The Relative Contributions of NIH and Private Sector Funding to the Approval of New Biopharmaceuticals. *Ther Innov Regul Sci* **57**, 160–169 (2023). https://doi.org/10.1007/s43441-022-00451-8

[13] See, for example, the statement made by Rep. Ocasio-Cortez in a January 2019 hearing of the House Committee on Oversight and Reform: "[T]he public is acting as early investor, putting tons of money into the development of drugs that then become privatized, and then they receive no return on the investment that they have made."

whereas the manufacturer of the drug and its commercial partners estimate their subsequent investment at approx. $2.2 billion[14] – how much of a lower price could the public be deemed to have "earned" by virtue of a federal research grant in such situations?

In general, arguments that the public is owed lower prices ignore the fact that the public and the private sectors, for the most part, fund research that is different but complementary, that the private sector spends significantly more than the public sector in monetary terms, and that the private sector assumes basically the entire risk that an experimental product will fail on the path of drug development.

Most important, proponents of so-called "reasonable pricing" fail to understand that their concept cannot work in the absence of a framework where *ex ante* bargaining can occur. At the time when a typical biomedical research grant is awarded, or a license to untested technology is offered, the parties will generally not know if the funded research will ever contribute to a drug product, when that drug product will come into existence, or who will bring it into existence. It will not be known how much it will cost to develop that drug, which conditions it will treat, or how it will be used in clinical practice. In such situations it is impossible to bind future parties to an agreement under which, if a drug is eventually developed against all odds, they could lose their investment and their rights if the government doesn't deem the drug's price reasonable. Businesses would simply walk away and invest their time and capital elsewhere.

Our current tech transfer system has been enormously successful. In 1980, prior to the enactment of the Bayh-Dole Act, less than 5% of the federal government's nearly 30,000 patents had been licensed for commercial development.[15] By empowering federally-supported universities and small businesses to hold and license patents, the Bayh-Dole Act fueled a vibrant innovation sector that, between 1996 and 2017, contributed to the development of more than 200 new drugs and vaccines, $865 billion in added GDP, 5.9 million jobs, and more than 13,000 startups.[16] It is hard to see how the American public could be said to have been "ripped off," as some critics now argue.

It may be superficially appealing to argue that U.S. payors should pay less for a new drug that was developed on the basis of seminal publicly-funded research. But it would be neither feasible nor rational to control a drug's price based on relative appraisals of the value and amount of underlying public research. Doing so would only put brakes on the pace of biomedical innovation and distract from other, more rational efforts to lower the cost of healthcare in the United States.

BIO looks forward to engaging further with the NIH on these important questions and thanks the agency for the opportunity to submit these comments.

Respectfully submitted,

Hans Sauer, Ph.D.
Deputy General Counsel, BIO

---

[14] https://newsroom.astellas.us/Astellas-Quote-and-Statement-on-the-Bayh-Dole-Act-and-XTANDI-June-14,-2022

[15] Government Accountability Office, Administration of the Bayh-Dole Act by Research Universities, GAO/RCED-98-126 at 3 (May 1998).

[16] AUTM, Driving the Innovation Economy (2018). Available at: https://autm.net/AUTM/media/Surveys-Tools/Documents/AUTM_FY2018_Infographic.pdf

Submission Date: 7/30/2023

Name: Mark Emalfarb

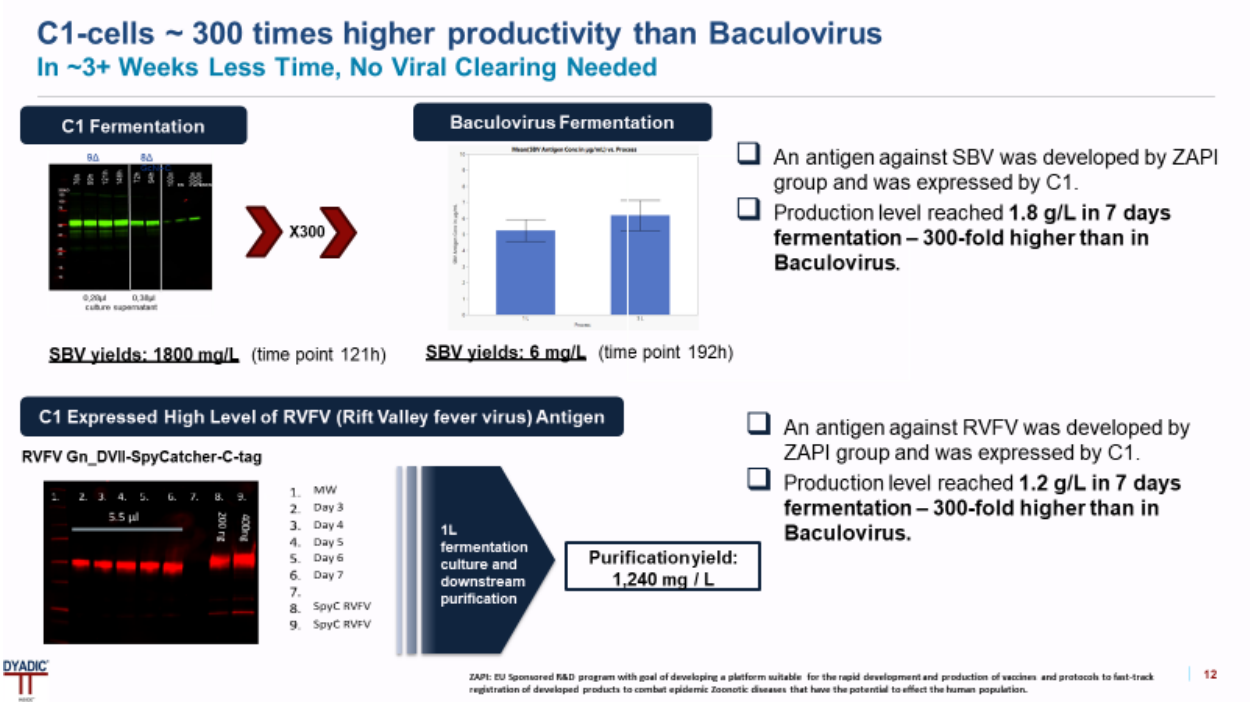
Name of Organization: Not Provided

Comment:

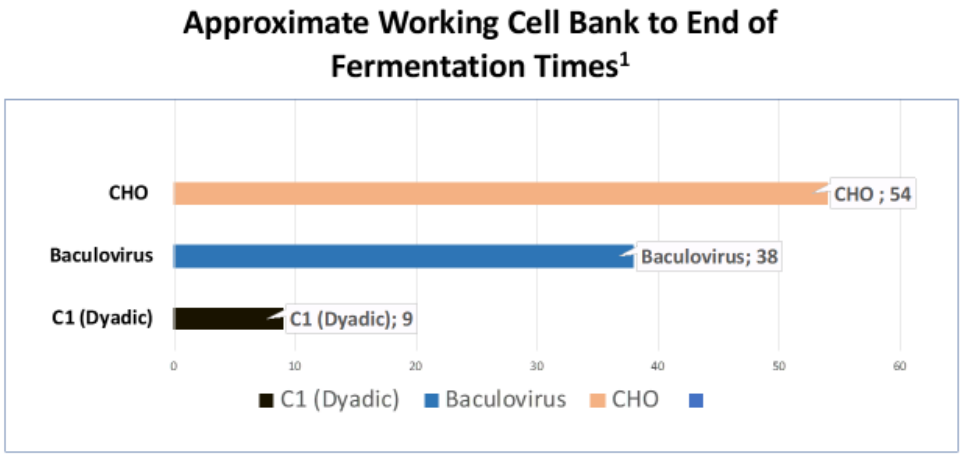
NIH and biotech/pharmaceutical companies need their scientists to utilize the most efficient cell lines in their discovery and development programs.

Too often this is overlooked by scientists early on, inefficiencies are locked in, and if a biologic makes it to commercialization the poor choice of inefficient cell lines at the beginning of the research and development stage ends up with less doses of a vaccine or a drug being available and the cost of manufacturing each dose is greater than it should be wasting tax payer's dollars and making the vaccine and/or drug less available for middle & lower income countries.

An example of this is as follows see two slides comparing yield (c1 cells are ~ 300 times more productive) and speed of manufacturing C1-cells vs Baculovirus and CHO cells (C1 production batches are much shorter).



Short Fermentation Timeline



[1]Ranges: C1 6-9 days; Baculovirus 28-38 days; CHO 41-54 days

Additional Comment (attachment): None

August 8, 2023

Lyric Jorgenson, Ph.D.
NIH Office of Science Policy
6705 Rockledge Dr. #750
Bethesda, MD 20817

Dear Director Jorgenson,

We appreciate the opportunity to contribute our insights and feedback after attending the National Institutes of Health (NIH) workshop on "Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer," held on July 31, 2023.

NIH through its intramural programs and extramural funding has played a critical role in advancing knowledge and the development of groundbreaking biomedical products. Throughout recent decades, there has been an extraordinary growth in novel drugs, medical devices, and diagnostics, thanks to NIH's unwavering support. However, it is now clear that academic research sponsored by NIH, while crucial, is not enough.

The workshop offered a critical platform to explore the disparity between academic research and the realization of accessible and affordable products. Though valuable conversations took place about NIH's potential to enhance product accessibility, the main challenges of transitioning early-stage products from research to patient evaluation were not fully addressed.

The focus of this discussion is on drug development, which represents the most intricate path in biomedical technologies. I aim to highlight our view on three key areas:

1. Understanding the increasing “Valley of Death”.
2. Current limitations to NIH’s efforts to boost early drug development.
3. Fannin's experience in this domain.

<u>The Valley of Death</u>:

Academic research conducted at the NIH has played a crucial role in advancing our understanding of human biology and identifying potential avenues for disease intervention and improved health outcomes. The advent of the "omics" revolutions, in particular, have been particularly transformative, opened up a vast array of potential targets for therapeutic development that present exciting opportunities for medical breakthroughs. Despite these remarkable strides in research, drug development has encountered a significant lag, leading to a growing disconnect between foundational discoveries and their practical implementation.

While considerable efforts have been dedicated to expediting clinical development and enhancing the affordability and accessibility of approved products, the true bottleneck lies in the transition from identifying a promising target to developing a drug suitable for clinical

3900 Essex Lane, Suite 575 Houston, TX 77027
www.fanninnovation.com

testing. The NIH and other academic institutions excel in knowledge creation, often resulting in the discovery of "pre-drugs" that demonstrate efficacy in laboratory mice. However, substantial additional work is required before these pre-drugs can progress to safe human testing.

This entails a comprehensive series of tasks, spanning multiple domains, including in-depth efficacy testing across various models, safety assessment in relevant animal models, clinical formulation development, GMP (Good Manufacturing Practice) manufacture of drug substance and drug product, establishment of a clinical trial strategy encompassing trial design and site/investigator identification, obtaining regulatory feedback, and evaluating commercial aspects such as the market and competitive landscape.

This critical stage, commonly referred to as the "first valley of death," poses a formidable challenge in the drug development process. Successfully navigating this phase is essential for translating promising pre-drugs into clinically applicable drugs that can benefit patients.

Limitations to Current NIH Efforts:

The process of drug development is complex, involving a diverse range of activities that demand a skill set distinct from academic research. While academic engagement is a vital component, it alone is insufficient. NIH has recognized this gap and we appreciate efforts made to address it.

Among the various institutes/centers at NIH, the National Center for Advancing Translational Sciences (NCATS) stands out for its specific focus on product development rather than fundamental research. However, despite NCATS' valuable contributions, the magnitude of innovation generated across NIH-funded research far exceeds NCATS' capacities.

NIH has several initiatives aimed at fostering successful product development in academic institutions, with the NCAI/REACH programs being prominent examples. These initiatives aim to provide "entrepreneurial training for innovators on how to bring technologies to market" and offer feedback from federal and industry experts. However, these programs face two critical limitations.

First, they do not fully acknowledge that the skill sets required for successful product development differ from those of accomplished researchers and inventors. Although these skills can be learned, they are complex and cannot be easily acquired solely through descriptive or didactic "entrepreneurial training." Second, while expert feedback is beneficial, it cannot replace the practical experience of product developers with real stakes in the outcome.

NIH dedicates significant resources to nurture talent development by providing support to early-career researchers through both intramural and extramural funding. This investment is crucial for sustaining the vitality of the research ecosystem. However, a notable gap exists as equivalent support is not readily available to foster the growth of product development talent.

While the emphasis on supporting academic research is vital, it is equally important to recognize the significance of growing expertise in product development. Bridging this gap and providing adequate resources and opportunities for individuals interested in pursuing careers in product development will not only bolster the translational potential of research but also

3900 Essex Lane, Suite 575 Houston, TX 77027
www.fannininnovation.com

ensure a robust pipeline of skilled professionals dedicated to transforming scientific discoveries into tangible healthcare solutions.

The Small Business Innovation Research (SBIR)/Small Business Technology Transfer (STTR) program represents another crucial area of support for early product development. The NIH SBIR/STTR program has demonstrated remarkable success in assisting numerous small businesses engaged in product development endeavors. However, a significant challenge arises from the fact that the criteria used at NIH to evaluate SBIR/STTR applications are the same as those employed for assessing academic research grant applications. This lack of tailoring to assess the likelihood of successful product development reduces the program's effectiveness on this front.

Moreover, the review panels responsible for evaluating these applications are often comprised largely of academic researchers with limited experience in product development. This further compounds the challenge, as their perspectives may not fully align with the specific needs and requirements of successful product development efforts.

Addressing these early barriers to drug development necessitates a comprehensive approach that recognizes the unique skill sets required, encourages and creates hands-on product development experience, and tailors evaluation criteria to better assess the potential for successful product development. By enhancing collaboration between academic research and product development expertise, NIH can maximize its impact and accelerate the translation of groundbreaking discoveries into tangible medical solutions that benefit society. This can be further enhanced by streamlining the process by which inventions are out-licensed to product developers.

The Fannin Approach:

Fannin is among the most active early-stage development groups in the life sciences, boasting a diverse portfolio of a dozen programs and platforms at various stages of development. Our unique approach involves advancing this pipeline internally and through Fannin-founded entities, utilizing a combination of investor and grant funding. This strategy was crafted to address the biotech development gap observed in the vast swathes of the U.S. outside biotech hubs like Boston, which lack a critical mass of experienced product developers and funders.

Early drug development encounters significant challenges, including an extraordinarily high failure rate and concerns related to non-reproducible academic data. Additionally, the substantial capital needs in the biotech industry compound this challenge particularly for NIH and universities located outside major biotech hubs. While successful product development necessitates early spin-outs to experienced product developers, attracting such talent to academic spin-outs is a challenging task. Furthermore, the absence of an experienced management team often deters investors from supporting promising technologies in the biotech space.

3900 Essex Lane, Suite 575 Houston, TX 77027
www.fannininnovation.com

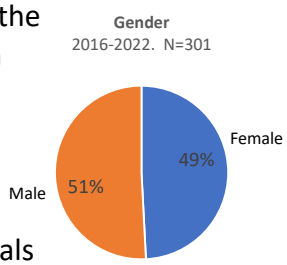
Pooled Management Team: To navigate this intricate landscape, Fannin has adopted a Pooled Management Team approach, where our experienced management team concurrently drives the development of multiple programs. Apart from being capital efficient, this approach provides the technology with an experienced drug development team much earlier in the process than may be possible with a single-asset startups. This strategy is made possible by the inherent time lags in early drug development, largely influenced by scientific factors and animal models.

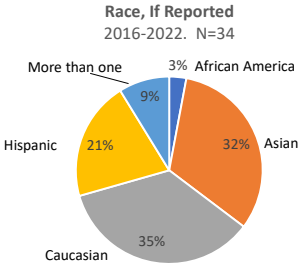
Since our establishment, Fannin has launched approximately 35 programs, with a dozen currently active, including one commercial product and two in clinic stages. A relevant example for NIH is an antibody targeting the IL-7 receptor, in-licensed from NCI. This antibody is in development for the treatment of childhood leukemias and is slated to enter clinical trials next year.

Funding: Fannin's innovative funding strategy also plays a pivotal role in reducing early failure costs. By leveraging grant funding for early de-risking, we raise investor capital and build out the team only after the initial de-risking phase is complete. Despite our location in Houston, far from the biotech investment hubs, our programs have seen around $190 million in funding, with $70 million from grants and $120 million from investors.

The SBIR/STTR program has been especially important for early-stage de-risking. Fannin's success in this approach has been recognized by SBIR with a prestigious 2016 Tibbetts Organization Award, which celebrates outstanding achievements in SBIR/STTR initiatives. Notably, Fannin is the only for-profit entity to have received this prestigious award.

Talent Development: Recognizing that Houston's biotech bottleneck was the scarcity of experienced product developers, compounded by the lack of opportunities for this talent to grow, Fannin created its own talent development program. Our program includes part-time interns and full-time fellows/associates, the latter accredited by the Department of Labor. The program has flourished over the last decade, attracting individuals from local and national institutions.[1] Our over 320 interns, fellows and associates hail from diverse backgrounds, including substantial numbers of under-represented minorities.





The majority of our program alumni remain in Houston, actively contributing to the local innovation ecosystem, working with local startups including those at Fannin. Those who ventured beyond Houston's borders, serve at major pharma companies, biotechs, VCs, and

[1] Baylor College of Medicine, Case Western Reserve, Cornell, Duke, Emory, Georgetown, Georgia Tech, Harvard, Johns Hopkins, MD Anderson, National Cancer Institute, Notre Dame, Princeton, Rice, Stanford, Texas A&M University, Trinity, UC Berkeley, University of Chicago, University of Houston, University of Georgia, University of Manchester, University of Texas (multiple campuses), University of Toledo, Villanova, and Washington University.

3900 Essex Lane, Suite 575 Houston, TX 77027
www.fannininnovation.com

consulting firms, with many maintaining connections to and investing in Houston technologies and startups.

Illustrative organizations employing Fannin alumni:

Pharma	Abbvie, AstraZeneca, BMS, J&J, Merck, Novartis, Pfizer, Roche, Sanofi, Takeda
Biotech	Amgen, Biogen, BridgeBio, Fannin, Genentech, Immatics, Seagen, Allovir
Med Device	3M, Alcon, Boston Scientific, Medtronic, Smith & Nephew, Stryker, Gore
Consulting	Accenture, Boston Consulting group, Deloitte, KPMG, McKinsey, PwC
Other	FDA, USPTO, Apple, GE, Intel, Lockheed Martin, Texas Instruments, GE Healthcare

Conclusion:

The remarkable expansion of novel drugs, medical devices, and diagnostics over the last few decades owes a debt of gratitude to academic research conducted at or supported by the NIH. Our understanding of human biology has grown exponentially, but the translation of this knowledge into practical products that can positively impact people's lives has not kept pace. The NIH can play a pivotal role in addressing this disparity and bridging the "valley of death".

A comprehensive four-pronged strategy can help bridge this gap:

1. Recognize the Distinct Skill Set: Acknowledge that product development requires a unique skill set that is distinct from academic research and that early involvement of experienced product developers can facilitate and accelerate successful product development.
2. Support Career Paths in Product Development: Provide resources and opportunities to individuals interested in pursuing careers in product development, particularly within for-profit drug development entities.
3. Facilitate Technology Transfer: Streamline the process of out-licensing NIH-owned technology to product developers, making it easier for promising discoveries to move into the commercial realm.
4. Refine SBIR/STTR Grant Application Review: Broaden the review pool and update the criteria used for reviewing SBIR/STTR grant applications to prioritize factors that promote and facilitate product development.

We are fully committed to engaging in further discussions with the NIH to advance this important mission. NIH has the opportunity to unlock the full potential of NIH-funded research and accelerate the transformation of cutting-edge science into tangible solutions that benefit individuals and society at large.

Sincerely,

Atul Varadhachary

Atul Varadhachary, MD, PhD
Managing Director

3900 Essex Lane, Suite 575 Houston, TX 77027
www.fannininnovation.com

Submission Date: 8/11/2023

Name: James Love

Name of Organization: Knowledge Ecology International

Comment:

Attached is a comment on the shrinking time the public has to comment on NIH exclusive patent licenses.

Jamie

Additional Comment (attachment):

The NIH has radically reduced the time for the public to comment on exclusive licenses

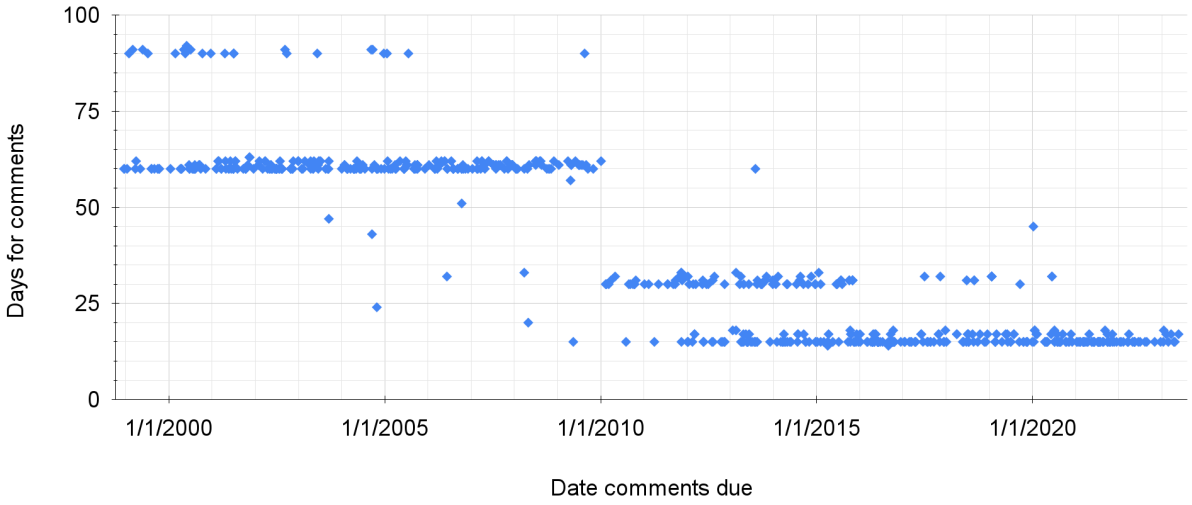
James Love, Marshall Pentes and Luis Gil Abinader
Knowledge Ecology International (KEI)
August 11, 2023

Introduction

Federal agencies in the U.S. have a limited authority to grant exclusive or partially exclusive licenses over government-owned patents, provided that they comply with the requirements set forth in 35 U.S. Code § 209, 37 CFR § 404, and other norms. Pursuant to 35 U.S. Code § 209, federal agencies may grant exclusive patent licenses only if they are “a reasonable and necessary incentive” to induce investments, and in most cases, after providing the public notice and an opportunity to file comments.

Since the Bayh-Dole Act was enacted, the National Institutes of Health (NIH) has drastically decreased the time available to the public to comment on exclusive patent licenses. These changes include a dramatic shift in the time given the public to comment in 2010, months after Dr. Francis Collins became the Director of the NIH, and another significant shift in 2016.

Figure: Days allowed for the public to comment on prospective NIH exclusive patent licenses



Shrinking the length of public comment periods is part of a broader set of policies implemented by NIH officials over the past fifteen years to make the NIH technology transfer practices less transparent, and to reduce the influence of consumer and taxpayer interests.

When the Bayh-Dole Act was first enacted through Public Law 96-517, statute 35 USC § 209 had a different title, “Restrictions on licensing of federally owned inventions,” and the statute did not set out the amount of time for public notice on an exclusive license. The implementing regulation, however, did set out a number of days for comment.

The March 12, 1985 version of 37 CFR § 404.7 required that the opportunity to file comments should be available for “a 60-day period.” The text of the regulation, as provided in 1985, was as follows:

> 37 CFR § 404.7, March 12, 1985 version
>
> (i) Notice of a prospective license, identifying the invention and the prospective licensee, has been published in the Federal Register, providing opportunity for filing written objections within a 60-day period;

The July 1, 1997 revision of 37 CFR § 404.7 still required federal agencies to provide “opportunity for filing written objections within a 60-day period.”

Public Law 106-404, enacted on November 1, 2000, amended several aspects of the Bayh-Dole Act, including 35 USC § 209. One of these amendments changed the title of Section 209 to “Licensing federally owned inventions,” and two changes were made regarding public notice. The statute now provided that the public was to be given “at least 15 days before the license is

granted" to comment, and the change also eliminated the public notice requirement for exclusive licenses granted to parties of Cooperative Research and Development Agreements (CRADAs).

> *35 U.S. Code § 209, as amended through Public Law 106-404*
>
> (e) Public Notice.—No exclusive or partially exclusive license may be granted under section 207(a)(2) unless public notice of the intention to grant an exclusive or partially exclusive license on a federally owned invention has been provided in an appropriate manner at least 15 days before the license is granted, and the Federal agency has considered all comments received before the end of the comment period in response to that public notice. This subsection shall not apply to the licensing of inventions made under a cooperative research and development agreement entered into under section 12 of the Stevenson-Wydler Technology Innovation Act of 1980 (15 U.S.C. 3710a).

Following this amendment, the implementing regulation was also changed on July 1, 2002, to reduce the deadline for public comments from 60 to "at least 15 days."

While the statute and regulation permitted the shorter comment period, the practice at the NIH was normally to give the public 60 or more days to comment on the non-CRADA exclusive licenses.

Data and descriptive analysis

Marshall Pentes (KEI) has reviewed each of the NIH Federal Register notices on prospective exclusive patent licenses, from October 19, 1998 to May 2023, and calculated the number of days given for the public to provide comments. (Link here).

From July 1, 2002 to December 31, 2009, the NIH published 222 notices in the Federal Register asking for comments on a prospective patent license. Ninety-six percent of these notices gave the public 60 days or more to comment. But beginning in 2010, a few months after Dr. Francis Collins became Director of the NIH, the practice changed.

From 2010 to 2015, the NIH published 155 notices. Only 1 of the 155 notices was open for 60 days or more. Among the 154 notices with a shorter comment period, half had a comment period of 30 to 33 days, and half had a period of 15 to 18 days.

Beginning in 2016 and through 2022, the NIH has given the public 15 to 18 days to comment on licenses 93 percent of the time.

Table: Number of days for public notice by year

Year	Total Federal Register Notices	Less than 60 days of public notice	24, 43, 45, or 47 days notice	30 to 33 days public notice	15 to 20 days public notice	Percent less than 60 days notice	Percent 30 to 33 days notice	Percent 15 to 18 days notice
2000	27	0	0	0	0	0.0%	0.0%	0.0%
2001	30	0	0	0	0	0.0%	0.0%	0.0%
July 1, 2001	11	0	0	0	0	0.0%	0.0%	0.0%
2002	36	0	0	0	0	0.0%	0.0%	0.0%
2003	26	1	1	0	0	3.8%	0.0%	0.0%
2004	30	2	1	0	0	6.7%	0.0%	0.0%
2005	28	0	0	0	0	0.0%	0.0%	0.0%
2006	30	2	0	1	0	6.7%	3.3%	0.0%
2007	28	0	0	0	0	0.0%	0.0%	0.0%
2008	18	2	0	1	1	11.1%	5.6%	5.6%
2009	15	2	0	0	1	13.3%	0.0%	6.7%
2010	13	13	0	12	1	100.0%	92.3%	7.7%
2011	18	18	0	14	4	100.0%	77.8%	22.2%
2012	20	20	0	9	11	100.0%	45.0%	55.0%
2013	39	38	0	17	21	97.4%	43.6%	53.8%
2014	32	32	0	12	20	100.0%	37.5%	62.5%
2015	33	33	0	13	20	100.0%	39.4%	60.6%
2016	33	33	0	0	33	100.0%	0.0%	100.0%
2017	26	26	0	2	24	100.0%	7.7%	92.3%
2018	24	24	0	8	16	100.0%	33.3%	66.7%
2019	23	23	1	1	21	100.0%	4.3%	91.3%
2020	30	30	0	2	28	100.0%	6.7%	93.3%
2021	38	38	0	0	38	100.0%	0.0%	100.0%
2022	17	17	0	0	17	100.0%	0.0%	100.0%
2023	6	6	0	0	6	100.0%	0.0%	100.0%
July 1, 2001 to 2009	222	9	2	2	2	4.1%	0.9%	0.9%
2010 to 2015	155	154	0	77	77	99.4%	49.7%	49.7%
2016 to 2022	191	191	1	13	177	100.0%	6.8%	92.7%

Why does the comment period matter?

The shorter notice periods, which include weekends and holidays, make it more difficult for the public to assess and influence the NIH's licensing policies. Why is this relevant? These are some examples of issues that may concern the public:

1. The proposed exclusive license may involve a company with a bad track record or no record at all of successfully bringing products to market.
2. A different licensee may be preferred if there is one that has better policies regarding pricing or access in developing countries.
3. The exclusive license may not be needed to bring a product to market, for example, if the product already has late-stage clinical trials results, and/or is eligible for other subsidies, such as the Priority Review Voucher, regulatory exclusivities on test data, or qualifies for orphan drug exclusivity, which are types of intellectual property protection that are significant, but also often shorter than the life of a patent. The scope of the rights in the license may be excessive for other reasons too. For example, it has been argued in some cases that the license need not be exclusive in the United States if the licenses are exclusive in Europe or other high-income markets.
4. The public may object to a license if the licensing process lacks transparency, regarding the terms offered, or the identity of the licensee. In some cases, the NIH licenses technologies to companies with no web pages or SEC filings, and where there is no information available at all regarding the ownership, board of directors, or management team.
5. An objection can be submitted if the license allows manufacturing outside the United States, or if the NIH failed to comply with the requirement in 40 USC § 559 regarding seeking the advice of the Attorney General with respect to antitrust law, for patents with a market value more than $3 million.
6. The NIH may propose a life of patent exclusivity for the license when a shorter term of exclusivity is more appropriate, and certainly consistent with the requirements in 35 USC § 209 that the scope of rights is limited to those which are reasonably necessary to induce investment.
7. The proposed royalty may be inadequate.
8. The NIH may have failed to provide sufficient rights for the use of the invention by third parties involved in research.
9. The NIH could be asked to provide for technology transfer on manufacturing at some point in the license.
10. The Field of Use may be too broad.
11. Understanding patent status globally is critical to examining a proposed license. Researching patent landscapes can be a complex and time-consuming endeavor. In recent years, the NIH has typically provided PCT numbers and identifiers for applications that have already entered into the national phase. Nevertheless, to adequately comment on a proposed license, interested parties may still need to cross-check the list of patent application numbers provided in the Federal Register notice with information available in databases hosted by national intellectual property offices. Without this cross-checking,

the procedural status, geographical scope, claimed subject matter, and legal strength of the patent rights may be unclear. This type of due diligence often takes significant time.

12. Whether the terms of a proposed license are appropriate may depend on the inventions claimed in the patents. Exclusive licenses over inventions relating to platform technologies and research tools are considered inappropriate by many experts and stakeholders. Determining the scope and nature of the inventions subject to a proposed exclusive license can require a relatively complex analysis of the patent claims. Given the diversity of technologies licensed by the NIH, interested parties often need to consult with subject matter experts to understand their nature. This again can take considerable time and resources.
13. The working requirements can be too lax.

These are just some of the issues that can be raised by the public during the comment period. In some cases, time is needed to evaluate the proposed license, and a 15 day window from the publication in the Federal Register makes this difficult. Not everyone reads the Federal Register daily, and it may take a while before people with an interest in the license even know about the request for comments. Additionally, the NIH itself is often unwilling to provide essential information about the license terms or the prospective licensee at all, or does not provide timely responses to questions asked.

The public not only has a right to provide comments to an agency on a prospective license, but they have some limited rights to appeal a decision by the agency to reject comments. This includes an administrative and a judicial appeal. In one licensing decision, KEI sued the NIH in federal court, but the case was dismissed on the grounds that KEI did not have staff or members who had the specific disease for the field of use in the license and therefore lacked standing. When KEI is faced with a 15-day notice period, there can be a scramble to analyze the technology, disease, and license, and if there are serious objections to be raised, it is necessary to reach out to patients or companies that would have sufficient standing to allow the public to sue the NIH in a federal court to enforce the public interest safeguards in the Bayh-Dole Act. A short 15-day comment period makes it very difficult to do any of this and has the practical and, we believe, intended result to undermine the public interest safeguards in the Bayh-Dole Act.

ANNEX:

The right of the public to appeal licensing decisions was narrowed to companies trying to commercialize inventions in 2023

It has always been challenging for the general public to appeal an NIH licensing decision in federal court, given the current requirements to obtain standing, but until 2023, it was possible to request an administrative appeal of a decision. There is an administrative appeal pending for

the NIH rejection of the Xtandi march-in request. The appeal was filed on March 23, 2023, by three prostate cancer patients, and supported by eight NGOs on May 2, 2023.

On March 24, 2023, the National Institutes of Standards and Technology (NIST) issued sweeping new changes in the regulations concerning Rights to Federally Funded Inventions and Licensing of Government Owned Inventions (88 FR 17730). These new rules became effective April 24, 2023, and included a significant change in 37 CFR 404.11, Appeals.

Before April 24, 2023, among the parties who could appeal a decision included:

> (1) A person whose application for a license has been denied;
>
> (2) A licensee whose license has been modified or terminated, in whole or in part; or
>
> (3) A person who timely filed a written objection in response to the notice required by § 404.7(a)(1)(i) or § 404.7(b)(1)(i) and who can demonstrate to the satisfaction of the Federal agency that such person may be damaged by the agency action.

The change in the regulations modified (3), which now reads:

> (3) A person who timely filed a written objection in response to the notice required by § 404.7 and who can demonstrate to the satisfaction of the Federal agency that such person may be damaged by the agency action due to being denied the opportunity to promote the commercialization of the invention.

By adding the words, “due to being denied the opportunity to promote the commercialization of the invention,” the Biden Administration, in adopting a rule proposed by the Trump Administration, has eliminated the right of anyone but an entity seeking “the opportunity to promote the commercialization of the invention” to appeal a decision. This change was designed to eliminate the right of patients or public interest groups to seek an administrative review of decisions that harm the public as consumers, taxpayers, or citizens, but does ensure that drug companies and other commercial entities have robust rights of appeal.

KEI had filed objections to this proposal on March 26, 2021, which were rejected by NIH in 2023. KEI’s 2021 comments, filed by Kathryn Ardizzone, included these passages:

> The NIST proposal on standing is inconsistent with the intent of the Bayh-Dole Act, as expressed through the licensing procedures at 35 U.S.C. § 209(e). By giving the public a right to comment on exclusive licenses and requiring agencies to consider their comments, Congress signaled its desire to give members of the public a powerful voice in these decisions. The right to comment cannot be meaningful if the public cannot appeal licenses. The proposal is also inconsistent with a stated policy and objective of

the Act: to “protect the public against nonuse or unreasonable use of inventions.” 35 U.S.C. § 200.

The proposal would likely contribute to agencies’ dismissiveness of public comment as it stands today. Over the past several years, the National Institutes of Health (NIH) has become increasingly unresponsive and non transparent about its licensing decisions, undermining the public’s voice. As an example of this lack of responsiveness and possible hostility to the public’s right to appeal, KEI’s previous counsel asked the NIH to provide him copy of the NIH’s appeals procedures for an appeal that KEI wanted to submit, but the NIH initially refused to forward him the policy, asserting that KEI did not have standing. It was impossible for the NIH to know that KEI did not have standing before KEI even had an opportunity to be heard on why it did. And despite KEI notifying the NIH on multiple occasions over the years, the link to the Department of Health and Human Services appeals procedures remains broken on the NIH Office of Technology Transfer website.

The failure of agencies to consider public comments and appeals would have a harmful impact. If this proposal is implemented and NIH licensing officers prefer to enter into licenses that violate the restrictions set forth at 35 U.S.C. § 209, the Public Health Service obligation to promote access in developing countries, and the requirement under 40 U.S.C. § 559 to seek the advice of the Attorney General, the officers would be even more willing to dismiss the comments on both process and substance, knowing that the public would not be able to seek review of their actions. These restrictions, however, are all important because they are all intended to protect the public interest concerning the licensing of inventions paid for and owned by the public. As such, they deserve serious assessment and consideration when making licensing decisions. It is also unreasonable to expect potential developers of federally-owned technologies to advocate for public interest safeguards, since they share the same interests as other companies seeking to commercialize federal inventions, such as by charging high prices and engaging in anticompetitive practices or under-serving persons living in developing countries. The public is uniquely situated to provide an important and necessary check on agencies’ licensing decisions.

. . .

Exclusive licenses in government-owned patents have broad implications, including on the price at which the technology would be available in the market. They give companies monopolies in inventions paid for and owned by the American public, and these monopolies have consequences. During the period of exclusivity, companies face no competition regarding the licensed inventions, and thus are able to set higher prices for the resultant products. High prices and other potential consequences of exclusive licenses can harm patients, payers and the public in general, all of whom should have the opportunity to comment on and appeal decisions that may damage them. They are no less damaged by the licenses simply because they themselves do not have the

opportunity to commercialize an invention. There can be no doubt that when the public pays for and owns an invention, it has a stake in how it is licensed.

. . .

I strongly believe that to preserve the public's role in the licensing process and best ensure agencies comply with their statutory requirements regarding exclusive patent licenses, NIST must rescind this proposal. But rescission, in my opinion, would not go far enough, because it is disturbing and highly concerning that NIST would issue this proposal in the first place. Upon reading this proposal together with the rest of NIST's regulatory package, a theme emerges: NIST is doing everything it can to maximize the privatization aspect of the Bayh-Dole Act and erode its public interest safeguards. When I joined KEI as their lawyer, I never expected, but increasingly learned the extent to which federal agencies like NIST and the NIH sidestep or distort Congressional intent on the Bayh-Dole Act, in order to diminish the public interest in the affordability of taxpayer-funded inventions in service of private interests.

Congress should conduct oversight on the NIST proposals in general, and ask NIST specifically why it thought that undermining the public's right to participate in the licensing process was beneficial and consistent with the text and intent of the Bayh-Dole Act.

Submission Date: 8/15/2023

Name: Katharine Ku

Name of Organization: Wilson Sonsini Goodrich & Rosati

Comment:

Additional Comment (attachment):

August 15, 2023

Lyric Jorgenson, PhD
Acting Associate Director for Science Policy
National Institutes of Health Office of Science Policy
6705 Rockledge Dr #750
Bethesda, MD 20817

Dear Director Jorgenson,

My name is Katharine Ku, and I currently serve as Chief Licensing Advisor at the law firm Wilson Sonsini Goodrich & Rosati. As someone who has worked in the field of technology transfer for over four decades -- including 27 years as Executive Director of Stanford University's Office of Technology Licensing[1] -- I would like to offer some personal comments on last month's "Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer."

Some participants suggested that the federal government should require that medicines developed with support from the National Institutes for Health (NIH) be sold at a "reasonable price." According to proponents of this policy, the authority to dictate prices in this manner can be found in the 1980 Bayh-Dole Act.

That position distorts both the letter and the intent of Bayh-Dole. Worse, it represents a major threat to the process of technology transfer that has powered America's innovation economy for decades.

The chief purpose of Bayh-Dole was to create a fair and uniform process by which universities and non-profits that received federal grants could patent any resulting discoveries and license them to private companies.

The tech-transfer system established by Bayh-Dole has proven wildly successful. By one estimate, academic tech transfer has contributed $1.9 trillion to the nation's gross domestic product and created 6.5 million jobs between 1996 and 2020 alone.[2] Before Bayh-Dole, technologies developed in university labs with the support of the federal government rarely found their way into commercial products.[3] Today, such commercialization is routine.

The pricing reforms discussed at last month's workshop could cripple the tech-transfer system that Bayh-Dole created. Companies that license government-backed research must take enormous financial risks to transform those technologies into practical, real-world products. Without the freedom to price their products as they see fit, these risks would be impossible to justify. As a result, researchers would have a vastly more difficult time turning their laboratory breakthroughs into real-world products.

---

[1] https://www.wsgr.com/en/people/katharine-ku.html
[2] https://autm.net/AUTM/media/Surveys-Tools/Documents/AUTM-Infographic-2021_1.pdf
[3] https://itif.org/publications/2019/03/04/bayh-dole-acts-vital-importance-us-life-sciences-innovation-system/

Efforts to impose reasonable-price requirements on NIH-funded technologies are nothing new, of course. The NIH added a reasonable pricing clause to its Cooperative Research and Development Agreements (CRADAs) beginning in 1990. This clause required those seeking a license to a particular technology to show "a reasonable relationship between pricing of a licensed product, the public investment in that product, and the health and safety needs of the public."[4]

The NIH rescinded that policy five years later after an "extensive review," the conclusion of which was that "the pricing clause has driven industry away from potentially beneficial scientific collaborations with [public health service] scientists without providing an offsetting benefit to the public," NIH Director Harold Varmus, M.D. said at the time.[5] Following the elimination of the pricing clause, the number of NIH CRADAs exploded.[6]

Despite this clear evidence that pricing restrictions discourage innovation, a number of advocates and policymakers seem determined to repeat the mistakes of the 1990s. This position was expressed most vocally at last month's workshop by James Love. But it also enjoys the support of lawmakers like Sens. Elizabeth Warren (D-MA) and Rep. Lloyd Doggett (D-TX), among others.[7] Bayh-Dole is not the problem, nor the solution, to the pricing of drugs.

The NIH serves an indispensable role in fostering basic research. But the agency is ill-equipped for the risky, expensive work of transforming that research into safe, effective products and should never be imposing arbitrary and nebulous price restrictions on a product so long before it ever becomes a reality.

I have devoted my career to helping researchers and entrepreneurs turn groundbreaking science into products that can benefit humanity on a massive scale. NIH-imposed pricing restrictions would threaten the technology transfer system that makes such innovation possible.

Thank you for allowing me to comment on this critical issue. If you have any questions, please don't hesitate to contact me.

Sincerely,

Katharine Ku

Katharine Ku
Executive Director Emerita
Office of Technology Licensing
Stanford University

[4] https://www.techtransfer.nih.gov/sites/default/files/documents/pdfs/NIH-Notice-Rescinding-Reasonable-Pricing-Clause.pdf
[5] https://www.techtransfer.nih.gov/sites/default/files/documents/pdfs/NIH-Notice-Rescinding-Reasonable-Pricing-Clause.pdf
[6] https://bayhdolecoalition.org/wp-content/uploads/2023/06/CRADA-QA-Nov-2021-FINAL.pdf
[7] https://www.warren.senate.gov/oversight/letters/senators-warren-king-and-representative-doggett-seek-answers-from-hhs-and-commerce-on-interagency-working-group-for-bayh-dole

Submission Date: 8/16/2023

Name: Peter Pitts

Name of Organization: Center for Medicine in the Public Interest

Comment:

Attached are my comments per the Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer.

Thank you,

Peter J. Pitts

Additional Comment (attachment):

August 16, 2023

Lyric Jorgenson, Ph.D.
Office of Science Policy
6705 Rockledge Drive, Suite 630
Bethesda, MD 20892

Dear Director Jorgenson:

On behalf of The Center for Medicine in the Public Interest (CMPI), I am writing in regard to the NIH's recent workshop on *Transforming Discoveries Into Products: Maximizing NIH's Levers to Catalyze Technology Transfer*.

CMPI is a nonprofit, nonpartisan organization committed to advancing the discussion and development of patient-centered health care. Collectively, we are troubled by the adversarial claims raised against intellectual property protections and the private sector's role in drug development during the workshop. The renewed discussions of including "reasonable pricing" clauses in NIH funding agreements were equally disconcerting.

The life sciences sector in America stands unrivaled in its innovative prowess globally. This isn't mere coincidence; it's a testament to our robust technology transfer system, which facilitates private enterprises in transforming basic lab research -- backed by federal investments -- into groundbreaking medicines.

To be sure, the term "basic research" is a bit of a misnomer. Undertaken primarily by NIH-supported labs and academic institutions, there is nothing basic about this form of research. It is foundational to our understanding of how certain scientific principles can be harnessed to craft life-saving treatments, vaccines, and medicines.

However, it's crucial to distinguish between basic research and drug development. While the responsibility for the former largely falls on NIH funded labs and academic institutions, the

responsibility for the latter falls to private firms that license federally-funded research to develop and commercialize breakthrough treatments. Indeed, in 2020, the biopharmaceutical industry invested $122 billion in research and development -- a figure nearly three times the NIH's total budget for FY2020.[12]

Indeed, it can take close to $3 billion to bring one new drug to market, accounting for the reality that around 90% of candidates in clinical trials fail to gain FDA approval.[34] Yet, private investors have been undeterred by these odds. They're driven by the potential of a single successful treatment benefiting millions and the opportunity to recover their initial investments, funding further research endeavors.

This system of technology transfer has existed for over four decades since the enactment of the Bayh-Dole Act, which gave federal labs the ability to license their research to private companies to develop and commercialize. And while the intricate journey of drug development often leads to setbacks, these risks are shouldered by the private sector. Yet, when they succeed, the ripple effects are profound -- benefiting patients, taxpayers, and the advancement of science as a whole.

To date, the Bayh-Dole Act has facilitated the creation of over 200 new drugs and vaccines, contributed nearly $2 trillion to our gross industrial output, and spurred the growth of 15,000 startups.[5] It is because of this legislation that NIH-funded basic research reaches patients in the form of new medicines. Given its pivotal role, it's perplexing that the agency has not firmly refuted claims that the Bayh-Dole Act grants the government authority to "march-in" for the purpose of controlling drug prices.

Those advocating for this scheme misinterpret the purpose of the law, and how it works. The Bayh-Dole Act's march-in provision gives the government the power to intervene if the holder of the patent rights is unwilling or unable to commercialize a discovery to the point it becomes available to the public. As NIH has historically recognized, march-in is not a price-control mechanism.[6]

To undermine the very technology transfer system that has enabled the United States to develop over half of all new drugs in the global market would be a mistake.[7] Our current R&D pipeline is flourishing thanks to the technology transfer process facilitated and protected by the Bayh-Dole Act. Those who wish to twist the law's intent to unilaterally determine drug prices would be responsible for the demise of U.S. biomedical innovation as we know it.

---

[1] https://www.researchamerica.org/wp-content/uploads/2022/09/ResearchAmerica-Investment-Report.Final_.January-2022-1.pdf
[2] https://sgp.fas.org/crs/misc/R43341.pdf
[3] https://pubmed.ncbi.nlm.nih.gov/26928437/
[4] https://ascpt.onlinelibrary.wiley.com/doi/10.1002/cpt.2568
[5] https://autm.net/AUTM/media/Surveys-Tools/Documents/AUTM-Infographic-2021_1.pdf
[6] https://www.techtransfer.nih.gov/sites/default/files/documents/policy/March-In-Norvir2013.pdf
[7] https://itif.org/publications/2019/03/04/bayh-dole-acts-vital-importance-us-life-sciences-innovation-system/ (fig. 1)

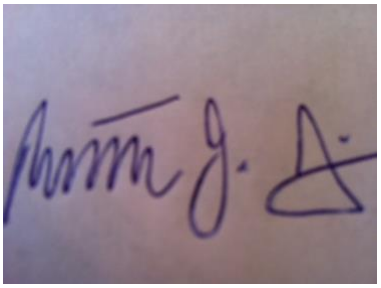
Just as the NIH should resist political pressure to "march-in" on the basis of price, the agency must resist calls to implement "reasonable pricing clauses" that would dictate prices for new products developed through cooperative R&D agreements.

Such policies do not achieve their intended goal of reducing drug costs. Instead, CRADA reasonable pricing clauses strain industry partnerships, often derailing promising drug candidates in the process. That was precisely what happened when the NIH experimented with the idea in the mid-1990s, leading the agency to quickly retract the plan. As then-NIH Director Dr. Harold Varmus aptly stated, the "[reasonable] pricing clause has "driven industry away from potentially beneficial scientific collaborations…without providing an offsetting benefit to the public."[8]

We are on the cusp of the next era of medical innovations. NIH research, coupled with the power of private industry, will ensure that medical breakthroughs get to our patients as soon as possible. Tampering with the current system will only lead to fractures between government and private industry that leave patients in the lurch.

On behalf of CMPI, thank you for your attention to our concerns.

Respectfully,



Peter J. Pitts
President
The Center for Medicine in the Public Interest

[8] https://www.techtransfer.nih.gov/sites/default/files/documents/pdfs/NIH-Notice-Rescinding-Reasonable-Pricing-Clause.pdf

Submission Date: 8/17/2023

Name: Robert Pavey

Name of Organization: Pavey Family Investments

Comment:

Attached is my statement s a Word document.

Prepared Statement of Robert D. Pavey

Partner, Morgenthaler Ventures and Manager, Pavey Family Investments
for
National Institutes of Health Workshop entitled
Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer

Thank you for allowing me to submit this prepared statement.

Bob Pavey
Managing Member
Pavey Family Investmenrs

Additional Comment (attachment):

PAVEY FAMILY INVESTMENTS

August 18, 2023

Prepared Statement of Robert D. Pavey

Partner, Morgenthaler Ventures and Manager, Pavey Family Investments
for: National Institutes of Health Workshop
entitled
Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer

Dr. Lyric Jorgenson
NIH Office of Science Policy
6705 Rockledge Dr #750
Bethesda, MD, 20817

VIA EMAIL: SciencePolicy@od.nih.gov

Dear Director Jorgenson,

My name is Bob Pavey. I have been a venture capitalist for more than 50 years, both as a partner in the firm Morgenthaler Ventures and currently on my own as Pavey Investments. I have invested in a number of companies pursuing breakthrough inventions in several different technologies, including both digital technology companies and biopharmaceutical companies. During the 1990s, I served as President of the National Venture Capital Association and in that role and subsequently have developed a broad perspective on the economic forces affecting investment in US early-stage technology. I am also currently a Trustee of Case Western Reserve University where my primary focus is on technology development and technology transfer.

I have reviewed a number of the written statements that were presented to the Office of Science Policy at the NIH workshop on "Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer," and I would like to add a few thoughts of my own for your consideration. In my opinion, transforming scientific discoveries and other novel ideas into products has been one of the greatest accomplishments of this country over the past fifty years and I would very much like to see the robust continuation of this great accomplishment. The remarkable growth we have enjoyed, particularly since 1980, can be attributed to a number of factors, chief among them the emergence of an investment community that was able to diversify the risks involved in investing in unproven technologies and, in many cases, unproven companies.

There always have been risk takers (known sometimes as angel investors) willing to back adventurous entrepreneurs on a one-off basis; the Spanish monarchy's willingness to provide funds to Christopher Columbus is a well-known example of "patron" style investments that have been with us throughout history. Many angel investors are still active worldwide, but what made the American venture capital experience different was the emergence of financial organizations that took a systematic approach to investing in multiple promising startups and small companies. When the risk is high that any given startup will fail, investments make more sense if a fund of investment dollars can be spread into multiple investments, in hopes that successful investments will more than offset the failures. At a

high level, this is the VC model today. And indeed when modern portfolio management theory became generally accepted about 40 years ago, institutional investors and university endowments began allocating a minority of their investment capital to private equity firms. This allowed firms such as mine to support many promising young companies while at the same time providing better returns of many non-profit institutional investors.

The American VC industry as we know it today began shortly after World War II. The industry progressed very slowly until about 1980, when the government agency responsible for regulating pension funds allowed pension funds to move to modern diversified portfolio management. At that point the entire venture capital industry exploded with growth and new investment capital. Several other forces converged about the same time that added to the growth – The reduction of capital gains taxes in 1978, the creation of the Court of Appeals for the Federal Circuit (rebuilding of a patent system that investors could rely on), and the passage of the Bayh-Dole Act that allowed the recipients of government research grants to own and license the patents that covered their work. As a result of these changes, thousands of new companies have been formed based on new and better technologies and more agile managements. Many of those small companies of the 1980s are the corporate giants of today.

Sadly, this growth cycle is showing signs of winding down. This is a key factor the agency should keep in mind as it pursues "Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer." For a variety of reasons, investors have become more risk averse, a trend that is not healthy for our future as a nation. To some extent, this increased aversion to risk is masked by the enormous influx of later stage investment capital. On closer look, however, we see that investment capital available at the seed stage is not growing. Put differently, much of private equity capital flowing into small companies over the last few years has gone into late-stage companies that no longer face startup risks. These trends become particularly important at the point where NIH is trying to maximize "technology transfer" to private companies that are willing to assume the extreme risks associated with drug development.

Much of the decline in risk taking is a direct result of government policies that increase the perceived risks facing the entrepreneur and the investor. For many investors, including myself, patents are no longer regarded as reliable protection for risky investments. My perception is based on personal experience trying to enforce a patent that is being infringed by a very large company. These large companies simply refuse to take a license and have told me that their policy is to fight every case as long as they can, because it deters other small companies from suing them. That experience is far from unique; it seems clear to me that few if any small companies can afford to enforce their patents, even strong patents. The cost is prohibitive and the time to win a patent battle can be a decade. Many venture capitalists today only invest in software, avoiding companies that depend on patents.

Perhaps an even greater threat to investors today comes from the demands by some people in Congress and the Biden Administration that they can make drugs cost less by exercising so-called "march-in rights" or by controlling the prices that private companies can charge for therapies. These ideas emanate largely from people with little or no knowledge of the return needed to justify the risk of new drug development. Such arguments are damaging the investing climate, which will only get worse unless NIH and other agencies firmly reject them.

Respectfully submitted Robert D. Pavey

Submission Date: 8/18/2023

Name: Karen Kerrigan

Name of Organization: Small Business & Entrepreneurship Council

Comment:

Thank you for the opportunity to submit comments regarding NIH's recent workshop: Transforming Discoveries Into Products - Maximizing NIH's Levers to Catalyze Technology Transfer.

I have attached comments regarding the role that small innovative firms and entrepreneurs play in innovation, and the incentives needed to continue to drive innovative discoveries and bring those to market for the betterment of consumers and our nation's health.

Please contact me if you have questions, or need additional information.

Thank you,
Karen Kerrigan

Karen Kerrigan
President & CEO
Small Business & Entrepreneurship Council
www.sbecouncil.org
@SBECouncil

Protecting small business, promoting entrepreneurship

Additional Comment (attachment):

August 16, 2023

Lyric Jorgenson, PhD
Acting Associate Director for Science Policy
National Institutes of Health Office of Science Policy
6705 Rockledge Dr #750
Bethesda, MD 20817

Dear Director Jorgenson,

On behalf of the Small Business & Entrepreneurship Council (SBE Council), I'd like to thank you for the opportunity to submit comments regarding the themes discussed at the National Institutes of Health's recent workshop, *Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer*.

SBE Council is an education, advocacy, and research organization dedicated to protecting small businesses and promoting entrepreneurship. Our members include small business owners, entrepreneurs, state and local business groups, and corporate partners and associations.

Many of them play an extraordinary role in driving U.S. innovation forward. Small businesses and startups make up the large majority of firms in high-patenting industries.[1] In the life sciences, for instance, nearly 80% of firms have fewer than 100 employees. Roughly half have fewer than 10.[2]

Despite their size, small businesses account for the lion's share of new drug approvals. Between 2015 and 2020, nearly two-thirds of new medicines were developed by small firms.[3]

Unlike larger pharmaceutical companies, small businesses and startups do not have the ample pipelines and previous successes to fund their ongoing research and development endeavors. Instead, they rely on venture capital to support their efforts.

[1] https://sbecouncil.org/about-us/facts-and-data/
[2] https://bayhdolecoalition.org/wp-content/uploads/2022/04/Attacks-on-Bayh-Dole-Webinar-Transcript.pdf pg. 2
[3] https://www.pharmavoice.com/news/2020-01-pharma-innovation/612330/

Naturally, attracting investors requires certain assurances. Drug development is a formidable process, often spanning a decade or longer and demanding $2 billion of capital or more. [4] A staggering 90% of development attempts don't succeed. [5] Startups, with their inherent vulnerabilities and limited safety nets, are particularly susceptible to failure -- making them high-risk investments.

If not for our world-leading system of intellectual property rights, few investors would dare to take the leap. IP protections offer venture capital firms an opportunity to recoup their investments - and turn a profit - should a development effort succeed. In so doing, IP rights function as a catalyst, incentivizing funders to commit capital to innovative startups developing groundbreaking new treatments.

It is for this reason that we were concerned by certain discussions that took place during the NIH's July 31 workshop. Rather than protect and build on critical IP rights, some panelists suggested reforms that would erode these protections - threatening the small business-led innovation ecosystem economy in the process.

Some activists and lawmakers have long believed undermining patent rights is key to lowering drug prices. They've repeatedly petitioned the government, for example, to misuse the "march-in" provision of the Bayh-Dole Act to force down the cost of prescription drugs.

The 1980 law permitted universities and small research institutions to retain the patent rights on discoveries their scientists made with federal funding and exclusively license them to private companies for development. It was designed to ensure taxpayer-funded inventions reached consumers -- rather than languish on government laboratory shelves, as many discoveries did pre-Bayh-Dole.

The law has proven to be an incredible success. Between 1996 and 2020, technology transfer between academic institutions and private companies led to the development of more than 200 vaccines and treatments. The Bayh-Dole system has helped launch more than 17,000 startups and support 6.5 million jobs.[6]

Unfortunately, that hasn't stopped activists from suggesting the government can misuse its "march-in" rights under Bayh-Dole as a price control mechanism. Those rights allow government to revoke an exclusive patent right on an invention in an extremely limited set of circumstances - namely, when the original licensee fails to commercialize the discovery. The price of a drug developed by private industry is simply not one of those circumstances, as the law's authors have reaffirmed.

---

[4] https://pubmed.ncbi.nlm.nih.gov/26928437/
[5] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9293739/
[6] https://autm.net/AUTM/media/Surveys-Tools/Documents/AUTM-Infographic-22-for-uploading.pdf pg. 1

To date, the NIH has rightfully denied all march-in requests. But if the agency were to reverse course, it would instill significant uncertainty regarding the intellectual property safeguards that have empowered startups and small businesses to emerge and bring treatments to patients.

With no guarantee of the exclusive patent rights that could help them recoup their investments in the life sciences, venture capital firms will no doubt look elsewhere. Innovative startups already struggling to find capital may go under. Others will never get off the ground.

March-in petitions aren't the only existential threat facing small businesses and entrepreneurs in the industry. There have also been renewed calls for the NIH to require any company licensing agency-funded research to set a "reasonable price" for the resulting product.[7] Those calls have since been taken up by scorned march-in advocates -- and even echoed during the NIH workshop.

A reasonable pricing clause would similarly destabilize intellectual property rights and the innovation ecosystem at large. Knowing NIH can set an ill-defined price for any product resulting from its research, few small businesses, entrepreneurs, and venture capitalists will partner with the agency to commercialize government-funded discoveries. The very technology transfer and innovation NIH is working to catalyze will grind to a halt.

Such a scenario is not theoretical. The NIH implemented a reasonable pricing clause in its Cooperative Research and Development Agreements in 1990. By 1995, the NIH director concluded that "the pricing clause has driven industry away from potentially beneficial scientific collaborations with [NIH] scientists without providing an offsetting benefit to the public" and subsequently removed it from future agreements.[8]

Put simply, small businesses and startups are advancing the next generation of innovative treatments. We urge the NIH to continue supporting and promoting the system of robust and assured intellectual property protections that make it all possible. SBE Council appreciates the opportunity to weigh in on this important matter.

Sincerely,

Karen Kerrigan, President & CEO

---

[7] https://www.statnews.com/pharmalot/2023/06/13/sanders-biden-nih-drugs-medicine/#:~:text=Sanders%20wants%20NIH%20to%20adopt,that%20agency%20research%20helps%20develop&text=In%20another%20bid%20to,Sanders%20(I%2DVt.)

[8] https://bayhdolecoalition.org/wp-content/uploads/2023/06/CRADA-QA-Nov-2021-FINAL.pdf pg. 2

800 Connecticut Ave. NW ● Suite 300
Washington, D.C. 20006
(703)-242-5840
www.sbecouncil.org
@SBECouncil

Protecting Small Business, Promoting Entrepreneurship

Submission Date: 8/18/2023

Name: Gerard Scimeca

Name of Organization: Consumer Action for a Strong Economy

Comment:

Dear NIH:

Please see our attached comments to the Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer.

If feasible, please send confirmation of receipt, thank you.

_____

Gerard Scimeca
Chairman, CASE

Additional Comment (attachment):

Submission Date: 8/18/2023

Name: Gerard Scimeca

Name of Organization: Consumer Action for a Strong Economy (CASE)

Comment:

August 18, 2023

National Institutes of Health (NIH) - Lyric Jorgenson, Ph.D.
NIH Office of Science Policy
6705 Rockledge Dr #750
Bethesda, MD, 20817

Dear Director Jorgenson,

Consumer Action for a Strong Economy (CASE) writes today to the National Institutes of Health (NIH) to provide feedback following the workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer.

American consumers greatly benefit from having access to more new drugs and treatments than many of their peers abroad. For example, the U.S. led the world in the search for solutions to COVID-19, and we delivered beyond expectations. The public-private cooperation encouraged by our current laws was vital to this success.

The Bayh-Dole Act helped solidify this unrivaled position for American patients because of the collaborations it fosters in medical research and development (R&D). Promoting technology transfers between public and private partners should remain a top priority. This will allow us to continue to advance scientific progress and incentivize the development of discoveries made through federally funded laboratories and universities nationwide.

Strong Intellectual Property (IP) protections promote the very collaborations that make our nation a leader in producing new cures and treatments, and these protections must never be taken for granted. Despite many misleading claims, Bayh-Dole's "march-in" rights are not supposed to be a free pass for government intrusion. Our elected officials should continue to reject requests to use "march-in" provisions to break the patents of specific drugs, and refuse broader calls to destabilize America's patent protections.

Consumers depend on our innovative healthcare system for lifesaving cures, and it's up to us to protect and defend this advantage.

Sincerely,

Consumer Action for a Strong Economy (CASE)

Consumer Action for a Strong Economy
1800 Diagonal Road, Suite 600
Alexandria, VA 22314

@CASE_forAmerica

Submission Date: 8/18/2023

Name: Patricia Kelmar

Name of Organization: U.S. Public Interest Research Group

Comment:

Please see attached our comments. Thank you very much.

Patricia Kelmar, JD
Senior Director, Health Care Campaigns
PIRG and PIRG EducationFund

Additional Comment (attachment):

U.S. PIRG

USPIRG.org
Info@USPIRG.org

August 18, 2023

Lawrence A. Tabak, D.D.S. Ph. D.
Acting Director
National Institutes of Health
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Tabak:

On behalf of the U.S. PIRG (Public Interest Research Group) and our state affiliates, I am submitting comments relating to the National Institutes of Health Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer on July 31, 2023.

PIRG is a nonprofit advocate for the public interest. We speak out for a healthier, safer world which includes promoting policies that support the delivery of high value healthcare. To succeed in this mission, we must address skyrocketing health care costs, including the cost of prescription drugs.

We have a strong history in finding ways to cut costs without impacting quality. There is no better model than the ability of patients to access lower cost generic and biosimilar prescription drugs. As such, we have been particularly concerned about market barriers and anticompetitive practices that block entry of generic and biosimilar medications. Two-thirds of U.S. adults rely on prescription drugs to live full lives and to treat their illnesses and medical conditions.[1] And yet 1 in 4 people struggle to pay for their medications.[2] The role of patents in the pharmaceutical market play an important role in whether there is true competition in prescription drug pricing. With even just one generic alternative, prices for that drug go down by as much as 40%.[3]

For this reason we watched with interest your recent workshop on how the NIH decides whether and how to patent and license discoveries made by publicly-funded NIH scientists. We applaud the public mission of NIH as presented in the workshop slides to act as a "steward of medical and behavioral research for the Nation." NIH should honor this goal in all of your operations. The agency should be a

[1] Emily Ihara, "Prescription Drugs", Georgetown University Health Policy Institute. https://hpi.georgetown.edu/rxdrugs/#:~:text=More%20than%20131%20million%20people,United%20States%20%E2%80%94%20use%20prescription%20drugs

[2] Ashley Kirzinger et al., "Poll: Nearly 1 in 4 Americans Taking Prescription Drugs Say it's Difficult To Afford Their Medicines, Including Larger Shares Among Those With Health Issues, With Low Incomes and Nearing Medicare Ages", KFF, March 1, 2019. https://www.kff.org/health-costs/press-release/poll-nearly-1-in-4-americans-taking-prescription-drugs-say-its-difficult-to-afford-medicines-including-larger-shares-with-low-incomes/

[3] FDA, Generic Competition and Drug Prices, Dec. 2019, https://www.fda.gov/media/133509/download, p. 2

model for all innovators – to make discoveries that can be shared with the public and built upon by other inventors.

NIH provides the backbone of research that launches many life-saving innovations. As such, you should center your decision-making on whether patients will be able to pay for the medicines which come to market because of NIH's ground-breaking discoveries. Indeed, you have an even greater obligation to consider how your decisions impact drug price competition. President Biden's executive order to end anti-competitive practices specifically called for greater availability of generic and biosimilar drugs in the marketplace to provide low-cost options for the people who need them.[4]

We urge the NIH to use its existing powers to ensure that prescription drugs and other medical products developed with public funds are not kept from the public because of price and anti-competitive practices.

Licensing terms to foster better prices.
The workshop focused on how NIH licenses its discoveries. Several strong ideas were offered to address the high prices of medications (based on NIH science) that are developed and marketed by pharmaceutical companies. We strongly urge NIH to include terms in its licensing agreements that better protect patients from price-gouging and unsupportable prices. Licensing agreements should include reasonable pricing requirements and other mechanisms that incentivize better prices for patients.

Transparency of NIH expenditures and licensures to ensure accountability.
Clear, timely and accurate information builds public trust. NIH should disclose how public funds are expended to bring about NIH discoveries. And recognizing that the public essentially owns NIH patents, the terms of NIH licenses, including royalty rates, should be open to view to the broadest extent possible. NIH should also disclose the costs of clinical trials supported by the agency's funds. Transparency allows for accountability and full assessment of the use of public funds.

Tracking NIH science in patents applications from private entities.
Drug patent applicants are required to disclose any federal funding in their patent applications. The NIH must fully enforce this provision and consider removing patent rights for those applicants who violate this requirement.

March-in rights to overcome price-gouging.
We urge the NIH to use its march-in rights for medications where there is no existing competition and the drugs' prices are not reasonable.

NIH has the opportunity to improve its operations to take the long view of its part in medicine science. By keeping a patient-centric approach to its work, the NIH should do its utmost to not simply help

[4] The White House, Executive Order on Promoting Competition in the American Economy, July 9, 2021 *accessed on* Feb 28, 2023 *at* https://www.whitehouse.gov/briefing-room/presidential-actions/2021/07/09/executive-order-on-promoting-competition-in-the-american-economy/

launch the discoveries that make new prescription drugs possible, but the agency should consider how to use its power to ensure the market prices allow the patients to access them. Thank you for your review of our comments.

Sincerely,

Patricia Kelmar
Senior Director, Health Care Campaigns
pkelmar@pirg.org

Submission Date: 8/18/2023

Name: Jon Soderstrom

Name of Organization: Wilson Sonsini Goodrich & Rosati

Comment:

Please see my comments in the attached.

Jon Soderstrom, PhD | Chief Licensing Advisor | Wilson Sonsini Goodrich & Rosati

Additional Comment (attachment):

Lyric Jorgenson, PhD.
Office of Science Policy
6705 Rockledge Drive, Suite 630
Bethesda, MD 20892

Director Jorgenson,

My name is Jon Soderstrom, and I served as the managing director of Yale University's Office of Cooperative Research for 25 years. As someone with over three decades of experience in technology transfer, I appreciate the opportunity to submit comments regarding the National Institutes of Health's July 31 workshop, *Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer*.

My entire career has tracked the remarkable trajectory of American life sciences innovation since the passage of the Bayh-Dole Act in 1980.[1] Prior to then, when I was a student researching intellectual property, the federal government held title to roughly 28,000 patents. Less than 5% of those patents had been licensed or commercialized.[2] And with the government's approach of predominantly issuing non-exclusive licenses for federal innovations, companies were reluctant to invest the time and resources necessary to develop an invention for the market.

Bayh-Dole established certainty of title by providing for patent ownership by the inventors: the universities and scientists who made the discovery. The law has been instrumental in promoting collaboration between government, universities, and the private sector -- facilitating the transfer of technology from the lab to the market.

Indeed, since I first joined Yale in 1996, over 15,000 new companies have been formed, and 200 drugs and vaccines, brought to market.[3] In New Haven, I was able to play a small role in this remarkable progress, overseeing the development of 74 new start-ups that have raised over $2 billion in venture capital backing and led to more than 50 different products -- all based on Yale intellectual property.[4]

Considering the extensive positive impacts of the Bayh-Dole Act, any changes should be approached with caution to avoid disruption of the entire innovation ecosystem.

Certain lawmakers, for instance, have called upon the NIH to impose so-called "reasonable pricing" clauses for all of the agency's grants, licenses, and Cooperative R&D Agreements

[1] https://www.academia.edu/86403600/Remarks
[2] https://www.gao.gov/assets/rced-98-126.pdf
[3] http://autm.net/AUTM/media/Surveys-Tools/Documents/AUTM-Infographic-2021_1.pdf
[4] https://news.yale.edu/2021/06/28/soderstrom-longtime-director-ocr-honored-25-years-leadership

(CRADAs).[5] Such clauses would deter private-sector partners from engaging in collaborative research with the NIH, hindering the progress that Bayh-Dole has made possible.

The concept of reasonable pricing clauses is not novel. In 1989, the NIH briefly adopted the policy for its CRADAs, thereby setting pricing restrictions on any products that stemmed from discoveries arising from its CRADAs or exclusive licenses.[6] While well-intentioned, this did not yield favorable outcomes for anyone involved, including patients. Rather, the number of CRADAs fell from 42 in 1989 to an average of 32 annually, as both universities and companies hesitated to partner with the NIH.[7]

As a result, NIH Director Harold Varmus rescinded the policy just six years later, stating that "the pricing clause has driven industry away from potentially beneficial scientific collaborations with [NIH] scientists without providing an offsetting benefit to the public."[8] Fortunately, collaborations between academia and the government soon recovered, with the number of CRADAs rebounding to more than 160 by 1997.[9]

This period well illustrates the deterrent effect that reasonable pricing clauses can exert on the technology commercialization process. Such requirements inject uncertainty into the ecosystem and weaken intellectual property rights -- stymying productive public-private collaborations and depriving patients of potentially life-changing medicines.

The NIH is at a pivotal juncture: the agency can either concentrate on propelling scientific advancements for patient benefits or upend its successful policies in an attempt to tackle broader healthcare challenges. These issues have dominated discussions recently – including during the July 31 workshop – and the NIH must be careful not to let them overshadow the agency's core mission.

Not disavowing the NIH's long-standing role in facilitating public-private partnerships allows basic scientific research to be more efficiently translated into tangible therapies. These fruitful collaborations not only offer a wealth of innovative medicine choices but naturally promote competitive prices. Straying from this course with restrictive rules or inappropriate interventions -- however well-intentioned -- would halt the progress patients so desperately need.

Consider that just four years after the passage of the Bayh-Dole Act -- at the height of the HIV/AIDS epidemic -- two Yale researchers began studying an antiviral therapy that had yet to be commercialized.[10] When their work suggested the drug had promise, they licensed it to Bristol

---

[5] https://www.washingtonpost.com/health/2023/06/12/sanders-hold-nih-director-drug-prices/
[6] https://www.techtransfer.nih.gov/sites/default/files/documents/pdfs/NIH-Notice-Rescinding-Reasonable-Pricing-Clause.pdf
[7] https://bayhdolecoalition.org/wp-content/uploads/2023/06/CRADA-QA-Nov-2021-FINAL.pdf
[8] 1995 - 1989 = 6 https://bayhdolecoalition.org/wp-content/uploads/2023/06/CRADA-QA-Nov-2021-FINAL.pdf
[9] https://bayhdolecoalition.org/wp-content/uploads/2023/06/CRADA-QA-Nov-2021-FINAL.pdf
[10] 1984 – 1980 = 4 https://www.academia.edu/86403600/Remarks

Myers Squibb, which shepherded the treatment through clinical trials and got fast-track approval from the FDA. Zerit would become the first effective medicine for HIV-AIDS.[11]

Absent the Bayh-Dole Act and a technology transfer framework that leverages intellectual property rights, medicines like Zerit -- along with hundreds of other cutting-edge treatments -- might never have reached the market to benefit patients. Millions of lives could be lost.

As the NIH looks to the future, it is crucial to acknowledge the importance of protecting intellectual property rights, fostering public-private partnerships, and driving the development of medical breakthroughs. And the agency must be careful not to inadvertently stifle the very engine that has propelled U.S. leadership in the life sciences.

Thank you for your consideration on this important matter.

Respectfully,

Jon Soderstrom

[11] https://www.academia.edu/86403600/Remarks

Submission Date: 8/18/2023

Name: Justin Mendoza

Name of Organization: Universities Allied for Essential Medicines

Comment:

Hello,

Please find attached comments from Universities Allied for Essential Medicines.

Thank you,
Justin Mendoza

Justin Mendoza, MPH
Executive Director, North America
Universities Allied for Essential Medicines
UAEM.org | Twitter | Facebook | Instagram

Additional Comment (attachment):

UNIVERSITIES ALLIED FOR ESSENTIAL MEDICINES

Washington DC • USA
+1 (510) 868-1159 • www.uaem.org

August 18, 2023

Lawrence A. Tabak, D.D.S. Ph. D.
Acting Director
National Institutes of Health
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Tabak,

Thank you for the opportunity to submit a written comment on the Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer.

Universities Allied for Essential Medicines (UAEM) is a global, student-driven organization with offices in the United States and members at more than 50 universities around the world. We represent researchers, future physicians, future attorneys, and more who aim to ensure that everyone has access to the medicines they need to survive.

The National Institutes of Health (NIH) are the world's largest government investors in biomedical research and development. With more than $42 B in funds, the decisions made by the NIH about how to ensure access and affordability for the medicines discovered and developed with these funds set a precedent for other investors from private philanthropy to companies and other nations. No matter how groundbreaking an innovation may be, its potential to save lives can only be realized if people from different socio-economic backgrounds, regions, and communities have access to it. Prioritizing accessibility and affordability is integral to NIH's mission of fostering scientific advances that enhance public health and wellbeing.

We submit the following comment to describe three areas for the NIH to consider in technology transfer: affordable access provisions, reasonable pricing clauses, and ensuring transparency and accountability for the NIH's licensing terms.

Ensuring Affordability

In doling out billions of dollars for the discovery and development of novel health technologies and licensing promising medical products, the National Institutes of Health (NIH) has a responsibility to ensure affordability and access to the American public that ultimately footed the bill. Here we submit two approaches to affordability that should be explored and pursued by the NIH: Affordable Access Provisions, and Reasonable Pricing Clauses.

UNIVERSITIES ALLIED FOR ESSENTIAL MEDICINES

Washington DC • USA
+1 (510) 868-1159 • www.uaem.org

Affordable Access Provisions:

A vast majority of NIH funding every year goes to university research centers and laboratories with academic affiliations. That means that academic institutions are responsible for the patenting and licensing of a majority of NIH-funded research products. Since the passage of the Bayh-Dole Act in 1980, research institutions take on the responsibility of patenting and licensing NIH-funded research products discovered on their campuses. With the end goal of commercialization, technology transfer officers have felt pressure to deliver exclusive licenses, with terms favorable to industry partners. Yet, when recommendations were made during COVID-19 to make pandemic-related technology licenses less exclusive, more than 96 universities opted to follow new industry-setting guidelines because it was a level playing field, with risks reduced.

To that end, UAEM recommends that the NIH act to level the playing field for university technology managers for access and affordability through contracting requirements such as affordable access provisions. The Affordable Access Plan provision was co-developed by the University of California Los Angeles Technology Development Group,[1] UAEM, and the Medicines Patent Pool. This provision is to our knowledge the first of its kind in exclusive licenses from U.S. universities, and places a forward-thinking but non-prescriptive obligation on the licensee to create and report on an affordable access plan to the university with strategies and timelines to ensure affordable access to licensed products in LMICs. The affordable access plan obligation is only triggered at a point where commercialization is imminent, allowing any licensee sufficient time to generate the resources needed to advance through the many stages of research and development. This provision has been utilized in licensing agreements by UCLA without issue since 2020.

Further, the University of California Berkeley Intellectual Property & Innovative Research Alliance has released their new exclusive license template,[2] which includes an affordable access plan provision of their own. This provision is substantively similar to the UCLA provision, *but with the important addition of extending the scope of the access plan beyond LMICs to also include underserved communities in the United States, giving the university some level of oversight for the high and rising costs of health products for communities around the country.*

These plans are also being considered in licensing agreements at UC Riverside, Yale University, and Columbia University, to varying degrees. However, these plans are not yet ubiquitous, and UAEM fears that university technology transfer offices may shy away from implementation of these plans or even including them out of fear that it will stymie interest from potential

[1] UCLA Technology Development Group, UCLA Considers Underserved Populations When Licensing Medical Research Discoveries, accessed August 18, 2023, at: https://tdg.ucla.edu/ucla-considers-underserved-populations-when-licensing-medical-research-discoveries.
[2] UC Berkeley Exclusive License Template, accessed August 18, 2023, at: https://ipira.berkeley.edu/sites/default/files/shared/docs/EXCL%20EQUITY%20therapeutics%20diagnostics%2007April2023.pdf

licensees, despite the fact that neither UCLA or Berkeley have reported any issues. Given the lack of utilization on behalf of technology transfer officers of past access provisions, frameworks, and policies it is clear that the industry of technology transfer is risk averse when it comes to access provisions in academic licensing agreements.[3]

If the NIH were to include language akin to an affordable access plan provision when granting funds, this could become part of the standard of practice and thus easier for academic institutions to implement without fear of retribution.

Reasonable Pricing Clauses

Between 1989-1995, the use of responsible pricing clauses in cooperative R&D agreements (CRADAs) was used by the federal government in contracts with the pharmaceutical sector [4]. This policy was incited by patient and family turmoil during 1987, when the pharmaceutical company Burroughs Wellcome launched a new AIDS drug developed with the help of NIH scientists at a cost of $10,000 per year [5]. This price point caused protests from AIDs activists which led to Congressional hearings conveyed by Henry Waxman (D-CA) resulting in the NIH inserting “fair” pricing clauses into the standard CRADA. From its inception, reasonable pricing clauses became a point of contention between the NIH and pharmaceutical manufacturers [6]. The event that led to the removal of the “fair” pricing clause in CRADAs was the legal dispute between Myriad Genetics and the National Institute for Health Sciences (NIEHS). In 1992, a collaboration began between researchers from the NIEHS and Myriad Genetics to locate the *BRCA1* breast cancer gene which was achieved after two years. The issue of the use of responsible pricing arose after hesitancy from corporate investors, Myriad refused to enter a CRADA with the NIEHS [7]. This led to the NIEHS researchers receiving acknowledgement as inventors but not listed as patent recipients. This led to the presumption that NIH collaborations would not be sought in the future by the private pharmaceutical sector if responsible pricing provisions were included in future CRADAs.

---

[3] Contreras, J. - Univ est' - University T ersity Technology T echnology Transfer and the er and the Nine Points Document – An Empirical Assessment. *University of Utah College of Law Research Paper No. 476 12(2) U.C. Irvine L. Rev. 435 (2023)*

[4] Jorge L. Contreras, "What Ever Happened to NIH's 'Fair Pricing' Clause?," Petrie-Flom Center Blog, Harvard Law School (August 4, 2020) https://blog.petrieflom.law.harvard.edu/2020/08/04/nih-fair-pricing-drugs-covid19/.

[5]

[6] Jorge L. Contreras, "What Ever Happened to NIH's 'Fair Pricing' Clause?," Petrie-Flom Center Blog, Harvard Law School (August 4, 2020) https://blog.petrieflom.law.harvard.edu/2020/08/04/nih-fair-pricing-drugs-covid19/.

[7] Jorge L. Contreras, "What Ever Happened to NIH's 'Fair Pricing' Clause?," Petrie-Flom Center Blog, Harvard Law School (August 4, 2020) https://blog.petrieflom.law.harvard.edu/2020/08/04/nih-fair-pricing-drugs-covid19/.

Despite the lack of reasonable pricing terms for NIH-funded projects in recent years, universities across the U.S. have been utilizing reasonable pricing terms in various licensing arrangements. In 2023, UAEM has worked to expand on existing efforts and establish affordable access plans, to help create pathways to enforcing affordability at the university licensing level. The University of California Los Angeles created an affordable access plan provision in 2019, and Berkeley expanded upon this policy earlier this year. These provisions create an affordable access plan for medicines in lower- and middle-income countries, and Berkeley's policy requires these plans be developed for vulnerable communities in the U.S. as well.[8] Additionally, the Innovative Genomics Institute at Berkeley just recommended reasonable pricing for the future of genetic therapies, the cutting edge of biomedical innovation, even going as far as to recommend a cost-plus model for future technologies.[9]

Additionally, during the COVID-19 public health emergency, where significant federal funds were used to bring COVID-19 treatments and vaccines to market, the federal government negotiated terms that are akin to reasonable pricing clauses. In advance purchase agreements between Novovax and the Department of Defense, the company agreed to give the U.S. the "lowest, best price" for five years for any doses administered in the U.S. Pfizer agreed to a most-favored nations clause that would allow the U.S. government to get a lower price if an economically equivalent nation (one of six high-income countries) were able to negotiate a lower price. These terms were not only accepted by these companies, but guaranteed the federal government and U.S. consumers would have timely and affordable access to COVID-19 technologies while these cutting edge technologies were coming to market.

With all of this in mind, it is imperative that the NIH consider reasonable pricing terms and strong licensing mechanisms to ensure that U.S. taxpayers no longer pay the highest prices in the world for prescription drugs while also footing the bill for discovery. Even without new legislation, the NIH has the ability to utilize March-In Rights as spelled out in Bayh-Dole, or enact a Royalty-free right to practice in order to increase competition and lower the cost of medicines. This is particularly important while considering the impact of NIH-funded medications that have been over-patented with increasing prices, despite a lack of true innovation.

Ensuring Transparency

Greater transparency about the NIH's operations and licensing transactions is crucial to patients, consumer advocates, and academic specialists in technology transfer. The University of California Berkeley publishes draft licensing agreements and terms on its website to show

[8] Policy available at Berkeley IPIRA, here: https://ipira.berkeley.edu/sites/default/files/shared/docs/EXCL%20EQUITY%20therapeutics%20diagnostics%2007April2023.pdf. Discussion of policy at UAEM Webinar "A New Standard in University Licensing," Available here: https://www.uaem.org/tools/recording-a-new-standard-in-university-licensing
[9] Making Genetic Therapies Affordable and Accessible, Report, available at: https://innovativegenomics.org/atf-report/.

future licensees and other institutions what its best practices are. This practice should be standard for the NIH's licenses as well.

We encourage the NIH to solicit feedback from the public about its policies regarding the accessibility of different types of information about patenting, licensing, and accessibility of products developed with NIH funding.

Greater information about NIH licenses must be made accessible to the public. If confidentiality concerns are justified, they may be appropriate to address through narrow redactions. But at some point, confidentiality concerns are no longer justifiable, and the public should receive full access, as it does to documents pertaining to national security.

While licenses are in effect, the public is entitled to know basic licensing information–such as royalty rates. Making this information available will allow the public to assess the impact of NIH investments and make more informed policy decisions. It will also facilitate accountability to the public and trust in the agency's operations.

Transparency will also increase the efficiency of licensing markets. Royalty rates are routinely disclosed in the course of patent litigation because they are evidence used to prove damages. Making this information available will reduce the cost of obtaining such information through litigation and make it more difficult for companies to use litigation costs to inflate patent licensing fees. This will make licensing markets more efficient, open to competition, and fair to small and new entrants which are most sensitive to litigation costs. Additionally, in the event that the U.S. government does decide to practice its right to government patent use, as described in 28 U.S.C. 1498, a public record of NIH licensing royalty rates would potentially prove useful in setting reasonable royalties when that use is challenged in court.[10]

In addition, we recommend that the NIH ensure transparency on a number of factors outside of licensing and royalty agreements, and have included the following as areas to consider broader transparency:

Trial costs

Any NIH-supported clinical trial should be required to report its total costs and the share funded by the federal government, using a standardized accounting format.

[10] Brennan, Hannah, Kapczynski, Amy, Monahan, Christine H., Rizvi, Zain. A Prescription for Excessive Drug Pricing: Leveraging Government Patent Use for Health. Yale Journal of Law & Technology. 2017. Available at: https://openyls.law.yale.edu/handle/20.500.13051/7810

UNIVERSITIES ALLIED FOR ESSENTIAL MEDICINES
Washington DC • USA
+1 (510) 868-1159 • www.uaem.org

Drug pricing and market information

We urge the NIH to implement the provisions in WHA72.8, which the World Health Organization (WHO) has developed specifically to improve the transparency of markets for medicines, vaccines, and other health products.

Enforcement of existing disclosure requirements

The NIH can and must do more to enforce the obligation to disclose federal funding in patent applications. There must be consequences for those who violate their disclosure obligation.

Conclusion

UAEM applauds the NIH's efforts to open up public comment on technology transfer and innovation. The agencies efforts have clearly demonstrated an effective system to drive biomedical products and health technology to commercialization. It is our view that the NIH's impact on both taxpayers and the public's health more broadly have been limited by licensing terms and transparency that favors commercial interest over the public. The proposals we have set forward in this comment, especially adoption of an affordable access plan provision, are friendly to both the public's interests in new medical innovations, and to the commercialization of those products.

Sincerely,

Justin Mendoza, MPH
Executive Director
Universities Allied for Essential Medicines North America
Justin@uaem.org

Submission Date: 8/18/2023

Name: Kevin Walters

Name of Organization: Wisconsin Alumni Research Foundation

Comment:

Dear NIH Office of Science Policy,

Please find attached a letter from the Wisconsin Alumni Research Foundation to Acting Associate Director Jorgenson in regards to the invitation to comment on your Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer. As noted in the letter, we have also attached our recent letter to the Senate HELP Committee due to its relevance to this topic.

Thank you for the opportunity to contribute to this important conversastion. Please let us know if we can be of any further assistance.

Best,

Kevin Walters

Wisconsin Alumni Research Foundation (WARF)
Public Affairs Analyst
Pronouns: he, him, his
www.warf.org

Additional Comment (attachment):

WARF
Wisconsin Alumni Research Foundation

P: 608-960-9850

614 Walnut Street, 13th Floor
Madison, WI 53726
warf.org

Lyric Jorgenson, PhD.
Office of Science Policy
6705 Rockledge Drive, Suite 630
Bethesda, MD 20892

August 18, 2023

Via email: SciencePolicy@od.nih.gov

Director Jorgenson,

The Wisconsin Alumni Research Foundation (WARF) values the opportunity to submit comments to the National Institutes of Health (NIH) regarding the agency's approach to biomedical innovation and access to NIH-funded discoveries as discussed in the recent workshop entitled, "Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer."

As the technology transfer office for the University of Wisconsin-Madison (UW-Madison), WARF's mission is to enable university research to solve the world's problems. For nearly a century, we have helped successfully develop health care innovations including vitamin D fortification; the revolutionary blood thinner warfarin; a life-changing organ transplant solution; multiple stem cell technologies; and treatments for anemia, cancer, and liver and kidney diseases. Our active intellectual property portfolio of 2,230 innovations includes more than 1,300 in the biological and pharmaceutical fields, close to 500 in agriculture and food, and more than 500 related to medical devices. Funding from NIH supported the basic research behind many of these technologies. We strongly support policies that facilitate the translation of federally funded research into accessible medical treatments and devices for the benefit of patients, health care professionals, and the public at large.

As the oldest university-based technology transfer office, WARF has had the opportunity to partner with NIH through multiple generations of tech transfer innovation and success. In addition to being an essential funding agency for UW-Madison research, NIH has been a strong partner in innovation and a leader in effective policymaking. An NIH initiative in the late 1960s and 1970s, implemented in partnership with WARF, led to the creation of a clear, balanced, and widely successful patenting framework, which Congress later passed into federal law as the Bayh-Dole Act of 1980.

For more than 40 years, WARF has been a champion of the Bayh-Dole framework because we have seen it serve the national interest while also empowering offices like ours to fulfill our charitable mission. We have been gratified to see NIH demonstrate a steadfast commitment to upholding and defending Bayh-Dole. Today, we encourage the agency, and all federal agencies, to extend and reinforce that commitment.

Bayh-Dole serves the national interest by providing the clear intent of Congress (to use the patent system to promote the utilization of inventions) and consistent expectations for government contractors (e.g., take steps to achieve practical application within a reasonable time). It empowers universities and research institutions to achieve their missions by delegating patent rights and trusts the expertise of tech transfer offices distributed throughout the nation. This arrangement furnishes the crucial incentives that drive the private sector to bring inventions to market and gives institutions like WARF the flexibility to pursue exclusive licensing agreements when necessary to achieve the best possible outcome for technologies.

The Bayh-Dole Act's emphasis on patent rights has been pivotal in fostering private R&D collaborations with academic institutions and fueling biomedical advancements. The incentive framework established by Bayh-Dole has been instrumental in attracting the private capital necessary to shoulder the risks of taking the basic research discoveries funded by federal agencies and commercializing them into technologies that benefit the public.

For all these reasons, Bayh-Dole is not simply a law (although the law itself is essential). It has become the signifier for an industry of institutions and a community of professionals across the public, private, and nonprofit sectors who have executed thousands of agreements and built decades of enduring partnerships. To understand why NIH has been central to sustaining the public-private industry and community, it helps to remember several crucial moments in the history of tech transfer.

In the late 1960s, WARF Patent Counsel Howard Bremer collaborated with NIH Counsel Norm Latker and UW-Madison Vice President Bill Young to craft the first Institutional Patent Agreement (IPA) with NIH. Over the course of the following decade, the successful IPA program demonstrated that government officials and university administrators could work together to bring federally funded technologies to market. The IPA concept provided the core components of what became Bayh-Dole. In the process, a patchwork system of laws that fostered micromanagement and suspicion among agencies and universities was replaced by a system of cooperation and productivity.

Since that early success, a number of special interest groups have attempted to undermine the Bayh-Dole framework, specifically by distorting its march-in provisions into a lever for stipulating product prices. NIH leaders who received march-in petitions for price controls, across multiple administrations, have correctly rejected them as an invalid use of the law. The agency deserves credit for its commitment to the rule of law in the face of political pressure. Upholding the integrity of Bayh-Dole remains essential to fortifying the technology transfer system that has made America the global leader in biomedical advances.

As a counterexample, on one occasion in the 1990s, NIH introduced reasonable pricing provisions into its Cooperative R&D Agreements (CRADAs) and the impact on innovation was disastrous: The number of new treatments stemming from NIH licenses declined dramatically. By undermining the university-industry partnerships needed to transform discoveries into consumer goods, these well-intentioned pricing policies actually reduced the development of new therapies.

Fortunately, the agency changed course. Former NIH Director Harold Varmus put it best when he announced the end of the CRADA pricing provisions in 1995: "The clause attempts to address the rare breakthrough product at the expense of a more open research environment and more vigorous scientific collaborations. One

has to have a product to price before one can worry about how to price it, and this clause is a restraint on the new product development that the public identified as an important return on their research investment."

In recent years, NIH has once again faced pressure to impose reasonable or reference pricing clauses on NIH grants, licenses, and CRADAs. We were glad to see that NIH officials once again rejected the idea. As history shows, inserting price controls into agreements with private sector partners creates uncertainty around the ability to earn a return on the commercialization of early-stage discoveries. This added risk discourages companies from licensing federally funded inventions and investing the vast sums of money required to bring them to the marketplace. And without industry taking on the costly and uncertain work of commercialization, many promising technologies would languish as basic research, failing to realize their potential as new therapies benefiting the public.

In the interest of providing full context and explanation for our positions, we are attaching a recent letter WARF submitted to the U.S. Senate Committee on Health, Education, Labor and Pensions during their recent consideration of staff proposals related to biomedical innovation as part of the reauthorization of the Pandemic and All-Hazards Preparedness Act (PAHPA).

The NIH has long been a strong and consistent partner in WARF's work, yielding life-saving medical breakthroughs and, just as important, effective policies that enable generations of future discoveries. We are grateful for your dedication to the public health mission and appreciate your support of Bayh-Dole and longstanding efforts to ensure that it continues to do great work for U.S. research and innovation.

Sincerely,

Erik Iverson
Chief Executive Officer
Wisconsin Alumni Research Foundation

Michael Falk
Chief IP and Licensing Officer
Wisconsin Alumni Research Foundation

WARF
Wisconsin Alumni Research Foundation

P: 608-960-9850

614 Walnut Street, 13th Floor
Madison, WI 53726
warf.org

The Honorable Bernie Sanders
Chair
Committee on Health, Education,
Labor and Pensions
United States Senate
Washington, D.C. 20510

The Honorable Dr. Bill Cassidy
Ranking Member
Committee on Health, Education,
Labor and Pensions
United States Senate
Washington, D.C. 20510

The Honorable Tammy Baldwin
Committee on Health, Education,
Labor and Pensions
United States Senate
Washington, D.C. 20510

The Honorable Bob Casey
Committee on Health, Education,
Labor and Pensions
United States Senate
Washington, D.C. 20510

The Honorable Mitt Romney
Committee on Health, Education,
Labor and Pensions
United States Senate
Washington, D.C. 20510

July 10, 2023

Via email: PAHPA2023Comments@help.senate.gov

Dear Chair Sanders, Ranking Member Cassidy, Senator Baldwin, Senator Casey, and Senator Romney,

The Wisconsin Alumni Research Foundation ("WARF") greatly appreciates the opportunity to provide feedback on the bipartisan discussion draft to reauthorize the Pandemic and All-Hazards Preparedness Act ("PAHPA").

We write to **oppose the Chair's staff proposal (Sections 601 and 602)** to require that all Biomedical Advanced Research and Development Authority ("BARDA") and Centers for Disease Control ("CDC")-supported products be sold to the Federal Government or in the U.S. commercial market at the lowest price among G7 countries and at a reasonable price.

We write to **support the Ranking Member's staff proposal (Section 611)** to incentivize the development of more medical countermeasures ("MCMs") by extending the Priority Review Voucher program through the duration of PAHPA and (1) providing a new, non-transferrable priority review voucher to companies that develop new MCMs on top of the transferrable voucher they currently receive; and (2) including threats to the Armed Forces.

As the technology transfer office for the University of Wisconsin-Madison ("UW-Madison"), WARF's mission is to enable UW-Madison research to solve the world's problems. For close to a century, WARF has helped successfully develop health care innovations including vitamin D fortification; the revolutionary blood-thinner warfarin; an organ transplant solution; multiple stem cell technologies; and treatments for anemia, cancer, and liver and kidney diseases. We are therefore very much in favor of policies that improve the development of new public health innovations as well as policies that improve public access to medicines, therapeutics, and medical devices.

The proposals from the Chair and Ranking Member offer a study in contrasts of how to achieve the dual goals of innovation and access. In WARF's long experience, policies like the Priority Review Voucher have proven successful by incentivizing industry investment in technology development and encouraging early-stage collaborations among universities, federal agencies, and private industry.

By contrast, price restrictions and price controls have proven to have a negative effect on innovation and access by disincentivizing additional investments, creating uncertainty throughout the development process, and involving government regulation at the consumer pricing stage of the process after investment and development have already taken place.

For a specific historical example of how pricing clauses impede innovation, we refer committee staff to a letter sent to President Biden by WARF's friends at the Bayh-Dole Coalition and co-signed by AUTM, our industry's professional association. That letter explains the disastrous results when the National Institutes of Health ("NIH") introduced reasonable pricing language into Cooperative R&D Agreements in the 1990s. Chair Sanders's proposal would be broader than what the NIH implemented, and it would assuredly have a broader and more severe impact on federally funded innovation.

The following points further explain our positions on both pricing and voucher proposals.

Pricing Clauses:

1. *Disincentivizing investment and collaboration on new technologies*
   Universities rely heavily on federal funding to conduct basic research and create new knowledge for public benefit. Indeed, the federal government fills a crucial role in funding basic research. However, funding for basic research does not cover the considerable cost of developing that research into consumer products. Universities lack the capacity for commercial production, not least because doing so falls outside the scope of their mission as institutions of higher education.

   University-industry partnerships are therefore essential for realizing the public benefits of federally funded research. Organizations like WARF were created for that purpose – to seek out industry partners. We know from hard-earned experience that, even in the best of circumstances, industry partners are often reluctant to take on the considerable and unpredictable risks of developing innovative technologies. By their very nature, these products are untested in the market because they are new and novel. Reasonable pricing clauses increase the risk and uncertainty further by placing limits on the eventual earning potential of federally funded inventions, even before investors have determined how much time and money will be required to bring the drug to market. In these situations, private investors and commercial manufacturers will refuse to license federally funded inventions, and treatments based on university research will not be accessible because they will not be developed.

2. *Hindering regional economic development*
   Bringing new innovations to consumers is not the only benefit for developing federally funded inventions at universities. The partnerships that WARF builds with industry attract investment to Wisconsin, which leads to jobs and economic growth in local communities. For that reason, WARF has been greatly encouraged by the place-based innovation initiatives enacted by the Inflation Reduction Act and the CHIPS & Science Act, and currently being implemented by the National Science Foundation ("NSF") and the Economic Development Administration ("EDA"). All of these programs seek to build up regional innovation ecosystems by building public-private partnerships and attracting private investment.

   Reasonable pricing clauses for federally funded research run counter to these economic development programs. Rather than erecting sound and consistent public policy, these clauses will pit government priorities against each other. Grant recipients of NSF and EDA

funds will be asked to build private partnerships for economic development, only to have that development undermined should any of their individual technologies be funded even in part by BARDA or CDC funds.

Priority Review Vouchers:

3. *Incentivizing investment and collaboration (at no additional cost to the federal government)*
   The voucher program invites industry collaboration by reducing the Food & Drug Administration ("FDA") review process by up to 4 months. A shortened process brings the resulting product to the public faster, provides the manufacturer an additional four months of sales, and often leads to wider adoption by the public due to the product appearing on the market earlier.

   But the voucher is most often used as a financial asset, which may be its greatest contribution to the development process. Knowing that a voucher can be sold gives manufacturers confidence that they will get a return on their investment in developing a product and have a source of funds for expenses such as clinical trials. The additional non-transferable voucher, proposed by the Ranking Member's staff, would provide an additional incentive, especially if a company could use it for any product in their pipeline.

   For all these reasons, the voucher program can be a vehicle for the government to not only mitigate but reduce the risks inherent to the development of technologies that meet particularly urgent health care needs or address undertreated disorders. Because of their ongoing benefits, we recommend that the sunset provisions be eliminated for all priority review voucher programs.

1. *Encouraging regional economic development (at no additional cost to the federal government)*
   While WARF has yet to pursue the MCM priority review vouchers covered by this proposal, we have direct experience with vouchers for rare pediatric diseases and have begun exploring vouchers for tropical diseases. These programs operate in the same way as MCM vouchers, only to treat different diseases.

   Specifically, UW-Madison researchers have developed a therapeutic that has the potential to restore vision in children afflicted with a form of Leber Congenital Amaurosis (LCA16), a rare genetic eye disorder that causes complete blindness before the age of ten. WARF is currently developing the LCA16 treatment together with Hubble Therapeutics, a startup company, and pursuing clinical trials at UW-Madison Hospital and Clinics. The research, development, and investment in this technology will all take place in Wisconsin.

We can state unequivocally that the founding of Hubble Therapeutics, and the ongoing development of their treatment of LCA16, could not have been possible without a priority review voucher. The economics and timeline would have simply been unsustainable.

WARF encourages your committee to adopt the language extending the MCM Priority Review Voucher Program. Should one of our technologies be applicable for the program, we would be glad to work with the FDA for a voucher that would increase the likelihood of bringing our technology to the public. For similar reasons, we ask that you reject the pricing clause language.

Sincerely,

Erik Iverson
Chief Executive Officer
Wisconsin Alumni Research Foundation

Michael Falk
Chief IP and Licensing Officer
Wisconsin Alumni Research Foundation

Submission Date: 8/18/2023

Name: Tom Giovanetti

Name of Organization: Institute for Policy Innovation

Comment:

_____

Tom Giovanetti
President | Institute for Policy Innovation (IPI)

Additional Comment (attachment):

August 18, 2023

Dr. Lyric Jorgenson
Acting Associate Director for Science Policy
National Institutes of Health
Office of Science Policy
6705 Rockledge Dr. #750
Bethesda, MD 20817

Dear Director Jorgenson:

I appreciate the opportunity to comment on the importance of private sector investment in prescription drug research and development and its relationship to NIH funding.

The Institute for Policy Innovation is a non-profit, non-partisan public policy "think tank" based in Irving, Texas, and founded in 1987 to research, develop and promote innovative and non-partisan solutions to today's public policy problems. IPI is supported wholly by contributions from individuals, businesses and non-profit foundations.

By way of background, I am a resident scholar with IPI. I am also a past president of the Health Economics Roundtable for the National Association for Business Economics, the largest trade association of business economists. And I currently serve as Chair of the Texas Advisory Committee to the U.S. Commission on Civil Rights.

Comparing Federal Funding for Research and Development: The Pharmaceutical Industry vs. the Clean Energy Industry

There is a small but vocal and influential group of people who have increasingly pushed the narrative that most research and development funding for prescription drugs in the United States comes from the government. While the federal government does provide some funding, primarily for initial drug research—as well as medical devices and other health care-related research—the private sector pharmaceutical companies provide the lion's share of R&D funding.

At a House Committee on Oversight and Reform meeting in January 2019, U.S. Representative Alexandria Ocasio-Cortez (D-NY) claimed, "the public is acting as early investor, putting tons of money into the development of drugs that then become privatized, and then they [the public] receive no return on the investment that they have made." Similar assertions have been made by other progressive elected officials and think tanks.

It's a strange argument given that this very week President Joe Biden toured the country boasting the one-year anniversary of the Inflation Reduction Act (IRA), which is pouring hundreds of billions of taxpayer dollars into funding basic research and development for various types of clean energy projects and products.

For example, Reuters reports, "While the biggest impacts will begin in 2024 and 2025, there have been more than 270 new clean energy projects announced since its [the IRA] passage, with

investments totaling some $132 billion, according to a Bank of America analyst report." And that's just the beginning.

Goldman Sachs recently released a report claiming the real cost of the IRA over 10 years will be $1.2 trillion, more than three times the initial estimate of $391 billion. According to Goldman, its estimate includes "electric vehicles (difference: $379 billion), green energy manufacturing ($156 billion), renewable electricity production ($82 billion), energy efficiency ($42 billion), hydrogen ($36 billion), biofuels ($34 billion) and carbon capture ($31 billion)."

We should also mention $39 billion in taxpayer-provided funding for the semiconductor industry—which has many very profitable companies—provided in the CHIPS and Science Act, which passed last summer.

The president and other progressives refer to all of these taxpayer-provided subsidies as "investments."

Countless for-profit companies, with many wealthy investors (and political donors), will benefit from these taxpayer-provided subsidies. Some of those companies may survive and reap hefty profits. Most will likely end up filing for bankruptcy, as the electric bus company Protera has recently done. And yet we never hear progressives complain that taxpayers may "receive no return on the investment that they have made" in clean energy.

While the government will use the subsidies to impose regulatory strings on the receiving companies, there is no indication yet that the government intends to impose price controls on the clean energy companies, as the White House proposes to do with prescription drugs.

In fact, the clean energy industry, with all of its branches, could not survive without massive government subsidies. The U.S. pharmaceutical industry has thrived for decades almost entirely on private sector funding. And the health of patients around the world has benefited from those investments.

How much has the pharmaceutical industry invested? About $1.1 trillion since 2000. But the funding pace is accelerating. While members of the Pharmaceutical Research and Manufacturers Association (PhRMA) invested $50.7 billion in R&D in 2010, that annual investment doubled to $102.3 billion by 2021.

Determining how much the National Institutes of Health (NIH) provides in basic research funding is complicated because money is fungible and can be used for a number of purposes that may or may not directly result in the discovery of a new molecule.

A 2019 study titled "Public sector financial support for late stage discovery of new drugs in the United States: cohort study" found, "Over the 10 year study period [2008-2017], the FDA approved 248 drugs containing one or more new molecular entities. Of these drugs, 48 (19%) had origins in publicly supported research and development and 14 (6%) originated in companies spun off from a publicly supported research program."

A 2020 research paper titled "Public research funding and pharmaceutical prices: do Americans pay twice for drugs?" reviewed several studies, concluding:

> "Detailed case studies reveal that public support has played at least some role in virtually all of the 26 most clinically and commercially significant drugs and drug classes approved over the past several decades. … But in a large majority of cases, the public sector's contribution to new drugs has been in the form of early scientific findings, unrelated to current or potential applications. The public sector supported key basic research for 19 of the 26 'transformative' drugs and drug classes cited above, contributed to the actual discovery of a new therapy in just 11, and could claim sole discovery credit in only four cases."

So, yes, NIH funding plays a role in basic research, but it's the innovator pharmaceutical companies that take a new molecule, or sometimes just a concept, and turn that into a product, guide it through the often very expensive clinical trials and time-consuming FDA approval process, manufacture the new drug, package, distribute and market it to health care providers and patients.

Of course, there are a number of factors that determine whether those drugs will actually make it to market. The Congressional Budget Office says, "Only about 12 percent of drugs entering clinical trials are ultimately approved for introduction by the FDA."

No one reimburses the drug companies for the 88 percent of drugs entering clinical trials that don't make it to market. And of those that do make it to market, only a handful are very profitable. But it is those very profitable drugs that cross-subsidize the ones that don't make it to market. Yet it's those profitable drugs that the government is targeting for price controls.

One more point. For the past two decades, the innovator drug companies have increasingly begun to target diseases that affect a relatively small percentage of the population—say, perhaps only 25,000 to 100,000 people—often referred to as "orphan drugs." In those cases, the companies do not have the ability to spread the cost of creating those drugs over millions of patients. The smaller the patient population, the higher the cost, relatively speaking.

In conclusion, it is true the government funds some initial work in identifying new molecules and therapies. But that funding pales in comparison to the cost, time and effort it takes to bring a new drug to market. Most investigational drugs won't make it. When that happens, it is the pharmaceutical industry and its investors who lose money, not taxpayers.

By contrast, the federal government is pouring hundreds of billions of taxpayer dollars into multiple clean energy projects. Most of those clean energy companies will fail. If a drug company were to fail, investors would lose their capital. When government-backed clean energy companies fail, taxpayer money is lost. If Rep. Ocasio-Cortez really wants to discover where "the public is acting as early investor," but then "receive no return on the investment that they have made," she should turn to the clean energy industry rather than the pharmaceutical industry.

Sincerely,

Merrill Matthews, Ph.D.
Resident Scholar
Institute for Policy Innovation

Submission Date: 8/18/2023

Name: Adam Mossoff

Name of Organization: Hudson Institute

Comment:

Dear Director Jorgenson,

Please find attached my second comment for consideration by the NIH in its report from the Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer.

If you have any questions, please feel free to contact me via email or by telephone at (703) 993-9577.

Best regards,

Adam Mossoff

Adam Mossoff
Senior Fellow
Chair, Forum for Intellectual Property
Hudson Institute

Additional Comment (attachment):

Hudson Institute
Forum for Intellectual Property

`

August 18, 2023

Via Email Submission

Lyric Jorgenson, Ph.D.
Office of Science Policy
6705 Rockledge Drive, Suite 630
Bethesda, MD 20892

Re: Comment for Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer Report

Dear Director Jorgenson,

I respectfully submit this written comment to offer additional data and economic evidence to the National Institutes of Health (NIH) for consideration in its report from the July 31 workshop, *Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer*. I am submitting this comment in my capacity as a Senior Fellow and Chair of the Forum for Intellectual Property at the Hudson Institute.

In my previous submission, I explained why the arguments to use the Bayh-Dole Act or 28 U.S.C. § 1498 to control the price of prescription drugs contradict the plain text and function of these two statutes. Aside from these legal arguments, the NIH should continue to engage in evidence-based policymaking in considering whether to revise its licensing and tech transfer policies. Although evidence-based policymaking is a general principle of good government, it is especially important for the NIH and the licensing policies that it adopts given the direct impact these policies have on biopharmaceutical innovation in the healthcare sector of the U.S. innovation economy.

Given the importance of evidence-based policymaking, the NIH should keep in mind that reliable and effective patent rights have been a key driver of the U.S. innovation economy for over 200 years, as economists, historians, and legal scholars have repeatedly demonstrated.[1] The patent

[1] *See, e.g.,* JONATHAN M. BARNETT, INNOVATORS, FIRMS, AND MARKETS: THE ORGANIZATIONAL LOGIC OF INTELLECTUAL PROPERTY (2021); DANIEL SPULBER, THE CASE FOR PATENTS (2021); B. ZORINA KHAN, INVENTING IDEAS: PATENTS, PRIZES, AND THE KNOWLEDGE ECONOMY (2020); Stephen Haber, *Innovation, Not Manna from Heaven* (Hoover Institution, Sep. 15, 2020), https://www.hoover.org/research/innovation-notmanna-heaven;; B. Zorina Khan, *Trolls and Other Patent Inventions: Economic History and the Patent Controversy in the Twenty-First*

system was central to the successes of the Industrial Revolution in the nineteenth century, the pharmaceutical and computer revolutions in the twentieth century, and the biotech and mobile telecommunications revolutions in the twenty-first century.[2] Patent systems that secure reliable and effective property rights to inventors consistently and strongly correlate with successful innovation economies.[3]

Reliable and effective patent rights, including the licensing of patented technologies, are the basis of U.S. global leadership in innovation and economic growth. Even when technological revolutions began in other countries, these revolutions have been completed in the U.S. The two most prominent examples, of course, are the Industrial Revolution, which originated in England in the eighteenth century,[4] and the pharmaceutical revolution, which originated in Germany in the late nineteenth century.[5] Both revolutions shifted to the U.S. in the nineteenth and twentieth centuries, respectively.[6] By the twentieth century, technological revolutions began in the U.S. The computer and the biotech revolutions in the twentieth century began—and continue—in the U.S.[7]

Dr. Zorina Khan, an award-winning economist, has demonstrated that reliable and effective property rights in innovation—patents—were a key factor in thriving markets for technology in the United States in the nineteenth century.[8] Other economists have also identified features of these robust nineteenth-century innovation markets—such as an increase in "venture capital" investment in patent owners, the rise of a secondary market in the sale of patents as assets, and the embrace of specialization via patent licensing—as robust indicators of value-maximizing economic activity

---

Century, 21 GEO. MASON L. REV. 825, 837-39 (2014); Naomi R. Lamoreaux, Kenneth L. Sokoloff & Dhanoos Sutthiphisal, *Patent Alchemy: The Market for Technology in US History*, BUS. HIST. REV. (Spring 2013).

[2] *See* Kevin Madigan & Adam Mossoff, *Turning Gold to Lead: How Patent Eligibility Doctrine is Undermining U.S. Leadership in Innovation*, 24 GEO. MASON L. REV. 939, 942-949 (2017) (describing how the U.S. patent system facilitated U.S. leadership in the biotech revolution).

[3] *See, e.g.*, Stephen Haber, *Patents and the Wealth of Nations*, 23 GEO. MASON L. REV. 811 (2016); Jonathan M. Barnett, *Patent Tigers: The New Geography of Global Innovation*, 2 CRITERION J. INNOVATION 429 (2017).

[4] *See* WILLIAM ROSEN, THE MOST POWERFUL IDEA IN THE WORLD: A STORY OF STEAM, INDUSTRY, AND INVENTION (2010).

[5] *See* THOMAS HAGER, THE DEMON UNDER THE MICROSCOPE: FROM BATTLEFIELD HOSPITALS TO NAZI LABS, ONE DOCTOR'S HEROIC SEARCH FOR THE WORLD'S FIRST MIRACLE DRUG (2006).

[6] *See* KHAN, *supra* note 1 (explaining why the U.S. patent system was more successful than the English patent system in promoting innovation and economic growth).

[7] *See* Madigan & Mossoff, *supra* note 2.

[8] *See* B. ZORINA KHAN, THE DEMOCRATIZATION OF INVENTION: PATENTS AND COPYRIGHTS IN AMERICAN ECONOMIC DEVELOPMENT, 1790–1920, at 9-10 (2005) ("[P]atents and . . . intellectual property rights facilitated market exchange, a process that assigned value, helped to mobilize capital, and improved the allocation of resources. . . . Extensive markets in patent rights allowed inventors to extract returns from their activities through licensing and assigning or selling their rights.").

made possible by reliable and effective patents.[9] This remains true today: a twenty-first-century startup with a patent *more than doubles* its chances of securing venture capital financing compared to a startup without a patent, and this patent-based startup has statistically-significant increased chances of success in the marketplace as well.[10]

The biopharmaceutical sector has been an exemplar of the economic and historical successes of reliable and effective patents. The U.S. is a global leader in biomedical innovation. More than 50% of new drugs are invented in the U.S.[11] More than 25% of active pharmaceutical ingredients are manufactured in the U.S.[12] Annual private investment in research and development (R&D) of new pharmaceutical and biotech innovations is approximately $129 billion (as of 2018).[13] This is almost triple the total amount of total public funding of $43 billion of R&D in healthcare innovations (as of 2018).[14] Medical diagnoses that once were either death sentences or led to a greatly diminished quality of life—cancer, hepatitis, and diabetes—are now treatable and manageable medical conditions that make possible a relatively normal lifespan. As the legal platform that spurred these successes by incentivizing investments and licensing activities, the U.S. patent system has been recognized as the "gold standard" innovation engine.[15]

This is the evidence that should inform the NIH's deliberations as it considers policy arguments from the July 31 workshop that would undermine the economic and life-enhancing function of the patent system. The burden is on anyone proposing new regulatory restrictions, additional licensing costs, and additional legal uncertainties to provide reliable and robust data that this is evidence-based policymaking. Scientists, entrepreneurs, and venture capital investors will not discover and develop breakthrough technologies in therapeutics, diagnostics, or vaccines if they are not secure in the same promise of reliable and effective patents made available to innovators since the early twentieth century that were the progenitor of the biopharmaceutical and biotech revolutions.

---

[9] *See, e.g.*, Naomi R. Lamoreaux, Kenneth L. Sokoloff & Dhanoos Sutthiphisal, *Patent Alchemy: The Market for Technology in US History*, 87 BUS. HIST. REV. 3, 4–5 (2013).

[10] *See* Joan Farre-Mensa, et al., *What Is a Patent Worth? Evidence from the U.S. Patent "Lottery,"* 75 J. FINANCE 639 (2019), https://doi.org/10.1111/jofi.12867.

[11] *See* Yali Friedman, *Where Are Drugs Invented, and Why Does It Matter?*, 16 ACS MEDICINAL CHEMISTRY LETTERS 589, 590 (May 2017), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5467189/# ("North America (largely the United States) accounts for more than half of drug patent inventorship . . . .").

[12] *See* Janet Woodcock, *Safeguarding Pharmaceutical Supply Chains in a Global Economy* (Oct. 30, 2019), https://www.fda.gov/news-events/congressional-testimony/safeguarding-pharmaceutical-supply-chains-global-economy-10302019.

[13] *See U.S. Investments in Medical and Health Research and Development 2013–2018*, at 7 (Research America, 2019), https://www.researchamerica.org/wp-content/uploads/2022/09/InvestmentReport2019_Fnl.pdf (estimating total private investment in biopharmaceutical R&D in 2018 is estimated to be $129 billion). For each drug approved by the FDA for use by patients, there is on average $2.6 billion in R&D expenditures incurred over 10–15 years. *See* Joseph A. DiMasi, Henry G. Grabowski, & Ronald W. Hansen, *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 47 J. HEALTH ECON. 20 (2016).

[14] *See U.S. Investments in Medical and Health Research and Development 2013–2018, supra note 14, at 8.*

[15] *See* Madigan & Mossoff, *supra* note 2, at 940-41.

As the NIH considers any new policies in patent licensing and tech transfer, it should remain committed to the fundamental principle of evidence-based policymaking. The Honorable David Kappos, former Director of the U.S. Patent and Trademark Office (USPTO) in the Obama Administration, testified before Congress in 2013 that "we are not tinkering with just any system here; we are reworking the greatest innovation engine the world has ever known . . . If there were ever a case where caution is called for, this is it."[16] Former USPTO Director Kappos cautionary remarks to Congress about changing the patent system reflect the same maxim in healthcare, "first, do no harm." The NIH should remain committed to this maxim of good government and healthcare. Its licensing and tech transfer policies should always be derived from the evidence of the key role of reliable and effective patent rights as a driver of biopharmaceutical innovation.

If you have any questions or need further information, please do not hesitate to reach out via email (amossoff@hudson.org) or by telephone (703-993-9577).

Sincerely,

Adam Mossoff

[16] *Innovation Act of 2013: Hearing on H.R. 3309 Before the Comm. on the Judiciary*, 113th Cong. (Oct. 29, 2013) (statement of David J. Kappos, Partner, Cravath, Swaine & Moore LLP).

Submission Date: 8/18/2023

Name: Stephen Ezell

Name of Organization: The Information Technology & Innovation Foundation

Comment:

To NIH Colleagues:

The Information Technology and Innovation Foundation herewith submits these comments with regard to the NIH "Workshop on Transforming Discoveries Into Products: Maximizing NIH's Levers to Catalyze Technology Transfer."

Kind regards,

Stephen Ezell

Stephen Ezell
Vice President, Global Innovation Policy | The Information Technology & Innovation Foundation

Additional Comment (attachment):

ITIF | INFORMATION TECHNOLOGY & INNOVATION FOUNDATION

Comments of:

Stephen Ezell
Vice President, Global Innovation Policy
Information Technology and Innovation Foundation

To the:

United States National Institutes of Health

Request for Public Comment on:

"Workshop on Transforming Discoveries Into Products: Maximizing NIH's Levers to Catalyze Technology Transfer"

August 18, 2023

INTRODUCTION

This submission represents the views of the Information Technology and Innovation Foundation (ITIF), a non-profit, non-partisan think tank focused on the intersection of technological innovation and public policy. ITIF offers them in response to a "Workshop on Transforming Discoveries Into Products: Maximizing NIH's Levers to Catalyze Technology Transfer" held on July 21, 2023, to which the National Institutes of Health (NIH) subsequently solicited public comment.[1]

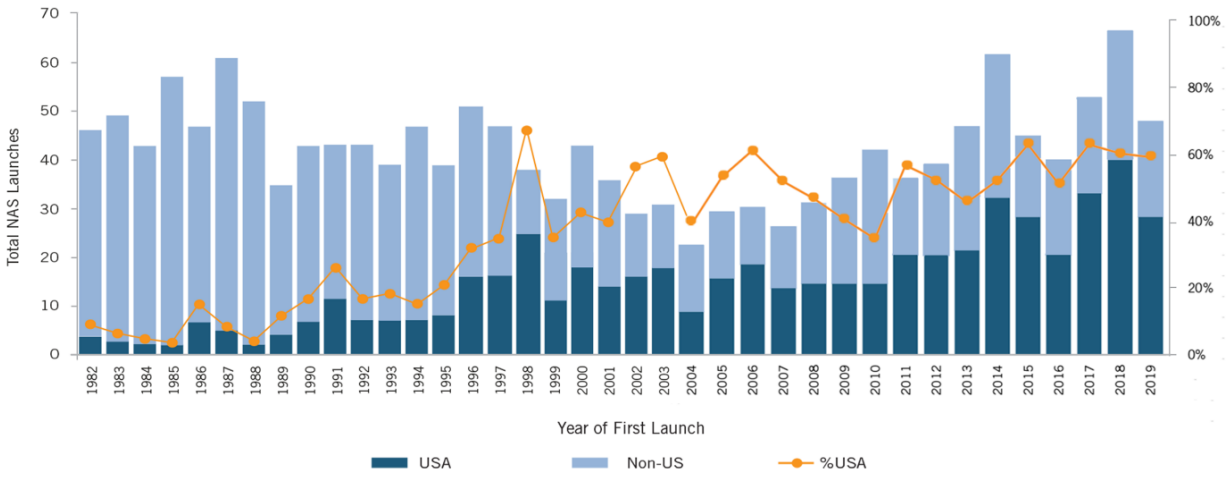
Broadly, ITIF contends that the technology transfer regime the United States has implemented over the past four decades, largely as enabled through the Bayh-Dole Act, has been tremendously effective in stimulating innovation, especially in the life-sciences. While all such processes should be continuously streamlined or tweaked where improvement is possible, the current system is not nearly broadly in need of serious modification or reform, which would likely be counterproductive to a largely well-functioning technology transfer dynamic that effectively transmits technologies to private-sector companies, especially entrepreneurial small businesses, which are willing to assume the risk and expense of turning NIH-supported inventions into useful therapies. This matters especially in light of new ITIF research finding that America is home to 85 percent of the world's small, research-intensive biopharma firms.[2] Such companies account for nearly two-thirds (66 percent) of U.S. biopharmaceutical firms, have an average R&D intensity of 62 percent, and account for more than seven in ten drug candidates currently in Phase III clinical trials.[3]

THE HISTORY OF U.S. LIFE SCIENCES COMPETITIVENESS

The United States has come to be the world's leader in life-sciences innovation, as it is across a number of advanced-technology industries. Indeed, in every five-year period since 1997, the United States has produced more new chemical or biological entities than any other country or region in the world. From 1997 to 2016, U.S.-headquartered enterprises accounted for 42 percent of new chemical or biological entities introduced in the world, far outpacing relative contributions from European Union (EU) member countries, Japan, China, or other nations.[4] Moreover, the United States has become the world's largest funder of biomedical research and development (R&D) investment in recent decades, with one (2008) study estimating that the U.S. share of global biomedical R&D funding reached as high as 80 percent over the preceding two decades.[5] Put simply, since the start of this millenium, U.S.-headquartered biopharmaceutical enterprises have accounted for almost half of the world's new drugs.

But U.S. leadership in life-sciences innovation wasn't always a given; in fact, for most of the post-World War II-era, the United States was a global "also-ran" in life-sciences innovation. Between 1960 and 1965, European companies invented 65 percent of the world's new drugs, and in the latter half of the 1970s, European-headquartered enterprises introduced more than twice as many new drugs to the world as did U.S.-headquartered enterprises (149 to 66).[6] In fact, throughout the 1980s, fewer than 10 percent of new drugs were introduced first in the United States.[7] (See Figure 1.) America wasn't inventing new-to-the world drugs, let alone getting them to its citizens first.

Figure 1: U.S. share of new active substances launched on the world market, 1982–2019[8]



That the United States subsequently flipped the script and has become the world's life-sciences innovation leader has not been accidental or incidental. Rather, as ITIF argues in "Why Life-sciences Innovation Is Politically Purple," U.S. life-sciences leadership today is rather the result of a series of conscientious and intentional public policy decisions designed to make America the world's preeminent location for life-sciences research, innovation, and product commercialization.[9] The United States did so with robust and complementary public and private investment in biomedical R&D; supportive incentives, including tax policies, to encourage biomedical investment; robust intellectual property (IP) rights; an effective regulatory and drug-approval system; a drug-pricing system that allows innovators to earn sufficient revenues to enable continued investment into future generations of biomedical innovation; and, lastly, the world's best system to support technology transfer and commercialization, especially with regard to translating technologies stemming from federally funded R&D to the private sector.

World-leading Public and Private R&D Investment

America's world-leading life-sciences innovation policy environment starts with world-leading levels of public and private investment in R&D.[10] For instance, in fiscal year (FY) 2022, America's National Institutes of Health invested the majority of its $45 billion of appropriations into research that seeks to enhance life while reducing illness and disability.[11] Meanwhile, America's life-sciences industry is the single most R&D-intensive industry in the world, in 2019 investing nearly one-quarter of its revenues in back into R&D, and in 2020 investing $122 billion in R&D.[12] In total, companies in global health industries invested about €235 billion ($255 billion) in R&D in 2021, accounting for 21.5 percent of total business R&D expenditure worldwide.[13]

But it's not just that America's public and private sectors lead the word in investing in biomedical research, it's that these public and private R&D investments and activities are highly complementary—and indispensable—to America's successful life-sciences innovation system. Historically, public-sector researchers have performed the upstream, earlier-stage research elucidating the underlying mechanisms of disease and identifying promising points of intervention, whereas corporate researchers have performed the downstream, applied research resulting in the discovery of drugs for the treatment of diseases and have carried out the development activities necessary to being them to market.[14] Federally funded basic life-sciences research tends to be concentrated in the basic science of disease biology, biochemistry, and disease processes, with a major goal of the research being the identification of biomarkers and biologic targets that new drugs could treat.[15] While the private sector does invest in basic scientific research, including at U.S. universities, the

preponderance of its activity is applied R&D focused on the discovery, synthesis, testing, and manufacturing of candidate compounds intended to exploit biologic targets, for the purpose of curing medical conditions.[16]

A number of studies have elucidated this dynamic. For instance, a 2000 study by the U.S. Senate Joint Economic Committee found that, "Federal research and private research in medicine are complementary. As medical knowledge grows, federal research and private research are becoming more intertwined, building the networks of knowledge that are important for generating new discoveries and applications."[17] Similarly, as an Organization for Economic Cooperation and Development (OECD) study asserted, "It is particularly important for government-funded research to continue to provide the early seeds of innovation. The shortening of private-sector product and R&D cycles carries the risk of under-investment in scientific research and long-term technologies with broad applications."[18]

Similarly, a 2017 National Bureau of Economic Research study examined whether there was evidence of NIH investments either "crowding out" or "crowding in" private-sector investment. As the authors wrote, their findings were "consistent with the absence of crowd out" and "suggest that NIH funding spurs private patenting by either increasing total firm R&D expenditure or increasing the efficiency of these expenditures."[19] Additionally, they wrote, "Even if NIH funding crowds out some private investment, it is offset by increases in the number of patents related to NIH funding through indirect citation channels, or by increases in the productivity of private R&D investments."[20]

Concurring findings were reported in a 2012 Milken Institute study, which found that $1 of NIH funding boosted the size of the bioscience industry by $1.70 and that the long-term impact may be as high as $3.20 for every dollar spent.[21] Likewise, a 2013 report by Battelle found that, looking solely at federal support for the Human Genome Project between 1988 and 2012, every dollar of federal funding helped generate an additional $65 dollars in genetics-related private activity.[22] Rutgers University Professor A.A. Toole identified a quantifiable correlation between investment in publicly funded basic research and corporate-funded applied research wherein an increase of 1 percent in the funding of public basic research led to an increase of 1.8 percent in the number of successful applications for new molecular entities (compounds that have not been approved for marketing in the United States) after a lag of about 17 years. Toole concluded that a $1 investment in public-sector basic research yielded $0.43 in annual benefits in the development of new molecular entities in perpetuity—a remarkable return on investment.[23]

In short, as Chakravarthy et al. aptly conclude in a 2016 study, "Industry's contributions to the R&D of innovative drugs go beyond development and marketing and include basic and applied science, discovery technologies, and manufacturing protocols"…"without private investment in the applied sciences there would be no return on public investment in basic science."[24]

Oher Factors Contributing to U.S. Life-sciences Leadership

Other factors have contributed substantially to U.S. life-sciences leadership. For instance, the United States' introduction of the world's first R&D tax credit in 1981 played a catalytic role in spurring greater levels of private-sector R&D. In the life-sciences sector, this was complemented by the 1986 introduction of the orphan drug tax credit, which allowed drug manufacturers to claim a tax credit on research costs for orphan drugs (i.e., drugs for rare diseases affecting 200,000 or fewer U.S. patients). The 1992 introduction of the bipartisan Prescription Drug User Fee Act (PDUFA), which authorized the Food and Drug Administration (FDA) to collect user fees associated with applications from the biopharmaceutical industry for regulatory approval of new human-drug submissions, has played a pivotal role in reducing the time it takes the FDA to make safety and efficacy determinations for new drugs—from the over 30 months it took on average in the mid-1980s to less than 10 months today.[25] The FDA's innovative use of breakthrough designations for novel drugs have also speeded time-to-market for promising therapies. The breakthrough-therapy designation has

helped expedite the development and review of drug and biological products for serious or life-threatening diseases or conditions when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies.

The United States has also benefitted greatly from having a drug-pricing system that permits companies to earn sufficient revenues from one generation of biomedical innovation to reinvest in the next.[26] That matters greatly because, as the OECD has clearly stated, "There exists a high degree of correlation between pharmaceutical sales revenues and R&D expenditures."[27] For instance, a correlation ITIF ran between net sales and R&D expenditures for 478 pharmaceutical companies (using 2021 data) resulted in a very strong coefficient of 0.92.[28]

Indeed, virtually all academic assessments find strong links between life-sciences company profits and R&D investments.[29] For instance, one study found that a real 10 percent decrease in the growth of drug prices would be associated with an approximately 6 percent decrease in pharmaceutical R&D spending as a share of net revenues.[30] Similarly, Lichtenberg found that a 10 percent decrease in cancer drug prices would likely cause a 5 to 6 percent decline in both cancer regimens and research articles.[31] Most recently, 2021 research by Tomas Philipson and Troy Durie at the University of Chicago estimated that a 1 percent reduction in pharmaceutical industry revenue leads on average to a 1.54 percent decrease in R&D investment.[32]

This is why the drug price controls recently introduced in the Inflation Reduction Act (IRA) are likely to be so delterious to U.S. biopharmaceutical innovation. All assessments agree the legislation will reduce life-sciences innovation and the discovery of new drugs; the only question is by how much. The Congressional Budget Office (CBO) estimated in July 2022 that the propsosed prescription drug legislation (that eventually largely became the IRA legislation) would cost the development of just 15 drugs over 30 years.[33]

But other analyses were far less sanguine. For instance, in examining the drug price controls proposed in HR 5376 (the Build Back Better Act), Philipson and Durie found the legislation would reduce revenues by 12 percent through 2039, with the reduced revenues meaning R&D spending would fall by about 18.5 percent, or $663 billion. The authors found that this reduction in R&D activity would lead to135 fewer new drugs, predicating that this drop in new drugs would generate a loss of 331.5 million life years in the United States. Similarly, Vital Transformations has modeled the impacts of the drug pricing provisions of President Biden's 2024 budget proposal, now proposed as legislation by Senator Baldwin (D-MN) as the "Smart Prices Act (SPA)," which would impose government price setting for selected Medicare drugs at only five years after initial FDA approval. Vital Transformations estimates that this expanded government price setting could result in roughly 230 fewer FDA approvals of new medicines over a 10-year period, once the impacts are fully reflected in the pipeline. They further estimate a loss of 146,000 to 223,000 direct biopharmaceutical industry jobs. Moreover, they find that had the drug pricing provisions of the SPA been in place prior to the development of today's top-selling medicines, 82 of the 121 therapies they identified as selected for price setting would likely have not been developed.[34]

And while these were just econometric modeling exercises, the real-world impact of IRA drug price controls are arriving quickly, and rapidly blasting through the 15 drugs CBO estimated would be lost over a 30-year period. One analysis found that in the first four months of 2023, at least 24 companies made announcements to curtail drug development because of the IRA.[35] For instance, in November 2022, Bristol-Myers Squibb announced it would cancel plans for some drug development programs and cancer treatments, citing the effects of the IRA.[36] Eli Lilly informed *Endpoints News* that it would abandon work on a blood-cancer drug in light of the IRA.[37] And Astra Zeneca has said that it, "may defer U.S. cancer drug launches in response to IRA."[38] In light of these announcements, a mere 15 drugs lost over 30 years as a result of the IRA—let alone more-aggressive drug price legislation—is likely to be a woeful undercount. Yet it highlights a broader point:

the system America has put in place over the prior quarter century to support life-science innovation has yielded tremendous results; calls to substantially reform it now—whether through drug price controls or by substantially altering existing, effective technology transfer policies, such as by including reasonable pricing provisions in license agreements—are likely to have deleterious and counterproductive effects.

And that brings the discussion to the final major factor that has allowed the United States to become the world's life-sciences innovation leader: imaginative and effective technology transfer and commercialization policies, particularly as embodied in the Bayh-Dole Act.

INNOVATIVE U.S. TECHNOLOGY TRANSFER AND COMMERCIALIZATION POLICIES

As with life-sciences innovation, the United States was long a laggard in technology transfer and commercialization practices, especially with regard to the licensing of technologies stemming from federally funded R&D. As late as 1978, the federal government had licensed less than 5 percent of the as many as 30,000 patents it owned.[39] Likewise, throughout the 1960s and 1970s, many American universities shied away from direct involvement in the commercialization of research.[40] Indeed, before the passage of Bayh-Dole, only a handful of U.S. universities even had technology transfer or patent offices.[41]

Aware as early as the mid-1960s that the billions of dollars the federal government was investing in R&D was not paying the expected dividends, President Johnson in 1968 asked Elmer Staats, then the comptroller general of the United States, to analyze how many drugs had been developed from NIH-funded research. Johnson was stunned when Staats's investigation revealed that "not a single drug had been developed when patents were taken from universities [by the federal government]."[42] As his report to Congress elaborated:

> At that time we reported that HEW [the Department of Health, Education, and Welfare, predecessor of the Department of Health and Human Services] was taking title for the Government to inventions resulting from research in medicinal chemistry. This was blocking development of these inventions and impeding cooperative efforts between universities and the commercial sector. We found that hundreds of new compounds developed at university laboratories had not been tested and screened by [the] pharmaceutical industry because the manufacturers were unwilling to undertake the expense without some possibility of obtaining exclusive rights to further development of a promising product.[43]

The Congressional response to this conundrum was the Bayh-Dole Act, passed in 1980, which afforded contractors—such as universities, small businesses, and nonprofit research institutions—rights to the intellectual property generated from federal funding. The legislation's impact was immediate, powerful, and long-lasting. It has been widely praised as a significant factor contributing to the United States' "competitive revival" in the 1990s.[44] In 2002, *The Economist* called Bayh-Dole:

> Possibly the most inspired piece of legislation to be enacted in America over the past half-century. Together with amendments in 1984 and augmentation in 1986, this unlocked all the inventions and discoveries that had been made in laboratories throughout the United States with the help of taxpayers' money. More than anything, this single policy measure helped to reverse America's precipitous slide into industrial irrelevance.[45]

Allowing U.S. institutions to earn royalties through the licensing of their research has provided a powerful incentive for universities and other institutions to pursue commercialization opportunities.[46] Indeed, the Bayh-Dole Act almost immediately led to an increase in academic patenting activity. For instance, while only 55 U.S. universities had been granted a patent in 1976, 240 universities had been issued at least one patent by 2006.[47] Similarly, while only 390 patents were awarded to U.S. universities in 1980, by 2009, that number had

increased to 3,088—and by 2015, to 6,680. Another analysis found that in the first two decades of Bayh-Dole (i.e., 1980 to 2002) American universities experienced a tenfold increase in their patents, and created more than 2,200 companies to exploit their technology.[48] In total, over 100,000 U.S. patents have been issued to academic research institutions over the past 25 years.[49] Moreover, academic technology transfer has supported the launch of over 13,000 start-ups since 1996 alone.[50] According to a report prepared for the Association of University Technology Managers (AUTM) and the Biotechnology Industry Organization (BIO), from 1996 to 2015, academic patents and their subsequent licensing to industry—substantially stimulated by the Bayh-Dole Act—bolstered U.S. gross domestic product by up to $591 billion, contributed to $1.3 trillion in gross U.S. industrial output, and supported 4,272,000 person years of employment.[51] Perhaps most importantly for public health, more than 200 drugs and vaccines have been developed through public-private partnerships since the Bayh-Dole Act entered force in 1980.[52]

On average, three new start-up companies and two new products are launched in the United States every day as a result of university inventions brought to market, in part thanks to the Bayh-Dole Act.[53] And as Harvard University's Naomi Hausman has written, "The sort of large scale technology transfer from universities that exists today would have been very difficult and likely impossible to achieve without the strengthened property rights, standardized across granting agencies, that were set into law in 1980."[54]

The Bayh-Dole Act has produced a number of additional benefits. For example, Hausman analyzed the impact of Bayh-Dole in shaping university relations with local economies and found that the increase in university connectedness to industry under the IP regime created by Bayh-Dole produced important local economic benefits. In particular, Hausman found that long-run employment, payroll, payroll per worker, and average establishment size grew differentially more after the 1980 Bayh-Dole Act in industries more closely related to innovations produced by a local university or hospital.[55] There is also evidence that the Bayh-Dole Act contributed to university faculty responding to royalty incentives by producing higher-quality innovations.[56] Evidence further suggests that patenting increased most after Bayh-Dole in lines of business that most value technology transfer via patenting and licensing.[57]

Finally, countries throughout the world—including Brazil, China, Indonesia, Japan, Korea, Malaysia, the Philippines, Singapore, South Africa, and Taiwan—have since followed the United States' lead in establishing policies that grant their universities IP ownership rights.[58] Even Kazakhstan and Zimbabwe are currently looking at implementing Bayh-Dole-like legislation, recognizing its power to help turn their universities into engines of innovation and commercialization. Likewise, the California Senate Office of Research conducted a comprehensive analysis of the Bayh-Dole Act and concluded: "After reviewing the literature and interviewing key experts, we recommend the Legislature consider adopting a statewide IP policy replicating the principles of the Bayh–Dole Act for research granting programs."[59] U.S. states and foreign countries have supported adoption of Bayh-Dole-like policies because they recognize that Bayh-Dole works. Simply put, the Bayh-Dole Act has created a powerful engine of practical innovation, producing many scientific advances that have extended human life, improved its quality, and reduced suffering for millions of people.[60]

The Risks Inappropriate Use of March-In Rights Pose to the Bayh-Dole Act

In short, the Bayh-Dole Act has been an unparalleled success. Yet some have advocated for policies that would undermine some of its key provisions and effects. At issue are so-called march-in rights, a provision within the Bayh-Dole Act that permits the U.S. government, in specified, proscribed, and limited circumstances, to require patent holders to grant a "nonexclusive, partially exclusive, or exclusive license" to a "responsible applicant or applicants."[61] As the following section explains, the architects of the Bayh-Dole Act

principally intended for march-in rights to be used to ensure patent owners commercialized their inventions.[62] As Senator Birch Bayh explained:

> When Congress was debating our approach fear was expressed that some companies might want to license university technologies to suppress them because they could threaten existing products. Largely to address this fear, we included the march-in provisions.[63]

Yet a number of civil society organizations and some members of Congress have called on NIH to exploit Bayh-Dole march-in rights to "control" allegedly unreasonably high drug prices. (Though, as ITIF has written, these advocates' assertions that U.S. drug prices, on net, are unreasonably high are fundamentally unwarranted and unsubstantiated.)[64] Nevertheless, at least seven petitions requesting NIH to "march in" with respect to a particular pharmaceutical drug have been filed (six as of the referenced CRS report).[65] In four of these cases, the petition was filed by civil society organizations alleging that a company was pricing a drug too high.[66] Some 50 members of Congress, led by Representative Lloyd Doggett (D-TX), have called on the NIH to cancel exclusivity when patented drugs are not available with reasonable terms.[67] Senator Angus King (I-ME) proposed legislation in 2017 that would require the Department of Defense (DOD) to issue compulsory licenses under Bayh-Dole "whenever the price of a drug, vaccine, or other medical technology is higher in the U.S. than the median price charged in the seven largest economies that have a per capita income at least half the per capita income of the U.S."[68] In other words, DOD would force a licensor to divulge their intellectual property so that a drug could be manufactured by other licensees, and in theory be sold at a lower price. (While it was not enacted, a similar provision was unfortunately included in the FY 2018 National Defense Authorization Act (NDAA) Senate Armed Services Committee report.) Yet the Bayh-Dole Act's designers did not intend for march-in rights to be used to control drug prices.

BAYH-DOLE MARCH-IN RIGHTS WERE NEVER INTENDED TO ADDRESS DRUG PRICE CONCERNS

The Bayh-Dole Act proscribes four specific instances in which the government is permitted to exercise march-in rights:

1) If the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention;
2) If action is necessary to alleviate health or safety needs not reasonably satisfied by the patent holder or its licensees;
3) If action is necessary to meet requirements for public use specified by federal regulations and such requirements are not reasonably satisfied by the contractor, assignee, or licensees; or
4) If action is necessary, in exigent cases, because the patented product cannot be manufactured substantially in the United States.[69]

In other words, lower prices are not one of the rationales laid out in the act. In fact, as senators Bayh and Dole have themselves noted, the Bayh-Dole Act's march-in rights were never intended to control or ensure "reasonable prices."[70] As the twain wrote in a 2002 *Washington Post* op-ed titled, "Our Law Helps Patients Get New Drugs Sooner," the Bayh-Dole Act:

> Did not intend that government set prices on resulting products. The law makes no reference to a reasonable price that should be dictated by the government. This omission was intentional; the primary purpose of the act was to entice the private sector to seek public-private research collaboration rather than focusing on its own proprietary research.[71]

The op-ed reiterated that the price of a product or service was not a legitimate basis for the government to use march-in rights, noting:

> The ability of the government to revoke a license granted under the act is not contingent on the pricing of a resulting product or tied to the profitability of a company that has commercialized a product that results in part from government-funded research. The law instructs the government to revoke such licenses only when the private industry collaborator has not successfully commercialized the invention as a product.[72]

Rather, Bayh-Dole's march-in provision was designed as a fail-safe for limited instances in which a licensee might not be making good-faith efforts to bring an invention to market, or when national emergencies require that more product is needed than a licensee is capable of producing. As Joseph P. Allen, a senate staffer for Bayh who played a key role in shaping the legislation, explains, Congress's introduction of Bayh-Dole was intended "to decentralize patent management from the bureaucracy into the hands of the inventing organizations, while retaining the long-established precedent that march-in rights were to be used in rare situations when effective efforts are not being made to bring an invention to the marketplace or enough of the product is not being produced to meet public needs."[73]

Likewise, the National Institute of Standards and Technology (NIST) report "Return on Investment Initiative: Draft Green Paper" agreed, noting, "The use of march-in is typically regarded as a last resort, and has never been exercised since the passage of the Bayh-Dole Act in 1980."[74] The report noted that, "NIH determined that that use of march-in to control drug prices was not within the scope and intent of the authority."[75]

In fact, there has only been one case in which Bayh-Dole's march-in criteria truly would have been met: a 2010 case in which Genzyme encountered difficulties in manufacturing sufficient quantities of Fabrazyme/agalsidase beta, an orphan drug for the treatment of Fabry disease.[76] Genzyme had to shut down the plant making the drug due to quality control issues and was therefore unable to manufacture the drug in sufficient quantities. NIH investigated the situation but did not initiate a march-in proceeding because it found that "Genzyme was working diligently to resolve its manufacturing difficulties" and that the company was likely to get back into production faster than a new licensee could get FDA approval to make the drug.[77]

March-in rights have never been exercised during the now over-40-year history of the Bayh-Dole Act.[78] NIH has denied all seven petitions to apply march-in rights, noting that the drugs in question were in virtually all cases adequately supplied and that concerns over drug pricing were not, by themselves, sufficient to provoke march-in rights.[79] NIH itself has expressed skepticism about the use of march-in rights to control drug prices, noting:

> Finally, the issue of the cost or pricing of drugs that include inventive technologies made using federal funds is one which has attracted the attention of Congress in several contexts that are much broader than the one at hand. In addition, because the market dynamics for all products developed pursuant to licensing rights under the Bayh-Dole Act could be altered if prices on such products were directed in any way by NIH, the NIH agrees with the public testimony that suggested that the extraordinary remedy of march-in is not an appropriate means of controlling prices.[80]

As Rabitschek and Latker wrote in "Reasonable Pricing—A New Twist for March-in Rights Under the Bayh-Dole Act" in the *Santa Clara University High Technology Law Journal*, "A review of the [Bayh-Dole] statute makes it clear that the price charged by a licensee for a patented product has no direct relevance to march-in rights."[81] As the authors concluded:

> There is no reasonable pricing requirement under 35 U.S.C. §203(l)(a)(1), considering the language of this section, the legislative history, and the prior history and practice of march-in rights. Rather, this provision is to assure that the contractor utilizes or commercializes the funded invention.[82]

The argument that Bayh-Dole march-in rights could be used to control drug prices was originally advanced in an article by Peter S. Arno and Michael H. Davis.[83] They contended that "[t]he requirement for 'practical application' seems clear to authorize the federal government to review the prices of drugs developed with public funding under Bayh-Dole terms and to mandate march-in when prices exceed a reasonable level" and suggested that under Bayh-Dole, the contractor may have the burden of showing that it charged a reasonable price.[84] While Arno and Davis admitted there was no clear legislative history on the meaning of the phrase "available to the public on reasonable terms," they still concluded that, "[t]here was never any doubt that this meant the control of profits, prices, and competitive conditions."[85]

But as Rabitschek and Latker explain, there are several problems with this analysis. First, the notion that "reasonable terms" of licensing means "reasonable prices" arose in unrelated testimony during the Bayh-Dole hearings. Most importantly, they note, "If Congress meant to add a reasonable pricing requirement, it would have explicitly set one forth in the law, or at least described it in the accompanying reports."[86] As Rabitschek and Latker continue, "There was no discussion of the shift from the 'practical application' language in the Presidential Memoranda and benefits being reasonably available to the public, to benefits being available on reasonable terms under 35 U.S.C. § 203."[87] As they conclude, "The interpretation taken by Arno and Davis is inconsistent with the intent of Bayh-Dole, especially since the Act was intended to promote the utilization of federally funded inventions and to minimize the costs of administering the technology transfer policies…. [The Bayh-Dole Act] neither provides for, nor mentions, 'unreasonable prices.'"[88]

Again, the Bayh-Dole Act's march-in provisions were included with commercialization in mind. Related to this, another reason the Bayh-Dole Act's architects inserted march-in right provisions was because, at the time the law was introduced, very few universities were experienced in patent licensing. The march-in provision therefore served as a fail-safe for cases in which universities were not effectively monitoring their agreements.[89] But universities have in fact proven proactive and effective in enforcing their licensing agreements, regularly including development milestones in their licenses—and when these milestones aren't being met without satisfactory reason (e.g., development is more difficult than expected), universities often terminate the deal and look for another developer. In other words, universities are enforcing their licensing agreements, not letting licenses just sit on the technologies—another example of why there has been no reason for the government to march in.

APPLYING MARCH-IN RIGHTS TO ADDRESS PRICING WOULD LEAD TO SIGNIFICANTLY REDUCED INNOVATION

Even if Congress were to amend Bayh-Dole to allow the federal government to use march-in rights to force lower pricing, the result would be a reduction of life-sciences innovation, as past experience clearly shows.

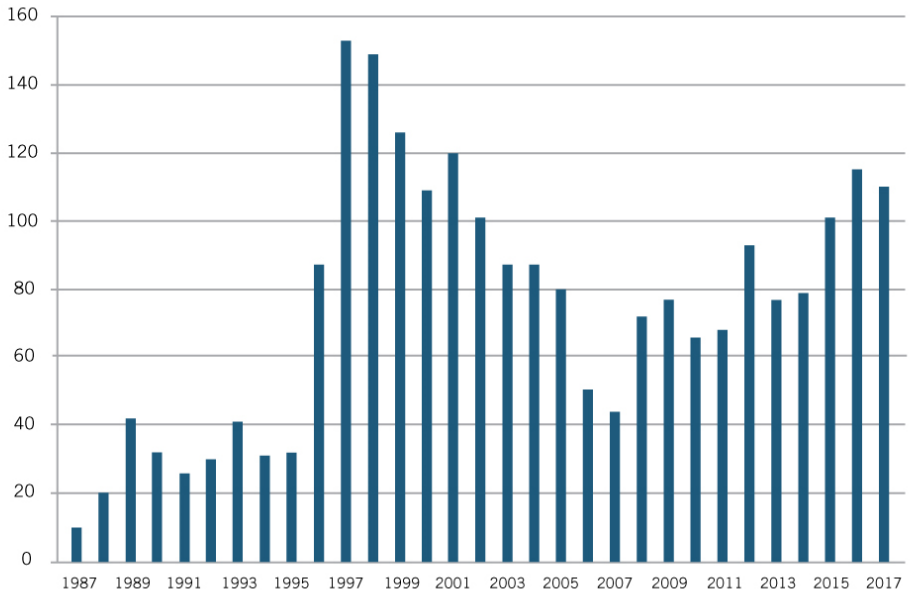
The debate around "reasonable pricing" of drugs stemming from licensed research goes back some time. The Federal Technology Transfer Act of 1986 (FTTA) authorized federal laboratories to enter into Cooperative Research and Development Agreements (CRADAs) with numerous entities, including private businesses. NIH has found that CRADAs "significantly advance biomedical research by allowing the exchange and use of experimental compounds, proprietary research materials, reagents, scientific advice, and private financial resources between government and industry scientists."[90]

In 1989, NIH's Patent Policy Board adopted a policy statement and three model provisions to address the pricing of products licensed by public health service (PHS) research agencies on an exclusive basis to industry, or jointly developed with industry through CRADAs. In doing so, the Department of Health and Human Services (DHHS) became the only federal agency at the time (other than the Bureau of Mines) to include a "reasonable pricing" clause in its CRADAs and exclusive licenses.[91] The 1989 PHS CRADA Policy Statement asserted:

> DHHS has a concern that there be a reasonable relationship between pricing of a licensed product, the public investment in that product, and the health and safety needs of the public. Accordingly, exclusive commercialization licenses granted for the NIH/ADAMHA [Alcohol, Drug Abuse, and Mental Health Administration] intellectual property rights may require that this relationship be supported by reasonable evidence.

But as Joseph P. Allen notes, such "attempts to impose artificial 'reasonable pricing' requirements on developers of government supported inventions did not result in cheaper drugs. Rather, companies simply walked away from partnerships."[92] Use of CRADAs began in 1987 and rapidly increased until the reasonable pricing requirement hit in 1989, after which they declined through 1995 (see Figure 2).

Figure 2: Private-Sector CRADAs With NIH, 1987–2017[93]



Recognizing that the only impact of the reasonable pricing requirement was undermining scientific cooperation without generating any public benefits, NIH eliminated the reasonable pricing requirement in 1995. In removing the requirement, then NIH director Dr. Harold Varmus explained, "An extensive review of this matter over the past year indicated that the pricing clause has driven industry away from potentially beneficial scientific collaborations with PHS scientists without providing an offsetting benefit to the public. Eliminating the clause will promote research that can enhance the health of the American people."[94] As Figure 2 shows, after NIH eliminated the requirement in 1995, the number of CRADAs immediately rebounded in 1996, and grew considerably in the following years.[95] The case represents a natural experiment showing the harm pricing requirements can inflict. Somewhat similarly, as the California Senate Office of Research has noted, "Granting agencies such as the National Institutes of Health (NIH) ultimately have

abandoned policies that require a financial return to the government after concluding that removing barriers to the rapid commercialization of products represents a greater public benefit than any potential revenue stream to the government."[96]

A more recent case involved biopharmaceutical company Sanofi possibly taking a license from the U.S. Army to develop a vaccine for the Zika virus. U.S. Army scientists from the Walter Reed Army Institute of Research developed two candidate vaccines for the Zika virus and posted a notice in the federal register offering to license them on either a nonexclusive or exclusive basis. No company responded to the nonexclusive license, and Sanofi was the only company that submitted a license application for the Army's Zika candidate vaccine, with the U.S. Army and Sanofi reaching a licensing agreement in June 2016 that would enable Sanofi to continue the development and clinical trial work necessary to turn the candidate vaccine into a market-ready product. As a U.S. Army official noted, "Exclusive licenses are often the only way to attract a competent pharma partner for such development projects," and are needed because the military lacks "sufficient" research and production capabilities to develop and manufacture a Zika vaccine.[97] Sanofi received a $43 million government grant to start undertaking clinical trial work on the virus candidate.

In July 2017, supported by Knowledge Economy International, an organization opposed to robust intellectual property rights, Sens. Bernie Sanders (D-VT) and Dick Durbin (D-IL) argued that the U.S. Army and Sanofi should insert reasonable pricing language into the exclusive license. Sanders even called on President Trump to cancel the deal.[98] In response, Army officials noted that they were not in a position to "enforce future vaccine prices." For its part, Sanofi representatives noted, "We can't determine the price of a vaccine that we haven't even made yet," and argued that "it's premature to consider or predict Zika vaccine pricing at this early stage of development. As noted earlier, ongoing uncertainty around epidemiology and disease trajectory make any commercial projections theoretical at best."[99] Sanofi noted that it had committed over 60 researchers to the effort, invested millions of dollars itself, and was "committed to leveraging its flavivirus vaccine development and manufacturing expertise to deliver and ultimately price a Zika vaccine in a responsible way."[100]

Sanofi also noted that the proposed license would require it to pay milestone and royalty payments back to the government, and its exclusive license would not prevent other companies—such as GlaxoSmithKline, Takeda, and Moderna, which also had all struck their own Zika vaccine partnerships with U.S. agencies—from bringing competing products to market, and allow for robust competition in the market for Zika vaccines.[101] However, with both partners continuing to be attacked in the media, in September 2017, Sanofi announced it would "not continue development of, or seek a license from, the Walter Reed Army Institute of Research for the Zika vaccine candidate at this time."[102] This is yet another case wherein certain policymakers' insistence on pricing requirements stifled innovation and the potential for a firm to bring a promising innovation to market.

It also takes the debate back to the central point that, in their push for lower drug prices through weaker private IP rights stemming from federally funded research, advocates fail to acknowledge *that no drugs were created from federally funded inventions* under the previous (to Bayh-Dole) regime.[103] In contrast, over 200 new drugs and vaccines have been developed through public-private partnerships facilitated in part by the Bayh-Dole Act since its enactment in 1980.[104]

CONCLUSION

America's innovation system is fragile, and while America today leads the world in life-sciences innovation, that was not always the case, nor is it guaranteed to be the case in the future. As ITIF wrote in a 2021 report, "Going, Going, Gone? To Stay Competitive in Biopharmaceuticals, America Must Learn From Its Semiconductor Mistakes," "Taking the industry for granted and believing that government can impose

regulations with no harmful effect—common policy views in Washington—will almost certainly mean passing the torch of global leadership to other nations, especially China, within a decade or two."[105]

As ITIF commented to the Senate HELP Committee as it considered the Pandemic and All-Hazards Preparedness Act (PAHPA), policymakers should reject the inclusion of reasonable pricing clauses in that (or other related) legislation, recognizing the long history of failure with efforts to include reasonable pricing clauses in NIH licensing activities.[106] Reasonable or reference pricing clauses should not be included in NIH grants, licenses, or CRADAs. Similarly, with regard to the broader cross-agency application of the Bayh-Dole Act, the price of resulting products should not be considered as a basis for the application of march-in provisions. Not only did Congress never establish price as a basis for march-in, such a practice would be deleterious to the effective mechanisms America has designed to promote the transfer of technologies stemming from federally funded R&D and to the broader cause of U.S. biomedical innovation.

Weakening the certainty of access to IP rights provided under Bayh-Dole by employing march-in or reasonable pricing requirements to address drug pricing issues—especially if it meant a government entity could walk in and retroactively commandeer innovations private-sector enterprises invested hundreds of millions, if not billions, to create—would significantly diminish private businesses' incentives to commercialize products supported by federally funded research.[107] As David Bloch notes, "The reluctance of such [biopharmaceutical] companies to do business with the government is almost invariably tied up in concerns over the government's right to appropriate private sector intellectual property."[108] As he continues, "Each march-in petition potentially puts at risk the staggeringly massive investment that branded pharmaceutical companies make in developing new drug therapies."[109] In conclusion, ITIF believes that any proposals to add "reasonable pricing" requirements to agreements between the NIH and private companies would be strongly misguided and deleterious to the cause of biopharmaceutical innovation.

Thank you for your consideration and the opportunity to comment.

Stephen Ezell
Vice President Global Innovation Policy
Information Technology and Innovation Foundation

REFERENCES

1. National Institutes of Health (NIH), "Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer" (NIH, July 31, 2023), https://osp.od.nih.gov/events/workshop-on-transforming-discoveries-into-products-maximizing-nihs-levers-to-catalyze-technology-transfer/.
2. Trelysa Long, "Preserving U.S. Biopharma Leadership: Why Small, Research-Intensive Firms Matter in the U.S. Innovation Ecosystem" (ITIF, August 2023), 1, https://itif.org/publications/2023/08/21/preserving-us-biopharma-leadership-why-small-research-intensive-firms-matter/.
3. John Wu and Robert D. Atkinson, "How Technology-Based Start-Ups Promote U.S. Economic Growth" (ITIF, November 2017), https://itif.org/publications/2017/11/28/how-technology-based-start-ups-support-us-economic-growth; Congressional Budget Office (CBO), "Research and Development in the Pharmaceutical Industry" (CBO, April 2021), https://www.cbo.gov/system/files/2021-04/57025-Rx-RnD.pdf.
4. Joe Kennedy, "How to Ensure That America's Life-sciences Sector Remains Globally Competitive" (ITIF, March 2018), 37, https://itif.org/publications/2018/03/26/how-ensure-americas-life-sciences-sector-remains-globally-competitive; European Federation of Pharmaceutical Industries and Associations (EFPIA), "The Pharmaceutical Industry in Figures, Key Data 2017," 8, https://www.efpia.eu/media/219735/efpia-pharmafigures2017_statisticbroch_v04-final.pdf.
5. Justin Chakma et al., "Asia's Ascent—Global Trends in Biomedical R&D Expenditures" *New England Journal of Medicine* 370, No. 1 (January 2014); ER Dorsey et al., "Funding of US Biomedical Research, 2003-2008" *New England Journal of Medicine* 303 (2010): 137–43, http://www.ncbi.nlm.nih.gov/pubmed/20068207.
6. Neil Turner, "What's gone wrong with the European pharmaceutical industry," *Thepharmaletter*, April 29, 1999, https://www.thepharmaletter.com/article/what-s-gone-wrong-with-the-european-pharmaceutical-industry-by-neil-turner; David Michels and Aimison Jonnard, "Review of Global Competitiveness in the Pharmaceutical Industry" (U.S. International Trade Commission, 1999), 2-3, https://www.usitc.gov/publications/332/pub3172.pdf.
7. John K. Jenkins, M.D., "CDER New Drug Review: 2015 Update" (PowerPoint presentation, U.S. Food and Drug Administration/CMS Summit, Washington, D.C., December 14, 2015), http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM477020.pdf.
8. Jenkins, "CDER New Drug Review," 23; Ian Lloyd, "Pharma R&D Annual Review 2020 NAS Supplement," *PharmaIntelligence*, April 2020, 3, https://pharmaintelligence.informa.com/~/media/informa-shop-window/pharma/2020/files/whitepapers/rd-review-2020-nas-supplement-whitepaper.pdf
9 Robert D. Atkinson, "Why Life-Sciences Innovation Is Politically "Purple"— and How Partisans Get It Wrong" (ITIF, February 2016), https://www2.itif.org/2016-life-sciences-purple.pdf.
10 Ranjana Chakravarthy et al., "Public- and Private-Sector Contributions to the Research and Development of the Most Transformational Drugs in the Past 25 Years: From Theory to Therapy" *Therapeutic Innovation and Regulatory Science* Vol. 50, Issue 6 (July 2016), https://www.ncbi.nlm.nih.gov/pubmed/30231735.
11. National Institutes of Health, "Grants & Funding," https://www.nih.gov/grants-funding.
12. Beth Snyder Bulik "The top 10 ad spenders in Big Pharma for 2020," *Fierce Pharma*, April 2021, https://www.fiercepharma.com/special-report/top-10-ad-spenders-big-pharma-for-2020.
13. European Federation of Pharmaceutical Industries and Associations, "The Pharmaceutical Industry in Figures, 2023" (EFPIA, 2023), 10, https://www.efpia.eu/media/rm4kzdlx/the-pharmaceutical-industry-in-figures-2023.pdf.
14. Ashley J. Stevens et al., "The Role of Public-Sector Research in the Discovery of Drugs and Vaccines" *The New England Journal of Medicine* Vol. 364, Issue 6 (February 2011): 1, https://www.nejm.org/doi/full/10.1056/NEJMsa1008268.
15. Benjamin Zycher, Joseph A. DiMasi, and Christopher-Paul Milne, "The Truth About Drug Innovation: Thirty-Five Summary Case Histories on Private Sector Contributions to Pharmaceutical Science" (Center for Medical Progress at the Manhattan Institute, June 2008), 3–4, https://www.manhattan-institute.org/html/truth-about-drug-innovation-thirty-five-summary-case-histories-private-sector-contributions.
16. Ibid.

17. U.S. Senate Joint Economic Committee, "The Benefits of Medical Research and the Role of the NIH," May 17, 2000, https://www.faseb.org/portals/2/pdfs/opa/2008/nih_research_benefits.pdf
18. Organization for Economic Cooperation and Development (OECD), "Science, Technology and Innovation in the New Economy" (OECD: 2000), http://www.oecd.org/science/sci-tech/1918259.pdf.
19. Bhavan N. Sampat and Frank R. Lichtenberg, "What Are The Respective Roles Of The Public And Private Sectors In Pharmaceutical Innovation?" *Health Affairs* 30, No. 2 (2011): 332–339, https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2009.0917.
20. Ibid.
21. Anusuya Chatterjee and Ross C. DeVol, "Estimating Long-Term Economic Returns of NIH Funding on Output in the Biosciences" (Milken Institute, 2012, 4), http://www.milkeninstitute.org/publications/view/535.
22. "The Impact of Genomics on the U.S. Economy" (Battelle Technology Partnership Practice, UMR, June 2013), http://www.unitedformedicalresearch.com/advocacy_reports/the-impact-of-genomics-on-the-u-s-economy.
23. Andrew A. Toole, "The Impact of Public Basic Research on Industrial Innovation: Evidence from the Pharmaceutical Industry," *Research Policy* Vol. 41, Issue 1 (February 2012): 1–12, https://www.sciencedirect.com/science/article/abs/pii/S004873331100117X.
24 Ranjana Chakravarthy et al., "Public- and Private-Sector Contributions to the Research and Development of the Most Transformational Drugs in the Past 25 Years: From Theory to Therapy" *Therapeutic Innovation and Regulatory Science* Vol. 50, Issue 6 (July 2016), https://www.ncbi.nlm.nih.gov/pubmed/30231735.
25. Stephen Ezell, "How the Prescription Drug User Fee Act Supports Life-Sciences Innovation and Speeds Cures" (ITIF, February 2017), http://www2.itif.org/2017-pdufa-life-sciences-innovation.pdf; United States General Accountability Office (GAO), "FDA Drug Approval: Review Time Has Decreased in Recent Years" (Washington, D.C.: GAO, October 20, 1995), http://www.gao.gov/assets/230/221919.pdf; Jenkins, "CDER New Drug Review."
26. Stephen Ezell, "Comments to the Centers for Medicare & Medicaid Services on an International Pricing Index Model for Medicare Part B Drugs" (ITIF, December 2018), http://www2.itif.org/2018-CMS-pricing-index-comments.pdf?_ga=2.201095598.1236498136.1546543725-719207280.1528225744.
27. Organization for Economic Cooperation and Development, "Pharmaceutical Pricing Policies in a Global Market" (OECD, September 2008), 190, http://www.oecd.org/els/pharmaceutical-pricing-policies-in-a-global-market.htm.
28. Trelysa Long and Stephen Ezell, "The Hidden Toll of Drug Price Controls: Fewer New Treatments and Higher Medical Costs for the World" (ITIF, July 2023), https://itif.org/publications/2023/07/17/hidden-toll-of-drug-price-controls-fewer-new-treatments-higher-medical-costs-for-world/.
29 Joe Kennedy, "The Link Between Drug Prices and Research on the Next Generation of Cures" (ITIF, September 2019), https://itif.org/publications/2019/09/09/link-between-drug-prices-and-research-next-generation-cures.
30. Carmelo Giaccotto, Rexford E. Santerre, and John A. Vernon, "Drug Prices and Research and Development Investment Behavior in the Pharmaceutical Industry" *The Journal of Law & Economics* Vol. 48, Issue 1 April 2005, https://www.jstor.org/stable/10.1086/426882?seq=1#page_scan_tab_contents.
31. Frank R. Lichtenberg, "Importation and Innovation," NBER Working Paper No. 12539, September 2006, https://www.nber.org/papers/w12539.
32. Tomas J. Philipson and Troy Durie, "Issue Brief: The Impact of HR 5376 on Biopharmaceutical Innovation and Patient Health" November 9, 2021, https://cpb-us-w2.wpmucdn.com/voices.uchicago.edu/dist/d/3128/files/2021/08/Issue-Brief-Drug-Pricing-in-HR-5376-11.30.pdf.
33 U.S. Congressional Budget Office, "Estimated Budgetary Effects of Subtitle I of Reconciliation Recommendations for Prescription Drug Legislation" (CBO, July 8, 2022), https://www.cbo.gov/publication/58290.
34. Daniel Gassull, Harry Bowen, and Duane Schulthess, "The Impact of IRA Policy Expansion Proposals on the US Biopharma Ecosystem" (Vital Transformations, June 2023), https://vitaltransformation.com/2023/06/the-impact-of-ira-policy-expansion-proposals-on-the-us-biopharma-ecosystem/.

35. Tomas J. Philipson, "The Deadly Side Effects of Drug Price Controls," *The Wall Street Journal*, April 5, 2023, https://www.wsj.com/articles/medicare-drug-price-controls-will-make-america-sicker-research-innovation-negotiations-private-insurers-b503b4ba.
36. Paige Twenter, "Inflation Reduction Act will restrict oncology drug development, Bristol-Myers Squibb CEO says," *Becker's Hospital Review*, November 21, 2022, https://www.beckershospitalreview.com/pharmacy/inflation-reduction-act-will-restrict-oncology-drug-development-bristol-myers-squibb-ceo-says.html.
37. Max Gelman, "Updated: Eli Lilly blames Biden's IRA for cancer drug discontinuation as the new pharma playbook takes shape," *Endpoint News*, November 1, 2022, https://endpts.com/eli-lilly-rolls-snake-eyes-as-it-axes-two-early-stage-drugs-including-a-40m-cancer-therapy-from-fosun/.
38. Steve Usdin, "AstraZeneca may defer U.S. cancer drug launches in response to IRA," *Biocentury*, November 10, 2022, https://www.biocentury.com/article/645834/astrazeneca-may-defer-u-s-cancer-drug-launches-in-response-to-ira.
39. B. Graham, "Patent Bill Seeks Shift to Bolster Innovation," *The Washington Post,* April 8, 1978; Stevens, "The Role of Public Sector Research," 536.
40. Naomi Hausman, "University Innovation, Local Economic Growth, and Entrepreneurship," U.S. Census Bureau Center for Economic Studies Paper No. CES-WP- 12–10 (July 2012): 5, https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2097842.
41. Louis G. Tornatzky and Elaine C. Rideout, "Innovation U 2.0: Reinventing University Roles in a Knowledge Economy" (State Science and Technology Institute, 2014) 165, https://ssti.org/report-archive/innovationu20.pdf.
42. Joseph P. Allen, "When Government Tried March In Rights to Control Health Care Costs," *IPWatchdo*g, May 2, 2016, http://www.ipwatchdog.com/2016/05/02/march-in-rights-health-care-costs/id=68816/.
43. Statement of Elmer B. Staats, comptroller general of the United States, Before the Committee on the Judiciary United States Senate, "S. 414-The University and Small Business Patent Procedures Act," May 16, 1979, https://www.gao.gov/assets/100/99067.pdf.
44. David Mowery, "University-Industry Collaboration and Technology Transfer in Hong Kong and Knowledge-based Economic Growth," (working paper, University of California, Berkeley, 2009), http://www.savantas.org/cmsimg/files/Research/HKIP/Report/1_mowery.pdf.
45. "Innovation's Golden Goose," *The Economist*, December 12, 2002, http://www.economist.com/node/1476653.
46. Wendy H. Schacht, "Patent Ownership and Federal Research and Development (R&D): A Discussion of the Bayh-Dole Act and the Stevenson-Wydler Act" (Congressional Research Service, 2000), http://ncseonline.org/nle/crsreports/science/st-66.cfm.
47. Hausman, "University Innovation, Local Economic Growth, and Entrepreneurship," 7. (Calculation based on NBER patent data.)
48. John H. Rabitschek and Norman J. Latker, "Reasonable Pricing—A New Twist for March-in Rights Under the Bayh-Dole Act" *Santa Clara High Technology Law Journal* Vol. 22, Issue 1 (2005), 150, https://digitalcommons.law.scu.edu/cgi/viewcontent.cgi?article=1399&context=chtlj; The Economist, "Innovation's Golden Goose."
49. AUTM, "Driving the Innovation Economy: Academic Technology Transfer in Numbers," https://autm.net/AUTM/media/Surveys-Tools/Documents/AUTM_FY2018_Infographic.pdf.
50. Ibid.
51. Lori Pressman et al., "The Economic Contribution of University/Nonprofit Inventions in the United States: 1996–2015" (Report prepared for AUTM and Biotechnology Industry Organization (BIO), June 2017), 3, https://www.bio.org/sites/default/files/June%202017%20Update%20of%20I-O%20%20Economic%20Impact%20Model.pdf.
52. AUTM, "Driving the Innovation Economy."
53. Phone interview with Joe Allen, July 24, 2018.
54. Hausman, "University Innovation, Local Economic Growth, and Entrepreneurship," 8.

55. Ibid.
56. Saul Lach and Mark Schankerman, "Incentives and Invention in Universities," *RAND Journal of Economics* Vol 39, No. 2 (2008): 403–433, https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.0741-6261.2008.00020.x.
57. Scott Shane, "Encouraging University Entrepreneurship? The Effect of the Bayh-Dole Act on University Patenting in the United States" *Journal of Business Venturing* 19 (2004): 127–151, https://papers.ssrn.com/sol3/papers.cfm?abstract_id=1495504.
58. Robert D. Atkinson, Stephen J. Ezell, and Luke A. Stewart, "The Global Innovation Policy Index" (ITIF and the Ewing Marion Kauffman Foundation, March 2012), 65, http://www2.itif.org/2012-global-innovation-policy-index.pdf?_ga=2.21733243.1175485471.1531853145-719207280.1528225744.
59. California Senate Office of Research, "Optimizing Benefits From State-Funded Research" *Policy Matters* (March 2018), 12, https://sor.senate.ca.gov/sites/sor.senate.ca.gov/files/0842%20policy%20matters%20Research%2003.18%20Final.pdf.
60. Rabitschek and Latker, "Reasonable Pricing," 150.
61. John R. Thomas, "March-In Rights Under the Bayh-Dole Act" (Congressional Research Service, August 2016), 7, https://fas.org/sgp/crs/misc/R44597.pdf.
62. David S. Bloch, "Alternatives to March-In Rights" *Vanderbilt Journal of Entertainment and Technology Law*, Vol. 18:2:247 (2016): 253, http://www.jetlaw.org/wp-content/uploads/2016/03/Bloch_SPE_6-FINAL.pdf.
63. Statement of Senator Birch Bayh to the National Institutes of Health (May 24, 2004), https://www.ott.nih.gov/sites/default/files/documents/2004NorvirMtg/2004NorvirMtg.pdf.
64. Stephen Ezell, "No, America's Drug Prices Aren't Climbing Radically Out of Control," *The Innovation Files*, June 17, 2022, https://itif.org/publications/2022/06/17/no-americas-drug-prices-arent-climbing-radically-out-of-control/.
65. Thomas, "March-In Rights Under the Bayh-Dole Act," 11.
66. Ibid.
67. Ibid, 14.
68. Joseph Allen, "Proposal from Senator King Won't Reduce Drug Prices, Just Innovation," *IPWatchdog*, July 17, 2017, https://www.ipwatchdog.com/2017/07/17/senator-king-reduce-drug-prices-innovation/id=85702/.
69. Thomas, "March-In Rights Under the Bayh-Dole Act," 10.
70. Birch Bayh, "Statement of Birch Bayh to the National Institutes of Health," May 25, 2014, http://www.essentialinventions.org/drug/nih05252004/birchbayh.pdf.
71. Birch Bayh and Bob Dole, "Our Law Helps Patients Get New Drugs Sooner," *The Washington Post*, April 11, 2002, https://www.washingtonpost.com/archive/opinions/2002/04/11/our-law-helps-patients-get-new-drugs-sooner/d814d22a-6e63-4f06-8da3-d9698552fa24/?utm_term=.ddbf6876a380.
72. Ibid.
73. Allen, "When Government Tried March In Rights to Control Health Care Costs."
74. National Institute of Standards and Technology (NIST), "Return on Investment Initiative: Draft Green Paper" (NIST, December 2018), 30, https://nvlpubs.nist.gov/nistpubs/SpecialPublications/NIST.SP.1234.pdf.
75. Ibid, 30.
76. Thomas, "March-In Rights Under the Bayh-Dole Act," 9.
77. Ibid.
78. Ibid.
79. Thomas, "March-In Rights Under the Bayh-Dole Act," 11–12.
80. Elias A. Zerhouni, director, NIH, "In the Case of Norvir Manufactured by Abbott Laboratories, Inc.," July 29, 2004, http://www.ott.nih.gov/sites/default/files/documents/policy/March-In-Norvir.pdf.
81. Rabitschek and Latker, "Reasonable Pricing," 160.

82. Ibid, 167.
83. Peter Amo and Michael Davis, "Why Don't We Enforce Existing Drug Price Controls? The Unrecognized and Unenforced Reasonable Pricing Requirements Imposed upon Patents Deriving in Whole or in Part from Federally Funded Research," *Tulane Law Review* Vol. 75, 631 (2001), https://engagedscholarship.csuohio.edu/cgi/viewcontent.cgi?article=1754&context=fac_articles.
84. Ibid.
85. Rabitschek and Latker, "Reasonable Pricing," 162–163.
86. Ibid, 163.
87. Ibid. Here, the Presidential Memoranda refers to memoranda produced by the Kennedy and Nixon administrations that pertained to government policy related to contractor ownership of inventions.
88. Ibid.
89. Stephen Ezell interview with Joseph P. Allen, November 18, 2018.
90. National Institutes of Health, "NIH News Release Rescinding Reasonable Pricing Clause," news release, April 11, 1995, https://www.ott.nih.gov/sites/default/files/documents/pdfs/NIH-Notice-Rescinding-Reasonable-Pricing-Clause.pdf.
91. Ibid.
92. Allen, "Compulsory Licensing for Medicare Drugs—Another Bad Idea from Capitol Hill."
93. National Institutes of Health, "OTT Statistics," accessed January 13, 2019, https://www.ott.nih.gov/reportsstats/ott-statistics.
94. National Institutes of Health, "NIH News Release Rescinding Reasonable Pricing Clause."
95. Allen, "Compulsory Licensing for Medicare Drugs—Another Bad Idea from Capitol Hill."
96. California Senate Office of Research, "Optimizing Benefits From State-Funded Research," 11.
97. Eric Sagonowsky, "Sanofi Pulls Out of Zika Vaccine Collaboration as Feds Gut its R&D Contract," *FiercePhrma*, September 1, 2017, https://www.fiercepharma.com/vaccines/contract-revamp-sanofi-s-Zika-collab-u-s-government-to-wind-down; Ed Silverman, "Sanofi Rejects U.S. Army Request for 'Fair" Pricing' for a Zika Vaccine," *PBS*, May 20, 2017, https://www.pbs.org/newshour/health/sanofi-army-request-pricing-Zika-vaccine.
98. Bernie Sanders, "Trump Should Avoid a Bad Zika Deal," *The New York Times*, March 10, 2017, https://www.nytimes.com/2017/03/10/opinion/bernie-sanders-trump-should-avoid-a-bad-Zika-deal.html?_r=0.
99. Eric Sagonowsky, "Sanofi Executive Lays Out Case For Taxpayer Funding—And Exclusive Licensing—on Zika Vaccine R&D," *FiercePhrma*, May 25, 2017, https://www.fiercepharma.com/vaccines/exec-says-corporate-responsibility-not-potential-profits-drove-sanofi-s-Zika-vaccine-r-d.
100. Jeannie Baumann, "Sanofi Never Rejected Fair Pricing for Zika Vaccine: Exec," *BloombergNews*, July 18, 2017, https://www.bna.com/sanofi-rejected-fair-n73014461930/.
101. Sagonowsky, "Sanofi Executive Lays Out Case For Taxpayer Funding—And Exclusive Licensing—on Zika Vaccine R&D."
102. Sagonowsky, "Sanofi Pulls Out of Zika Vaccine Collaboration as Feds Gut its R&D Contract."
103. Joseph Allen, "Bayh-Dole Under March-in Assault: Can It Hold Out?" *IP Watchdog*, January 21, 2016, http://www.ipwatchdog.com/2016/01/21/bayh-dole-under-march-in-assault-can-it-hold-out/id=65118/.
104. AUTM, "Driving the Innovation Economy."
105. Stephen Ezell, "Going, Going, Gone? To Stay Competitive in Biopharmaceuticals, America Must Learn From Its Semiconductor Mistakes" (ITIF, November 2021), https://itif.org/publications/2021/11/22/going-going-gone-stay-competitive-biopharmaceuticals-america-must-learn-its/
106. Stephen Ezell, "Comments Before the US Senate Help Committee Regarding the "Pandemic and All-Hazards Preparedness Act" (ITIF, July 2023), https://itif.org/publications/2023/07/10/comments-regarding-the-pandemic-and-all-hazards-preparedness-act/.

107. Stephen J. Ezell, "Why Exploiting Bayh-Dole 'March-In' Provisions Would Harm Medical Discovery," *The Innovation Files,* April 29, 2016, https://www.innovationfiles.org/why-exploiting-bayh-dole-march-in-provisions-would-harm-medical-discovery/.
108. Bloch, "Alternatives to March-In Rights," 261.
109. Ibid.

Submission Date: 8/18/2023

Name: Michael Mohr-Ramirez

Name of Organization: Taxpayers Protection Alliance

Comment:

To Whom It May Concern,

Please find comments from the Taxpayers Protection Alliance attached. Let me know if you have any questions – thank you!

Best,
Michael

--
Michael Mohr-Ramirez
Federal Policy Manager
Taxpayers Protection Alliance

Additional Comment (attachment):

Submission Date: 8/18/2023

Name: David Williams

Name of Organization: Taxpayers Protection Alliance

Comment:

Taxpayers Protection Alliance, 1101 14th Street, NW., Suite 1120, Washington, D.C. 20005
(202) 930-1716
www.protectingtaxpayers.org

TAXPAYERS PROTECTION ALLIANCE

August 18, 2023

Lyric Jorgenson, Ph.D.
NIH Office of Science Policy
6705 Rockledge Dr #750
Bethesda, MD, 20817

Dear Director Jorgenson,

The Taxpayers Protection Alliance (TPA) writes today in response to your agency's recent workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer.

Public-private partnerships in medicine significantly strengthen the advances made through federally funded research. This relationship ensures that taxpayer money ultimately leads to many new treatments and products being brought to market for consumers. Intellectual Property (IP) protections form the backbone of this dynamic, driving the eventual commercialization of potentially lifesaving discoveries.

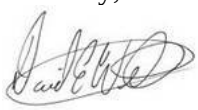
For example, the Bayh-Dole Act was originally passed in 1980 for this very reason. The law leverages the private incentives that come from strong patent protections to promote tech transfer and ensure that federally funded research doesn't waste away. As a result, more than 200 new drugs have been developed through the Bayh-Dole framework. The United States stands today as a world leader in medical innovation because of this important foresight.

The current system maintains the proper incentives for discoveries made in federal labs and universities to be taken to the next level through private development. This was not the case prior to the Bayh-Dole Act, when universities lacked the appropriate framework to license patents to private companies. The private sector's ability to pour resources into finding applications for federally supported discoveries has served a critical role in offering Americans access to cutting edge treatments and cures.

Policymakers must be careful to avoid political pressures that would upset this balance. Recent calls to abuse the Bayh-Dole Act or bring back misguided policies like the "reasonable pricing clause," which the NIH trashed in 1995, are examples of such dangerous pressures. While the Bayh-Dole Act does give the federal government "march-in" rights that allow it to step in and relicense discoveries, the purpose of this tool is not to manipulate pricing. And the "reasonable pricing clause" has already proven itself as a disastrous policy that drives away private investments.

NIH has played a crucial role in upholding the legal framework that drives American medical innovation. TPA urges you to continue to promote The United States system of IP protections that provides countless benefits for American taxpayers, patients, and the economy.

Sincerely,



David Williams
President

Submission Date: 8/18/2023

Name: Emily Michiko Morris

Name of Organization: The University of Akron School of Law

Comment:

Dear Director Jorgenson:

Please accept the attached cover letter and law review article for consideration in relation to the July 31, 2023 NIH Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer.

Please do not hesitate to contact me if you have any questions.

Thank you for your time and consideration.

Emily Michiko Morris (she/her/hers)
David L. Brennan Endowed Chair and Associate Professor
The University of Akron School of Law
Support Akron Law

Additional Comment (attachment):

School of Law

Emily Michiko Morris
David L. Brennan Endowed Chair
Assoc. Dir., Ctr. for Intell. Prop. Law & Techn.
C. Blake McDowell Law Center
302 Buchtel Common
Akron, OH 44325-2901
t: 330-972-6486
e: emichikomorris@uakron.edu

August 18, 2023

Submitted via email

Lyric Jorgenson, Ph.D.
NIH Office of Science Policy
6705 Rockledge Dr #750
Bethesda, MD, 20817

Comments on the July 31, 2023 NIH Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer

Dear Director Jorgenson,

In response to the invitation by the National Institutes of Health (NIH) to comment on its workshop on *Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer*, I respectfully submit the attached article. Although the article nominally addresses government-funded research on nanotechnology, it also addresses government-funded research on other "science-based" technologies, such as biotechnology, more generally. As such, I hope it may be of some relevance to the NIH as it considers its policies on the patenting and – in particular – its licensing of NIH-funded inventions and discoveries.

I published this article, *The Irrelevance of Nanotechnology Patents*, in 2016 to respond to the common criticism that patenting government-funded basic research causes anticommons or other obstacles to free use of the research. In science-based technologies such as nanotechnology and biotechnology – fields that rely mostly on academic research and discoveries of natural phenomena – government-conducted and government-funded research provides pivotal and yet very early stage, basic research that is at best no more than a proof-of-concept requiring many additional developmental stages before commercialization can be achieved. Basic research in science-based fields thus does not provide a direct societal benefit but instead simply a foundation on which socially valuable applications later can be developed – but only if others in either the public or private sector are willing to invest in such development.

The attached article shows that, for this reason, as important and valuable as government-funded research is to science-based technologies, patents on such upstream basic research have little effect on downstream research and development. For one thing, downstream application development in scienced-based technologies frequently takes so long that any upstream basic research patents will have expired. More importantly, the unpredictability, complexity, cost, and risk involved in developing usable applications of science-based technologies poses a far greater deterrent to investment in such endeavors than do patents on government-funded basic research. Even for government-funded research that is more directly translatable into products usable by the public, in biopharmaceuticals in particular the typically privately born cost of modifying and testing those products for safe and effective use greatly outweighs the government's contribution toward inventing those products. As a result making such investments in commercializing technologies still in such early and risky stages of development is well beyond the comfort zone of most private investors. Because of the difficulties inherent in science-based technologies, development in these fields is especially prone to underdevelopment.

The NIH and other government agencies that fund basic research should be aware of these issues in

licensing patents on government-funded basic research, whether the NIH itself or grant recipients such as university researchers hold those patents. For example, although many have called for government exercise of its "march-in" rights under the Bayh-Dole Act or even government imposition of "reasonable pricing" or other price-controls in their patent licenses, such clauses serve only to magnify the uncertainty and risk of developing basic research, thereby further exacerbating underdevelopment in biotechnology and other science-based fields. Although they may not otherwise be particularly relevant, restrictive licensing of patents on basic, government-funded research could thus greatly deter further development.

Thank you very much for this opportunity to contribute to the conversation and for your consideration.

Sincerely,

Emily Michiko Morris
David L. Brennan Endowed Chair and Associate Professor of Law
Senior Fellow for Life Sciences & Scholar, Center for Intellectual Property x Innovation Policy, Antonin Scalia Law School, George Mason University

CONNECTICUT
LAW REVIEW

VOLUME 49 DECEMBER 2016 NUMBER 2

Article

The Irrelevance of Nanotechnology Patents

EMILY MICHIKO MORRIS

Although scientists have for decades now had the ability to manipulate matter at the atomic level, we have yet to see the nanotechnological revolution that these scientists predicted would follow. Despite the years of effort and billions of dollars that have been invested into research and development thus far, nanotechnology has yielded surprisingly few end-user applications. A number of commentators have blamed this lack of progress on the Bayh-Dole Act and other changes to patent law, arguing that, although these laws are supposed to stimulate technological development, they have in fact had the exact opposite effect when it comes to nanotechnology. Because universities now own too many "upstream" patent rights with the potential to obstruct "downstream" development of usable applications, their argument goes, the Bayh-Dole Act has caused an unnecessary drag on nanotechnology development. This Article shows, however, that contrary to this common criticism, patents on university-based nanotechnology research are most often simply irrelevant.

While nanotechnology applications have been slow to emerge, this Article shows that the latency in development is due not to patents but rather to the fact that nanotechnology is a science-based technology and as such faces various additional hurdles that far outweigh the potential effect of any upstream patenting by universities. Just the inherent technological difficulties alone of working in science-based fields makes development cycles in these fields unavoidably long. To make matter worse, science-based fields typically also face issues with tacit knowledge and the lack of widespread expertise as well as the "valley of death" and the difficulties of attracting investment in intermediate-stage development. Add to this mix constraints due to concerns about public health and safety along with limited access to proprietary materials and equipment and it is not difficult to understand why nanotechnology development has not advanced as quickly as some might have hoped. Thus, while nanotechnology and other science-based technologies may occasionally experience patent-related holdup problems, development in these fields would be more effectively addressed by looking instead at the multitude of other, nonpatent factors that pose well-recognized obstacles in such science-based technologies.

ARTICLE CONTENTS

The Irrelevance of Nanotechnology Patents

EMILY MICHIKO MORRIS*

INTRODUCTION

Once the stuff of science fiction, nanotechnology is now expected to be the next technological revolution.[1] For over thirty years, the United States government has invested several billion dollars into research and development of technologies that exploit the unusual qualities of matter at the atomic level.[2] All of this enthusiasm has yielded thousands of nanotechnology patents[3] but little in the way of revolutionary new products and applications. We have yet to see the brave new world of efficient energy sources and targeted, cell-specific chemotherapy delivery systems that nanotechnology researchers have been working to develop for years, and the self-replicating nanobots we see in Star Trek and other science fiction seem to be nothing more than that—science fiction.[4] "Nanotechnology" has become less of a technological revolution and instead more of buzzword to create hype for otherwise mundane products that have little to do with actual

* Visiting Associate Professor, University of Maine School of Law, and Eastern Scholar, Shanghai University of Political Science and Law. Many thanks to Miriam Bitton, Bernard Chao, David Friedman, Deborah Halbert, Matthew David, Stuart Graham, Lital Helman, Peter Lee, Mark Lemley, John Golden, Lateef Mtima, Xuan-Thao Nguyen, Lucas Osborn, Laura Pedraza-Farina, Ted Sichelman, Ofer Tur-Sinai, and Greg Vetter; the Ono Academic College Faculty of Law, Kiryat Ono, Israel. This project was made possible in part by generous grants from The Program for Professors of Special Appointment (Eastern Scholars) at Shanghai Institutions of Higher Learning, and from the Shanghai University of Political Science and Law, to whom the author expresses her gratitude.

[1] Graham Reynolds, *Nanotechnology and the Tragedy of the Anticommons: Towards a Strict Utility Requirement*, 6 U. OTTAWA L. TECH. J. 79, 81 (2009).

[2] Requests for federal funding of nanotechnology research and development totaled almost two-billion dollars in fiscal year 2013 alone. JOHN C. MONICA, NANOTECHNOLOGY LAW § 2:116 (2014); *see also* Ted Sabety, *Nanotechnology Innovation and the Patent Thicket: Which IP Policies Promote Growth?*, 15 ALB. L.J. SCI. & TECH. 477, 504–05 (2005) (noting that venture capital investments are much smaller by comparison); Rachel Lorey Allen, *Venture Capital Investment in Nanotechnology*, JONES DAY, http://www.jonesday.com/practiceperspectives/nanotechnology/venture_capital.html [https://perma.cc/T4G3-R3VY] (last visited Nov. 16, 2016) (similar).

[3] Raj Bawa, *Nanotechnology Patent Proliferation and the Crisis at the U.S. Patent Office*, 17 ALB. L.J. SCI. & TECH. 699, 707 n.26 (2007); Mark A. Lemley, *Patenting Nanotechnology*, 58 STAN. L. REV. 601, 604, 604 n.14 (2005); Siva Vaidhyanathan, *Nanotechnologies and the Law of Patents: A Collision Course*, *in* NANOTECHNOLOGY: RISK, ETHICS AND LAW 225, 227 (Geoffrey Hunt & Michael Mehta eds., 2006).

[4] Lemley, *supra* note 3, at 602; MONICA, *supra* note 2, § 1:10; Douglas Sharrott & Sachin Gupta, *How to Cope with the Expiration of Early Nanotechnology Patents*, 8 NANOTECH. L. & BUS. 159, 160 (2011).

nanotechnological breakthroughs.[5] Any real nanotechnological shift in the way we manufacture goods and the materials we use seems to remain a distant future, stuck in a holding pattern as a perpetually *immature* field, an "emerging science," and a "new technology."[6] Why?

Professor Mark Lemley and a number of others have suggested that the answer to this puzzling question is simple: nanotechnology differs from all of the technologies that came before it.[7] As the first major new technological field after the Bayh-Dole Act[8] and other related statutes and changes to patentability standards,[9] nanotechnology has experienced an unprecedented boom in patenting, particularly on basic research and research tools. What is more, an unprecedented number of these patents are held by universities.[10] Patents on "upstream" research of this nature have the potential to obstruct "downstream" development of usable products and other applications.[11] Lemley and others argue that the Bayh-Dole Act, which now encourages recipients of government research funding to patent the resulting basic research, has caused an anticommons—or a thicket—of patents so dense and overwhelming that it is stunting nanotechnology development, a problem yet further exacerbated by nanotechnology's potentially cross-disciplinary nature.[12] Although patents are supposed to promote technological progress, Bayh-Dole has created simply *too many* patents in nanotechnology.

This Article shows that a "tragedy of the anticommons" characterization

---

[5] JOHN C. MILLER ET AL., THE HANDBOOK OF NANOTECHNOLOGY: BUSINESS, POLICY, AND INTELLECTUAL PROPERTY LAW 151–52 (2005); Jue Wang & Philip Shapira, *Partnering with Universities: A Good Choice for Nanotechnology Start-Up Firms?*, 38 SMALL BUS. ECON. 197, 203 (2012), http:/link.springer.com/article/10.1007/s11187-009-9248-9 [https://perma.cc/Z55S-ZLAF].

[6] *E.g.*, Zia Akhtar, *Nanotechnology: Meeting the Challenges of Innovation, Production, and Licensing*, 9 NANOTECH. L. & BUS. 133, 133–34 (2012); Frederick A. Fiedler & Glenn H. Reynolds, *Legal Problems of Nanotechnology: An Overview*, 3 S. CAL. INTERDISC. L.J. 593, 594–95 (1994); Lemley, *supra* note 3, at 605; Frank Murray et al., *Defense Drivers for Nanotechnology Commercialization: Technology, Case Studies, and Legal Issues*, 9 NANOTECH. L. & BUS. 4, 5 (2012). Most commentators agree that the field of nanotechnology has existed since at least the mid-1980s. *See, e.g.*, Francisco Castro, *Legal and Regulatory Concerns Facing Nanotechnology*, 4 CHI.-KENT J. INTELL. PROP. 140, 140 (2004) (citing nanotechnology's "formal existence" to the publication of K. ERIC DREXLER, ENGINES OF CREATION: THE COMING ERA OF NANOTECHNOLOGY (1st ed. 1986)); Reynolds, *supra* note 1, at 87 (same).

[7] Lemley, *supra* note 3, at 605–06.

[8] *See* 35 U.S.C. §§ 200–12 (2000) (incorporating the Bayh-Dole Act's provisions into the Patent Act).

[9] *See infra* text accompanying notes 60–68.

[10] Lemley, *supra* note 3, at 601, 605–06.

[11] *Cf.* Sabety, *supra* note 2, at 481 n.12 (describing "upstream" as "seminal breakthrough inventions" and "downstream" as "follow-on . . . innovations").

[12] Lemley, *supra* note 3, *passim*; *see also* Joel D'Silva, *Pools, Thickets and Open Source Nanotechnology*, 31 EUR. INTELL. PROP. REV. 300, *passim* (2009); Terry K. Tullis, Comment, *Application of the Government License Defense to Federally Funded Nanotechnology Research: The Case for a Limited Patent Compulsory Licensing Regime*, 53 U.C.L.A. L. REV. 279, *passim* (2005); Bawa, *supra* note 3, *passim*; Reynolds, *supra* note 1, at 81–85, 96–98.

of development in nanotechnology is too simple. Lemley is correct that nanotechnology development has been slow, but not for the reasons he suggests. In fact, for many, if not most, aspects of nanotechnology development, patents on university-based research are simply *irrelevant*. This Article shows that in nascent but complex fields like nanotechnology, technological and economic uncertainty, long development cycles, tacit knowledge, lack of funding, and even regulatory and safety issues are likely to be much more significant and rate-limiting than patents are. In this way, nanotechnology is not nearly as unique as Lemley suggests; nanotechnology's developmental difficulties are the same, well-known difficulties that other science-based technologies face. This is not to say that all nanotechnology patents are irrelevant or that an "anticommons" could never interfere in the development of nanotechnology applications. The point here is simply that patenting of basic research, whether by universities or any other entities, is not the problem. Those concerned about the lack of progress in nanotechnology would be better served to look at the multitude of other factors, such as lack of funding, limited access to expertise and materials, long development cycles, and public-safety concerns, that are well known to slow research-intensive fields such as nanotechnology and biotechnology.[13]

The following discussion examines the characteristics of science-based technologies and explains why patents likely play a minimal role, at least at this point, in nanotechnology development, particularly with regard to university patenting on upstream technology under the Bayh-Dole Act and its related statutes. Section I provides a general description of nanotechnology, its origins, and its potentially cross-disciplinary effect. Section II then briefly describes the concern, as put forth by Professor Lemley and other commentators, that high levels of university patenting on basic research has created and continues to create an anticommons that is stifling nanotechnology development. Section III provides a different story, however. First, as in biotechnology, anticommons in nanotechnology are probably more feared than real at this stage. Second, and more importantly, Section III shows why it is more likely that development of early-stage university research in nanotechnology is suffering not from problems caused by patenting under Bayh-Dole but from many of the same nonpatent problems that have always affected science-based technologies. This latter group of problems—including tacit knowledge,[14] the valley of death,[15] safety concerns,[16] and more[17]—are currently much larger obstacles than any

[13] *See infra* Section III.B.

[14] For a discussion of tacit knowledge, see *infra* Section III.B.4.

[15] For a discussion of the valley of death, see *infra* Section III.B.2.

[16] For a discussion of safety concerns, see *infra* Section III.B.6.

[17] *Infra* Section III.B.

that patents might pose at this point in nanotechnology's development.

I. NANOTECHNOLOGY: THE BASICS

Named after the nanometer, or one billionth of a meter,[18] nanotechnology is the study of the unique physical and chemical characteristics of matter at the sub-microscopic level.[19] At this scale, substances often display different physical and chemical properties because the high surface-area-to-volume ratio allows otherwise very weak quantum forces to dominate over other physical forces.[20] This difference causes the melting points, electrical conductivity, reflectivity, tensile strength, and magnetic and optical properties of matter to vary in surprising ways from their macroscopic forms.[21] By leveraging these differences, scientists have been able to create some amazing new materials. Researchers have now been successful in synthesizing miraculously light, yet strong materials, such as carbon nanotubes that are one-sixth the weight but one hundred times the strength of steel,[22] carbon fullerenes ("buckyballs") that can be used for targeted drug delivery to individual cells,[23] and semiconductor nanocrystals ("quantum dots") small enough to map DNA sequences.[24] Bar-coded nanowires can be used to create nanoscale sensors that can identify biowarfare pathogens at sensitivity levels never before seen.[25] The branched structure of dendrimers can be used as drug-release mechanisms that simultaneously monitor body vitals to regulate dosages.[26] Nanotechnology is expected to revolutionize a wide array of industries, including medicine,

---

[18] As a point of reference, a single helium atom is approximately one tenth of a nanometer in diameter, and a ribosome, a very small intracellular organelle, is approximately twenty nanometers in diameter. D'Silva, *supra* note 12, at 300.

[19] *Id.*; Bawa, *supra* note 3, at 704; Amit Makker, Note*, The Nanotechnology Patent Thicket and the Path to Commercialization*, 84 S. CAL. L. REV. 1163, 1164 (2011).

[20] SOCIETAL IMPLICATIONS OF NANOSCIENCE AND NANOTECHNOLOGY: NAT'L SCI. FDN. NSET WORKSHOP REPORT *passim* (Mihail C. Roco & William Sim Bainbridge eds., 2001) [hereinafter SOCIETAL IMPLICATIONS], http://www.wtec.org/loyola/nano/NSET.Societal.Implications/nanosi.pdf [https://perma.cc/4KKY-U3CK]; Bawa, *supra* note 3, at 705; Gunter Festel et al., *Importance and Best Practice of Early Stage Nanotechnology Investments*, 7 NANOTECH. L. & BUS. 50, 50 (2010); Siddarth Khanijou, *Patent Inequity?: Rethinking the Application of Strict Liability to Patent Law in the Nanotechnology Era*, 12 J. TECH. L. & POL'Y 179, 187 (2007).

[21] SOCIETAL IMPLICATIONS, *supra* note 20; Bawa, *supra* note 3, at 705; Festel et al., *supra* note 20, at 50; Khanijou, *supra* note 20, at 187.

[22] William J. Simmons, *Nanotechnology as a Nascent Technological Model for Immediate Substantive United States and Japan Patent Law Harmonization*, 17 ALB. L.J. SCI. & TECH. 753, 774 (2007).

[23] Behfar Bastani & Dennis Fernandez, *Intellectual Property Rights in Nanotechnology*, INTELL. PROP. TODAY 36, at text accompanying note 19 (Aug. 2002), http://www.iploft.com/Nanotechnology.pdf [https://perma.cc/MWB7-WVLU].

[24] David S. Almeling, Note, *Patenting Nanotechnology: Problems with the Utility Requirement*, 2004 STAN. TECH. L. REV. 1, P8 (2004).

[25] Murray et al., *supra* note 6, at 14.

[26] *Id.* at 15.

energy, textiles, and electronics, leading many to hail nanotechnology as "a key technology for economic development in the twenty-first century"[27] and to compare nanotechnology to the steam engine, transistor, and the Internet in its potential effect on society.[28]

Like many pioneering technologies, nanotechnology originated largely through basic research performed by government-funded universities and federal laboratories. Governments around the world have invested billions of dollars in nanotechnology research, with private industry and investors quickly following suit.[29] In the United States, for example, both federal and state government support for nanotechnology has expanded geometrically over the last two decades.[30] By 2001, Congress and President Clinton had established the National Nanotechnology Initiative (NNI) to promote and coordinate nanotechnology research among several federal agencies, including the Department of Defense, the Department of Energy, the National Institutes of Health, and the Department of Justice;[31] by 2017 the NNI's total investment in nanotechnology will exceed $24 billion.[32] Developed countries around the world have made similar investments in anticipation of the "next industrial revolution."[33]

The field continues to be very much in its infancy, however, and the value of nanotechnology innovations remains highly speculative.[34] Much of nanotechnology is still in the early research stages and has yet to be developed into marketable products.[35] According to the Project on Emerging

---

[27] Maryam Ahmadi & Leila Ahmadi, *Intellectual Property Rights of Bionanotechnology in Related International Documents*, 8 NANOTECH. L. & BUS. 289, 289 (2011).

[28] *E.g.*, Neal Lane & Thomas Kalil, *The National Nanotechnology Initiative: Present at the Creation*, 21 ISSUES IN SCI. & TECH. (2005), http://issues.org/21-4/lane/ [https://perma.cc/8YES-AJB4].

[29] Bawa, *supra* note 3, at 701.

[30] Simmons, *supra* note 22, at 775–76.

[31] Jordan Paradise, *Reassessing Safety for Nanotechnology Combination Products: What Do Biosimilars Add to Regulatory Challenges for the FDA?*, 56 ST. LOUIS L.J. 465, 474 (2012).

[32] NAT'L SCI. & TECH. COUNCIL COMM. ON TECH. & THE SUBCOMM. ON NANOSCALE SCI., ENG'G, & TECH., THE NATIONAL NANOTECHNOLOGY INITIATIVE: SUPPLEMENT TO THE PRESIDENT'S 2017 BUDGET 3 (Mar. 2016), https://www.whitehouse.gov/sites/default/files/microsites/ostp/nni_fy17_budget_supplement.pdf [https://perma.cc/2GXB-DXMK]. This author has been unable to find a reliable estimate of what proportion of the U.S. government's overall R&D spending is devoted to nanotechnology, however, because of the interdisciplinary nature of nanotechnology and the consequent difficulty of identifying nanotechnology funding separately from funding in other fields.

[33] *See* Allen, *supra* note 2 (noting China, South Korea, and the E.U.'s nanotechnology investments); Simmons, *supra* note 22, at 777–78 (noting Japan's multibillion dollar investments in nanotech); *see also* NAT'L SCI. & TECH. COUNCIL, COMM. ON TECH. & THE SUBCOMM. ON NANOSCALE SCI., ENG'G, & TECH., NATIONAL NANOTECHNOLOGY INITIATIVE: RESEARCH AND DEVELOPMENT SUPPORTING THE NEXT INDUSTRIAL REVOLUTION, SUPPLEMENT TO THE PRESIDENT'S 2004 BUDGET 1 (2003), http://www.nano.gov/sites/default/files/pub_resource/nni04_budget_supplement.pdf [https://perma.cc/U3KD-456H] (referring to nanotech as an "industrial revolution"). For more detail on private-industry investment in nanotechnology R&D, on the other hand, see *infra* text accompanying notes 257–62.

[34] Lane & Kalil, *supra* note 28.

[35] Lemley, *supra* note 3, at 604.

Nanotechnologies' survey, 1,628 consumer products on the market contained nanomaterials as of 2013,[36] and many products contain only small amounts of nanotechnology.[37] Most of these products represent incremental improvements to existing technologies, such as stain-resistant nanocoatings, high-tech tennis rackets, ski wax, and sunscreen.[38] Yet other products bear the "nano" name more to create buzz than to give an accurate description of the underlying product.[39] The radical new "disruptive" technologies that many expected nanotechnology to produce have yet to appear, however,[40] leading many to note that, despite the large sums of money invested in the field thus far, surprisingly few groundbreaking nanotechnology products have reached the market.[41] The lack of current commercial value notwithstanding, a surprisingly large number of patents on basic nanotechnology research have been filed by both universities and private firms. In fact, critics claim that very few of the nanotechnology inventions created thus far have not been patented; patents have issued on carbon nanotubes, quantum dots, nanowires, dendrimers, atomic-force microscopes, and many other basic tools and materials.[42]

At first glance, it is not surprising that everyone wants to get in early on the patent "gold rush" of the next major industrial revolution. Closer inspection reveals that basic research patents in nanotechnology are something of an oddity. Patents are popularly conceived of as a mechanism for incentivizing investment in technological research and development (R&D) by helping investors appropriate returns on their investments *ex post* by charging for access to the patented inventions.[43] Because the vast majority of nanotechnology research conducted thus far has been funded through the federal government,[44] patent protection would seem unnecessary; technologies that have been funded *ex ante* through

---

[36] *Inventory Finds Increase in Consumer Products Containing Nanoscale Materials*, PROJECT ON EMERGING NANOTECHNOLOGIES (Oct. 28, 2013), http://www.nanotechproject.org/news/archive/9242/ [https://perma.cc/2ZAP-UQHY].

[37] Josh Wolfe, *Blue Chips Stack Up on Nanotechnology*, FORBES (Oct. 24, 2005, 1:00 PM), http://www.forbes.com/2005/10/24/motorola-lucent-hp-nano-ppg-cz_jw_1024soapbox_inl.html.

[38] Akhtar, *supra* note 6, at 134; Andrew Wasson, *Protecting the Next Small Thing: Nanotechnology and the Reverse Doctrine of Equivalents*, 2004 DUKE L. & TECH. REV. 10, 10 (2004).

[39] MILLER ET AL., *supra* note 5, at 151–52.

[40] Allen, *supra* note 2.

[41] *E.g.*, Sean O'Neill et al., *Broad Claiming in Nanotechnology Patents: Is Litigation Inevitable?*, 4 NANOTECH. L. & BUS. 29, 31 (2007) (noting the lack of nanotechnology products in the marketplace); Lemley, *supra* note 3, at 604, 623 (stating that nanotechnology "has so far produced few actual products"); *see also* Dennis S. Karjala, *Protecting Innovation in Computer Software, Biotechnology, and Nanotechnology*, 16 VA. J.L. & TECH. 42, 46 (2011) (arguing that few nanotech products on the market truly represent the unique characteristics of nanotechnology).

[42] Lemley, *supra* note 3, at 613–14; Reynolds, *supra* note 1, at 86.

[43] Rebecca S. Eisenberg, *A Technology Policy Perspective on the NIH Gene Patenting Controversy*, 55 U. PITT. L. REV. 633, 648 (1994).

[44] Sabety, *supra* note 2, at 504–05.

government or other monies do not require the incentive of patent exclusivity.[45] Patenting on research already funded by the government also violates the "reward theory" of patenting, by which patents serve primarily to afford the opportunity to appropriate private returns on investments in invention and innovation.[46] Allowing patents on inventions that have been funded through government-collected taxpayer funds also effectively charges the public twice.[47]

Indeed, the type of research and development that governments are most likely to fund *ex ante* are exactly those that the prospect of patent exclusivity is unable to incentivize. Basic—or, "pure"—research, particularly in complex and unpredictable fields such as biotechnology and nanotechnology, is often thought to be too uncertain and distant in value to be attractive as investments to private firms.[48] Even when protected by patents, the expected value of such basic research will be less than its expected cost, and private firms will invest their resources in areas with more certain returns.[49] Because basic scientific and technological research has great public value, however, governments step in and use public funds to subsidize research that otherwise might never be funded.[50]

In the wake of the Bayh-Dole and the Stevenson-Wydler Acts, however, university patenting on government-funded and other research increased dramatically.[51] Levels of university patenting increased by more than eightfold between the late 1970s and the 1990s, with universities spending almost six times as much on patenting in 2004 as they did in 1991, and this upward trend continues to this day.[52] How much of this increase in

---

[45] Rebecca S. Eisenberg, *Public Research and Private Development: Patents and Technology Transfer in Government-Sponsored Research*, 82 VA. L. REV. 1663, 1666–67 (1996); Arti K. Rai & Rebecca S. Eisenberg, *The Public Domain: Bayh-Dole Reform and the Progress of Biomedicine*, 66 LAW & CONTEMP. PROB. 289, 300–01 (2003).

[46] Donald G. McFetridge & Douglas A. Smith, Comment, *Patents, Prospects and Economic Surplus: A Comment*, 23 J.L. & ECON. 197, 198 (1980).

[47] Eisenberg, *supra* note 45, at 1666; Michael S. Mireles, *Adoption of the Bayh-Dole Act in Developed Countries: Added Pressure for a Broad Research Exemption in the United States?*, 59 ME. L. REV. 259, 261 (2007); Jacob H. Rooksby, *University Initiation of Patent Infringement Litigation*, 10 J. MARSHALL REV. INTELL. PROP. L. 623, 631 (2011).

[48] Suzanne Scotchmer & Stephen M. Maurer, *Innovation Today: Private-Public Partnership*, *in* SUZANNE SCOTCHMER, INNOVATION AND INCENTIVES 227, 230 (2004); Eisenberg, *supra* note 45, at 1695–96.

[49] GEORGE S. FORD ET AL., PHOENIX CENTER FOR ADVANCED LEGAL & ECONOMIC PUBLIC POLICY STUDIES, A VALLEY OF DEATH IN THE INNOVATION SEQUENCE: AN ECONOMIC INVESTIGATION 11 (2007); Brett Frischmann, *Innovation and Institutions: Rethinking the Economics of U.S. Science and Technology Policy*, 24 VT. L. REV. 347, 352 (2000).

[50] Scotchmer & Maurer, *supra* note 48, at 244, 246.

[51] David E. Adelman, *A Fallacy of the Commons in Biotech Patent Policy*, 20 BERKELEY TECH. L.J. 985, 989 (2005); Mireles, *supra* note 47, at 264.

[52] ASS'N UNIV. TECH. MANAGERS, AUTM U.S. LICENSING SURVEY: FY 2014 (2016); Richard R. Nelson, *Observations on the Post-Bayh-Dole Rise of Patenting at American Universities*, 26 J. TECH.

university-based, upstream patenting is actually due to changes in the law is unclear. Much of the increase in university-centered biomedical research patenting occurred simultaneously with an increase in government funding for such research,[53] and the high proportion of university-owned patents that we see in nanotechnology may likewise be due to the fact that government funding continues to be one of the main drivers of research in the area.

Regardless of the reasons for the increase in university patenting of upstream research, however, a number of commentators have expressed grave doubts about the wisdom of such patenting patterns. Commentators like Professor Lemley and others argue that the large volume of upstream, university-owned patenting makes nanotechnology development uniquely ripe for anticommons and other holdup problems.[54] But are patents truly the problem? Or is development in a science-based technology like nanotechnology unavoidably slow for a variety of reasons that have little to do with patenting at this point in time? The following two sections address each of these explanations to show that upstream patents held by universities and other government funding recipients likely have little to do with the slow rate of nanotechnology development thus far.

II. LEMLEY'S STORY: THE TRAGEDY OF THE ANTICOMMONS

Lemley and other commentators on nanotechnology development argue that a combination of three patent-related factors have paradoxically slowed progress in nanotechnology. First, liberalization of both patentable subject matter restrictions and patentable utility standards in the 1980s and 1990s paved the way for patenting on technology much earlier in the research and development process.[55] Second, because nanotechnology is a uniquely cross-disciplinary field, the increase in upstream research patents may have a particularly broad effect on downstream development.[56] Third, enactment of the Bayh-Dole Act in 1980 encouraged patenting of government-funded research, resulting not only in a marked surge in upstream patenting but also a new class of patent holders that lack either the expertise or the orientation to license their patent effectively.[57] The combined effect of these three changes in patenting patterns is to create an anticommons, or overparcelization of patent rights, that inflates transaction costs and hinders

---

TRANSFER 13, 13 (2001); Kristen Osenga, *Rembrandts in the Research Lab: Why Universities Should Take a Lesson from Big Business to Increase Innovation*, 59 ME. L. REV. 407, 419 (2007).

[53] David C. Mowery & Arvids A. Ziedonis, *Academic Patents and Materials Transfer Agreements: Substitutes or Complements?*, 32 J. TECH. TRANSFER 157, 158 (2007). *But see* Eisenberg, *supra* note 45, at 1702–05 (questioning whether pre-Bayh-Dole government patents were actually underutilized).

[54] Lemley, *supra* note 3, at 620.

[55] *Id.* at 613.

[56] *Id.* at 614.

[57] *Id.* at 617.

downstream development.[58] And as the first major technological field to emerge since these changes, critics argue, nanotechnology development may now suffer from the same tragedy of the anticommons and other holdup problems that these changes may have caused in biotechnology as well.[59]

First, many commentators assert that nanotechnology has experienced a high level of patenting on upstream, basic research due to relaxation of both patentable subject matter and patentable utility standards, both of which occurred around the same time in the early 1980s.[60] According to the critics, changes in the patentability of both basic research and federally-funded research now allow universities to patent more of their nanotechnology research and to patent it earlier in the research process than ever before. For example, naturally occurring products, laws of nature, and abstract ideas have long been held to be unpatentable subject matter.[61] The Supreme Court's 1980 decision in *Diamond v. Chakrabarty*[62] is widely thought to have relaxed these restrictions, however, by lowering the bar for what can be deemed a patentable modification or "application" of a naturally occurring product or law of nature.[63] As a result, basic nanotechnology research on previously unrecognized characteristics of substances at the nanoscopic level have become more likely to be patentable with only minor modifications over the substances' naturally occurring forms.[64] Similar case law on the utility requirement, such as *In re Brana*,[65] in addition to revisions to the United States Patent and Trademark Office's (USPTO's) 1995 Utility Guidelines, also have loosened the utility requirements for so-called research tools or research intermediates.[66] As a result, much basic, upstream research has now become patentable even though it typically requires a good deal of further downstream investment and development to be incorporated

---

[58] *Id.* at 618.

[59] *See* Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698, 698 (1998) (discussing the tragedy of the anticommons in scientific research in biotechnology); Eisenberg, *supra* note 43, at 640 (same).

[60] *E.g.*, Lemley, *supra* note 3, at 613, 628; Simmons, *supra* note 22, at 783–85.

[61] Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980); *see also* Mark Williamson & James Carpenter, *Traversing Art Rejections in Nanotechnology Patent Applications—No Small Task*, 7 NANOTECH. L. & BUS. 131, 137–38 n.40 (2010) (citing cases).

[62] 447 U.S. at 303.

[63] *Id.* at at 309 (declining to hold genetically modified bacteria to be unpatentable subject matter simply because they are living organisms and because they derive from products of nature); Symposium, G. Nagesh Rao, Note, *Nanotechnology: A Look into the Future of Arising Legal Dilemmas*, 17 ALB. L.J. SCI. & TECH. 835, 848 (2007); Tullis, *supra* note 12, at 287.

[64] Simmons, *supra* note 22, at 785; Nicholas M. Zovko, Comment, *Nanotechnology and the Experimental Use Defense to Patent Infringement*, 37 MCGEORGE L. REV. 129, 141,141 n.130 (2006).

[65] 51 F.3d 1560, 1568 (Fed. Cir. 1995) (holding that patents do not have to reach FDA approval in order to meet the utility requirement).

[66] Utility Examination Guidelines, 60 Fed. Reg. 36, 263 (July 14, 1995).

into usable end products with real-world utility.[67] The creation of the United States Court of Appeals for Federal Circuit in 1982 and its perceived pro-patent stance are alleged to have softened the various patentability requirements, further intensifying upstream patenting in new fields such as nanotechnology.[68]

The overall effect of these and other changes in the patent system has led to early-stage research patents on "incomplete" inventions that have little in the way of immediate application. By patenting incomplete inventions, researchers leave much of the development work to others while reserving to themselves the ability to charge downstream royalties or licensing fees, effectively allowing upstream patentees to extract rents from downstream developers. To make matters worse, the boundaries of upstream research patents are also thought to be more vague. Because upstream research itself tends to be more conceptual and abstract, it has the potential to cover broad ranges of downstream developments, further enhancing its preemptive effects.[69]

In a related vein, many commentators complain that nanotechnology suffers from not only greater upstream patenting but also poorer patent quality.[70] In addition to common criticisms about the USPTO's high application backlog, high examiner turnover rates, and so on,[71] any new field such as nanotechnology presents obvious difficulties for the USPTO. New technologies, particularly complex ones like nanotechnology, pose steep learning curves for USPTO examiners, few of whom will have the necessary expertise for evaluating nanotechnology patent applications.[72] New technologies obviously also lack the kind of robust prior art that exists in more established fields, making it more challenging to identify inventions that fail to meet the novelty or nonobviousness requirements.[73] The fact that many nanotechnological details are easily maintained as trade secrets means that patenting likely does not reflect the total level of nanotechnology innovation and, more importantly, does not adequately reflect the existing

---

[67] David E. Adelman & Kathryn L. DeAngelis, *Patent Metrics: The Mismeasure of Innovation in the Biotech Patent Debate*, 85 TEX. L. REV. 1677, 1689–90 (2007); Reynolds, *supra* note 1, at 105.

[68] *E.g.*, Sabety, *supra* note 2, at 488 n.47; *see also* Dov Greenbaum, *Academia to Industry Technology Transfer: An Alternative to the Bayh-Dole System for Both Developed and Developing Nations*, 19 FORDHAM INTELL. PROP. MEDIA & ENT. L.J. 311, 349 (2009) (noting that the Federal Circuit has been "largely perceived as propatent").

[69] Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839, 884 (1990); Arti K. Rai, *Fostering Cumulative Innovation in the Biopharmaceutical Industry: The Role of Patents and Antitrust*, 16 Berkeley Tech. L.J. 813, 839–40 (2001).

[70] *E.g.*, Bawa, *supra* note 3, at 717–18.

[71] *Id.* at 724–27.

[72] Carl Shapiro, *Navigating the Patent Thicket: Cross Licenses, Patent Pools, and Standard Setting*, 1 INNOVATION POL'Y & ECON. 119, 121 (2001); Heller & Eisenberg, *supra* note 59, at 699.

[73] Akhtar, *supra* note 6, at 138; Bawa, *supra* note 3, at 707–09.

level of applicable prior art in the field.[74]

Moreover, even standardizing terminology can present challenges for new technologies. The USPTO did not have a separate nanotech classification until 2004, when it first established Class 977 for patent applications in this field, and even then, the 977 category includes only inventions that exploit those phenomena occurring at one hundred nanometers or less.[75] Because experts in nanotechnology argue that characteristics occurring at up to three hundred nanometers in size should also qualify as nanotechnology for regulatory purposes,[76] 977's current parameters may be too narrow to include all relevant nanotechnology applications and prior art, particularly with regard to nanomedicine and nanobiotechnology, which often lie outside of 977's one hundred nanometer size limit.[77] And with high patenting levels and steep learning curves come inevitable delays in examining and issuing patents; the backlog of nanotech patent applications and their average pendency have both increased over the years.[78] The uncertainty caused by long patent pendencies can deter downstream developers from entering a field for fear of infringing yet-unissued patents.[79]

A second fact that concerns many commentators is nanotechnology's cross-disciplinary nature, a characteristic that may be unique to nanotechnology. Nanotechnology is unusual in that it is defined solely by size;[80] the exact size limits on what constitutes nanotechnology are in dispute,[81] but any phenomenon that occurs at the nanoscopic level could be argued to qualify as nanotechnology. Given the breadth of this definition, nanotechnology has the potential to revolutionize any number of fields, including biotechnology, electronics, energy, medicine, and materials sciences.[82] Nanotech is thus more size-specific than discipline-specific, which creates some additional issues not seen in most fields. Relevant prior

---

[74] Lemley, *supra* note 3, at 617.

[75] U.S. PATENT & TRADEMARK OFFICE, CLASS 977 NANOTECHNOLOGY CROSS-REFERENCE ART COLLECTION, http://www.uspto.gov/patents/resources/classification/class_977_nanotechnology_cross-ref_art_collection.jsp [https://perma.cc/SBQ3-G7RE] (last visited Nov. 16, 2016); *see also* Bawa, *supra* note 3, at 706–07 (discussing the USPTO's decision to establish the Class 977 category).

[76] *E.g.*, FRIENDS OF THE EARTH, OUT OF THE LABORATORY AND ON TO OUR PLATES: NANOTECHNOLOGY IN FOOD & AGRICULTURE 3 (2008), http://www.foe.org/system/storage/877/b5/4/547/Nanotechnology_in_food_and_agriculture_-_web_resolution.pdf [https://perma.cc/2ZY2-W2U2]; Policy Memorandum from Miles V. McEvoy, Deputy Adm'r, U.S. Dep't of Agric., to Stakeholders & Other Interested Parties 1 (Mar. 24, 2015), https://www.ams.usda.gov/sites/default/files/media/NOP-PM-15-2-Nanotechnology.pdf [https://perma.cc/87N8-W8ES].

[77] Bawa, *supra* note 3, at 707.

[78] Raj Bawa, *Patents and Nanomedicine*, 2 NANOMEDICINE 351, 358 (2007).

[79] Heller & Eisenberg, *supra* note 59, at 699; Shapiro, *supra* note 72, at 121.

[80] Bawa, *supra* note 3, at 704.

[81] *Id.*

[82] Lemley, *supra* note 3, at 614.

art becomes more difficult to identify and the appropriate skill level by which to measure patentability becomes more difficult to define.[83] More importantly, nanotechnology's cross-disciplinarity multiplies its potential applications, giving patents in nanotechnology unusually broad effects in many different areas of development.[84] Those who work in downstream nanotech development may need to negotiate licensing from patent holders outside of their own fields and often may be caught infringing patents from fields well outside of what they might reasonably have been expected to review.[85]

The third factor on which Professor Lemley and others predicate their nanotechnology anticommons argument is the Bayh-Dole Act.[86] Before Bayh-Dole took effect, universities and other government-funding recipients had frequently been unable to patent their research, as government agencies sometimes would not allow retention of intellectual property rights on research funded through government grants.[87] The Bayh-Dole Act specifically changed these policies, not only to allow patenting but in fact to promote patent ownership by the recipients of federal funds. Specifically, the Bayh-Dole Act (formally, the Patent and Trademark Law Amendments Act of 1980) set a policy for all federal agencies funding technological research to encourage small businesses and nonprofit organizations such as universities to retain title to their research by filing for patents on it.[88] The somewhat controversial justification for this change was to address the perceived underutilization of government-funded research and to attract private investment in developing and commercializing such research.[89] The post-Bayh-Dole era saw a marked increase in patenting on government-funded research in not only nanotechnology but also other research fields, particularly biotechnology.[90]

One particular twist that Bayh-Dole adds to the mix, moreover, is the concomitant growth in universities as patentees. Bayh-Dole has increased university patenting by about sixteen fold,[91] with estimates putting

---

[83] Williamson & Carpenter, *supra* note 61, at 139–40.

[84] Lemley, *supra* note 3, at 614–15.

[85] *Id.*

[86] Adelman, *supra* note 51, at 989.

[87] Sabety, *supra* note 2, at 484–85.

[88] 35 U.S.C. § 202 (2012); *see* Eisenberg, *supra* note 45; Peter Lee, *Transcending the Tacit Dimension: Patents, Relationships, and Organizational Integration in Technology Transfer*, 100 CALIF. L. REV. 1503 (2012); Mireles, *supra* note 47, at 260.

[89] Wei-Lin Wang, *A Critical Study on the Cooperative Research and Development Agreements of U.S. Federal Laboratories: Technology Commercialization and the Public Interest*, 9 NANOTECH. L. & BUS. 50, 53 (2012); Eisenberg, *supra* note 45, at 1669, 1680–82; Sabety, *supra* note 2, at 487–88.

[90] David C. Mowery, *The Bayh-Dole Act and High Technology Entrepreneurship in U.S. Universities: Chicken, Egg, or Something Else?*, *in* 16 ADVANCES IN THE STUDY OF ENTREPRENEURSHIP, INNOVATION & ECONOMIC GROWTH: UNIVERSITY ENTREPRENEURSHIP AND TECHNOLOGY TRANSFER 39, 51 (Gary D. Libecap ed., 2005).

[91] Bawa, *supra* note 3, at 722, 733–34; Lemley, *supra* note 3, at 615–16.

university patenting at about 12% of all nanotechnology patenting and 20.2% of all biomedical nanotech patenting, levels far exceeding university patenting of approximately 1% in other technologies.[92] Universities do not and cannot further commercialize their own research, however, and this uncoupling between invention and commercialization means that universities and private industry must incur the costs of finding and transacting with one another in order for research to be developed into usable end products.[93]

As a result, patent-licensing negotiations after Bayh-Dole now more frequently involve unwonted partners in the form of academically oriented universities transacting with commercially oriented firms. The transactions necessary to develop research-based technologies have become not only more numerous—because patents now exist where they had not before—but also more complicated, because private industry must now negotiate with universities in ways that they had not before. Universities are still disinclined to view themselves as commercial entities, moreover,[94] and even university technology transfer offices (TTOs) do not have the market-based approaches that private commercial entities do.[95] Almost thirty-five years after Bayh-Dole was enacted, universities are still unaccustomed to the commercial world and lack the experience and expertise necessary for patent licensing.[96] Universities also have very different internal authority structures than do more commercial laboratories, and universities serve multiple different constituencies whose often differing goals and agendas often prolong licensing negotiations.[97]

According to Professor Lemley and other critics, the combination of lowered patentability standards, cross-disciplinarity, and increases in university patenting created a perfect storm of nanotechnology patents that

---

[92] Lemley, *supra* note 3, at 615–16; Murray et al., *supra* note 6, at 31.

[93] David Blumenthal et al., *Relationships Between Academic Institutions and Industry in the Life Sciences–An Industry Survey*, 334 NEW ENG. J. MED. 368, 370 (1996); Osenga, *supra* note 52, at 421.

[94] Osenga, *supra* note 52, at 421.

[95] *See* Riccardo Fini & Nicola Lacetera, *Different Yokes for Different Folks: Individual Preferences, Institutional Logics, and the Commercialization of Academic Research*, *in* 21 ADVANCES IN THE STUDY OF ENTREPRENEURSHIP, INNOVATION AND ECONOMIC GROWTH: SPANNING BOUNDARIES AND DISCIPLINES: UNIVERSITY TECHNOLOGY COMMERCIALIZATION IN THE IDEA AGE 1, *passim* (2010); Nicholas S. Argyres & Julia Porter Liebeskind, *Privatizing the Intellectual Commons: Universities and the Commercialization of Biotechnology*, 35 J. ECON. BEHAV. & ORG. 427, 444 (1998).

[96] Celestine Chukumba & Richard Jensen, *University, Invention, Entrepreneurship, and Start-Ups* 13, 18–19 (Nat'l Bureau of Econ. Research, Working Paper No. 11475, 2005), http://www.nber.org/papers/w11475 [https://perma.cc/Q4NX-298Y]; Lay Leng Tan, *Generating Dollars from Nanotechnology*, INNOVATION: THE SING. MAG. OF RES., TECH. & EDUC., http://www.innovationmagazine.com/innovation/volumes/v4n3/features4 [https://perma.cc/GVY2-L3YS] (last visited Nov. 16, 2016); Interview with Marie Kerbeshian, Vice President of Tech. Commercialization, Ind. U. Research & Tech. Corp. (Mar. 5, 2015).

[97] Richard Jensen & Marie Thursby, *Proofs and Prototypes for Sale: The Licensing of University Inventions*, 91 AMER. ECON. REV. 240, 244 (2001); Interview with Kerbeshian, *supra* note 96; *see also* Blumenthal et al., *supra* note 93, at 370 (reporting university bureaucracy and regulations as the most frequent obstacle to life science companies forming research relationships with universities).

are not just numerous but also broad, overlapping, and fragmented in ownership.[98] Extrapolating from Michael Heller and Rebecca Eisenberg's famous article on the tragedy of the anticommons in biomedical research, Lemley posits that the explosion of university-owned upstream research patents poses an even greater risk of an anticommons in nanotechnology as well.[99] Anticommons and other holdup problems occur when rights to a particular piece of property are distributed among too many owners, resulting in decreased use of those property rights because of the difficulties of bringing all the rights holders to agreement on how to use their collective property.[100] In the case of technology, "overparcelization" of patent property rights may similarly cause underdevelopment of a given technology.[101] In some cases, a patent may cover a component used only in combination with one or more complementary components that themselves may be subject to separate patent rights, requiring horizontal patent coordination to be used in a productive way.[102] In other cases upstream and downstream patent rights cover "cumulative" technologies, in which separate patented technologies must be vertically coordinated in order to create a single product or process.[103] The need for horizontal or vertical patent coordination could be particularly likely in nanotechnology given that so many basic nanotechnology tools and nanomaterials have been patented.[104] Another source of holdup problems are patent thickets, in which patent rights are particularly dense because patents overlap with one another in scope.[105] This latter type of holdup problem is also thought to pose a particular risk to nanotechnology development, where large numbers of potentially overlapping patents cover multiple aspects and versions of materials like carbon nanotubes and semiconducting nanocrystals.[106] Because patents on upstream nanotechnology already number in the thousands, with the rate of

---

[98] Reynolds, *supra* note 1, at 83 (citing *Nanotechnology Gold Rush Yields Crowded, Entangled Patents*, LUX RESEARCH INC. (Apr. 21, 2005), http://www.prnewswire.com/news-releases/nanotechnology-gold-rush-yields-crowded-entangled-patents-54373177.html [https://perma.cc/G8CL-GZ6W].

[99] *Id.* at 97.

[100] Heller & Eisenberg, *supra* note 59, at 698.

[101] *Id*.

[102] Mark A. Lemley, *The Myth of the Sole Inventor*, 110 MICH. L. REV. 709, 740 (2012); *see also* Michael Mattioli, *Communities of Innovation*, 106 NW. U.L. REV. 103, 113–14 (2012) (discussing AUGUSTIN COURNOT, RESEARCHES INTO THE MATHEMATICAL PRINCIPLES OF THE THEORY OF WEALTH 103–04 (Nathaniel T. Bacon trans., Augustus. M. Kelley ed., 1971) (1838)). These types of complementary technologies are sometimes referred to as Cournot complements. Mattioli, *supra*, at 123.

[103] Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law*, 89 VA. L. REV. 1575, 1612–13 (2003); Richard R. Nelson, *The Market Economy, and the Scientific Commons*, 33 RES. POL'Y 455, 464 (2004); Shapiro, *supra* note 72, at 123.

[104] Lemley, *supra* note 3, at 613–14; Reynolds, *supra* note 1, at 86.

[105] Shapiro, *supra* note 72, at 119–20. *But see* Burk & Lemley, *supra* note 103, at 1627 (distinguishing patent thickets as occurring from the need to integrate multiple overlapping intellectual property rights and patent anticommons as occurring from the need to integrate multiple inputs, including intellectual property rights).

[106] D'Silva, *supra* note 12, at 301–02; Lemley, *supra* note 3, at 618.

new patent applications accelerating over time, the risk of underuse and obstruction due to anticommons or other hold ups could just grow worse.

In a Coasean world of zero transaction costs,[107] however, even highly balkanized patent rights could be easily overcome through bargaining and exchange. Where parcelized patent rights are owned by the same entity in a patent portfolio, for example, holdup problems are unlikely to occur. When patent rights are distributed among multiple owners, however, transaction costs become an issue, particularly when conflicting interests, rent-seeking, strategic behavior, and cognitive biases frustrate agreement to use the patents jointly.[108] University ownership of patents as well as the potentially cross-disciplinary relevance of those patents make transaction costs an even greater concern in nanotech.

Again, university TTOs have different interests, expertise levels, and governance structures than do the private industry actors with whom they might negotiate licenses, a factor that can significantly exacerbate transaction costs. Horizontal competitors with similar values and interests will find it easier to come to formal or informal agreements, particularly if repeated over time.[109] Similarly situated private firms with patent portfolios of similar value, for example, may face little difficulty in cross licensing their portfolios. Universities obviously have very different interests and incentives than private industry, however, and agreeing on terms for licensing university patents is often a long and laborious process. These types of conflicts are what this author has previously termed "qualitative," as opposed to a "quantitative" anticommons, in which, regardless of the number of rights holders, the heterogeneity of transacting parties and the divergence of their respective interests and incentives can multiply transaction costs.[110]

Differences of opinion may hinder patent licensing in other ways as well. Rights holders may attempt to hold out for a disproportionate share of any joint rents, for example, knowing that their contribution is essential to the success of the project.[111] Universities in particular tend to overestimate the value of their contributions to downstream development, as the academic mindset typically places greater value on research than on commercialization.[112] Universities frequently demand reach-through

---

[107] Reynolds, *supra* note 1, at 84.

[108] Heller & Eisenberg, *supra* note 59, at 698.

[109] *See* Lemley, *supra* note 3, at 622.

[110] Mark D. West & Emily M. Morris, *The Tragedy of the Condominiums: Legal Responses to Collective Action Problems After the Kobe Earthquake*, 51 AM. J. COMP. L. 903, 928 n.69 (2003); *see also* Henry E. Smith, *Intellectual Property as Property: Delineating Entitlements in Information*, 116 YALE L.J. 1742, 1776 (2007) (noting heterogeneity of interests increases transaction costs); Heller & Eisenberg, *supra* note 59, at 698 (same); MILLER ET AL., *supra* note 5, at 76 (same).

[111] Burk & Lemley, *supra* note 103, at 1611–12.

[112] Heller & Eisenberg, *supra* note 59, at 701. Unlike so-called patent trolls, however, universities are unlikely to try to extort rents from unwitting infringers. *See* Mark A. Lemley, *Are Universities Patent*

licenses to downstream products as well, allowing them to extract an even greater share of any returns from commercialization.[113]

The cross-industry applicability of basic nanotech inventions and research also allows universities and other upstream patent holders to exert unusually broad influence over downstream development in a wide number of fields. Universities and even private industry may be able to influence nanotechnology development not only in their own industries but also in other industries as well. The cross-industry applicability of nanotech patents thus raises the risk of both qualitative and quantitative anticommons, as the number of parties needing to license nanotech patents, as well as the number of nanotech patents themselves, increase with the number of industries affected.[114]

Simply having to pay licensing fees or royalties for one or more "upstream" patents reduces incentives to invest in downstream development,[115] and the more patents that must be licensed, the more that royalties must be stacked, and the more that incentives to invest in development are reduced.[116] And where invention costs are low, such as when invention costs are subsidized by the government, patents serve not so much to spur technological development as to deter it.[117] In these circumstances, a fully competitive environment at the margins—i.e., one without patent protections—would better foster downstream development.[118] Releasing government-funded university research into the public domain, for example, would permit interested firms free access to the research to commercialize it.[119] For many technologies competition is more effective than monopoly in spurring development; inventive concepts are nonrivalrous, allowing every interested firm to try their hands at developing downstream applications.[120]

Some of the concerns about nanotech patents have been tempered already, however. For example, some critics suggest tightening the utility and patentable subject matter standards to restrict patenting of upstream research largely in reaction to the flood of biotechnology research patent

---

Trolls?, 18 FORDHAM INTELL. PROP. MEDIA & ENT. L.J. 611, 629 (2008).

[113] A PATENT SYSTEM FOR THE 21ST CENTURY 71 (Stephen A. Merrill et al. eds., 2004) [hereinafter A PATENT SYSTEM]; Heller & Eisenberg, *supra* note 59, at 699; Osenga, *supra* note 52, at 427.

[114] *Cf.* Mattioli, *supra* note 102, at 113–14 (discussing Cournot's theory that the more rights that have to be licensed, the greater the cost as compared to rights ownership by single entity).

[115] Michael J. Meurer, *Business Method Patents and Patent Floods*, 8 WASH. U.J.L. & POL'Y 309, 323 (2002).

[116] Mark A. Lemley & Carl Shapiro, *Patent Holdup and Royalty Stacking*, 85 TEX. L. REV. 1991, 2012 (2007); Michael S. Mireles, *An Examination of Patents, Licensing, Research Tools, and the Tragedy of the Anticommons in Biotechnology Innovation*, 38 U. MICH. J.L. REFORM 141, 170 (2004).

[117] Burk & Lemley, *supra* note 103, at 1620–24.

[118] Merges & Nelson, *supra* note 59, at 843–44.

[119] Eisenberg, *supra* note 45, at 1702, 1710–11.

[120] Burk & Lemley, *supra* note 103, at 1604–08 (and sources cited therein); Merges & Nelson, *supra* note 69, at 843–44.

applications.[121] The Supreme Court's recent decisions in *AMP v. Myriad*[122] and *Mayo v. Prometheus*[123] have done exactly that, increasing the likelihood that "discoveries" of naturally occurring materials or principles will be found unpatentable.[124] The courts and the USPTO similarly have tightened the utility requirement to require "specific, substantial, and credible utility" as more than just an object of further research.[125] Moreover, the patent system now also limits patentability by interpreting many patents in new technologies rather narrowly through both the enablement requirement and the written description requirement, the latter of which also is most often applied to narrow university-held biotechnology patents.[126] And regardless, those who advocate for tightening patentability standards acknowledge that more stringent requirements will not completely solve any anticommons problem in nanotechnology, nor will it eliminate upstream research patenting.[127]

Moreover, tightening patentability standards does little to address the other issues that may predispose nanotechnology and other fields to holdup problems with the increase in university patenting under Bayh-Dole. Commentators have therefore proposed various mechanisms to diminish the risk of anticommons and other obstacles. Some of these proposals, such as resurrecting an experimental-use exception in patent law[128] and resurrecting

---

[121] *E.g.*, Reynolds, *supra* note 1, at 101–12 (arguing for adoption of a stricter utility requirement).

[122] Ass'n Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107 (2013).

[123] Mayo Collaborative Servs. v. Prometheus Labs., 132 S. Ct. 1289 (2012).

[124] *See Ass'n Molecular Pathology*, 133 S. Ct. at 2109–11 (holding isolated DNA sequences to be unpatentable products of nature); *Mayo Collaborative Servs.*, 132 S. Ct. at 1290–91 (holding dosing method based on blood metabolite levels to be an unpatentable law of nature).

[125] Heightened utility standards were first promulgated in an interim form in 1999 and later finalized in 2001. Utility Examination Guidelines, 66 Fed. Reg. 1,092 (Jan. 5, 2001); Revised Utility Examination Guidelines, Request for Comments, 64 Fed. Reg. 71,440 (Dec. 21, 1999); *see also In re* Fisher, 421 F.3d 1365 (Fed. Cir. 2005) (adopting the 2001 Utility Examination Guidelines); Adelman & DeAngelis, *supra* note 67, at 1687–90 (noting that the number of biotech applications granted have decreased due to the USPTO's tightened utility requirement in its 1999 Guidelines, among other factors); Rai, *supra* note 69, at 840 (characterizing the new standards as "a more balanced position").

[126] Dan L. Burk & Mark A. Lemley, *Biotechnology's Uncertainty Principle*, 54 CASE W. RES. L. REV. 691, 695–700 (2004); Burk & Lemley, *supra* note 103, at 1653–54; Rai, *supra* note 69, at 840–41.

[127] *See, e.g.*, Reynolds, *supra* note 1, at 84. For more detailed discussion of patentability requirements and upstream university patenting under the Bayh-Dole Act, see Emily M. Morris, *The Many Faces of Bayh-Dole*, 54 DUQ. L. REV. 81, 117–18 (2016).

[128] *E.g.*, Rochelle Dreyfuss, *Protecting the Public Domain of Science: Has the Time for an Experimental Use Defense Arrived?*, 46 ARIZ. L. REV. 457, 470 (2004); Janice M. Mueller, *No "Dilettante Affair": Rethinking the Experimental Use Exception to Patent Infringement for Biomedical Research Tools*, 76 WASH. L. REV. 1, 5, 9–10, 17 (2001) [hereinafter Mueller, *Dilettante*]; Mireles, *supra* note 47, at 276–77; *see also* Maureen A. O'Rourke, *Toward a Doctrine of Fair Use in Patent Law*, 100 COLUM. L. REV. 1177, 1180–81, 1191, 1198, 1205 n.118 (2000) (proposing import into patent law of fair-use type of exemption similar to that in copyright law under 17 U.S.C. § 107 (2000)). Patent law in the U.S. has, in modern times, reduced its experimental-use exception into near nonexistence. *See* Madey v. Duke Univ., 307 F.3d 1351, 1362 (Fed. Cir. 2002) (concluding that no experimental-use exemption applies where research is the "legitimate business" of the alleged infringer); Janice M. Mueller, *The*

the reverse doctrine of equivalents,[129] are designed to reduce transaction costs by removing the need to license upstream patents. Other proposals, such as less frequent injunctive relief,[130] more accurate apportionment of damages,[131] and limitations on treble damages for willful infringement,[132] seek to lessen the effect of royalty stacking by limiting infringement remedies. A third proposal, specific to Bayh-Dole, calls for the use of a funding agency's "march-in" rights under the Act to grant, under certain circumstances, what are effectively compulsory licenses that allow third parties greater access to patented technologies.[133] A similar proposal calls for government agencies to invoke their rights under the Act to disallow retention of patent rights by funding recipients in "exceptional circumstances" where it "will better promote the policy and objectives" of Bayh-Dole.[134] Finally, private ordering may also help reduce transaction

---

Evanescent Experimental Use Exemption from United States Patent Infringement Liability: Implications for University and Nonprofit Research and Development, 56 BAYLOR L. REV. 917, 918 (2004); Katherine J. Strandburg, *What Does the Public Get? Experimental Use and the Patent Bargain*, 2004 WIS. L. REV. 81, 99 (2004); Peter Lee, Note, *Patents Paradigm Shifts, and Progress in Biomedical Science*, 114 YALE L.J. 659, 683–84 (2004). The only substantial experimental-use exception that currently exists in patent law is the statutory exception limited to uses "reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products." 35 U.S.C. § 271(e)(1) (2012).

[129] *E.g.*, Burk & Lemley, *supra* note 103, at 1657–58; Dreyfuss, *supra* note 128, at 469. The reverse doctrine of equivalents is an equitable doctrine that states that, even if an accused device falls within the literal meaning of a patent claim, no infringement liability will be found if the accused device "so far changed in principle from a patented article that it performs the same or a similar function in a substantially different way." Scripps Clinic & Research Found. v. Genentech, Inc., 927 F.2d 1565, 1581 (Fed. Cir. 1991) (internal quotation marks omitted) (quoting Graver Tank & Mfg. Co. v. Linde Air Prod. Co., 339 U.S. 605, 607, 608 (1950)).

[130] *E.g.*, Peter Lee, *The Evolution of Intellectual Infrastructure,* 83 WASH. L. REV. 39, 102–20 (2008); Mark A. Lemley, *Ten Things to Do About Patent Holdup of Standards (And One Not To)*, 48 B.C. L. REV. 149, 161, 166–67 (2007); Burk & Lemley, *supra* note 103, at 1665–68. *But see* F. Scott Kieff, *Property Rights and Property Rules for Commercializing Inventions*, 85 MINN. L. REV. 697, 732–36 (2001) (advocating for continued use of injunctive relief).

[131] *E.g.*, Lemley, *supra* note 130, at 165–66.

[132] *See, e.g.*, Katherine J. Strandburg, *Curiosity-Driven Research and University Technology Transfer*, *in* 16 UNIVERSITY ENTREPRENEURSHIP AND TECHNOLOGY TRANSFER: PROCESS, DESIGN, AND INTELLECTUAL PROPERTY 93, 113 (Gary D. Libecap ed., 2005); A PATENT SYSTEM, *supra* note 113, at 108–09; Lemley, *supra* note 130, at 164–65; Lemley, *supra* note 3, at 630; *see also* Mireles, *supra* note 47, at 261 (discussing more robust research exemptions in the EU and Japan).

[133] Specifically, a funding government agency may force a funding recipient to grant nonexclusive or exclusive license to another under four circumstances: where the patentee is not expected to achieve "practical application" of the patented invention within "reasonable time;" where necessary to address health and safety needs; where necessary to meet requirements for public use specified under federal law; or to make sure that any manufacturing is substantially domestic. 35 U.S.C. § 203 (a)(1)–(4) (2012); Peter S. Arno & Michael H. Davis, *Why Don't We Enforce Existing Drug Price Controls? The Unrecognized and Unenforced Reasonable Pricing Requirements Imposed upon Patents Deriving in Whole or in Part from Federally Funded Research*, 75 TUL. L. REV. 631, 647 n.93, 648 (2001); Rai & Eisenberg, *supra* note 45, at 294.

[134] *See e.g.*, Rai & Eisenberg, *supra* note 45, at 293, 303, 310 (discussing 35 U.S.C. § 202 (a)(i)–(ii)); *see also* Tullis, *supra* note 12, at 306 (discussing possibility of compulsory licensing under agencies'

costs. Universities can join with other patent holders to form patent portfolios, patent pools, open-source pools, collective-rights organizations, or research and development consortia, all of which can simplify the process of gaining access to relevant patents.[135]

In the end, however, all of these proposals to fix patent holdup problems in nanotechnology matter little if the seemingly slow development is not due to patenting, as a closer look at the technology strongly suggests. The next Section explores this possibility in more detail.

III. THE STORY OF SCIENCE-BASED TECHNOLOGIES: THE IRRELEVANCE OF PATENTS

Contrary to Professor Lemley's assertion, nanotechnology may not be so different from other technologies that have also been affected by the Bayh-Dole Act. Many of the concerns voiced about nanotechnology patents are the same concerns that have been voiced about patents in other fields of university research. Patent floods, for example, have been seen in other new technologies such as molecular biology, superconductors, and petroleum refining, where scientific breakthroughs suddenly spur a rush of new opportunities.[136] Patent floods, in turn, often breed poor patent quality, as the sheer volume of new patent applications strains the USPTO's resources and low-quality and overlapping patents may lead to patent thickets.[137] Indeed, patent thickets have been cropping up since long before the Bayh-Dole Act and the recent expansion of upstream research patenting by universities; thickets were a well-recognized issue in the sewing machine war of the 1850s and in conflicts over airplane patents in the early 1900s, for example.[138] More recently, biotech has seen similar complaints about overly broad patenting, poor patent quality, unpatentable subject matter, and high

---

§ 202(c)(4) right to "nonexclusive, nontransferable, irrevocable, paid-up license to practice or have practiced for or on behalf of the United States any subject invention") (citations omitted).

[135] *See* Peter Lee, *Contracting to Preserve Open Science: Consideration-Based Regulation in Patent Law*, 58 EMORY L.J. 889, 915–16 (2009) (giving examples of patent pools and open-source software); Robert P. Merges, *Contracting into Liability Rules: Intellectual Property Rights and Collective Rights Organizations*, 84 CAL. L. REV. 1293, 1298 (1996) (suggesting that the law should allow "private collective rights organizations" to develop); Shapiro, *supra* note 72, at 119 ("Cross licenses and patent pools are two natural and effective methods used by market participants to cut through the patent thicket . . . ."); Lemley, *supra* note 3, at 623–27 (arguing that open licensing may be the solution to patent floods); Rai, *supra* note 69, at 845–46 ("[P]roperly designed cross-licensing and patent pooling arrangements can promote innovation markets.").

[136] Merges & Nelson, *supra* note 69, at 907–08; Meurer, *supra* note 115, at 319, 324–25.

[137] Meurer, *supra* note 115, at 323–24; *see also* Adelman & DeAngelis *supra* note 67, at 1710–11 (noting backlog of patent applications in complex technologies such as biotechnology).

[138] Adam Mossoff, *The Rise and Fall of the First American Patent Thicket: The Sewing Machine War of the 1850s*, 53 Ariz. L. Rev. 165, *passim* (2011).

patent clearance costs.[139]

In these and other ways, nanotech appears to be fairly typical of science-based technologies, as this Section explains.[140] There is therefore good reason to believe that at least some of future downstream nanotech development will follow in the footsteps of biotech development, where upstream patenting has turned out to be largely irrelevant. Rather, there are much more important obstacles than upstream patents to development in science-based fields such as biotechnology and nanotechnology: long development cycles; difficulties in attracting private investment; limited access to materials and equipment; high dependence on tacit knowledge; the low expected commercial values; multidisciplinarity; and likely regulatory hurdles. Science-based fields arise from university research, but even when present, access or lack of access to upstream university research patents often takes a back seat to other more salient characteristics of such technologies.

A. *Anticommons Require More Than Upstream Patenting*

As a first matter, the fact that universities hold such a high number of early-stage nanotechnology research patents is not by itself sufficient to cause either qualitative or quantitative holdup problems. Anticommons require more than just a large volume of patents. Patents vary a great deal in scope and importance,[141] and of the small percentage that have commercial value, few will be important enough to create obstacles. Rather, the effect of a patent depends on a number of variables, and the effect of patenting under the Bayh-Dole Act therefore will vary greatly across and even within technologies and their developmental pathways.[142]

To see this point, we can compare nanotechnology to biotechnology. As in nanotechnology, basic academic research and other government-funded research have played a large role in the development of biotechnology.[143] And like nanotech, biotech experienced a surge in university patenting after Bayh-Dole; universities currently hold about 18% of all patents in genetics

---

[139] *See, e.g.*, MICHAEL HELLER, THE GRIDLOCK ECONOMY 65 (2008) (summarizing studies suggesting overabundance and poor quality of biotechnology patents); Gary Pulsinelli, *Share and Share Alike: Increasing Access to Government-Funded Inventions Under the Bayh-Dole Act*, 7 MINN. J.L. SCI. & TECH. 393, 438 n.280 (2006) (noting criticisms of USPTO's evaluation of biotechnology patents).

[140] *See, e.g.*, Ulrich Schmoch & Axel Thielmann, *Cyclical Long-Term Development of Complex Technologies—Premature Expectations in Nanotechnology?*, 21 RES. EVAL. 126, 126 (2012) (characterizing nanotechnology as a "science-based complex technology").

[141] Adelman & DeAngelis, *supra* note 67, at 1682.

[142] Brett M. Frischmann, *Commercializing University Research Systems in Economic Perspectives: A View from the Demand Side*, *in* 16 UNIVERSITY ENTREPRENEURSHIP AND TECHNOLOGY TRANSFER: PROCESS, DESIGN, AND INTELLECTUAL PROPERTY 156–57 (Gary D. Libecap ed., 2005); Burk & Lemley, *supra* note 103, at 1584–87; Merges & Nelson, *supra* note 69, at 843.

[143] Bawa, *supra* note 3, at 722; Tullis, *supra* note 12, at 286–90.

and molecular biology.[144] In fact, some observers suggest that as a science-based field, nanotech now is following the same developmental trajectory that biotech charted about fifteen to twenty years ago.[145] The trends seen in biotech can therefore be informative in studying development trends in nanotech.

The empirical evidence thus far is equivocal at best as to whether the increase in university patenting has in fact either impeded or aided downstream development of university-based research as a whole,[146] largely because of the difficulties of testing such a hypothesis.[147] In biotech, however, the empirical data suggests that while anticommons and other holdup effects have affected specific fields such as genetics,[148] biotech more generally does not suffer from significant holdup problems, whether qualitative or quantitative.[149] Some studies suggest that biotechnological development and commercialization have in fact skyrocketed since the 1980s.[150]

The reasons for this surprising absence of evidence of holdup problems in biotech are manifold.[151] First, researchers, especially those in academia, just ignore patents as a general rule.[152] University researchers do not look at

---

[144] Adelman, *supra* note 51, at 997 (although Adelman notes that biotech patenting levels overall may be declining); Lee, *supra* note 135, at 939–40.

[145] Frank T. Rothaermel & Marie Thursby, *The Nanotech Versus the Biotech Revolution: Sources of Productivity in Incumbent Firm Research*, 36 RES. POL'Y 832, 842 (2007); Michael R. Darby & Lynne G. Zucker, *Grilichesian Breakthroughs: Inventions of Methods of Investing and Firm Entry in Nanotechnology* 2 (Nat'l Bureau of Econ. Research, Working Paper No. 9825, 2003), http://www.nber.org/papers/w9825 [https://perma.cc/RP29-2Y59].

[146] Osenga, *supra* note 52, at 410; Wolrad Prinz zu Waldeck und Pyrmont, *Research Tool Patents After* Integra v. Merck*–Have They Reached a Safe Harbor?*, 14 MICH. TELECOMM. & TECH. L. REV. 367, 387–88 (2008); Mireles, *supra* note 47, at 261, 274.

[147] *See* Charles R. McManis & Sucheol Noh, *The Impact of the Bayh-Dole Act on Genetic Research and Development: Evaluating the Arguments and Empirical Evidence to Date*, *in* PERSPECTIVES ON COMMERCIALIZING INNOVATION 435, 440, 475 (F. Scott Kieff & Troy A. Paredes eds., 2012) (giving examples of practical barriers to researching whether university patents inhibit innovation).

[148] *See, e.g.*, Mildred K. Cho et al., *Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services*, 5 J. MOLECULAR DIAGNOSTICS 3, 8 (2003); Jon F. Merz et al., Letter to the Editor, *Industry Opposes Genomic Legislation*, 20 NATURE BIOTECHNOLOGY 657 (2002). *But see* Andrew W. Torrance, *Open Source Biotechnology: Open Source Human Evolution*, 30 WASH. U.J.L. & POL'Y 93, 123 (2009) (pointing out that empirical evidence of anticommons due to gene patenting is scarce and that some empirical evidence in fact suggests the exact opposite).

[149] *See, e.g.*, John P. Walsh et al., *Effects of Research Tool Patents and Licensing on Biomedical Innovation*, *in* PATENTS IN THE KNOWLEDGE-BASED ECONOMY 289, 331 (Wesley M. Cohen & Stephen A. Merrill eds., 2003); Adelman, *supra* note 51, at 1023, 1028–29.

[150] *See* Kieff, *supra* note 130, at 725–26.

[151] Rebecca S. Eisenberg, *Noncompliance, Nonenforcement, Nonproblem? Rethinking the Anticommons in Biomedical Research*, 45 HOUS. L. REV. 1059, 1063–75 (2008); Rebecca S. Eisenberg, *Proprietary Rights and the Norms of Science in Biotechnology Research*, 97 Yale L.J. 177, 197–205 (1987).

[152] Eisenberg, *supra* note 151, at 1076.

patents in selecting their topics and conducting research,[153] and many report that they regularly use patented technologies in the belief that research is exempted from liability under an experimental-use exception.[154] Although the Federal Circuit has held that no such experimental-use exception applies even to university research,[155] research patent infringement is often too difficult to detect and police,[156] particularly when it involves "problem-specific" rather than foundational research, and in any event it is unlikely to be worth enough in damages to justify filing suit.[157] Not surprisingly, patent holders have been ill disposed toward suing academic infringers,[158] but universities may be reaching a point where they can no longer rely on effective immunity from suit for infringement. Universities have increasingly become the instigators and even targets of patent-enforcement threats,[159] and with the growing view of universities as commercial actors, they have increasingly become the targets of patent enforcement as well.[160]

A second, more specific, and perhaps more important reason why biotech has not experienced many hold ups is that biotech still offers so many research and development prospects that neither those in academia nor in private industry need bump into one another in order to research and develop their own patch of biotech.[161] As Professor David Adelman has argued, the opportunities in biotech still far outnumber current research and development capacity, such that those in the field still have plenty of

---

[153] *See*, *e.g.*, John P. Walsh et al., *View from the Bench: Patents and Material Transfers*, 309 SCI. 2002 (2005) (noting that only 5% of scientists surveyed regularly check for patents when conducting research).

[154] A PATENT SYSTEM, *supra* note 113, at 72; Walsh et al., *supra* note 149, at 331.

[155] Madey v. Duke Univ., 307 F.3d 1351, 1362–63 (Fed. Cir. 2002); *see also* A PATENT SYSTEM, *supra* note 113, at 73, 76–77 (noting the effect of *Madey*).

[156] Lemley, *supra* note 3, at 623; Mireles, *supra* note 47, at 275–76 (and sources cited therein).

[157] Lemley, *supra* note 3, at 623; *see also* Victor H. Polk, Jr. & Roman Fayerberg, *When Patented Technologies Get Put to Experimental Use: Practical Considerations for Nanotech R&D*, 8 NANOTECH. L. & BUS. 152, 153–54 (2011) (noting that damage remedies may be muted, depending on the method of infringement).

[158] Walsh et al., *supra* note 149, at 326–27; Heller & Eisenberg, *supra* note 59, at 700–01.

[159] *See* Christopher Brown, *Ayresian Technology, Schumpeterian Innovation, and the Bayh-Dole Act*, 43 J. ECON. ISSUES 477, 479 (2009) ("[U]niversities are heavily involved in patent litigation."); A PATENT SYSTEM, *supra* note 113, at 73, 76–77; Lemley, *supra* note 3, at 622; *see also* Mueller, *Dilettante*, *supra* note 128, at 3–4 (describing Roche's suit against more than forty U.S. universities and others for alleged infringement of patents on the use of "Taq" and PCR).

[160] *See*, *e.g.*, Jay P. Kesan, *Transferring Innovation*, 77 FORDHAM L. REV. 2169, 2183 (2009) ("[O]verpatenting by universities could lead to universities being treated more like commercial actors . . . ."); Peter Lee, *Patents and the University*, 63 DUKE L.J. 1, *passim* (2013); Mireles, *supra* note 47, at 275–76; Nelson, *supra* note 103, at 466. If the infringement occurs within public universities and research institutions, however, the Supreme Court's decision in *Florida Prepaid Post-Secondary Ed. Expense Bd. v. Coll. Savings Bank*, 527 U.S. 627 (1999) may provide sovereign immunity from suit. BUREAU OF NATIONAL AFFAIRS, INTELLECTUAL PROPERTY TECHNOLOGY TRANSFER 28, 59–60 (Aline C. Flower ed. 2d ed. 2014) [hereinafter BNA]; A PATENT SYSTEM, *supra* note 113, at 78–79; Eisenberg, *supra* note 151, at 1092.

[161] Adelman, *supra* note 51, at 998–99; Walsh et al., *supra* note 149, at 331–32.

freedom to operate within the biotech field.[162] In those cases where researchers were deterred by the cost of licensing upstream patents, the researchers were easily able to redirect their research efforts to alternative strategies, given that most subject matter offered a range of research approaches.[163] Similarly, patented processes and even research-method patents can often be circumvented if other processes for achieving the same result are available.[164] Studies have shown that biotech firms and other researchers will often invent around patented research or use other research tools if any given project would require too many patent licenses.[165] And although biotech has also seen a surge in overall patenting and in upstream patenting in particular,[166] the concentration of patenting in any one subfield of biotech remains small.[167]

Patent ownership also remains fairly diffuse, with no one entity able to exert much control over the field and few barriers to patenting and entry by newcomers.[168] Diffuse patent ownership can lead to increased transaction costs, but in the case of biotech, the number of patents that have to be evaluated and negotiated for any given biotech project remains manageable and is rarely reported as an obstruction.[169]

Without a similar mapping of nanotech-patenting patterns, it is difficult to tell whether nanotechnology also provides wide range of research avenues, but it seems likely. The youth of the field and its vast number of subfields suggest that nanotech is still wide open for exploration without fear of an anticommons.[170] Again, the likelihood of upstream patenting deterring downstream development is a question of how important those upstream patents are. Much like biotech, nanotech is new enough and complex enough that, even with the high levels of patenting on upstream research that nanotech has already seen, many more research opportunities likely have yet

---

[162] *See* Adelman & DeAngelis, *supra* note 67, at 1699.

[163] Walsh et al., *supra* note 149, at 303; *see also* Adelman, *supra* note 51, at 1003–04 (noting that most diseases offer more potential research targets than there are available researchers).

[164] *See* Rebecca S. Eisenberg, *Limiting the Role of Patents in Technology*, 5 J. NIH RES. 20, 22 (1993); *see also* A PATENT SYSTEM, *supra* note 113, at 72 (noting that patents can be circumvented by inventing around them, using substitute research tools, and locating research activity offshore).

[165] Eisenberg, *supra* note 151, at 1064–65.

[166] Adelman & DeAngelis, *supra* note 67, at 1687 (noting a decline in biotech patents issued as utility standards and USPTO resources tightened).

[167] *Id.* at 1701–02 (noting that most subclasses of biotechnology contained fewer than one hundred patents).

[168] *Id*.

[169] *Id.* at 1697 (citing Walsh et al., *supra* note 149, at 299–304); A PATENT SYSTEM, *supra* note 113, at 72.

[170] *Cf.* Adelman & DeAngelis, *supra* note 67, at 1698–1700 (explaining how biotechnology's relative youth continues to allow new avenues for exploration).

to be identified.[171]

Likewise, although many basic nanomaterials such as carbon nanotubes, quantum dots, fullerenes, nanowires, dendrimers, and nanorods have been patented,[172] it seems likely that useful additions and alternatives to these materials can be found in the near future. Organic nanotubes and polymer nanotubes, for example, can serve as alternatives to carbon nanotubes for many applications,[173] and carbon nanotubes can be both synthesized and purified through a wide variety of alternative methods.[174] Nanoscopic dendrimers also come in a huge variety of forms, including graphite-like dendrimers, dendrimers with cross-linked surfaces, hyper-branched dendrimers, and more.[175] Most or all of these alternative nanotubes, dendrimers, and processes have been patented (and therefore could create patent thickets or other holdup issues),[176] but their number and range demonstrate the breadth of the field and suggest that in nanotech, as in biotech, R&D opportunities far exceed capacity and that nanotech is thus also "an effectively unbounded, uncongested common resource."[177]

A few critical patents may be important enough, however, that despite their relatively small number, restricted access to these patents could create bottlenecks.[178] Many technologies rely on a few pivotal research tools to enable further research and development;[179] without these foundational inventions, further progress in their respective fields would be difficult or impossible.[180] Although very few upstream research patents fall within this

---

[171] David E. Adelman, *The Irrationality of Speculative Gene Patents*, *in* 16 ADVANCES IN THE STUDY OF ENTREPRENEURSHIP, INNOVATION & ECONOMIC GROWTH: UNIVERSITY ENTREPRENEURSHIP & TECHNOLOGY TRANSFER 125 (Gary D. Libecap ed. 2005).

[172] Lemley, *supra* note 3, at 613–14; Reynolds, *supra* note 1, at 86, 96.

[173] Michael Lounsbury et al., *The Politics of Neglect: Path Selection and Development in Nanotechnology Innovation*, *in* 21 ADVANCES IN THE STUDY OF ENTREPRENEURSHIP, INNOVATION & ECONOMIC GROWTH: UNIVERSITY ENTREPRENEURSHIP AND TECHNOLOGY TRANSFER 51 (Gary D. Libecap ed. 2010). The fact that carbon nanotubes have become the better-known form is more a matter of "technological momentum" than importance to the field. *Id.*

[174] M. Henry Heines, *Carbon Nanotubes: Tracing Growth of a Young Technology Through Patents*, 7 NANOTECHNOLOGY. L. & BUS. 21, 26–30 (2010) ("The impact of these synthesis patents is further lessened by the existence of a variety of [carbon nanotube] synthesis methods, presenting the manufacturer with a host of alternatives for avoiding infringement of a single patent.").

[175] Alexander Lee, *Examining the Viability of Patent Pools for the Growing Nanotechnology Patent Thicket*, 3 NANOTECH. L. & BUS. 317, 321–22 (2006).

[176] *See, e.g.*, *id.* at 323 (describing dendrimers as being subject to patent thickets).

[177] Adelman, *supra* note 51, at 987; *cf. id.* (discussing why biotech has not suffered from anticommons).

[178] Walsh et al., *supra* note 149, at 305–06.

[179] *See, e.g.*, Lee, *supra* note 130, at 86–91.

[180] Brett M. Frischmann, *An Economic Theory of Infrastructure and Commons Management*, 89 MINN. L. REV. 917, 928, 932 (2005); Brett M. Frischmann & Mark A. Lemley, *Spillovers*, 107 COLUM. L. REV. 257, 268–69 (2007); Lee, *supra* note 130, at 89–91. Foundational inventions have also been referred to variously as "common-method research tools," Adelman, *supra* note 171, at 139, "platform technologies," McManis & Noh, *supra* note 147, at 485, or even "Grilichesian breakthroughs," Darby & Zucker, *supra* note 145, at 1–2 (citing Zvi Griliches, *Hybrid Corn: An Exploration in the Economics of*

category,[181] exclusive rights over foundational tools obviously can stifle development and competition within a field.[182] Evidence suggests that foundational research tools are frequently dedicated to the public domain, however.[183]

Although nanotubes and other nanomaterials have been referred to as the "basic building blocks,"[184] nanotechnology's true foundational tool is probe microscopy; without probe microscopy, nanotechnology could not have become anything more than an interesting theory.[185] Nobel Prize-winning physicist Richard Feynman first suggested the idea of manipulating individual atoms in 1959, but it was not until the invention of the scanning tunneling microscope in 1981 that scientists could actually visualize matter at a high enough magnitude to begin to construct materials atom by atom.[186] The scanning tunneling microscope was followed by the invention of the atomic force microscope in 1989, which became commercially available shortly thereafter and proved to be superior to the scanning tunneling version.[187] Subsequent iterations on probe microscopy have also yielded the magnetic force microscope and the near-field scanning optical microscope.[188] Because nanotechnology could not exist without probe microscopy, patent rights on these foundational research tools could pose a risk to nanotech development.

According to Professor Lemley, nanotech is nevertheless different from other pioneering technologies like computers, biotech, integrated circuits, and lasers; although these fields experienced patent floods after Bayh-Dole, Lemley claims that those patents covered mainly downstream applications or improvements, not foundational technologies.[189] Instead, according to Lemley, the foundational tools in this latter group of technologies were

---

Technological Change, 25 ECONOMETRICA 501, 501 (1957)).

[181] Adelman, *supra* note 51, at 1020; Adelman, *supra* note 171, at 139; McManis & Noh, *supra* note 147, at 486.

[182] Nelson, *supra* note 103, at 464.

[183] Adelman, *supra* note 51, at 997–1001; Adelman, *supra* note 171, at 140; Walsh et al., *supra* note 149, at 324–29.

[184] Lemley, *supra* note 3, at 613–14; Reynolds, *supra* note 1, at 86.

[185] *See* MONICA, *supra* note 2, § 1:1 ("Most important to the development of nanotechnology [were] . . . entirely new forms of electron microscopes . . . ."); Zovko, *supra* note 64, at 156 ("[T]echniques such as scanning probe microscopy are essential for manipulating atoms and arranging them in particular molecular configurations . . . . If scanning probe microscopy, carbon nanotubes, or similar fundamental tools are unavailable to research and development entities through purchase or license from patent owners, the scientific progress of nanotechnology will be stifled."); Darby & Zucker, *supra* note 145, at 13–14.

[186] MONICA, *supra* note 2, § 1:1.

[187] Cyrus M. Mody, *Corporations, Universities, and Instrumental Communities: Commercializing Probe Microscopy, 1981-1996*, 47 TECH. & CULTURE 56, 68–69 (2006); Rothaermel & Thursby, *supra* note 145, at 833, 835.

[188] Mody, *supra* note 187, at 56, 57 n.1.

[189] Lemley, *supra* note 3, at 613.

unpatented, freely licensed, or tied up in interference proceedings and litigation for so long that they were effectively unenforceable.[190] In nanotechnology, by contrast, patents cover all but a very few foundational building blocks, making holdup problems much more likely than in previous technologies.[191]

Again, however, whether nanotech is truly different from biotech or other technologies is a matter for debate for a number of reasons. First, many of the basic nanotech building blocks to which Lemley refers are not truly pivotal, even though they may be basic. Again, carbon nanotubes and even quantum dots, fullerenes, nanowires, dendrimers, and nanorods may be basic in the sense that they can be incorporated into a vast variety of downstream applications,[192] but because meaningful substitutes likely can be found, these materials may not pose as great a holdup risk as Lemley suggests.

Second, to the extent that its development has been stifled by patents on foundational research tools like probe microscopy, nanotech is not as unique as Lemley would suggest. Contrary to Lemley's assertion otherwise, some studies suggest that biotech research has in fact experienced holdup effects.[193] Although Cohen and Boyer liberally granted inexpensive, nonexclusive licenses to their patented recombinant DNA technology,[194] foundational research tools such as Cetus Corporation's polymerase chain-reaction technology, Harvard's OncoMouse, and the University of Wisconsin's human embryonic stem cell technology are thought to have hampered progress in biotechnology because of the patent holders' restrictive licensing practices.[195] Thus, although foundational nanotechnology research tools have been patented, it is likely that development in this field is not significantly different from the other science-based technologies that have preceded it.

Third, even foundational technologies become less foundational as

---

[190] *Id.* at 610–14.

[191] *Id.* at 613–14.

[192] *Id.*; *see also* Reynolds, *supra* note 1, at 86, 97 ("[N]anotechnology anticommons occurs at the building block level . . . [where] patent holders will likely attempt to stack licenses on future downstream discoveries.").

[193] Nelson, *supra* note 103, at 464.

[194] MARYANN P. FELDMAN, ALESSANDRA COLAIANNI & CONNIE K. LIU, LESSONS FROM THE COMMERCIALIZATION OF THE COHEN-BOYER PATENTS: THE STANFORD UNIVERSITY LICENSING PROGRAM, *in* INTELLECTUAL PROPERTY MANAGEMENT IN HEALTH AND AGRICULTURAL INNOVATION: A HANDBOOK OF BEST PRACTICES 1797, 1797–98 (Anatole Krattiger et al. eds., 2007), http://www.iphandbook.org/handbook/ch17/p22/ [https://perma.cc/M5U5-DR8S].

[195] *See* Lee, *supra* note 130, at 93–96 ("Cetus threatened to aggressively enforce its patent against firms engaged in pharmaceutical development, and even threatened suit against noncommercial, academic researchers who shared their PCR-enabled research with industry. While Cetus did not follow through with its threats, this example demonstrates the risks of strong exclusive rights on an infrastructural resource subject to rapid and widespread adoption."); Mowery, *supra* note 90, at 56; Walsh et al., *supra* note 149, at 296–309.

newly invented alternatives supplement or replace earlier technologies,[196] as illustrated by the multiple forms of probe microscopy that have become available in nanotechnology.[197] Although probe microscopes are not perfectly interchangeable substitutes for one another, the progression from scanning tunneling microscope to atomic force microscope and beyond does at least illustrate the shift in technological bottlenecks over time.[198]

B. *Obstacles to Development in Science-Based Technologies*

Besides patents, nanotechnology faces a number of other, more significant hurdles common in science-based technologies. "Science-based" technologies such as biotechnology and nanotechnology, also known as "research-based" technologies, derive not from practical experience in industrial design and production but instead from the academic pursuit of knowledge for the sake of knowledge, which may then only later have practical application.[199] As Professor Liza Vertinsky has explained, science-based technologies are "knowledge-intensive"[200] and driven primarily by basic research and scientific breakthroughs outside the norm of private industry.[201] And because inventions in science-based fields such as nanotechnology are typically in no more than proof-of-concept form, they are high in development costs and investment risk but low in expected market value.[202] Commercializing technologies still in such early and risky stages of development is well beyond the comfort zone of most private investors.[203] The difficulties inherent to science-based technology

---

[196] Kieff, *supra* note 130, at 730–31; *cf.* Mossoff, *supra* note 138, at 204 (noting that patent thickets are contextual "depending on such things as time, available technology, and even commercial or legal norms").

[197] *See* Mody, *supra* note 187, at 56, 57 n.1.

[198] *See* Lee, *supra* note 130, at 74, 86–91 (discussing the "basic suite of infrastructural assets necessary to invent in a given field shift[ing] as technology progresses").

[199] Nelson, *supra* note 103, at 457–59.

[200] Liza Vertinsky, *Universities as Guardians of Their Inventions*, 4 UTAH L. REV. 1949, 1980 (2012).

[201] Bawa, *supra* note 3, at 722; Merges & Nelson, *supra* note 69, at 880, 907–08 (explaining how further innovation can become more "cumulative than science-based"); Mowery, *supra* note 90, at 42–43 (and sources cited therein); *see* Heather Hamme Ramirez, Comment, *Defending the Privatization of Research Tools: An Examination of the "Tragedy of the Anticommons" in Biotechnology Research and Development*, 53 EMORY L.J. 359, 378 (2004) ("Compared to other industries, the biotechnology sector is highly dependent on academic research . . . . [T]he private sector depends on universities for expanding their research capabilities and expertise and for staying informed about important advances in science."). Nanotechnology pioneer K. Eric Drexler describes science-based technologies by distinguishing them from engineering as curiosity-driven rather than results-driven. K. ERIC DREXLER, RADICAL ABUNDANCE: HOW A REVOLUTION IN NANOTECHNOLOGY WILL CHANGE CIVILIZATION 105–10 (2013).

[202] Mowery, *supra* note 90, at 42–43 (and sources cited therein); Chun Hsien Wang et al., *A Study of Nanotechnology R&D Alliance Networking*, 2012 PROC. PICMET '12: TECH. MGMT. EMERGING TECHS. 3497, *passim* (2012); Ramirez, *supra* note 201, at 378.

[203] *See* Bawa, *supra* note 3, at 722.

development are thus much more likely than patents to slow development in these embryonic fields, which are especially prone to suffer from underdevelopment.[204]

Much of the early optimism about pioneering new technologies such as biotech and nanotech and discussion about the effect of patenting in these fields overlook the significant nonpatent obstacles, however, which can often prove to be insurmountable.[205] Very little of the research in these fields and other government-funded research areas is even worth patenting, presumably because of the same lack of commercial value that made it dependent on government funding.[206] Universities must be highly selective in using their limited resources to patent faculty research, and university TTOs usually will avoid the high costs of obtaining patent protection unless industry expresses an interest in a particular technology.[207] Even when universities do decide to assume the cost of obtaining a patent, very few of those patents earn any profit.[208]

Thus, although development of some of the more straightforward nanotechnology applications may be less difficult, much if not most of the field seems to be as yet in a more inchoate state, requiring many additional developmental stages before commercialization can be achieved. Delays or even failure can occur at any one of these stages for any number of reasons. The following are some of the main reasons why much of nanotechnology as science-based technology is so challenging to commercialize.

---

[204] Michael Abramowicz, *The Danger of Underdeveloped Patent Prospects*, 92 CORNELL L. REV. 1065, 1070–71 (2007).

[205] Adelman, *supra* note 171, at 125.

[206] Frischmann, *supra* note 142, at 155, 175; Walsh et al., *supra* note 149, at 309 (reporting that only a minority of university-based inventions are patented, even in genetics).

[207] *See* David S. Siegel & Phillip H. Phan, *Analyzing the Effectiveness of University Technology Transfer: Implications for Entrepreneurship Education* 7 (Rensselaer Working Papers in Economics, Number 0426, 2004), www.economics.rpi.edu/workingpapers/rpi0426.pdf [https://perma.cc/M5ZD-R2RL] (noting that TTO and other research administrators "protect[] the university's intellectual property portfolio [and] . . . actively seek to market university-based technologies to companies and entrepreneurs"); BNA, *supra* note 160, at 225, 227–32; McManis & Noh, *supra* note 147, at 454; Interview with Kerbeshian, *supra* note 96. University TTOs often opt to file much less expensive provisional patent applications, but these expire after twelve months unless a fuller and more expensive nonprovisional application is filled. Margo A. Bagley, *Academic Discourse and Proprietary Rights: Putting Patents in Their Proper Place*, 47 B.C. L. REV. 217, 247 (2006).

[208] Brian J. Love, *Do University Patents Pay Off? Evidence from a Survey of University Inventors in Computer Science and Electrical Engineering*, 16 YALE J.L. & TECH. 285, 308–12 (2014) (finding that life science patents are at least more likely to be profitable than other high tech patents); Scotchmer & Maurer, *supra* note 48, at 235; Bagley, *supra* note 207, at 259; *see also* Greenbaum, *supra* note 68, at 359–60 ("[W]hile some licenses may be a boon for universities and some academic inventors, the majority of income derived from licensing of academic innovation nationwide comes out of a handful of licensing offices, most of which predated Bayh-Dole, and even those take relatively little revenue home relative to the costs necessary to generate those innovations.").

1. *Long Development Cycles*

First and most significant is the fact that commercializing science-based technologies requires a good deal of further experimentation and work; regardless of patent burdens, it is simply a laborious and slow process to develop basic research and "bridge the gap from the laboratory to the marketplace."[209] Science-based technologies often explore pioneering new areas well outside existing art but consequently require far more downstream development than other technologies.[210] Having been invented by scientists rather than business people, emerging technologies do not come out of the laboratory in ready-to-market form,[211] and even patentable inventions in these fields typically require several additional stages of development.[212] Taking research-intensive technologies from laboratory proofs of concept to industrial practice necessitates perfecting the invention so that it will perform reliably and can be reproduced in a cost-efficient manner.[213] For example, producing even basic nanotechnology building blocks such as nanotubes, metal oxide nanoparticles, and fullerenes in consistently high-quality form, took quite some time.[214] Each of these additional steps may also be complex and time-consuming, making overall commercialization quite lengthy. Long development cycles and time lags are therefore common in research-intensive fields such as physics, mathematics, and the physical sciences,[215] and nanotechnology has proven to be no exception, with long

---

[209] Thomas A. Kalil, *Nanotechnology and the "Valley of Death*," 2 NANOTECH. L. & BUS. 265, 265–66 (2005) (quoting *Nanotechnology Research and Development Act of 2003: Hearing on H.R. 766 Before the H. Comm. on Sci.*, 108th Cong. 57–58 (2003) (Statement of Alan Marty, Executive-in-Residence of JP Morgan Partners and Advisory Board Member of Nanobusiness Alliance); *accord* Roberto Mazzoleni & Richard R. Nelson, *Economic Theories About the Benefits and Costs of Patents*, 32 J. ECON. ISSUES 1031, 1048 (1998); Mowery, *supra* note 90, at 43; Schmoch & Thielmann, *supra* note 140, at 126.

[210] Bawa, *supra* note 3, at 719; Mowery, *supra* note 90, at 42–43; Wang et al., *supra* note 202, *passim*.

[211] Stuart J.H. Graham & Maurizio Iacopetta, *Nanotechnology and the Emergence of a General Purpose Technology*, 115/116 ANNALS ECON. & STAT. 5, 8 (2014).

[212] Mowery, *supra* note 90, at 44–45 (and sources cited therein); Merges & Nelson, *supra* note 69, at 880, 907–08; Nelson, *supra* note 103, at 457–59; *see also* Jerry G. Thursby & Marie C. Thursby, *University Licensing and the Bayh-Dole Act*, 301 SCI. 1052, 1052 (2003) (citing survey evidence that 45% of university inventions are simply "proof[s] of concept").

[213] *See* Philip E. Auerswald & Lewis M. Branscomb, *Valleys of Death and Darwinian Seas: Financing the Invention to Innovation Transition in the United States*, 28 J. TECH. TRANSFER 227, 229, 229 fig.2 (2003) (outlining a sequential model of development and funding); Kalil, *supra* note 209, at 265–66 (discussing the time and investment required to move a product from the "laboratory to the marketplace") (quoting *Nanotechnology Research and Development Act of 2003: Hearing on H.R. 766 Before the H. Comm. On Sci.*, 108th Cong. 57–58 (2003) (statement of Alan Marty, Executive-in-Residence of JP Morgan Partners and Advisory Board Member of Nanobusiness Alliance).

[214] Lane & Kalil, *supra* note 28, at 52.

[215] 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 30 (2004); Mowery, *supra* note 90, at 43.

development spans frequently delaying commercialization.[216]

Commercializing research-based technologies often entails development of new equipment and new materials as well. Translating scientific knowledge into industrial application generally involves implementation through one of the applied sciences such as engineering, information technology, or materials science.[217] The more pioneering these technologies are and the more widespread their effects, the more their successful commercialization will depend on separate scientific and technological developments in infrastructure such as machinery and processes, as well as correlative technologies such as supporting software and information technology.[218] In nanotechnology, for example, the need to develop secondary equipment and processes may be particularly acute, given the cross-disciplinary nature of nanotechnology and the need to adapt it to specific sectors.[219]

The technological translation process may also depend on the cost and availability of existing material assets and machinery.[220] Probe microscopy development, for example, has been heavily influenced by what materials were cheaply and easily available at the time.[221] When academic researchers were working on improving the STM for their own uses, they opted for graphite because it happened to be cheaply available as waste material from United Carbide.[222] Similar material availability issues also shaped the divergent development efforts by STM researchers working in different locations.[223] And even now, lack of access to high quality and reliably reproducible and manufacturable nanomaterials continues to be a stumbling

---

[216] Bawa, *supra* note 3, at 719; Festel et al., *supra* note 20, at 55; Lane & Kalil, *supra* note 28, at 50, 52; Rasmus Davidsen, *Nanotechnology Startups: Not the Usual Growth Pattern*, DAFTBLOGGER EJOURNAL (June 15, 2013, 6:36 PM), http://www.daftblogger.com/nanotechnology-startups-not-the-usual-growth-pattern/ [https://perma.cc/Z3DX-64YA].

[217] Merges & Nelson, *supra* note 69, at 880; *see also* Mowery, *supra* note 90, at 43.

[218] Abramowicz, *supra* note 204, at 1071; Auerswald & Branscomb, *supra* note 213, at 230; Graham & Iacopetta, *supra* note 211, at 12; Schmoch & Thielmann, *supra* note 140, at 127. Of course, where the development of auxiliary technologies depends on access to the upstream technologies to which they are complementary, hold up due to patents on those upstream technologies can further exacerbate overall developmental delays. *See, e.g.*, Howard F. Chang, *Patent Scope, Antitrust Policy, and Cumulative Innovation*, 26. RAND J. OF ECON. 34, 34 (1995). It is in the patentees' best interests, however, to license their upstream patents liberally where the value of their upstream technologies in turn depends on the development of complementary technologies. *Id* at 52.

[219] *See* Graham & Iacopetta, *supra* note 211, at 8–9 (noting that nanotechnology's success as a "general purpose technology" depends on the development of related technologies).

[220] *See* Lee, *supra* note 175, at 323 (explaining that the number of nanotechnology applications currently considered commercially viable is small because of the cost of producing even small quantities of dendritic molecules).

[221] Mody, *supra* note 187, at 65–66.

[222] *Id*.

[223] *Id.*

block for nanotech development[224] because materials such as carbon nanotubes and dendritic molecules are rate-limitingly expensive and difficult to find in sufficiently high quantities and quality.[225] Access to materials or research materials can be restrictive in other fields as well; for example, in biofuels the production cost of enzymes and ethanologens is a significant barrier to research.[226] Similarly, the fixed capital costs of retooling or buying new machinery can be prohibitively burdensome.[227] Nanotechnology depends on access to probe microscopes, nanofabrication equipment, modeling software, and other essential but often proscriptively costly tools.[228] For example, faster drying, more efficient autobody nanocoatings have been available for some time now, but the cost of retooling has kept the cash-strapped automobile industry from taking advantage of the new technology.[229]

Given the extreme length of development cycles in science-based technologies, then, those engaged in the commercialization process often simply ignore potential clashes with the patent rights of others, and rationally so.[230] Even when they receive cease-and-desist letters threatening legal action for patent infringement, emerging technology developers know that litigation to enforce patent rights is often more costly than it is worth.[231] In addition, patent holders usually will refrain from filing suit until an infringing development project produces something of enough commercial value to warrant the bother, but given the high failure rates in research-intensive technologies, threatening patent holders seldom actually file.[232] Litigation always poses a risk for the patent holders as well, as even the strongest patents may be subject to invalidation in whole or in part.[233] And if the critics are correct, filing infringement suits in science-based technologies may be particularly fraught with danger, as upstream patents

---

[224] NAT'L RESEARCH COUNCIL, MANAGING UNIVERSITY INTELLECTUAL PROPERTY IN THE PUBLIC INTEREST 7–8, 31, 38–40 (Stephen A. Merrill & Anne-Marie Mazza eds., 2010) [hereinafter NRC]; Lane & Kalil, *supra* note 28.

[225] Lee, *supra* note 175, at 323 ("[T]here are only a handful of [nanotechnology] applications and discoveries that are currently considered commercially viable and worth pursuing due to the very high cost of producing even small quantities of dendritic molecules."); MONICA, *supra* note 2, § 1:10.

[226] Daniel R. Cahoy & Leland Glenna, *Private Ordering and Public Energy Innovation Policy*, 36 FLA. ST. U.L. REV. 415, 448–49 (2009).

[227] Wolfe, *supra* note 37; *see also* Graham & Iacopetta, *supra* note 211, at 8–9 (noting that the "general purpose technologies," potentially including nanotechnology, often experience slow-downs as existing equipment is replaced with relevant new equipment).

[228] MILLER ET AL., *supra* note 5, at 189; Graham & Iacopetta, *supra* note 211, at 12.

[229] Wolfe, *supra* note 37.

[230] Mark A. Lemley, *Ignoring Patents*, 2008 MICH. ST. L. REV. 19, 20–22 (2008); Walsh et al., *supra* note 149, at 327.

[231] Lemley, *supra* note 230, at 22; Lemley, *supra* note 3, at 623; Polk & Fayerberg, *supra* note 157, at 153–54; Walsh et al., *supra* note 149, at 327.

[232] Lemley, *supra* note 230, at 22.

[233] *See id.* at 27 (noting that as many as three-fourths of litigated patents are found invalid or not infringed); Walsh et al., *supra* note 149, at 328.

are particularly vulnerable to invalidation for lack of specific and substantial utility, failure to claim patentable subject matter, and, especially in nanotechnology, inherency or obviousness.[234]

Finally, development cycles may also span so many years that patents on foundational or other potentially blocking upstream research inputs often will expire in the interim.[235] Patents on many of the basic nanotech building blocks, such as those on carbon nanotubes, buckyballs, quantum dots, dendrimers, and nanorods, for example, have already expired or are due to expire in the very near future,[236] and foundational inventions in particular may be used through several development cycles, such that their patents expire long before their utility does.[237] Thus, by the time science-based technologies finally achieve commercialization, many patents will no longer be in effect.[238] As a result, upstream patenting's capacity to exert holdup effects is rather low in these technologies.

2. *The Valley of Death*

The technological difficulties of commercializing science-based technologies bring economic difficulties as well. Again, commercialization of research-intensive technologies is usually an expensive, risky, multistage undertaking. The government will invest in the basic research stages, but private investors prefer to wait and invest only in the very last stages of development; private firms and investors generally favor development projects closer to completion so as to minimize risk and maximize the time-value of their funds.[239] The long, expensive, and uncertain development stages in between the early, basic research stage and the final, marketing stage are consequently left to languish for lack of investment.[240] Indeed, many scholars note that it is government funding of basic research that "causes" the valley of death because the government tends to subsidize exactly the kind of basic research in which private industry is unwilling to

---

[234] HELLER, *supra* note 139, at 65; Akhtar, *supra* note 6, at 138; Bawa, *supra* note 3, at 707–10; Pulsinelli, *supra* note 139, at 438 n.280 ; Williamson & Carpenter, *supra* note 61, at 139–40.

[235] Ted Sichelman, *Commercializing Patents*, 62 STAN. L. REV. 341, 366 (2010); Adelman, *supra* note 51, at 1015–16.

[236] Sharrott & Gupta, *supra* note 4, at 159–60.

[237] Adelman, *supra* note 51, at 1015–16; Sichelman, *supra* note 235, at 366.

[238] To see the inverse relationship between development cycle length and the risk of patent-related hold ups, contrast biotech and nanotech with the software industry, where development cycles are so short that new software may run afoul of patents still covering previous generations of software. Burk & Lemley, *supra* note 103, at 1622–23.

[239] Allen, *supra* note 2; Frischmann, *supra* note 142, at 172; FORD ET AL., *supra* note 49, at 4.

[240] Auerswald & Branscomb, *supra* note 183, at 232; FORD ET AL., *supra* note 49, at 10; Kalil, *supra* note 209, at 265–66. Private investors' willingness to invest in intermediate-stage commercialization has apparently varied somewhat over the years, however. Auerswald & Branscomb, *supra* note 213, at 231; T. Randolph Beard et al., *A Valley of Death in the Innovation Sequence: An Economic Investigation*, 18 RES. EVALUATION 343, 350–51 (2009).

assume the risk.[241] Development of many otherwise valuable science-based inventions never attain commercialization because of lack of funding for the intermediate stages of development in what has been termed the "Valley of Death."[242]

Private investors are reluctant to fund the intermediate stages of technology development for a variety of reasons, many of which are the same reasons that they do not invest in early-stage, basic research. Other things being equal, the more rapidly an investment yields returns the more likely investors are to invest, but research-intensive technologies do not lead to the kind of rapid innovation that can yield the immediate returns that investors want.[243] Instead, science-based technologies still in the early and even intermediate stages of development take too many years to yield returns, if they in fact yield any returns at all.[244] Much of the current development in nanotechnology, for example, commonly requires twice the time needed for commercialization in other venture-capital supported technologies[245] and is well beyond the accepted investment timetables of private industry.[246] Plus, the longer the development cycle, the more costly it is likely to be, making development even more unattractive as an investment.[247]

And it is not just the length of development cycles but also the uncertainty and risk inherent in science-based technologies that deter investment in the intermediate stages of development. Commercialization of basic research is a painstaking process of trial and error,[248] and university-initiated inventions in particular experience higher failure rates than private firm-initiated inventions, with up to half of university inventions failing during commercialization.[249] In addition to the technological uncertainties

---

[241] *See, e.g.*, Beard et al., *supra* note 240, at 344; *see generally* FORD ET AL., *supra* note 49, at 12–14 (providing an explanation and conceptualization of the "valley" in order to find out why it exists in the first place).

[242] The chronic underfunding of intermediate technological development has also been referred to as the "Darwinian seas" or "innovation gap." Auerswald & Branscomb, *supra* note 213, at 231. It has also been called the "funding gap." Beard et al., *supra* note 240, at 343.

[243] Abramowicz, *supra* note 204, at 1097.

[244] Auerswald & Branscomb, *supra* note 213, at 232.

[245] Schmoch & Thielmann, *supra* note 140, at 134; Allen, *supra* note 2; *see also* Wolfe, *supra* note 37 (explaining that development in nanotechnology start-ups average seven years from inception to market). *But see* Rothaermel & Thursby, *supra* note 145, at 846 (surmising, on the other hand, that nanotechnology development cycles are half as long as those typical of biotechnology).

[246] Lane & Kalil, *supra* note 28, at 52; *see also* Beard et al., *supra* note 240, at 345 n.3 (citing a Department of Energy report that venture capitalists, as a rule, expect a ten-time return on investments within five years).

[247] Abramowicz, *supra* note 204, at 1093.

[248] Mazzoleni & Nelson, *supra* note 209, at 1048.

[249] Emmanuel Dechenaux et al., *Appropriability and Commercialization: Evidence from MIT Inventions*, 54 MGMT. SCI. 893, 894 (2008); Frank T. Rothaermel & Marie Thursby, *Incubator Firm Failure or Graduation? The Role of University Linkages*, 34 RES. POL'Y 1076, 1078 (2005); *see also*

already mentioned, commercializing science-based inventions also involves the business uncertainties of defining markets and market demand.[250] Technological difficulties account for only about half of the failure rate among university inventions, with the remainder failing due to the business difficulties of identifying market opportunities for university inventions whose ultimate applications so frequently differ from what was expected during the early stages of commercialization.[251] Nanotechnology again has proven to be no exception, with both technological and marketing difficulties leading to high failure rates during commercialization efforts.[252]

Considering the time and expense involved and their minimal capacity even to assess risk, investors are understandably risk averse. The information gaps between inventing research scientists and investors are significant,[253] and few private investors can afford the fixed capital costs of acquiring the expertise necessary to assess the risks.[254] The intermediate stages of development are thus in many ways the most critical because they are the stages that resolve much of the technological and business uncertainty of commercialization.[255] Only once intermediate-stage development is complete, these uncertainties resolved, and a valid commercial plan proven are private investors willing to become involved.[256]

In this way the valley of death and the information gap between private interests and university researchers can create greater obstacles to downstream development than patents do. The difficulties of attracting investment in technologies with long and uncertain development cycles are often a more intractable problem than is the need to license upstream or complementary patents. As a matter of fact, identifying downstream firms to develop university research is one of the most difficult obstacles for technology transfer offices to overcome.[257]

Some private investors such as angel and seed investors specialize in early- and intermediate-stage development, however.[258] Indeed, a few angel

---

Thursby & Thursby, *supra* note 212, at 1052 (additional citations omitted) (citing evidence that university inventions have 72% failure rate for proof-of-concept inventions).

[250] Auerswald & Branscomb, *supra* note 213, at 229; Dechenaux et al., *supra* note 249, at 894; Kalil, *supra* note 209, at 265–66.

[251] Dechenaux et al., *supra* note 249, at 894.

[252] Allen, *supra* note 2; Wang et al., *supra* note 202, at 3498.

[253] Auerswald & Branscomb, *supra* note 213, at 230; Graham & Iacopetta, *supra* note 211, at 8–9; Atul Nerkar & Scott Shane, *Determinants of Invention Commercialization: An Empirical Examination of Academically Sourced Inventions*, 28 STRATEGIC MGMT. J. 1155 (2007); Scott Shane, *Selling University Technology: Patterns from MIT*, 48 MGMT. SCI. 122, 123 (2002); Charles W. Wessner, *Driving Innovations Across the Valley of Death*, 48 RES. TECH. MGMT. 9, 9 (2005).

[254] FORD ET AL., *supra* note 49, at 33–34.

[255] Auerswald & Branscomb, *supra* note 213, at 229–30; FORD ET AL., *supra* note 49, at 10; Kalil, *supra* note 209, at 265–66.

[256] Abramowicz, *supra* note 204, at 1071; Auerswald & Branscomb, *supra* note 213, at 229.

[257] Osenga, *supra* note 52, at 421.

[258] Auerswald & Branscomb, *supra* note 213, at 230.

investment companies, such as the Nano Business Angels network and the Central Coast Angel Network, have come to specialize in nanotech specifically.[259] Over time other venture capitalists and other potential investors will become less reluctant to invest in new technologies such as nanotechnology as investors develop expertise in and a level of comfort with the technologies and the technologies themselves mature, such that the perceived risk of investment attenuates.[260] Venture capital's interests in nanotechnology, for example, have waxed and waned over the years,[261] and venture capitalists have constituted only a small minority of overall funding of nanotechnology research for the past couple of decades.[262] Only once revenue streams from nanotechnology-based products finally began to grow in recent years did private industry funding for nanotechnology R&D finally begin to overtake government funding.[263]

Because of private capital's wariness of emerging technologies, development projects that are too uncertain and risky to attract private funding can obtain government funding from several federal agencies.[264] The Small Business Innovation Research (SBIR) program enacted in 1982, for example, allows federal agencies to grant funds to small businesses for the commercialization of government-sponsored R&D.[265] A number of agencies that fund nanotechnology basic research also issue SBIR grants, and the National Institutes of Health have even implemented a Bioengineering Nanotechnology Initiative to grant SBIR funds for biomedical nanotech projects.[266] The Small Business Technology Transfer (STTR) subpart of SBIR also funds collaborations between private industry and nonprofit educational and research facilities.[267] In the late 1980s, Congress also created the Advanced Technology Program (ATP) to provide matching funds for private investments in early-stage technological developments that face significant risk but are likely to yield significant and wide-ranging benefits.[268] Overall, government funding steps in to provide

---

[259] MILLER ET AL., *supra* note 5, at 190.

[260] Auerswald & Branscomb, *supra* note 213, at 232–34.

[261] Allen, *supra* note 2; Mark Boslet, *Nanotech Falls Out of Favor (Again) with VCs*, PE HUB (Nov. 11, 2010), http://www.pehub.com/2010/11/nanotech-falls-out-of-favor-again-with-vcs/ [https://perma.cc/J6NU-R3GX]; Tan, *supra* note 96; Wolfe, *supra* note 37.

[262] Bawa, *supra* note 3, at 702 n.6.

[263] NANOTECHNOLOGY UPDATE: CORPORATIONS UP THEIR SPENDING AS REVENUES FOR NANO-ENABLED PRODUCTS INCREASE, LUX RESEARCH INC. 1–2 (Dec. 2013), https://www.nsf.gov/crssprgm/nano/reports/LUX14-0214_Nanotechnology%20StudyMarketResearch%20Final%2017p.pdf [https://perma.cc/XC8A-QPBJ].

[264] BNA, *supra* note 160, at 285–86.

[265] Kalil, *supra* note 209, at 266–67.

[266] *Id.* at 266–68 (describing inter alia the National Institutes of Health "Bioengineering Nanotechnology Initiative"); MONICA, *supra* note 2 (listing federal agencies funding basic nanotech research).

[267] BNA, *supra* note 160, at 285; Vertinsky, *supra* note 200, at 1959 n.30, 2007, 2010.

[268] Kalil, *supra* note 209, at 266; Wessner, *supra* note 253, at 9–10.

about 20% to 25% of all funds for early-stage technology development,[269] with state governments also increasingly providing public funds for the same purposes, such as funding university start-ups.[270] Nanotechnology companies can also apply for Defense Advanced Research Projects Agency grants for high-risk projects that offer advances in military preparedness.[271]

3. *Limitations on Equipment and Materials*

Furthermore, constraints on access to the necessary tools and materials as well as skills raise imitation costs in a way that makes patent protections largely inconsequential and even unnecessary in science-based technologies.[272] Private control over relevant research facilities and materials, for example, create nonpatent exclusivities affecting downstream development. Not just industry but also universities are often perceived as being quite proprietary over their materials and instruments, particularly biotech materials, and frequently do not allow the public free access to their research materials and tools.[273] In point of fact, a survey of biotech researchers documents that the need to negotiate access to necessary materials such as cell lines was a more limiting factor than upstream patents.[274] And even when they do agree to share materials and equipment, universities often employ materials-transfer agreements that include reach-through royalty provisions or other restrictive conditions such as limits patenting to downstream products.[275]

Of course, proprietary university policies on sharing research materials may be a part of an overall shift toward less liberal sharing caused by Bayh-Dole's emphasis on university ownership of their research. Universities may feel that they need to be more protective of their research materials and tools as a way of simultaneously protecting their research patents,[276] for instance, or universities may be forced to be more possessive of their materials because of the restrictions imposed under industry-sponsored research

---

[269] Auerswald & Branscomb, *supra* note 213, at 232.

[270] *See* Michael MacRae, *Commercializing University Research*, ASME (Mar. 2011), https://www.asme.org/engineering-topics/articles/high-tech-startups/commercializing-university-research [https://perma.cc/RYQ2-QWCZ] (reporting on the state of Oregon's program to help its public university-based start-ups).

[271] MILLER ET AL., *supra* note 5, at 193. Government funding programs for intermediate stage development also may help by signaling to the market which technologies are worth investing in. Wessner, *supra* note 253, at 9–10.

[272] Adelman, *supra* note 51, at 986–87.

[273] BNA, *supra* note 160, at 215–16.

[274] Eisenberg, *supra* note 151, at 1066.

[275] Greenbaum, *supra* note 68, at 362–64; Mowery & Ziedonis, *supra* note 53, at 159.

[276] BNA, *supra* note 160, at 429; Rebecca S. Eisenberg, *Bargaining Over the Transfer of Proprietary Research Tools: Is This Market Failing or Emerging?*, *in* EXPANDING THE BOUNDARIES OF INTELLECTUAL PROPERTY: INNOVATION POLICY FOR THE KNOWLEDGE SOCIETY 223–28 (Rochelle C. Dreyfuss et al. eds., 2001); Mowery & Ziedonis, *supra* note 53, at 159.

agreements relying on the expectation of university patent ownership under Bayh-Dole.[277] On the other hand, universities may be protective simply because producing research materials and tools requires effort and investment and because those materials and tools help universities establish a competitive edge as leading research institutions.[278] Regardless of the motivation, however, the fact stands that exclusive access to research materials and tools is a more significant problem in technology commercialization efforts than patents are.[279]

One method that has been used to address the holdup problems created by the need for research materials is to standardize materials-transfer agreements, at least as between equally situated research institutions such as universities, as proposed by the NIH and endorsed by the AUTM for use in the transfer of biotechnology research materials.[280] This effort fell somewhat flat, however, as universities often may continue to place their economic self-interest over Mertonian norms and social welfare.[281]

Universities have, however, begun to set up technology incubators and research and science parks to house both university- and industry-based start-ups; to facilitate closer relationships between universities and private industry for joint projects, consultation, and other endeavors; and to provide access to research materials and tools.[282] Industry- and university-based "precompetitive" research and development consortia have also recently evolved to share research and development resources, such as research tools,

---

[277] BNA, *supra* note 160, at 241; James Flanigan, *Collaborating for Profits in Nanotechnology*, N.Y. TIMES, July 15, 2009, at B6; Arti K. Rai, *Proprietary Rights and Collective Action: The Case of Biotechnology Research with Low Commercial Value* 4 (Duke L. Sch. Legal Stud., Research Paper No. 59, 2004), http://ssrn.com/abstract=568521 [https://perma.cc/UT6Y-YX9P] (noting also a significant increase in proprietary rights over upstream materials in biotechnology research over the past two decades).

[278] Walsh et al., *supra* note 149, at 320 (noting that universities themselves rank commercial concerns at the bottom of the list of reasons for their proprietary attitudes toward research materials and tools).

[279] Eisenberg, *supra* note 151, at 1062; *cf.* Greenbaum, *supra* note 68, at 363 (noting that materials transfer agreements are not subject to the same exceptions that patent and copyright rights are). *But see* Mowery & Ziedonis, *supra* note 53, at 157 (finding evidence that materials transfer agreements do not hinder commercialization of university research).

[280] Uniform Biological Material Transfer Agreement: Discussion of Public Comments Received; Publication of the Final Format of the Agreement, 60 Fed. Reg. 12,771 (Mar. 8, 1995); Arti K. Rai, *Regulating Scientific Research: Intellectual Property Rights and the Norms of Science*, 94 NW. U.L. REV. 77, 113 nn.201–04 (1999); Lee, *supra* note 135, at 925.

[281] Rai, *supra* note 277, at 13; Rai & Eisenberg, *supra* note 45, at 289, 305–06.

[282] Matthew M. Mars & Sherry Hoskinson, *The Organizational Workshop: A Conceptual Exploration of the Boundary Spanning Role of University Entrepreneurship and Innovation Centers*, *in* ADVANCES IN THE STUDY OF ENTREPRENEURSHIP, INNOVATION AND ECONOMIC GROWTH: SPANNING BOUNDARIES AND DISCIPLINES: UNIVERSITY TECHNOLOGY COMMERCIALIZATION IN THE IDEA AGE, *supra* note 95, at 120; BNA, *supra* note 160, at 266–67; Rothaermel & Thursby, *supra* note 249, at 1076–77; Siegel & Phan, *supra* note 207.

materials, and even data.[283] These precompetitive consortia are probably the most effective means of providing public access to otherwise proprietary materials, as the consortia allow multiple downstream developers to share foundational resources. Such precompetitive consortia are difficult to organize, however, and face steep transaction costs that may require governmental intervention, or changes in relevant law, to overcome.[284]

4. Tacit Knowledge

Moreover, limited access to research materials and tools is not the only type of nonpatent exclusivity that can obstruct downstream development. Another form of effective exclusivity is tacit knowledge, a phenomenon common in fields such as biotechnology and nanotechnology, where university research can lead to such major advances over the prior art that learning curves become too steep for others in the field to be able to acquire the necessary expertise.[285] As a result, the knowledge and skills necessary for downstream development in the field remain concentrated in the hands of just a few researchers and impose an unavoidable limit on downstream development that often eclipses other types of exclusivity, including both patent protection and first-mover advantages.[286]

First, commercialization of most university research, whether or not patented, requires the participation of the inventing researcher. Estimates indicate that somewhere between 40% and 71% of licensed university research requires faculty involvement to be successfully commercialized.[287] Even genetics remained dependent on tacit knowledge for decades after Cohen & Boyer's seminal invention of recombinant DNA technology.[288] Nanotechnology also remains highly knowledge-intensive, such that success in the field is limited to firms with access to researchers with the requisite specialized skills in the area.[289]

---

[283] Liza Vertinsky, *Making Knowledge and Making Drugs? Experimenting with University Innovation Capacity*, 62 EMORY L.J. 741, 763–64 (2013) [hereinafter Vertinsky, *Making Knowledge*]; BNA, *supra* note 160, at 299; *see also* Liza S. Vertinsky, *Patents, Partnerships, and the Pre-Competitive Collaboration Myth in Pharmaceutical Innovation*, 48 U.C. DAVIS L. REV. 1509, 1530–37 (2015) [hereinafter Vertinsky, *The Pre-Competitive Collaboration Myth*]; Matthew Herder, *Patents & the Progress of Personalized Medicine: Biomarkers Research as Lens*, 18 ANNALS HEALTH L. 187, 220 (2009).

[284] Vertinsky, *Making Knowledge*, *supra* note 283, at 808–20; Vertinsky, *The Pre-Competitive Collaboration Myth*, *supra* note 283, at 1517.

[285] Darby & Zucker, *supra* note 145, at 1; Rothaermel & Thursby, *supra* note 145, at 833.

[286] Rothaermel & Thursby, *supra* note 145, at 833; *see generally* Darby & Zucker, *supra* note 145.

[287] Jerry G. Thursby & Marie C. Thursby, *Pros and Cons of Faculty Participation in Licensing*, *in* 16 ADVANCES IN THE STUDY OF ENTREPRENEURSHIP, INNOVATION AND ECONOMIC GROWTH: UNIVERSITY ENTREPRENEURSHIP AND TECHNOLOGY TRANSFER, *supra* note 95, at 192; Darby & Zucker, *supra* note 145, at 4; Rothaermel & Thursby, *supra* note 249, at 1078–79.

[288] *See* Darby & Zucker, *supra* note 145, at 9–10 (suggesting dependence on tacit knowledge in genetics lasted at least as long as the early 2000s after Cohen and Boyer's invention in the early 1970s).

[289] MILLER ET AL., *supra* note 5, at 189; Wang et al., *supra* note 202, at 3497–99.

For example, tacit knowledge was a significant factor in the development of the scanning tunneling microscope and the atomic force microscope, two of the foundational research tools through which the entire field of nanotechnology even became possible.[290] Invented by IBM employees Heini Rohrer and Gerd Binnig in 1979, the STM was at first a commercially valueless dud in which IBM lost interest.[291] Rohrer and Binnig did not want their brainchild to fall into oblivion, however, so they cultivated a select few academic researchers from a variety of disciplines who were interested in using the STM for basic research.[292] This core group of STM enthusiasts struggled for years to acquire enough of Binnig and Rohrer's expertise to replicate the microscope.[293] Only once a critical mass of enthusiasts finally had the expertise to construct STMs on their own and to spark the interests of their home institutions in the research benefits of these new devices did IBM decide to begin commercial STM production in the late 1980s.[294] Even then, for the first five years or so after they were invented, scanning tunneling and atomic-force microscopes were accessible only to those with the resources and skills necessary to construct the microscopes on their own.[295] Moreover, the facilities that invested in STMs still had to train someone to use the microscopes, given that the simple act of using an STM continued to require some degree of expertise and tacit knowledge for decades.[296]

Second, faculty involvement is often crucial to locating licensees for university research. A researcher's tacit knowledge can be important to bridging the information gaps between investors and researchers that contribute to valley-of-death issues and can help to inspire investor confidence by establishing a researcher's reputation and status.[297] In fact, potential licensees are often identified only through a faculty researcher's contacts with industry players[298] and through personal relationships rather than arm's-length marketing.[299]

Of course, like patent protection, first-mover advantages, and other

---

[290] *See* Mody, *supra* note 187, at 56.

[291] *Id*. at 60.

[292] *Id.* at 60–61.

[293] *Id.* at 56–57, 60–61.

[294] *Id.* at 60–61.

[295] Darby & Zucker, *supra* note 145, at 14, 25.

[296] Mody, *supra* note 187, at 68.

[297] BNA, *supra* note 160, at 429; *see also supra* notes 253–57 and accompanying text (discussing information gaps between researchers and investors as exacerbating the valley of death).

[298] Samuel Estreicher & Kristina A. Yost, *University IP: The University as Coordinator of the Team Production Process* 12–13 (N.Y.U. Pub. L. & Legal Theory Working Papers, Working Paper No. 489, 2016), http://lsr.nellco.org/nyu_plltwp/489 [https://perma.cc/27QG-RWE7].

[299] Donald Siegel et al., *Assessing the Impact of Organizational Practices on the Productivity of University Technology Transfer Offices: An Exploratory Study* 29–30 (Nat'l Bureau of Econ. Res., Working Paper No. 7256, 1999), http://www.nber.org/papers/w7256 [https://perma.cc/UL2K-8VVS].

types of exclusivity, tacit knowledge is time-limited; tacit knowledge can remain tacit for only so long. As understanding of an emerging technology matures and spreads, others will gain access to the technology. Exactly how long any such tacit knowledge might provide some sort of exclusivity in nanotech development is an open question and likely depends on the particular development at issue, but that being said, at least one study by economists strongly suggests that the duration of nonpatent exclusivity based on tacit knowledge and access to research tools was twice as long in biotech as in nanotech.[300]

While tacit knowledge and other natural exclusivities over university research continue to be in force, however, it is not surprising that commercialization efforts in science-based technologies tend to concentrate geographically around university faculty with the requisite expertise and materials.[301] Geographic collocation has the advantage of allowing hands-on participation by faculty members or others with pivotal tacit knowledge, access to university technology incubators and research parks, and collaboration or even acquisition of university-initiated start-up companies.

Indeed, in the last three decades or so, universities have begun to license their upstream research patents to start-up companies at increasing rates.[302] University start-ups could help solve some of the nonpatent problems in developing upstream research.[303] For example, start-ups may help both transfer tacit knowledge and provide access to research tools and materials. Faculty researchers and their graduate students commonly are active parts of university-based start-ups and have become increasingly active participants in private industry more generally, as research scientists now commonly move between universities and industry and private firms host postdoctoral fellows.[304] The tacit knowledge these students and faculty researchers possess continues to be exclusive to them,[305] of course, until such time that understanding of the underlying technology matures and spreads and becomes less tacit over time.[306] Nonetheless, faculty involvement in start-ups and other private enterprises does at least provide a conduit by

---

[300] Rothaermel & Thursby, *supra* note 145, at 846.

[301] Darby & Zucker, *supra* note 145, at 17; *see also* Giovanni Abramo et al., *The Role of Information Asymmetry in the Market for University-Industry Research Collaboration*, 36 J. TECH. TRANSFER 84, 87 (2011) (and sources cited therein).

[302] BNA, *supra* note 160, at 261; Estreicher & Yost, *supra* note 298, at 11–12. As a practical matter, licensing government-funded university research to start-ups fits neatly within Bayh-Dole's preference for licensing to small-businesses. BNA, *supra* note 160, at 29, 207, 261; Rothaermel & Thursby, *supra* note 145, at 833. University-based start-ups are still a relatively infrequent form of technology transfer, however. Kesan, *supra* note 160, at 2189; Estreicher & Yost, *supra* note 298, at 13.

[303] BNA, *supra* note 160, at 261.

[304] Lee, *supra* note 160, at 47.

[305] For this reason, private acquisition of university-based start-ups can aggravate holdup problems by consolidating ownership of pivotal upstream patents, research tools and materials, and knowledge.

[306] Lee, *supra* note 88, at 1525.

which tacit knowledge can be transferred to the commercial sector. Likewise, to the extent that university-based start-ups make use of university research tools and materials, start-ups can provide the commercial sector with at least some, albeit limited, access to tools and materials over which the university might exert proprietary rights.

To a lesser extent, start-ups may also help bridge the valley of death. Although larger or at least established firms might have more expertise in commercializing and marketing generally,[307] start-ups offer their own advantages.[308] University start-ups generally are more nimble and less risk-averse than not only universities but also larger, more established firms.[309] Unlike their parent universities, moreover, university-based start-ups are designed to be commercial entities that presumably will have the kinds of market orientations that universities lack while also avoiding the bureaucracy of university administrations and constituencies. And to the extent that they are funded through alternatives to private investment, university start-ups represent an intermediate (and separately funded and executed) step between upstream research and marketable downstream applications.[310] Start-ups work on the intermediate development stages, making commercialization less risky and more attractive to private investors. And although only a small percentage of licensed university research is introduced through start-ups rather than through more established firms,[311] university-based start-ups are by far the most common way for new nanotechnology businesses to get their start;[312] most nanotech companies today are university-based start-ups.[313]

5. *Multidisciplinarity and Personnel*

One of the most exciting aspects of nanotechnology is its potential to revolutionize an amazingly wide variety of technological and scientific fields. As noted above, however, this cross-industry potential is also one of nanotechnology development's potential drawbacks, although not for the reasons that Professor Lemley and others have posited. Development in multidisciplinary fields involves not just the need to coordinate patents and other legal rights but also the need to coordinate technological expertise from among the relevant fields.[314] Although mixing disciplines can create

---

[307] BNA, *supra* note 160, at 261.

[308] Chukumba & Jensen, *supra* note 96, at 4.

[309] BNA, *supra* note 160, at 261; Rothaermel & Thursby, *supra* note 145, at 833.

[310] *See* Heller & Eisenberg, *supra* note 59, at 698.

[311] Mowery, *supra* note 90, at 53.

[312] MILLER ET AL., *supra* note 5, at 140.

[313] *Id.* at 136.

[314] Laura G. Pedraza-Fariña, *Patent Law and the Sociology of Innovation*, 2013 WIS. L. REV. 813, 838–40 (2013); Sharon Tsai-hsuan Ku, *Forming Interdisciplinary Expertise: One Organization's*

new paradigms that spur innovation, such "intellectual migration" is not without its own transaction costs and uncertainty, completely independent of patent rights or their distribution.[315]

That is to say, "nanotechnologists" do not simply appear out of thin air. Nanotechnologists instead must be developed from other disciplines with other technological paradigms.[316] Like some other pioneering new technologies, nanotechnology was born of parallel but independent tracks of research in various fields. For instance, someone who started out as a materials scientist may create a nanotech advance with promising implications for medical research. To develop the invention further, the materials scientist will need to collaborate with an expert in medicine, biotechnology, or other fields, however, and the transaction costs of identifying and coordinating with others from different fields to collaborate on a new project can be steep. And even then, many factors create significant social barriers to the multidisciplinary cooperation necessary to design usable nanotechnology end products; institutional differences, lack of interdisciplinary standards and protocols, peer and institutional support, and other infrastructure, and even cultural differences between disciplines and the "inertia of disciplinary tradition," all can create a drag on the development process.[317] In these and other ways, the sociological aspects of technology development and any attendant "culture shock" may slow commercialization.

Perhaps because of nanotechnology's multidisciplinary nature and the need to unite specialists from many different areas, the majority of federal funding in nanotechnology thus far has been through government research laboratories rather than through university or private research facilities and thus falls under the provisions of the Stevenson-Wydler Act rather than Bayh-Dole.[318] The Stevenson-Wydler Act allows government-operated laboratories to enter into cooperative research and development agreements (CRADAs) with private contractors and to license, exclusively or nonexclusively, or even to assign title to, any resulting patents.[319] In this

---

Journey on the Road to Translational Nanomedicine, 4 WIRES NANOMEDICINE & NANOBIOTECH. 366 (2012).

[315] Pedraza-Fariña, *supra* note 314, at 820; *see also* Wang, *supra* note 202, at 3497 (identifying the costs associated with intellectual migration).

[316] Ku, *supra* note 314, at 367.

[317] *Id*. at 374.

[318] MILLER ET AL., *supra* note 5, at 146; Wang, *supra* note 89, at 53.

[319] The Stevenson-Wydler Technology Innovation Act of 1980 originally directed federal agencies to transfer federally owned technology to both state and local governments, and to the private sector, but it was later amended and expanded to its present form. Wang, *supra* note 89, at 54–55; *see also* Arno, *supra* note 133, at 644 (referring to amendments to Federal Technology Transfer Act of 1986); Eisenberg, *supra* note 45, at 1707–08 (referring also to the National Technology Transfer and Advancement Act of 1995). Under Stevenson-Wydler, federal laboratory research must be transferred to private industry for commercialization, mostly through groups such as the Federal Laboratory Consortium for Technology

regard, CRADAs are effectively cost-sharing agreements, with the government contributing access to government equipment, facilities, and personnel rather than research funds.[320] The most relevant virtue of CRADAs, moreover, is that they can pool the expertise of federal laboratory researchers and private researchers from among a variety of disciplines—a point particularly important to multidisciplinary areas such as nanotechnology research.[321]

The federal government has also used public funds to establish other types of research centers that can help solve many of the problems of science-based technology development.[322] One such center devoted specifically to nanotechnology development is the Nanotechnology Characterization Laboratory (NCL) at the National Cancer Institute, a federally funded laboratory created as a collaborative effort among pharmaceutical companies, university researchers, and government agencies to offer free molecule-characterization services to universities and industrial nanodrug developers working in translational medicine.[323] The NCL thus serves not only to standardize the metrics for nanoparticle characterization but also to collect the necessary expertise from diverse institutions and disciplines, including biologists, chemists, toxicologists, immunologists, pathologists, technicians, and biomedical and chemical engineers, thus helping to overcome interdisciplinary gaps.[324] The NCL has the further advantage of helping to usher nanodrugs through the riskier intermediate development stages and to make those drugs more attractive to private investors.[325] Finally, the NCL is also a noncommercial organization that produces no scientific publications or intellectual property but is nonetheless more commercially oriented and flexible than any university could be.[326]

One unique and perhaps more significant aspect of nanotechnology that may be slowing down its development, according to nanotech expert Eric Drexler, is that government, private investors, and even scientists

---

Transfer that are specially created to facilitate private acquisition of federal research. MILLER ET AL., *supra* note 5, at 146. Unlike research funded under the Bayh-Dole Act, however, federal laboratories typically retain patent rights over research created under a CRADA, Wang, *supra* note 89, at 63, but generally avoid granting exclusive licenses to their research whenever possible, MILLER ET AL., *supra* note 5, at 149.

[320] Wang, *supra* note 89, at 54–55.

[321] Frischmann, *supra* note 49, at 391–92; Vertinsky, *Making Knowledge*, *supra* note 283, at 760–65; Wang, *supra* note 89, at 69–70.

[322] *See, e.g.*, John C. Reed, *NCATS Could Mitigate Pharma Valley of Death: National Center for Advancing Translational Sciences Essential to Capitalize on Basic Research*, 31 GENETIC ENG'G & BIOTECH. NEWS, May 2011, 6–8, http://www.genengnews.com/gen-articles/ncatscould-mitigate-pharma-valley-of-death/3662/ [https://perma.cc/2KLX-BALB].

[323] Ku, *supra* note 314, *passim*.

[324] *See generally id.*

[325] Reed, *supra* note 322, at 7.

[326] Ku, *supra* note 314, *passim*.

themselves still do not fully appreciate what a true nanotechnology revolution would mean.[327] According to Drexler, the real definition of nanotechnology is a radical and comprehensive transformation in how things are manufactured, or what Drexler terms "atomically precise manufacturing" (APM).[328] Although closely related, the diffuse and largely piecemeal innovations that society currently identifies as nanotechnology have distracted from the bigger picture of what nanotechnology can offer and delayed realization of this promise as a result.[329]

Specifically, Drexler argues that although development efforts in nanotechnology thus far have led to the fabrication of new materials that exploit the unique phenomenon occurring at the nanoscopic level,[330] these advances have led mostly to use of the new nanomaterials as incremental improvements to existing technologies rather than fundamental changes in manufacturing methods or APM.[331] As one science historian put it, nanotechnology "consists of different, largely 'mono-disciplinary fields' which are rather unrelated to each other and which hardly share more than the "nano" prefix."[332] Drexler contends that nanotechnology is not just about improving existing technologies, however, but rather about the profound change in manufacturing globally that would come from APM.[333] Although a more scientific explanation of APM is obviously beyond the scope of the discussion here, atomically precise manufacturing is in many ways analogous to 3D printing or intracellular protein synthesis in that APM allows fabrication of an infinite variety of materials and objects through meticulous, sequential assembly of individual molecules of common elements.[334] Atomically precise manufacturing allows less expensive, environmentally cleaner, and thus "ultra-efficient" industrial-level production to take place not just in factories but also on desktops or anywhere else.[335] Atomically precise manufacturing will revolutionize fabrication processes because APM uses less raw material to create objects

---

[327] DREXLER, *supra* note 201, at xi.

[328] *Id.* at x, xii.

[329] *Id.* at xi, 121, 178, 195–96.

[330] *Id.* at xi.

[331] *Id.* at ix, 198; MILLER ET AL., *supra* note 5, at 151–52; Akhtar, *supra* note 6, at 134; *see also* Wasson, *supra* note 38, at 10 n.6 (explaining that nanotechnology has "focused on enhancing traditional products").

[332] Ku, *supra* note 314, at 367.

[333] DREXLER, *supra* note 201, at xi.

[334] PRODUCTIVE NANOSYSTEMS: A TECHNOLOGY ROADMAP v, 4 (K. Eric Drexler et al. eds., 2007) [hereinafter ROADMAP]; Bruce Dorminey, *Nanotechnology's Revolutionary Next Phase*, FORBES (Feb. 26, 2013), http://www.forbes.com/sites/brucedorminey/2013/02/26/nanotechnologys-civilization-changing-revolutionary-next-phase/; *Productive Nanosystems: From Molecules to Superproducts*, NANO WERK, http://www.nanowerk.com/nanotechnology/videos/Productive_nanosystems_From_molecules_to_superproducts.php [https://perma.cc/76LJ-LYLV] (last visited Nov. 15, 2016).

[335] DREXLER, *supra* note 201, at ix–xii.

that are stronger and yet lighter, thereby reducing both shipping costs and energy costs.[336] It is perhaps this kind of technologically brave new world that many predicted nanotechnology would bring and that critics worry that the Bayh-Dole Act has helped stymy.

And in fact, progress in APM has not been as rapid as Drexler and others had hoped,[337] but Drexler attributes the logjam to a lack of investment and focus, not to upstream patenting.[338] APM does exist to a limited extent in some isolated fields, but systemic changes in manufacturing technologies have yet to emerge.[339] According to Drexler, this is due in part to the fact that nanotechnology development continues to be scattered among divergent scientific disciplines, a cohesive vision of APM is still lacking.[340] Government agencies and other investors have focused instead on the development of nanoparticles and other lower hanging fruit with more readily attainable and yet less impressive returns.[341]

6. *Safety Fears*

A different risk that some nanotechnology enthusiasts mention as a problem for nanotech development is the health, environmental, and other dangers that nanotech applications may pose. Nanotechnology's relative unfamiliarity has provoked the same kinds of fears that have beset research in other research-based fields such as pharmaceuticals, genetically modified organisms, cloning, and human embryonic stem cells.[342] And because nanotech is such a uniquely cross-disciplinary area of research, it has applications and therefore potential safety ramifications in a number of heavily regulated fields.[343] In fact, to avoid triggering governmental regulatory review or public apprehension, some companies may try to keep their products "below the radar" by failing to identify products containing nanomaterials.[344] More importantly, concerns about possible regulatory barriers have also dampened investment in nanotech development: the specter of regulatory restrictions and potential liability for consumer, environmental, or other harms create additional uncertainties that yet further

---

[336] *Id*. at 162–63.

[337] *Id*. at 195.

[338] *Id*. at 178.

[339] *See* ROADMAP, *supra* note 334, at v, 4 (listing technologies using living tissue and scanning probe manipulation on crystal surfaces as examples of currently employed APM).

[340] DREXLER, *supra* note 201, at 121.

[341] *Id*. at 178, 195.

[342] *See* SOCIETAL IMPLICATIONS, *supra* note 20, at 203; 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, 127–28 (2007); Gary E. Marchant et al., *What Does the History of Technology Regulation Teach Us About Nano Oversight?*, 37 J.L. MED. & ETHICS 724, 727–28 (2009) (noting that society often has strong social and ethical concerns about emerging technologies such as nanotechnology).

[343] Marchant, *supra* note 342, at 724.

[344] Wolfe, *supra* note 37.

deter private and even government funding in nanotech R&D.[345] Public fears about nanotechnology have also negatively influenced enthusiasm for the field, and therefore its success.[346]

Some of the health and environmental concerns about nanotechnology are well-founded. Graphene particles, for example, may present some risk of respiratory damage, although review of graphene is ongoing.[347] Similarly, carbon nanotubes and buckyballs may be toxic when used in humans, whereas dendrimers may be a less toxic alternative for use in living organisms.[348] Particular instances of environmental and health dangers have apparently led to overgeneralization, however, and are leading some commentators to worry that the toxicity of some nanomaterials has created a stigma that encompasses all of nanotechnology in one stroke of the brush.[349]

And the science-fiction-level hype around nanotechnology has indeed led to popular but distorted fears about its safety. Some have even drawn on science fiction to dream up sensationalist, apocalyptic scenarios for how nanotechnology could herald the end of the world as we know it. Perhaps the most infamous of this latter category is the late Michael Crichton's "gray goo:" self-replicating nanobots that escape the laboratory and run amok, devouring the entire biosphere and turning it into copies of themselves.[350]

Such a nano-apocalypse is unlikely and perhaps even scientifically impossible,[351] but whether outlandish or reasonable, these fears have been enough to spur calls for caution in and even a moratorium on nanotechnology development until further research can be done on the potential safety impact of the field and appropriate regulations can be put in place.[352] A 2000 article by Bill Joy of Sun Microsystems even went so far as to call for a ban on nanotechnology because of its perceived perils to human health and safety.[353] Whether such moratoria or outright bans are warranted and whether nanotechnology threatens health and environmental harms significantly greater than those in other technologies are open questions.[354]

---

[345] Allen, *supra* note 2; Lee, *supra* note 175, at 323; Schmoch & Thielmann, *supra* note 140, at 133.

[346] Marchant, *supra* note 342, at 725.

[347] Philip Shapira et al., *Early Patterns of Commercial Activity in Graphene*, 14 J. NANOPART. RES. 811, 812 (2012).

[348] Lee, *supra* note 175, at 323.

[349] *See id*.; Schmoch & Thielmann, *supra* note 140, at 133 (noting that lack of conclusive toxicity studies could give nanotech a negative image and hinder its commercialization).

[350] *See* DREXLER, *supra* note 6, at 172–73; Bawa, *supra* note 3, at 703; Glenn Harlan Reynolds, *Nanotechnology and Regulatory Policy: Three Futures*, 17 HARV. J.L. & TECH. 179, 188 (2003).

[351] *See* Fiedler & Reynolds, *supra* note 6, at 605–06 (stating that nanorobot existence has a science fiction resonance, but "the reality is less dramatic").

[352] *See* Bawa, *supra* note 3, at 703; Rao, *supra* note 63, at 861–62.

[353] Bill Joy, *Why the Future Doesn't Need Us*, WIRED (Apr. 1, 2000, 12:00 PM), https://www.wired.com/2000/04/joy-2/ [https://perma.cc/D54F-XBDP].

[354] *See* Marchant et al., *supra* note 342, at 726.

What is clear, however, is that apprehension about nanotechnology's potential hazards have helped obstruct progress in the field.

C. *So Why Bother Patenting Science-Based Technologies at All?*

The discussion above demonstrates that to attribute the lack of progress in nanotechnology development solely or even primarily to the Bayh-Dole Act and upstream patenting, university patenting, or the combination thereof overlooks a whole host of other factors that play a much more significant role in science-based technologies. This is not to say upstream research patenting by universities is *entirely* inconsequential. On the one hand, the costs of licensing upstream university patents may at the margin occasionally tip the scales toward nondevelopment, as Professor Lemley and others have argued.[355] Alternatively, as this author has argued, upstream patents may on very rare occasions facilitate downstream development.[356] The vast majority of upstream patents held by universities in science-based technologies, however, are simply irrelevant either as a handicap or as a help in downstream development.

The question then becomes, why would universities take the trouble to patent their research at all? And why did Congress believe it to be a good idea to pass the Bayh-Dole Act and to encourage universities to patent their research? If patents on basic university research have so little effect on downstream commercialization of that research, at the very least universities are simply wasting their already limited resources in bothering to file and prosecute patent applications.

And in fact, universities do not patent the vast majority of their faculties' research, as noted above.[357] Very little of university research is eligible for patenting, an even smaller percentage is worth the costs of patenting, and almost no university research yields profits from patent licensing.[358] As a result, most university TTOs operate at a loss; again, patenting and licensing university research is a money-losing proposition for all but the fortunate few.[359]

That being said, not all university patents and university research fall into the category of basic upstream research, and not all university research

---

[355] *See supra* Section II.

[356] Morris, *supra* note 127, Part I; Emily Michiko Morris, *Flexing Bayh-Dole* (unpublished manuscript) (on file with author).

[357] *See supra* notes 177–79 and accompanying text.

[358] *Id.*

[359] *See* Greenbaum, *supra* note 68, at 331, 358–59 (citing a lack of interest in scientists who wish to develop university-owned inventions because almost none of university research yields profits from licensing); Thomas K. Grose, *A Challenging Matchup*, 15 AM. SOC'Y ENG'G EDUC. PRISM 20 (2006) (discussing that companies complain that too many university technology transfer administrators have an "unrealistic notion that they can make money off of all research").

is performed solely for the sake of knowledge. As a first matter, patents on university inventions in applied rather than basic research, such as university research in engineering, applied sciences, and some areas of biotechnology, require fewer and less risky additional steps to achieve commercialization and therefore are easier to license and higher in commercial value.[360] And even in the basic sciences, patented university research often serves dual roles both as upstream building blocks for downstream development and as "completed" products ready for use as commercially available research tools.[361] Second, private firms that sponsor university research will often ask the university to patent any consequent inventions and to grant these firms exclusive licenses to those patents.[362] Patents therefore can be worthwhile for the small percentage of university research conducted under private sponsorship agreements.[363] Third, universities may be willing to invest in patenting because of the reputational benefits patents provide,[364] although publication and other less costly signals of productivity may serve just as well.[365]

But as for why universities patent research outside of these rather narrow categories, the most likely explanation is the "home run mentality" of some university TTOs and even faculty.[366] Because of what has now become the near-mythological status of the patents on Harvard's OncoMouse and the University of Wisconsin's human stem cell technology, whose unusually high commercial value garnered millions in revenue for their respective universities,[367] many TTOs have come to regard university research patents as a sort of lottery ticket through which the TTOs hope eventually to hit it big on the one blockbuster patent that will earn untold fame and fortune for

---

[360] David C. Mowery & Bhaven N. Sampat, *The Bayh-Dole Act of 1980 and University-Industry Technology Transfer: A Model for Other OECD Governments?*, 30 J. TECH. TRANSFER 115, 116 (2005).

[361] *See* Dreyfuss, *supra* note 128, at 468.

[362] Jensen & Thursby, *supra* note 97, at 252. Although Bayh-Dole does not allow universities to assign the rights to their patents ahead of time if the covered research is also funded in part through federal funds (because Bayh-Dole reserves the government's right to veto such transfers). Sean M. O'Connor, *Intellectual Property Rights and Stem Cell Research: Who Owns the Medical Breakthroughs?*, 39 NEW ENG. L. REV. 665, 669 (2005). The potential to patent and exclusively license the research is made clear under the Act. *Id.* at 687. When it comes to university patents, as opposed to other forms of university technology transfer, private firms also tend to be more interested in readily commercializable, applied research. Wesley M. Cohen et al., *Links and Impacts: The Influence of Public Research on Industrial R&D*, 48 MGMT. SCI. 1, 16–17 (2002); Fini & Lacetera, *supra* note 95, at 10.

[363] Eisenberg, *supra* note 45, at 1700; Nelson, *supra* note 103, at 463.

[364] *See, e.g.*, Lee, *supra* note 128, at 676 ("Furthermore, centralized government registration of patents helps establish scientific consensus."); Love, *supra* note 208, at 332–34 (presenting research that more than a third of the respondents reported that patents enhanced their universities' and their own reputations).

[365] Adelman, *supra* note 171, at 127; Kesan, *supra* note 160, at 2184.

[366] Robert E. Litan et al., *Commercializing University Innovations: Alternative Approaches*, 8 INNOVATION POL'Y & ECON. 31, 43–44 (2007).

[367] *Cf.* Walsh et al., *supra* note 149, at 296–309 (discussing the commercial success of these patents).

the university and the inventing faculty.[368] This home-run mindset has led TTOs to hold some arguably unrealistic expectations about their patents' value and to focus too much of their limited resources on pursuing patents on the technologies with the greatest perceived blockbuster potential.[369] Because of the uncertainty inherent in science-based technologies, however, the eventual commercial value of upstream patents in these fields is highly variable and difficult to predict,[370] much like a lottery ticket. Not surprisingly, the home-run mentality has caused universities to invest in filing and accumulating patents that ultimately have little to no commercial value.

It is therefore not surprising that, when stuck with patents that turn out to have no market value, universities often decide not to pay maintenance fees for the patents and allow them to fall into the public domain instead.[371] Professor Kimberly Moore's study of patent-renewal rates and maintenance-fee payments provides corroborative evidence, documenting that early-stage patents are more likely to lapse for nonpayment of maintenance fees where the underlying technologies' development costs are high and where private industry has shown little interest in the technologies.[372] And recently, Pennsylvania State University went so far as to use an auction of fifty-nine of its unlicensed engineering patent portfolios to gather useful information on what types of patents were no longer worth the cost of paying maintenance fees.[373] Thus, although university TTOs may in the short term be overly optimistic about patenting their research, in the longer term universities seem to recognize that most of those patents are pointless to maintain.

CONCLUSION

Nanotechnology is promised to be the next technological revolution, but

---

[368] Bagley, *supra* note 207, at 259; Greenbaum, *supra* note 68, at 360.

[369] *See, e.g.*, Grose, *supra* note 359, at 20; Litan et al., *supra* note 366, at 43.

[370] *See* Kimberly A. Moore, *Worthless Patents*, 20 BERKELEY TECH. L.J. 1521, 1544, 1547–48 (2005).

[371] *Id.* at 1525 (surveying payment of maintenance fees on patents issued in 1991). Increasing maintenance fees must be paid at 3.5 years, 7.5 years, and 11.5 years after a patent is issued; failure to pay any of these fees leads to patent expiration in six months. *Id*. at 1525.

[372] *Id.* at 1534, 1544, 1547–48 (noting this phenomenon in biotech, pharmaceutical and chemical fields).

[373] Goldie Blumenstyk, *Penn State's Patent Auction Produces More Lessons Than Revenue*, CHRONICLE OF HIGHER EDUC. (May 1, 2014), http://chronicle.com/blogs/bottomline/penn-states-patent-auction-produces-more-lessons-than-revenue/ [https://perma.cc/2456-MCLU]. One of the reasons that Penn State sold so few patents may have been the restrictions that the university placed on the auction to prevent so-called patent trolls—nonpracticing entities that use patents to extract rents from unknowing infringers—from acquiring the patents. Neil Kane, *Patents for Sale: How to Separate the Valuable from the Worthless*, FORBES (May 22, 2014), http://www.forbes.com/sites/neilkane/2014/05/22/a-modest-proposal-for-licensing-patents/; *cf.* NRC, *supra* note 224, at 6–7 (advocating against university patent sales to patent aggregators and other nonpracticing entities).

development in the field has been slower than many had hoped. As Professor Siva Vaidhyanathan observed in 2005, "right now nanotechnology is more science than technology (some would argue more science fiction than science)."[374] The question is, why? Given the relatively high levels of patenting on university research in the area, it is understandable that Professor Lemley and several other commentators suspect that these patents are hindering nanotech's development transfer from university research to commercialized application. Translating research and knowledge into useable technologies depends on more than just intellectual property rights,[375] and the importance of patents versus other methods of technology transfer varies widely from case to case.[376] For nanotechnology, many if not most of university patents will have little effect on future nanotechnology development. Although some very small percentage of nanotech development may experience anticommons or other holdup problems because of upstream university patenting, development of other applications may be experiencing delays that have little to do with patenting ownership patterns or the degree of patenting on upstream research.

First, with regard to the risk of patent-induced holdup problems: a patent that covers "basic" or "upstream" research will not necessarily have enough preemptive breadth to hold up downstream development.[377] Many upstream nanotech patents may resemble gene sequence patents in that they require downstream work to be of commercial value but still are narrow enough that they can be easily designed around using meaningful substitutes. Such upstream but substitutable patents are unlikely to cause holdup problems.[378] Unless a patent covers one of the few foundational or "common-method research tools" and unless those patents are not licensed freely, little in the way of hold up is likely to occur.[379]

As compared to patents, moreover, other technological, economic, and sociologic issues may be much more significant drags on technological development than commonly realized. Nonpatent exclusivities, as well as risk aversion, lack of funding, and information gaps, play significant roles in the development of science-based technologies such as nanotech. Where access to research materials and tools, tacit knowledge, lack of private capital, and lack of public support are more rate-limiting than patents, as appears to be the case in most of nanotechnology development at this point in time, patents are for most intents and purposes simply irrelevant. Likewise, the overall effect of patenting depends greatly on the inherent

---

[374] Vaidhyanathan, *supra* note 3, at 232.

[375] NRC, *supra* note 224, at 2.

[376] Cahoy & Glenna, *supra* note 226, at 433; Jeannette Colyvas et al., *How Do University Inventions Get into Practice?*, 48 MGMT. SCI. 61, 62 (2002).

[377] *See* Adelman, *supra* note 171, at 133.

[378] *See* Kieff, *supra* note 130, at 730–31 (noting that the availability of market alternatives limits patent holders' power to set a price).

[379] Adelman, *supra* note 171, at 139.

uncertainties of and the time and expense necessary to developing downstream applications. Especially in revolutionary new fields like nanotechnology, the more time- and resource-intensive downstream development becomes, the more uncertainty attaches, and the less likely it is that upstream university patents will be important to the outcome.

Submission Date: 8/18/2023

Name: Lori Pressman

Name of Organization: Not Provided

Comment:

Additional Comment (attachment):

Lyric Jorgenson, Ph.D.
NIH Office of Science Policy
6705 Rockledge Dr #750
Bethesda, MD, 20817

August 18, 2023

Dear Director Jorgensen,

Thank you for the opportunity to submit comments to the National Institutes of Health (NIH) after workshop held on July 31, 2023: "Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer".

With respect to availability and accessibility:

-Stay the course within the Bayh-Dole and Stevenson-Wydler framework.
-Exclusivity attracts private sector investment which would not occur otherwise.
-Licenses with exclusivity in them can contain more diligence provisions and thus contractually incentivize more development than licenses without exclusivity.
-Absent private sector investment the taxpayers will pay for substantially more applied R&D
-Public-private partnerships are essential for making and distributing health innovations at scale.
-Price controls will work against availability and accessibility.
-Improve patient recruitment to clinical trials.

With respect to affordability:

-Since biomarkers greatly, *in the case of oncology, by a factor of ten*[i], improve the probability of moving from an IND to approval, incentivize the discovery of biomarkers both for patient recruitment and as surrogate endpoints, including multivariate biomarkers.
- Incentivize creation of appropriately secure, anonymized training sets, and/or synthetic datasets which will help discover such biomarkers and the underlying mechanisms of action. These training sets can include patient images and heatmaps of DNA. RNA, or protein expression.
-Incentivize secondary outcome research from existing clinical trials, -including by creating grant programs for this purpose. These secondary outcomes could include biomarker discovery and analysis and patient experience studies. Patient experience studies can encompass compliance, symptom relief, side effects, and understanding how patients find out about and decide to participate in clinical trials.
-Reward researchers who confirm results and publish negative results.
-Recognize the importance of novel formulations which lead to patient benefit, including improved therapeutic index, more convenient administration routes (e.g. oral versus intravenous) more convenient dosing (e.g. weekly v hourly), longer and easier storage (e.g. retains activity over time and over a large temperature range), and sponsor work in this area.
-Continue developing, validating, and advertising pre-clinical assays and models which better predict results in humans, such as the work on Wildings, the syngeneic lab mice with a wild mouse microbiome, from the Rehermann lab[ii].

[i] https://projectalpha.mit.edu/pos/ Table on approvals with and without biomarkers is about halfway down the page, and copied into this letter as Appendix B as a convenience.
[ii] https://pubmed.ncbi.nlm.nih.gov/31371577/

My forty plus years of technology transfer experience, including NIH funded work[iii], [iv] on academic patents and licensing is described here[1].

With respect to availability and accessibility

Stay the course with Bayh-Dole and Stevenson-Wydler:
Public -private partnerships are needed to assure availability and access to the fruits of NIH funded and performed research at scale. There is a natural and expected synergy among basic researchers, who are encouraged to try new ideas many of which will fail, and industry, which must produce and distribute tightly quality controlled products at scale.

In support of the critical importance of public-private partnerships, see Appendix A to this letter, which shows patterns of support for selected U.S. clinical trials, first by trial count, and then by enrollee count. Nonindustry players (light blue) play a significant role early in the process, and when considered by participation in trials. However, when the data are considered by enrollee count, it is clear that there would be no availability absent industry (dark blue) participation. Some trials have support from both industry and nonindustry (cross hatched light and dark blue), accounting perhaps for some of the different perspectives on relative contribution.

Patents create incentives both for disclosure and for investment by industry. Patents both disclose inventions and protect investments, simultaneously fulfilling the academic directive to share information and lowering the risk of for-profit partners to invest in early technologies. Patents can and do start conversations between the for-profit and nonprofit sectors, or between companies. Unlike trade secrets, they expire, thereby inherently incentivizing subsequent development. The opposite of patents is trade secrets. Exclusivity is virtually essential for new company formation and new product development:

Start-ups need exclusivity to start. AUTM data, collected between 1998- 2006 (the only years the data were collected in this form, both by exclusivity and type of company), show that more than ninety percent (90%) of the licenses to start-ups were exclusive or exclusive by field of use[2]. Figure 5 of "The licensing of DNA patents by US academic institutions: an empirical survey"[3], shows that for start-ups from various AUTM members that licensed patents with DNA sequences in the claims, only one of the 43 licenses was nonexclusive, -the rest were exclusive, all fields of use (29/43), or exclusive by field of use (13/43).

A "reasonable pricing" clause in licenses to federal funded inventions will cause industry partners to step away from these vital public-private partnerships. This has been documented for the case of NIH CRDA's. See "The NIH Experience with the Reasonable Pricing Clause in CRADAs FY1990- 1995, November 15, 2021."[4]. Why would an industry partner start a project with an uncertain outcome, requiring long investments of time, personnel, and money which, from that company's point of view, is at a disadvantage relative to its competitors, who may opt out of public-private partnerships just to avoid the "reasonable pricing" provision? The letter prepared by Robert P. Taylor has an insightful discussion of this topic.

[iii] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2726797/
[iv] https://www.uspto.gov/sites/default/files/aia_implementation/gene-comment-pressman.pdf

Exclusivity and patents incentivize new product development: It is not possible yet to investigate an alternative universe where, because there are more or fewer or different patents than there are today, there are more, or fewer, or different kinds of products. However, it is possible to study product development outcomes under patent licensing frameworks with more or less exclusivity. Bayh-Dole gives licensors more discretion regarding exclusivity in patent licenses than Stevenson-Wydler, so a comparison of the outcomes of licensing practices under Bayh-Dole and under Stevenson-Wydler may shed light on the question of whether more exclusivity leads to more or faster product commercialization and availability.

Figure 3 of the 2012 paper "DNA Patent Licensing Under Two Policy Frameworks" [5] suggests that a greater percentage of patents (with DNA sequences in the claims) are licensed under Bayh-Dole than under Stevenson-Wydler. Figure 6A suggests that products associated with these patents get to market faster under Bayh-Dole than under Stevenson-Wydler. Figure 4 shows that nonexclusivity does not guarantee availability of product.

The paper as a whole, simply by looking at timing of license execution relative to product introduction, shows that exclusive licenses are more consistent with incentive creation than nonexclusive ones. Exclusive licenses, or more accurately, licenses with some exclusivity in them (licenses can be and often are exclusive by field of use) occur for the most part before the products are introduced, and the licensees seem to keep them longer, as would be expected with the enhanced diligence provisions found in licenses with exclusivity. (Diligence provisions are contractual requirements to develop the technology. If there is insufficient measurable progress, the license can be terminated or made nonexclusive. These provisions are typically found in licenses with exclusivity and absent in licenses without exclusivity.) In contrast, nonexclusive licenses tend to be "just-in-time" or "just-in-case" licenses, executed close to or after product introduction, and simply not kept as long.

With respect to biological materials, those that are patented, per the full 2005 Walsh Cho Cohen[6] study, are transferred *more* easily than those that are not.

> "In contrast to the effects of access to intellectual property, access to tangible property in the form of material transfers is more likely to impede research."

A 2016 Master's Thesis[7] from the Utrecht University revisits in detail the question of patents and availability of diagnostic products. There are observations both about the lack of bad things associated with patents and the good things which do happen, such as product development and competition. An excerpt of the thesis is here[8].

Patents are consistent with an academic mission, trade secrets are not: Patents, aka, time-limited monopolies to the claimed invention, are visible. Trade secrets, such as the manufacturing know-how which is in a drug master file are not visible. Patents and trade secrets can both attract investment, yet academic institutions and organizations such as the NIH cannot use trade secrets to attract the public private partnerships which are essential to scaling availability of their inventions.

Exclusivity in licenses helps nonprofit licensors strengthen requirements to make and distribute licensed products in license agreements. Weakening patents either by weakening enforceability in the courts, or by prohibiting exclusive licensing only strengthens organizations that have the luxury of relying on trade

secrets, and reduces the ability of nonprofit organizations, including the NIH to "protect the public against nonuse or unreasonable use of inventions[v]".

Research is infrastructure. The word "returns" and "investment" have been taken from a financial and accounting context, where these terms have a well-defined, time-delineated meaning, and applied them to federal research policy, where they do not. Research has impacts far in time and place from when and where it was performed, and conversely, was performed far in time and place from where it bears fruit.

Some of the best new research on the distant, in time and place, impacts of research is Chapter 3 of the October 2021 World Economic Outlook report produced by the IMF. "Research and Innovation: Fighting the Pandemic and Boosting Long-Term Growth"[9]. Research is an "investment" and has "returns" in the sense that it can, over time, change the productivity and by implication health and well-being of entire nations and national economies. Basic research, per this IMF report has less localized and longer lasting impact than applied research, which has relatively shorter duration and more regional benefits. Of interest to this discussion, the IMF economists use citations by patents to either scientific publications, or to other patents as indicators of basic and more applied research, respectively. They then correlate patents with national account productivity (e.g. GDP) measures by country and by region. It is at this scale and in this sense that government funded research can be called an "investment".

With respect to affordability: Use our research resources more efficiently.

Biomarkers unambiguously increase the probability of a trial succeeding. See https://projectalpha.mit.edu/pos/ The phase-by-phase method is explained here[10]. These biomarkers have the potential to change the failure rates, and thus make is less expensive to develop new drugs, which has the potential to reduce the cost of drugs to patients. Because the data are so astounding, and still so little appreciated, I include them as Appendix B to this letter, and provide an excerpt below.

Of the nearly 20,000 oncology trials with biomarkers that were considered about two thirds did not have biomarkers, and one third did. The ones with biomarkers were ten times more likely to be approved. Considering non oncology trials, 15,960 did not have biomarkers, and only 185 (about one percent) did. Those with biomarkers were more than 2.5 times as likely to be approved. Why don't all trials have biomarkers?

Estimates of PoS, Biomarkers – 2022Q1 Update		
Estimated using the phase-by-phase approach.		
Therapeutic Area	**#Paths**	**PoS:1-A (%)**
Oncology w/o biomarkers	**13,367**	**1**
Oncology w/ biomarkers	**6,381**	**10.6**
Total w/o biomarkers	**29,327**	**4.2**
Total w/ biomarkers	**6,566**	**11.1**
All except oncology w/o biomarkers	**15,960**	**6.4**
All except oncology w/ biomarkers	**185**	**17.7**

[v] §35 USC 200

One potential answer is that DNA and RNA biomarkers are more likely to be readily identifiable in oncology trials, and that other diseases are more likely to have protein biomarkers, or highly multivariate biomarkers . Embrace machine learning approaches to identify such multivariate biomarkers.

Incentivize biomarker discovery especially in areas outside of oncology. Patient accrual biomarkers and surrogate endpoint biomarkers reduce drug trial costs several ways. First if fewer trials fail, the risk statistics reflect this change. A manager of a research budget should thus expect to pay less for their pipeline of innovative drugs, and this saving should be reflected when the drugs are priced.

To the extent that the biomarkers are indicative of an understanding of the basic mechanism of action of the drug, the efficacy of the drug should increase. This should shorten the time needed to conduct the trial because it should reduce the number of patients needed to get a statistically significant result. This alone reduces the clinical trial cost.

Validated surrogate endpoint biomarkers can also shorten the time to obtain a statistically significant result. Thus, improving our understanding of the underlying science and mechanisms of actions has both clinical and financial benefits.

Incentivizing development of biomarkers can be done by funding work directly on biomarkers. Also, the NIH could leverage existing clinical trials by supporting more collection and study of the secondary outcomes in current clinical trials. This is discussed more in the section on secondary outcomes.

Incentivize development of multivariate biomarkers: It is reasonable to expect more multivariate phenotypes moving forward, and therefore for the NIH to embrace machine learning to help define clinically useful phenotypes, including phenotypes that would be otherwise unobservable to the investigators, and are only discoverable by computers.

Incentivize creation of appropriately secure and/or anonymized curated and labeled training sets, and/or synthetic datasets which can be used to i) help discover such multivariate not-necessarily-discernable-by-humans biomarkers and ii) enhance our understanding of mechanisms of action. These training sets can include patient images and heatmaps of DNA, RNA, or protein expression.

Leverage existing clinical trials by funding more secondary outcome research -including by creating grant programs for this purpose. These secondary outcomes could include biomarker discovery and analysis and patient experience studies. Patient experience studies can encompass everything from patient compliance to symptom relief and their experience of side effects. Simply tracking how patients found out about the trial and how they decided to participate may lead to insights which enable better patient recruitment strategies. Reducing clinical trial accrual time will also reduce overall costs. Recruiting more diverse participants to clinical trials will enhance the robustness of the clinical trial results. Diverse participants provide additional opportunities for secondary outcome studies.

Reward researchers with money and/or accolades who confirm results and publish negative results.

Recognize the importance of novel formulations which lead to patient benefit, including improved therapeutic index, accessibility via easier administration routes (e.g. oral versus intravenous) more

convenient dosing (e.g. weekly v hourly), longer and easier storage (e.g. retains activity over time and over a large temperature range), and sponsor work in this area.

Continue developing, validating, and advertising pre-clinical assays and models which better predict results in humans, such as the work on Wildings, the syngeneic lab mice with a wild mouse microbiome, from the Rehermann lab[vi].

Thank for organizing this workshop and providing an opportunity to discuss the NIH mission and policy goals. Use illustrations and analogies when appropriate. Analogies can be helpful at times. Avoid metaphor. Metaphors are not helpful because there is too much risk of miscommunication, whether in personal conversations or in policy discussions.

Thank you very much for the opportunity to submit these comments.

Kind regards,

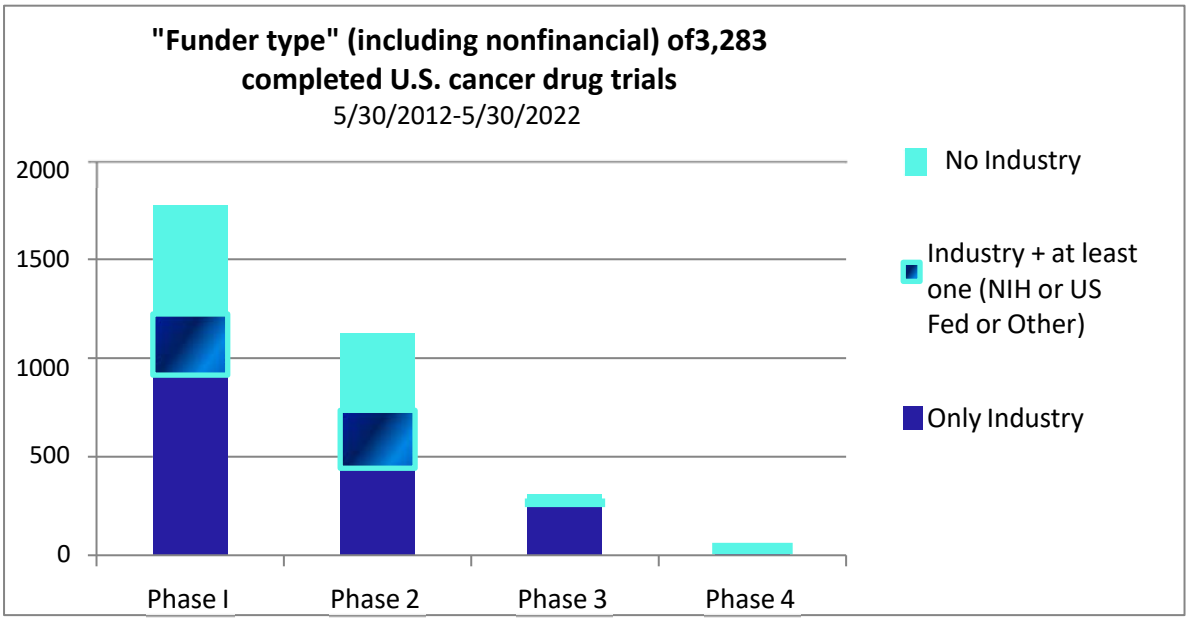
Lori Pressman
Cambridge, MA.

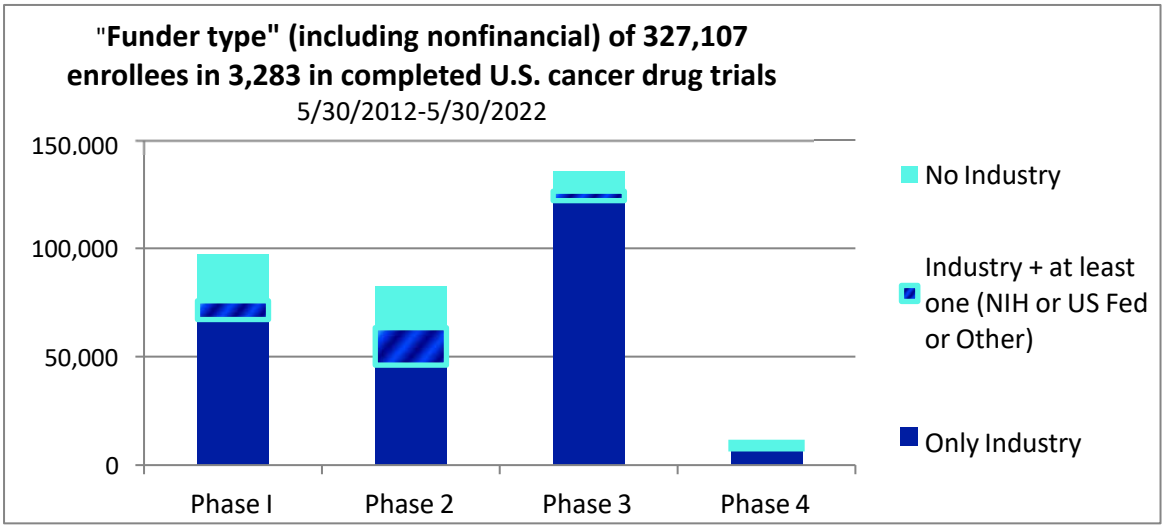
[vi] https://pubmed.ncbi.nlm.nih.gov/31371577/

Funder type https://clinicaltrials.gov/ct2/about-studies/glossary Describes the organization that provides funding or support for a clinical study. **This support may include activities related to funding, design, implementation, data analysis, or reporting.** Organizations listed as sponsors and collaborators for a study are considered the funders of the study. ClinicalTrials.gov refers to four types of funders:

- •U.S. National Institutes of Health
- •Other U.S. Federal agencies (for example, Food and Drug Administration, Centers for Disease Control and Prevention, or U.S. Department of Veterans Affairs)
- •Industry (for example: pharmaceutical and device companies)
- •All others (including individuals, universities, and community-based organizations)

Search string, run 6/2/2022: Completed Studies | Interventional Studies | Cancer | Drug | United States | Phase Early Phase 1, 1, 2, 3, 4 | Start date from 05/30/2012 to 05/30/2022





Appendix B.

Estimates of PoS, Biomarkers – 2022Q1 Update		
Estimated using the phase-by-phase approach.		
Therapeutic Area	**#Paths**	**PoS:1-A (%)**
Oncology w/o biomarkers	**13,367**	**1**
Oncology w/ biomarkers	**6,381**	**10.6**
Metabolic/Endocrinology w/o biomarkers	2,606	6.6
Metabolic/Endocrinology w/ biomarkers	29	16.8
Cardiovascular w/o biomarkers	1,940	7.5
Cardiovascular w/ biomarkers	16	25.3
CNS w/o biomarkers	3,517	4
CNS w/ biomarkers	83	11.5
Autoimmune/Inflammation w/o biomarkers	3,677	5.3
Autoimmune/Inflammation w/ biomarkers	17	14
Genitourinary w/o biomarkers	534	4.6
Genitourinary w/ biomarkers	17	--
Infectious Disease w/o biomarkers	2,698	6.6
Infectious Disease w/ biomarkers	12	37.4
Ophthalmology w/o biomarkers	245	8.2
Ophthalmology w/ biomarkers	1	53.8
Vaccines (Infectious Disease) w/o biomarkers	743	18
Vaccines (Infectious Disease) w/ biomarkers	10	--
Total w/o biomarkers	**29,327**	**4.2**
Total w/ biomarkers	**6,566**	**11.1**
All except oncology w/o biomarkers	**15,960**	**6.4**
All except oncology w/ biomarkers	**185**	**17.7**

.

[1] I've been an enthusiastic participant in our innovation ecosystem for more than 40 years, as an engineer, inventor, investor, license negotiator, academic technology transfer professional, and scholar. Since 2000 I have been a self-employed Boston based technology transfer practitioner, business development, licensing, and IP strategy consultant.

My degrees are S.B. physics from MIT 1979, and MSEE from Columbia 1983. I was an engineer at Lasertron, an MIT start-up, from 1984-1989 and experienced the patent and inventor friendly environment of AT&T Bell Labs in the early 1980's. I worked at the MIT TLO from 1989-2000, the last four years as assistant director with signatory authority. I was a director of a publicly traded investment company from 2002-2012 (NASDAQ:TINY). I am an inventor. I have been a reasonable royalty expert in patent damages litigation.

I have published NIH funded research on patent policy and licensing practices using ROC analysis, and applying the Bradford Hill criteria to assess causation , in a technology transfer context. I am the author of a series of BIO and AUTM funded studies estimating the economic impact of academic technology transfer using the Leontief I-O approach[1] and also, under NIST, funding applied the same approach to federal laboratory technology transfer[1].

I have been a reviewer for the USPTO Patents for Humanity awards and played various roles within AUTM. I was Chair of the Survey Statistics and Metrics Committee for their surveys covering FY99-FY01 and remain active with the Public Policy Committee. I am a volunteer grant reviewer and mentor for various organizations, including the MIT Deshpande Center. I received the Bayh-Dole award in 2017.

Recent activities include business development for individual start-ups and working with academic institutions on management of non-patented inventions, particularly data, software, and biological materials.

[2] Table 1. Fraction of licenses to start-ups that are exclusive. Data are from the AUTM STATT database These are the only years that the information is available in this form. Subsequent years have data by exclusivity, but not further categorized by company type (large entity, small entity or start-ups) and data by company type, but not further categorized by exclusivity.

Year	Start Up Exclusive	Startup Nonexclusive	% Startup Exclusive
1998	291	28	91%
1999	346	38	90%
2000	477	47	91%
2001	467	52	90%
2002	491	51	91%
2003	491	32	94%
2004	558	60	90%
2005	514	53	91%
2006	638	60	91%

[3] Pressman, L, Burgess, R. , Cook-Deegan, RM, Stephen J McCormack, SJ, Nami-Wolk, I, Melissa Soucy, M, &Walters, L 2006 "The licensing of DNA patents by US academic institutions: an empirical survey" Nature Biotechnology 24:1 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2726797/

[4] The NIH Experience with the Reasonable Pricing Clause in CRADAs FY1990- 1995, November 15, 2021 https://www.techtransfer.nih.gov/sites/default/files/CRADA%20Q%26A%20Nov%202021%20FINAL.pdf

[5] Pressman, L. 2012. "DNA Patent Licensing Under Two Policy Frameworks: "*Implications for Patient Access to Clinical Diagnostic Genomic Tests and Licensing Practice in the Not-For-Profit Sector"*, Life Sciences Law & Industry Report (March) https://www.uspto.gov/sites/default/files/aia_implementation/gene-comment-pressman.pdf

[6] Walsh, JP, Cho, C, Cohen, WM . 2005 "Final Report to the National Academy of Sciences' Committee Intellectual Property Rights in Genomic and Protein-Related Inventions Patents, Material Transfers and Access to Research Inputs in Biomedical Research" September 20, 2005 https://www.cambridge.org/core/books/abs/perspectives-on-commercializing-innovation/patents-material-transfers-and-access-to-research-inputs-in-biomedical-research/29169FA29D631C8FBEFEF26A5A4F1D65

[7] Gottardi, S. 2016 The effects of patenting on the development of diagnostic products. How patents influence incremental innovations and monopolies in market niches. https://studenttheses.uu.nl/bitstream/handle/20.500.12932/24462/Official%20Thesis.%20Simone%20Gottardi.pdf?sequence=2

[8] ''The research [about the effects of patenting on the development of diagnostic products] showed that patenting does not affect the product development in a significantly different way than other types of patenting. This rejects the hypothesis advanced by Heller and Eisenberg (1998) that gene patenting would hamper the downstream product development. This is in line with the findings of Walsh et al. (2003) that suggested that gene patents do not grant an effective monopoly over products or processes and that working solutions around the IP remain within the reach of competitors.

The presence of patents in a market niche promotes the number of incremental innovations in that market and decreases the strength of the monopoly. These results are in line with literature as it suggested that the number of IP rights present in a market niche supports product development and competition (Cohen & Merrill, 2003; Pressman, 2012; The Lewin Group 2005). At the same time the presence of patents strengthens the barriers to entry. In line with literature this confirms that patents support the production of technological products, promote competition and at the same time raises the barriers to entry for competitors (Hellmann, 2007; Kitch, 1977; Leten et al., 2010)." Id pp 41-42

[9]International Monetary Fund. 2021. World Economic Outlook:Recovery during a Pandemic—Health Concerns, Supply Disruptions, Price Pressures. Washington, DC, October. Chapter 3 "Research and Innovation: Fighting the Pandemic and Boosting Long-Term Growth" https://www.imf.org/en/Publications/WEO/Issues/2021/10/12/world-economic-outlook-october-2021

[10] Chi Heem Wong and others, Estimation of clinical trial success rates and related parameters, *Biostatistics*, Volume 20, Issue 2, April 2019, Pages 273–286, https://doi.org/10.1093/biostatistics/kxx069

Submission Date: 8/18/2023

Name: Ashlyn Roberts

Name of Organization: Incubate

Comment:

Good afternoon:

On behalf of Incubate, a coalition of early-stage life sciences venture capital firms representing the patient, corporate, and investment communities, please find the attached comment in response to the NIH's workshop, *Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer*.

Thank you for your consideration in these comments, please do not hesitate to contact myself or John@incubatecoalition.org for additional information.

Best Regards,
Ashlyn

Ashlyn Roberts
Coalition Director
@incub8coalition | incubatecoalition.org

Additional Comment (attachment):

incubate

August 18, 2023

Lyric Jorgenson, PhD
Acting Associate Director for Science Policy
National Institutes of Health Office of Science Policy
6705 Rockledge Dr #750
Bethesda, MD 20817

Dear Director Jorgenson:

On behalf of Incubate, the largest coalition of venture capital organizations that finance the early-stage life sciences ecosystem, we appreciate the opportunity to comment on the NIH's July 31 "Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer."

Specifically, we are troubled by certain panelists' misguided claims regarding the balance between public discovery and private development within America's innovation ecosystem. Furthermore, there's growing concern about attempts to divert the NIH's primary mission of advancing science towards addressing systemic healthcare policy issues.

Efforts to develop effective new therapies that meet unmet medical needs rely on strong and predictable intellectual property protections. While basic NIH research leads to important early-stage discoveries, it is private capital that funds efforts to turn those promising discoveries into life-saving medicines. Without strong IP protections, companies and their investors simply would not be able to take such risks.

Prior to 1980, federally-backed research frequently yielded promising discoveries that never benefited the public. That's because the U.S. government owned the patents on those discoveries and rarely licensed them out to companies with the expertise to successfully commercialize them. As of 1980, just 5% of 30,000 government-held patents were licensed out for further development.[1]

Recognizing the urgent need to fix this broken system, Senators Birch Bayh (D-IN) and Bob Dole (R-KS) authored legislation permitting universities and other institutions to own, patent, and license federally-funded discoveries.

The Bayh-Dole Act, as it came to be known, helped ensure promising scientific discoveries no longer gathered dust. From 1996 to 2020, over 200 drugs and vaccines were developed through the technology transfer system Bayh-Dole established -- including the Covid-19 mRNA shots that have saved millions of lives.[2] [3]

[1] https://www.google.com/url?q=https://techtransfer.syr.edu/about/bayh-dole/&sa=D&source=docs&ust=1691639467985331&usg=AOvVaw0_6b7Bk1vtGBwZq9UDVqJY
[2] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9975718/#:~:text=The%20US%20federal%20government%20invested,in%202020%20through%20March%202022.
[3] https://bayhdolecoalition.org/wp-content/uploads/2023/04/Driving-the-Innovation-Economy-Academic-Technology-Transfer-in-Numbers-2021.pdf

The economic impacts of the law are equally hard to ignore. Since 1996, the Bayh-Dole Act has added $1 trillion to U.S. GDP, supported 6.5 million jobs, and aided the formation of 15,000 start-ups.[4]

Unfortunately, we are seeing the Bayh-Dole system be misrepresented. The law's "march-in" provision should not be misused to impose price controls on life-saving medications. March-in is only permitted in rare instances, such as when a patent holder refuses to commercialize research altogether.[5] The law's authors never intended march-in to be used as a means of setting prices on successful products.[6]

More importantly, the suggested proposal would backfire by disincentivizing private companies from licensing government-backed research in the first place.

Developing a new medicine costs on average $2.6 billion and can take well over a decade.[7] [8] Some 90% of potential treatments fail during clinical trials.[9] Investors are able to fund so many drug development projects because one or two successful medicines can cover losses from dozens of failures. Robust and reliable IP protections allow private sector companies to recoup R&D costs and earn revenue to fund additional drug development activities for a defined period of time before generic and biosimilar competitors enter the market.

Allowing the government -- rather than private companies themselves -- to set prices on successful drugs undermines this entire system and will give life sciences investors no choice but to redirect their money elsewhere.

Another cause for concern is that certain lawmakers are asking NIH to insert "reasonable pricing" clauses in all future grants, licenses, and Cooperative Research and Development Agreements (CRADAs). This too amounts to government price-setting and would dissuade innovative life sciences companies from licensing early-stage research from the federal government.

This isn't theoretical. The NIH established a "reasonable pricing" requirement for CRADAs in 1989.[10] As a result of the policy, the number of private sector CRADAs with the NIH plummeted and the agency was forced to end the requirement in 1995.[11] [12] A year later, the number of CRADAs skyrocketed once again.[13]

History could not be clearer: "reasonable pricing" requirements led to reductions in public-private collaboration critical to developing life-saving therapies. It would be a mistake to revive these failed policies.

---

[4] https://bayhdolecoalition.org/wp-content/uploads/2023/04/Driving-the-Innovation-Economy-Academic-Technology-Transfer-in-Numbers-2021.pdf
[5] https://www.law.cornell.edu/uscode/text/35/203
[6] https://www.washingtonpost.com/archive/opinions/2002/04/11/our-law-helps-patients-get-new-drugs-sooner/d814d22a-6e63-4f06-8da3-d9698552fa24/
[7] https://pubmed.ncbi.nlm.nih.gov/26928437/
[8] https://ncats.nih.gov/about
[9] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9293739/
[10] https://itif.org/publications/2019/03/04/bayh-dole-acts-vital-importance-us-life-sciences-innovation-system/
[11] https://itif.org/publications/2019/03/04/bayh-dole-acts-vital-importance-us-life-sciences-innovation-system/
[12] https://itif.org/publications/2019/03/04/bayh-dole-acts-vital-importance-us-life-sciences-innovation-system/
[13] https://itif.org/publications/2019/03/04/bayh-dole-acts-vital-importance-us-life-sciences-innovation-system/

Incubate shares the NIH's desire to strengthen the U.S. technology transfer system while "promoting the application of knowledge to enhance human health."[14] Eroding IP protections and advancing mistaken "reasonable pricing" policies works directly against these goals.

In acknowledging the above, it's crucial to recognize that there are real and pressing concerns regarding access to and affordability of medicines. High out-of-pocket costs render essential medications unattainable for many American patients. But the solution isn't one that would reduce overall investment into these life-saving tools. Instead, the focus should be on improving the quality of insurance coverage, holding industry middlemen accountable, and ensuring that all patients have access to the medicines prescribed by their doctors.

When considering these broader healthcare challenges, it is also important to remember the distinct role of the NIH. Rather than modifying agency policies in ways that could stifle innovation, we should harness the NIH's capabilities to foster innovation and bolster competition. The value of strong public-private partnerships becomes evident here, as they serve as a bridge between research and real-world applications.

By fast-tracking groundbreaking innovations from the lab to the market, the NIH -- with the support of these public-private partnerships -- fosters a dynamic environment brimming with various therapeutic choices. Such diversity organically leads to more competitive pricing. Imposing restrictions will only hinder the very medical innovations vital for advancing public health.

Thank you again for the opportunity to comment. Please do not hesitate to email john@incubatecoalition.org or ashlyn@incubatecoalition.org with any questions.

Sincerely,

John Stanford
Executive Director
Incubate

###

[14] https://osp.od.nih.gov/events/workshop-on-transforming-discoveries-into-products-maximizing-nihs-levers-to-catalyze-technology-transfer/

Submission Date: 8/18/2023

Name: Drew Johnson

Name of Organization: Not Provided

Comment:

Good afternoon-

Thank you for allowing me the opportunity to comment on the NIH's July 31, 2023 workshop, focusing on the future of technology transfer in the context of biomedical innovation. Please find my comments attached and pasted below.

Respectfully,
Drew Johnson

Additional Comment (attachment):

Lyric Jorgenson, Ph.D.
Office of Science Policy
6705 Rockledge Drive, Suite 630
Bethesda, MD 20892

RE: NIH Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer

Director Jorgenson,

As a policy analyst, longtime government watchdog, and former national director of a technology-focused think tank, I appreciate the opportunity to comment on the NIH's July 31, 2023 workshop, focusing on the future of technology transfer in the context of biomedical innovation.

In observing the NIH's recent workshop, I noted an overrepresentation of panelists who were adversarial to patent rights and in favor of more agency control over the private sector.

The NIH has reached a point where it must decide whether to remain focused on advancing scientific discoveries for patients' benefit or alter its tried-and-true policies with the intent of addressing larger healthcare concerns. Certain lawmakers and advocates are pushing the latter aim to the forefront, as witnessed during the NIH's workshop.

However, it is imperative that the agency's central objectives do not waver. The NIH has long played a key role as a nexus between public initiatives and private ventures, expediting the transformation of scientific insights into practical medical treatments. These partnerships bring about a surge in life-changing innovation, while also cultivating a competitive marketplace. Shifting from this well-charted trajectory -- influenced by seemingly prudent, but restrictive, interventions -- would impede essential health advancements.

I recognize the importance of NIH's partnership with the private sector to continue to drive American biomedical innovation in an increasingly competitive global market. The NIH's advancements in basic research are unparalleled. However, without the resources and expertise the biomedical industry provides, few of the NIH's discoveries would make it through the regulatory process and into the hands of patients.

Private sector investment continues to dwarf the funds provided by government sources. One study highlighted the contrast in the allocations of funds for a cohort of 18 FDA-approved drugs. Researchers found that the private sector investment to bring these drugs to market was over 66 times that of the NIH's investment in the basic research that ultimately led to those drugs.

But to continue to make such substantial investments, private sector participants must have confidence that the intellectual property rights they obtain are honored. The Bayh-Dole Act has provided the private sector this comfort for over 40 years by facilitating commercialization through the transfer of intellectual property rights.

The law succeeded by restoring a long-standing principle of American intellectual property law wherein ownership follows inventorship. Prior to the Bayh-Dole Act, the government retained patents on federally funded inventions and only 5% of those patents were ever licensed for use in the private sector.

Restoring this principle allows the recipients of public funds (i.e., universities) to own their inventions despite funding from the federal government. Private sector companies can then license those inventions

and attempt to develop them into life-saving medicines and other marketable goods. This framework creates incentives for private entities to invest heavily in R&D and clinical trials, navigate the regulatory approval process, and optimize end-user distribution channels. When successful, much of the revenue generated flows back into additional research creating a virtuous cycle of innovation.

The results of this technology transfer framework have been remarkable. Between 1996 and 2020, an estimated $1 trillion was infused into the US economy, fueling the rise of America's globally acclaimed biotechnology industry. Beyond the monetary gains, since its enactment in 1980, Bayh-Dole has catalyzed the development of over two hundred drugs and vaccines. These aren't mere numbers; they represent tangible medications that enhance the lives of countless individuals worldwide.

Given this track record of success, proposals for the NIH to increase its oversight over the private sector and insert price control mechanisms in NIH research licenses are misguided. Doing so would risk upsetting the finely-tuned public-private partnerships developed over the last several decades.

Indeed, when the NIH introduced a "reasonable pricing" clause in its Cooperative Research and Development Agreements (CRADAs) from 1989 to 1995, there was significant pushback from both scientists and industry. The fallout was so pronounced that the then-NIH Director Harold Varmus stated: "The pricing clause has driven industry away from potentially beneficial scientific collaborations with [NIH] scientists without providing an offsetting benefit to the public… Eliminating the clause will promote research that can enhance the health of the American people."

The longstanding relationships between the NIH and the private sector have yielded marvelous results over the past four decades. The stability and predictability of the current systems have achieved the intended goal of more efficiently taking biopharmaceutical innovation from the chalkboard to the medicine cabinet. Any efforts to disrupt this delicate balance are short-sighted and will ultimately lead to less favorable results for the American people.

Once again, I commend the NIH for accepting additional comments on this matter. I believe it is vital to drive innovation through mutually beneficial technology transfer. To that end, please contact me should you have any questions or require additional information.

Respectfully,

Drew Johnson, MPP
Las Vegas, Nevada

Submission Date: 8/18/2023

Name: Claire Cassedy

Name of Organization: Knowledge Ecology International

Comment:

To Whom It May Concern:

On behalf of Knowledge Ecology International, please find attached the following written comments regarding the NIH "Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer":

- The Need for Increased Transparency and Public Safeguards in NIH Licenses. Claire Cassedy. August 18, 2023.
- The NIH does not enforce the statutory requirement to restrict the scope of exclusive rights in a patent license as set out in 35 USC § 209(a)(1-2). James Love. August 18, 2023. (Apologies if you have already received a copy of these comments).

Thank you for your consideration of these comments.

Best regards
Claire Cassedy

--
Claire Cassedy
Knowledge Ecology International
www.keionline.org

Additional Comment (attachment):

The Need for Increased Transparency and Public Safeguards in NIH Licenses

August 18, 2023

Claire Cassedy
Knowledge Ecology International

Overview

United States taxpayers have entrusted the National Institutes of Health (NIH) with conducting research and developing technologies that benefit the public's health and wellbeing. In order to do so, the NIH is supported with $45 billion in taxpayer funding. The Bayh-Dole Act was enacted to promote the commercialization of federally-funded inventions, while including critical safeguards to ensure that America's interest in innovation was balanced with access for the public who supported that innovation.

Before an agency such as the NIH may license a federally-owned invention, it must notify the public of its intent to do so, consider any objections submitted during a public comment period, and determine that certain statutory criteria have been met, including that "the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application[.]"[1]

Knowledge Ecology International (KEI) is a nonprofit non governmental organization that focuses on solutions to ensure affordable and accessible medicines. KEI has pushed the NIH for greater transparency of the process through which the NIH grants exclusive licenses to private companies for taxpayer funded inventions. Through the licenses, the NIH grants exclusive rights to potentially ground-breaking and budget-breaking medical technologies to

[1] 35 USC § 209(a)(2).

companies to further develop and commercialize. It is critical that the NIH use this mechanism to ensure that any resultant technology is affordable and accessible to the public.

Beginning in 2015, KEI has engaged the NIH on these licenses through the public comment period required by the Bayh-Dole Act. As of June 2023, KEI had drafted and submitted comments to the NIH regarding 105 proposed exclusive licenses. A list of the comments submitted is included in the Annex. KEI has also previously raised our concerns regarding the NIH's exclusive licensing practices with the House of Representatives' Committee on Oversight and Reform in 2019.[2]

KEI's comments to the NIH have included in-depth reviews of the technologies to be licensed, discussions of the companies seeking the licenses, critiques of the lack of transparency on the part of the NIH in noticing the licenses and responding to public requests for information, and comments on the licensing terms.

Beginning with the Federal Register notices themselves, the NIH appears to consider the public comment period for exclusive licenses to be a pro forma box to be checked in the process of handing over taxpayer-funded technologies to private companies with few public safeguards. The content of the notices comply with the Bayh-Dole requirements, but give the public very little data on which to assess the need for the technology to be licensed exclusively, or whether the company to receive the license is qualified to develop the product. Typically the only information given on the company is the name and a city and state location. Sometimes, the company listed has little to no web presence, and may not even be listed in the respective state's business registry.

In the presentation of the technology to be licensed, the NIH's Federal Register notices list the intellectual property and its assignee, the field of use covered by the license, the territory (most often worldwide), and a paragraph describing what the technology may be useful in treating.

The public that may wish to comment on the proposed licenses is left with many questions that are critical for informing whether exclusive licenses are necessary to incentivize development of the technologies or how the NIH has come to that determination and whether a particular company is the appropriate partner to further its development and ensure any resultant technology is accessible and affordable to the US public, or that other terms in a license are reasonable or appropriate.

Presented with this dearth of information, prior to the close of the comment period KEI has repeatedly asked for more information about the technology, proposed terms of the license, and the company set to receive the license. Examples of questions asked by KEI include:

1. At what development stage are the inventions listed?

---

2 https://www.keionline.org/wp-content/uploads/KEI_Letter_HouseOversightCommittee_-NIH_Lack_of_Transparency_22July2019.pdf

2. Are there any clinical trials of the licensed technology planned or already conducted?
3. Has the government funded any clinical trials relevant to these technologies? If so, please provide NCT numbers.
4. If the government has provided funding, how much has been spent by the government on these trials? Can you please provide relevant grant and/or contract numbers?
5. Is the term in the proposed licenses to be life of patent or less than life of patent?
6. In working towards executing this license, has the NIH sought advice from the Attorney General (as is required under 40 USC § 559) to determine if the "disposal to a private interest would tend to create or maintain a situation inconsistent with antitrust law"?
7. Is there a Cooperative Research and Development Agreement associated with this technology?
8. What analysis did the NIH undertake, if any, in order to conclude that exclusivity is a reasonable and necessary incentive?
9. How will the NIH ensure that the scope of exclusivity is not broader than reasonably necessary?
10. Would this technology be eligible for a priority review voucher?
11. Who are the principals in this company? For example, are the leading shareholders US residents or non-US residents?
12. Do any former NIH employees have leadership roles in the company?
13. (If proposed licensee is foreign firm) Is the NIH in any concurrent negotiations to waive the domestic manufacturing requirement (35 USC 204) for this license?

There were many times that the NIH did not provide responses to our questions. Indeed KEI received an email that was evidently intended for an NIH colleague, but was sent to us by mistake, instructing them not to reply to us.[3]

When the NIH did provide a response to our questions, it was often with limited responses, for example answering a question about how the NIH determined that an exclusive license was necessary to incentivize the development of a particular technology by responding that that "has been addressed previously", in earlier exchanges about other exclusive licenses.[4] If the NIH were properly assessing whether licensing a technology on an exclusive basis is necessary for a particular invention, it could not have been "addressed previously". It appears that the NIH does not conduct any analysis of what terms and exclusivity are actually necessary to incentivize the development of any of the publicly funded innovations it is offering up on the auction block to private companies.

KEI Exchange with the NIH Regarding EnZeta License

In 2023, the NIH has posted two notices in the Federal Register for the "Prospective Grant of an Exclusive Patent License: Manufacture, Distribution, Sale and Use of T-Cell-Based

[3] https://www.keionline.org/wp-content/uploads/Attachment-C-10Jan2020.pdf

[4] https://www.keionline.org/wp-content/uploads/KEI-NIH-Questions-86FR50895-License-Sana-Biotechnology.pdf

Immunotherapies for Solid Tumors" (88 FR 20544 in April and 88 FR 54629 in August). Both licenses were to be granted to entities with "EnZeta" in the name: EnZeta, Inc. and EnZeta, Immunotherapies, Inc.

Upon receiving an alert on April 5, 2023 that a notice would be published the next day, KEI immediately emailed Richard Girards, Jr. seeking information about EnZeta, Inc. as the firm did not appear to have a website or any other publicly available information. Mr. Girards replied on April 6, 2023 providing limited answers and directed us to search the Delaware state business registry (which yielded very limited information that we had to pay for). KEI asked further questions on April 7th, to which we did not receive a reply either before or after the comment period closed on April 21, 2023.[5] This exchange regarding EnZeta is one of many similar exchanges KEI has experienced when trying to obtain basic information about these exclusive licenses.

The NIH has recently posted another Federal Register notice (88 FR 54629) for nearly the same technologies, this time to EnZeta Immunotherapies, Inc. Again, no firm by this name appears in a Google search, and a search of the Delaware business registry returns very limited results. KEI asked the NIH a set of questions about the prospective license and how this notice related to the April EnZeta notice.[6] The NIH has responded to those questions in a timely manner, but has provided limited information.

For example, KEI's first question asked how the August notice related to the April notice, since they are both to EnZeta-named companies for overlapping IP for T-cell-based immunotherapies for solid tumors. The NIH declined to answer that question, stating "...we have determined that these queries either call for or inextricably implicate business confidential information that NIH is legally precluded from divulging."[7]

KEI has experienced exchanges such as this numerous times when trying to obtain basic information about these exclusive licenses. In order for the public to assess and comment on the necessity and appropriateness of the licenses, the NIH must be more transparent in the information both in the Federal Notices and in their responses to public questioning.

Increased Transparency in Public Notices for Exclusive Licenses

In addition to the information already provided, the NIH should include in the public notices regarding exclusive licenses:

1. A written analysis, or a discussion of the analysis that was undertaken, of how exclusivity has been deemed "reasonable and necessary" under 35 U.S.C. § 209,

[5] The full exchange with the NIH regarding the April EnZeta notice is available here: https://www.keionline.org/39002
[6] https://www.keionline.org/38976
[7] https://www.keionline.org/wp-content/uploads/NIH-Response-KEI-Questions-EnZeta-17Aug2023.pdf

2. The terms of the prospective license, including scope and time period of exclusivity, as well as royalty rate to be earned from the agreement, should be made public,

3. A description of the inventions' stage of development,

4. In order to increase transparency in the cost of drug development, the NIH should make available information on the total funds the government has spent on research and any clinical trials, including total and per patient cost,

5. A description of how the NIH solicited the licensee and an analysis of how it has vetted the licensee. The information should include physical addresses for the company's headquarters and the names of principals in the company. The NIH should also disclose what steps it has taken to ensure that the licensee has the infrastructure, know-how, experience, staff, and funds necessary to begin work on the invention as soon as the license is granted.

6. The NIH should disclose what safeguards it is taking to protect the public interest in this technology, and to ensure that prices charged will not be significantly higher in the United States than in other high income countries.

License Safeguard Term Requests in KEI Comments

In our comments, KEI asked that if the NIH decided to proceed with the exclusive license that the licenses include public interest safeguards. The content of the comments was tailored to the particular technology and company, but examples of terms that KEI requested be incorporated by the NIH included:

- Reference pricing,
- Limitations on geographic scope,
- Transparency, related to the 2019 WHO resolution on transparency (WHA72.8),
- Transparency of R&D outlays, sales/revenue,
- Domestic manufacturing waiver (for foreign firms),
- Non-exclusive/WHO/Medicines Patent Pool licenses,
- Acknowledgement of federal funding,
- Global registration and affordability,
- Limitations on exclusivity term,
- 40 U.S.C. § 559 - Attorney General consultation,
- Transfer of know-how and biologic resources; research permissions,
- 35 U.S.C. § 209 analysis,
- Limiting exclusivity to non-US high income countries,
- Requirement that US prices are set to ensure affordable Medicare co-pays,
- Requirement that US prices do not exceed the estimated value of treatment,

- Limitations on the geographic scope of test data rights,
- Working the patent requirement,
- Products should be priced such that access is not restricted by payors.

Below are brief discussions of and examples of language for selected terms noted above.

Affordable Access for US Patients

Reference pricing. KEI included requests for the NIH to incorporate reference pricing to ensure affordable access to treatments for US patients in 101 of the 105 comments submitted. Below is an example of that request:

> "a provision in the license that requires that any medical technology using the patented invention be available in the United States at a price that does not exceed the median price in the seven largest economies by GDP that have at least 50 percent of the GNI per capita as the United States, using the World Bank Atlas method."

As KEI noted in our comments numerous times,

> "The above is a modest safeguard. The US government has recently incorporated similar terms in agreements related to COVID-19 vaccines and other technology contracts. For example, in the contract with Sanofi Pasteur (Sanofi) for a COVID-19 vaccine, the federal government included a term that stated that Sanofi will not sell the vaccine to any member of the G7 or Switzerland at a price lower than what the U.S. government paid. The NIH should apply this standard to its exclusive licensing practices, and prevent licensees from charging U.S. residents a higher price for products embodying the licensed invention than they charge residents of these high-income countries."

Limitations on years of exclusivity. KEI proposed that the NIH include limitations on the term of the exclusivity, tied to the revenue generated by the product sales. As KEI suggested in 71 comments,

> "We propose that the exclusivity of the license be reduced when the global cumulative sales from products or services using the inventions exceed certain benchmarks. For example, the period of exclusivity in the license could be reduced by one year for every $500 million in global cumulative revenue after the first one billion in global sales. This request is consistent with the statutory requirements of 35 USC § 209, which requires that "the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application.""

Limiting exclusivity to non-US high income countries. KEI also proposed that the NIH include in its licenses a term that would limit exclusivity to the European Union, Japan and other high-income countries, but not extend to the United States. This would ensure that countries that did not fund the R&D underlying the inventions would bear the costs of the exclusivity, while the US residents would not.

Limitations on US prices. KEI asked the NIH to seek terms that would put limitations on US prices of products, ensuring that 1) Medicare co-pays for the products are affordable, 2) that prices do not exceed the estimated value of treatment, and 3) that products are priced such that access is not restricted by payors.

Transparency

KEI's requests regarding transparency cover several areas, including clinical trial costs, R&D outlays more broadly, sales, and revenue, and also urge the NIH to include terms that adhere to the resolution on transparency adopted by the World Health Organization Member States (WHA72.8). KEI notes that this resolution was enthusiastically supported by HHS at its adoption.

Transparency of R&D outlays. In its exclusive licenses, the NIH should require that licensees file an annual report to the NIH, available to the public, on the research and development costs associated with the development of any product or service that uses the inventions, including reporting separately and individually the outlays on each clinical trial. This is not a request to see a confidential company business plan or license application but rather that going forward licensees (and any sublicensees) be required to report on actual R&D outlays to develop the subject inventions. Reporting on actual R&D outlays is important for determining if the NIH is meeting the requirements of 35 U.S.C. § 209, that "the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application[.]" Specifically, having data on actual R&D outlays on each clinical trial used to obtain FDA approval provides evidence that is highly relevant to estimating the risk-adjusted costs of bringing NIH licensed inventions to practical application.

Transparency of sales, revenue, grants, and credits. Through these licenses, the NIH should also require reporting on units of sales and revenue for sales, by country, as well as annual reporting on grants and research contracts received from government agencies, with data on the funding agency, the identifier of the grant or contract, and the amount of the grant or contact. Reporting would also include tax credits associated with R&D for the product, including the U.S. orphan drug tax credit, broken out by the type of credit and the expenditure the credit was associated with (such as a specific trial), as well as other government R&D subsidies.

Domestic Manufacturing Waiver

Innovations that are licensed under the Bayh-Dole Act must include a requirement that the products be "substantially" manufactured in the United States. Companies can obtain a waiver of this requirement. For licensees based outside the United States, KEI asked about and requested the NIH disclose whether the company had sought waiver of the domestic manufacturing requirement. When KEI asked about a potential waiver of the domestic manufacturing requirement in questions to the NIH prior to the close of the comment period, the NIH would refuse to provide that information.[8]

[8] For example: https://www.keionline.org/36442

Global Access

Limitation on geographic scope of exclusivity and test data rights. In order to ensure affordable access in low and middle income countries, KEI asked the NIH to ensure that the exclusive licenses did not extend to countries with a per capita income less than 30 percent that of the United States. In the "United States Public Health Service Technology Transfer Policy Manual, which outlines the technology transfer policies for the NIH, FDA, and CDC, the manual sets out as a policy objective, that "PHS seeks to promote commercial development of inventions in a way that provides broad accessibility for developing countries." KEI's proposal seeks to give action to those words.

Additionally, KEI requested in its comments that the NIH to include provisions that would require the licensed patent holders to waive any exclusive rights regarding test data and any patent-registration linkage rights that may exist in any country with a per capita income less than 30 percent of U.S. per capita income. This is important because a number of trade agreements and bilateral pressures force low and middle income countries to enact laws granting exclusive rights in test data, in most cases, without the possibility of exceptions, even in cases involving excessive prices.

Non-exclusive, World Health Organization, and Medicines Patent Pool licenses. KEI has urged in its comments to the NIH that:

> "The NIH should retain a right to grant the WHO, the Medicines Patent Pool or other governments the rights to use the patent rights to procure the medical technology from competitive suppliers, including technology transfer, in LMICs, upon a finding by HHS or the WHO that people in these markets do not have sufficient access to the medical technology."

Global registration and affordability. KEI has asserted that, "The licenses should require the licensee to disclose the steps that each will take to enable the timely registration and availability of the medical technology at an affordable price in the United States and in every country with a demonstrated need, according to the Centers for Disease Control and Prevention (CDC) and/or the World Health Organization (WHO), either by supplying a country directly at an affordable, publicly disclosed price and with sufficient quantities, or by providing technology transfer and rights to all intellectual property necessary for third parties to do so."

NIH Due Diligence and Fostering Further Innovation

Acknowledgement of federal funding. In order to recognize the contributions that taxpayers make in the support of biomedical R&D, KEI urged that the licensee should be required to include, when issuing statements, press releases, and other documents describing the development of any product that includes the licensed inventions, a statement that describes

the role of the licensed inventions and the total and proportionate contribution of federal funding to the research and development performed to bring the inventions to market.

40 U.S.C. § 559 - Attorney General consultation. Per 40 U.S.C. § 559, the NIH is required to seek the advice of the Attorney General regarding antitrust issues when disposing of property. Patents with a market value more than $3 million fall under this requirement. When KEI asked whether the NIH had sought the advice of the Attorney General, the NIH would either not answer the question, or asserted that the requirement did not apply to their licensing practices.

35 U.S.C. § 209 analysis of the necessity of exclusivity. 35 U.S.C. § 209 has several restrictions on the grant of an exclusive license. In Section 209(a)(1), the agency has to determine if exclusivity is a reasonable and necessary incentive to induce the investments to bring an invention to practical application. Additionally, if some exclusivity is warranted, the agency still has to determine the scope of exclusivity, and is required to ensure that that the proposed scope of exclusivity is not greater than reasonably necessary.

No exclusive license should be granted until the NIH conducts an economic analysis to determine if exclusivity can be limited to less than the life of the patent, as was the case, for example, for all extramural-funded patents when the Bayh-Dole Act was passed in 1980, and under previous NIH Directors, as in the case of the ddI license for an HIV drug.

When asked by KEI the NIH has never provided a copy of the analysis carried out to determine that an exclusive license was necessary to induce investments, nor have they described how they conducted their analysis. Indeed, in other responses to KEI, the NIH has appeared to admit to not conducting analyses for each prospective license by stating that answers to questions about the analyses have been addressed in earlier licenses.[9]

Transfer of know-how and biologic resources, and research permissions. In order to address research by third parties on the inventions to be licensed, in many of our comments KEI proposed the NIH explicitly permit researchers worldwide to use the inventions for research purposes, regardless of whether or not research has a grant or contract from a U.S. government agency, and for both profit or non-profit organizations. KEI also urged the NIH to require the licensee to provide transfer of manufacturing know-how and access to relevant biologic resources, to any firm designed by the United States.

Examples of Notable Exclusive Licenses

CAR T Therapy for B-cell Cancers - Kite Pharma/Gilead Sciences

---

9 https://www.keionline.org/wp-content/uploads/KEI-NIH-Questions-86FR50895-License-Sana-Biotechnology.pdf

On Monday July 29, 2019, KEI submitted joint comments[10] to the NIH on behalf of KEI, Social Security Works (SSW), Universities Allied for Essential Medicines (UAEM), Union for Affordable Cancer Treatment (UACT), and Clare Love, a cancer patient, regarding two proposed exclusive licenses to Kite Pharma/Gilead Sciences for CAR T technologies to treat cancers.[11]

Both licenses concerned CAR T technologies that target both CD19 and CD20 proteins and were for the treatment of B-cell derived human cancers, which include Non-Hodgkins Lymphoma (NHL), acute lymphoblastic leukemia (ALL) and chronic lymphocytic leukemia (CLL). At the time, Kite/Gilead already had on the market Yescarta, a CAR T therapy to treat B-cell derived cancers. Yescarta was also developed from NIH-licensed technologies and was introducted at a price of $373,000 per treatment.

The dual targeting of CD19 and CD20 would provide more comprehensive therapy to B-cell cancers than treatments that have been approved that only target CD19, such as Yescarta. Granting a license to these technologies on an exclusive basis presents a troubling anti-competitive consolidation of these technologies with a company that has repeatedly been shown to charge extremely high prices for its treatments. Particularly in this case, KEI urged the NIH's compliance with 40 U.S.C. § 559, which requires the NIH to solicit the Attorney General's advice regarding antitrust issues in the disposal of government property.

Since 2012, Kite/Gilead have entered into several Cooperative Research and Development Agreements (CRADAs) and exclusive licenses related to CAR-technologies. In 2016, the New York Times chronicled the close relationship between the NIH and Kite/Gilead in an article titled, "NAME."[12]

As KEI noted in our comments, "The NIH license of yet another B-cell CAR T treatment to Gilead/Kite for the treatment of hematological malignancies will increase concentration, and protect Yescarta and Kymriah from price competition at a time when the new cell- and gene-therapies present emerging threats to health care budgets, and the high prices for treatments, which have nothing to do with R&D or cell manufacturing costs, are associated with rationing."

Ebanga - Ridgeback Therapeutic's Ebola treatment

On March 30, 2021, KEI filed comments regarding the "Prospective Grant of an Exclusive Patent License: Development, Production, and Commercialization of Ebola Neutralizing Single Monoclonal Antibody for the Treatment of Ebola Virus Disease in Humans" (86 FR 14331) to

---

[10] https://www.keionline.org/wp-content/uploads/Kite-Gilead-NIH-License-comments-29July2019.pdf

[11] "Prospective Grant of an Exclusive Patent License: Autologus Therapy Using Bicistronic Chimeric Antigen Receptors Targeting CD19 and CD20" (84 FR 33272) and "Prospective Grant of an Exclusive Patent License: Allogeneic Therapy Using Bicistronic Chimeric Antigen Receptors Targeting CD19 and CD20" (84 FR 33270).

[12] https://www.nytimes.com/2016/12/19/health/harnessing-the-us-taxpayer-to-fight-cancer-and-make-profits.html

Ridgeback Therapeutics.[13] Ridgeback has risen in profile in recent years, as it obtained and leveraged rights to COVID-19 treatment NAME.

In the 2021 license, the field of use of the license conveyed the rights to the, “development, production, and commercialization of Ebola neutralizing monoclonal antibody mAb114, as a single antibody not in combination with other monoclonal antibodies, for the treatment of Ebola virus disease in humans.”[14]

Ridgeback's Ebola treatment Ebanga (ansuvimab-zykl, formerly referred to as mAb114) was approved by the FDA on December 12, 2020, prior to the publication of the notice and grant of this exclusive license. Ridgeback also received a priority review voucher (PRV) for the treatment as well under the material threat medical countermeasure PRV as well as an orphan drug designation and approval.

The US government provided significant support and incentives for the development of mAb114, including sponsoring and conducting key clinical trials, granting Ridgeback rights to the technical data, and agreeing to contracts worth up to $168 million. The Ridgeback press release concerning Ebanga notes,

> “Ebanga development has been funded in whole or in part with federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response; Biomedical Advanced Research and Development Authority, under Contract Numbers 75A50119C00059 and 75A50120C00009.”[15]

As previously noted, when granting patent licenses to federally-owned inventions, the NIH may only grant an exclusive license when exclusivity is a necessary incentive and must limit the scope of patent licenses, including the period of exclusivity, to that which is reasonable and necessary. 35 U.S.C. §209(a)(1)-(2).

How was a license on an exclusive basis necessary to incentivize commercialization when the product was already approved by FDA? The clinical trials were already completed and/or underway, Ridgeback had rights to clinical trial data, and the company already brought in $168 million through contracts just to bring the invention to market. Granting exclusive rights in this case was in no way reasonable or necessary.

---

[13] https://www.keionline.org/wp-content/uploads/KEI-Comments-NIH-Exclusive-License-Ridgeback-30March2021.pdf

[14] “Prospective Grant of an Exclusive Patent License: Development, Production, and Commercialization of Ebola Neutralizing Single Monoclonal Antibody for the Treatment of Ebola Virus Disease in Humans” (86 FR 14331).

[15] https://www.businesswire.com/news/home/20201222005421/en/Ridgeback-Biotherapeutics-LP-Announces-the-Approval-of-EbangaTM-for-Ebola

ANNEX

TABLE:
Overview of Requests in KEI Comments on NIH Prospective Exclusive Licenses

The NIH does not enforce the statutory requirement to restrict the scope of exclusive rights in a patent license as set out in 35 USC § 209(a)(1-2).

August 18, 2023
James Love
Knowledge Ecology International

Submitted to: SciencePolicy@od.nih.gov

The NIH does not enforce the statutory requirement to restrict the scope of exclusive rights in a patent license as set out in 35 USC § 209(a)(1-2).

Any reform of NIH licensing policy should address this failure.

Introduction

There are two aspects of the NIH's failure to enforce the 35 USC § 209 restrictions.

First, 35 USC § 209(a)(1) only allows the grant of an exclusive license on a federally-owned invention when, "granting the license is a **reasonable and necessary incentive** to call forth the investment capital and expenditures needed to (A) bring the invention to practical application; or (B) otherwise promote the invention's utilization by the public." (emphasis added).

Second, 35 USC 209(a)(2) requires that for an exclusive license, "the proposed scope of exclusivity is not greater than **reasonably necessary to provide the incentive** for bringing the invention to practical application, as proposed by the applicant, or otherwise to promote the invention's utilization by the public." (emphasis added).

The two conditions on the grant of an exclusive license on patents owned by the federal government are designed to protect the public from a private party obtaining a legally enforced monopoly on an invention owned by the federal government, except when the terms of the exclusive right are both reasonable and necessary to achieve commercialization, and the exclusive rights are limited to what is reasonably necessary.

The scope of rights that should be limited under § 209 may involve many issues, including most importantly these five issues:

1. The specific inventions,
2. The field of use,
3. The geographic territory,
4. The amount of time the exclusivity applies (the term), and
5. Conditions on pricing.

NIH Practice

The covered inventions

The specific inventions are often listed in the public notice for a license and are not limited to inventions with granted patents. The covered inventions may be inventions where applications for patents have been submitted, but not yet granted, and even inventions where applications may be filed in the future. For example, in the current prospective exclusive license to the mystery company EnZeta, the licensed inventions will include, in addition to four specific and named patent applications, "any and all other U.S. and ex-U.S. patents and patent applications

claiming priority to any one of the foregoing, now or in the future." Among the four named patent applications in the EnZeta license, two were filed 2023 and the most recent application was filed May 9, 2023, less than four months ago.

The field of use

In some cases, the NIH limits the field of use in a license, to some degree, and in others, the field of use is "commensurate in scope with the patent rights," or unlimited by the license itself.

The degree that a field of use is limiting can be important and varies by license. These are a few examples:

- EnZeta Immunotherapies, Inc. August 2023. "manufacture, distribution, sale and use of T-cell-based immunotherapies for solid tumors."

- Elgia Therapeutics, Inc., July 2023. "Development, manufacture, use and commercialization of Caspase Inhibitors disclosed and claimed in the prospective licensed patent rights, for the treatment of inflammatory diseases, such as hidradenitis suppurativa (HS) in humans and animals."

- Affini-T Therapeutics, Inc., December 2022. "Development, manufacture and commercialization of T or Natural Killer cell therapy products genetically engineered to express the P53 R175H-reactive T cell receptor claimed in the Licensed Patent Rights for the treatment of cancer in humans."

- Australian National University, May 2023. "commensurate in scope with the patent rights."

- University College London Business, Ltd. ("UCLB"), incorporated in England and Wales, May 2023. "commensurate in scope with the patent rights."

- The Progeria Research Foundation ("PRF"), July 2021. "commensurate in scope with the patent rights."

The geographic territory

The NIH most commonly grants worldwide rights to its patented inventions.

Concerns over developing country access

KEI often asks the NIH to exclude exclusivity in developing countries, or more generally, to not grant exclusive rights in countries with a per capita income of less than 30 percent of the United

States. As far as we know, the NIH has always rejected KEI's proposals to limit the exclusive rights in lower-income countries, even when the license covers treatments for HIV or other illnesses that often benefit from voluntary open licenses from big drug companies to the Medicines Patent Pool (MPP).

Just one of many examples of exclusive licenses in developing countries concerns the 2020 license to RNAceuticals, a firm without a web page. The technology is for N6, which is a "Novel, Broad, Highly Potent HIV-Specific Antibody and a Broadly Neutralizing Human Anti-HIV Monoclonal Antibody (10E8) Capable of Neutralizing Most HIV-1 Strains." Eleven health and patient NGOs and nine individuals wrote to Dr. Fauci on July 20, 2020 objecting to the territory of the license, stating:

> "For existing HIV drugs, most companies that currently hold patents on useful antiretroviral drugs have demonstrated a willingness to license on a non-exclusive basis in roughly 115 lower and middle income countries, including South Africa and India, via the Medicines Patent Pool. Instead this proposed license would extend exclusivity to this mystery firm to HIV antibodies already in clinical trials to Brazil, China, India, South Africa, and Russia, and apparently Serbia.
>
> The USAID is aware that most persons living with HIV reside in countries with lower incomes and scarce resources to purchase medicines, and that the role of donors in supporting such areas is constantly at risk and is declining relative to the number of persons needing treatments. While only a handful of developing countries are included in the proposed license, several have large populations of persons living with HIV, and five countries (India, China, Brazil, Russia and South Africa) can play an important role in manufacturing generic versions of products covered by the license. The exclusive license would allow the licensee to prevent that manufacture."

The United States Public Health Service Technology Transfer Policy Manual, Chapter No. 300, PHS Licensing Policy, 12/08/2010, includes this often ignored statement:

> "PHS seeks to promote commercial development of inventions in a way that provides broad accessibility for developing countries."

As the NIH is fully aware, there is massive evidence of disparities in access to new drugs by geography, and while the United States has repeatedly endorsed the norm "to promote access to medicines for all" in regard to intellectual property rights, the NIH routinely grants worldwide rights to licensed patents, knowing full well that in most cases this will lead to unequal access globally. Of particular concern are the licenses that include exclusivity in India and other countries with the capacity to manufacture and sell generic or biosimilar versions of treatments.

KEI has often asked HHS and the NIH to include, in licenses, a provision that permits the NIH to enable more competitive licensing in developing countries, either through the Medicines Patent

Pool or other arrangements. These requests are generally ignored by HHS and the NIH, and most NIH-issued exclusive licenses, with few exceptions, have provided for worldwide rights.

We have asked the NIH to take into account the fact that the inclusion of India and other developing countries in the geographic territory of the exclusive rights has almost no impact on the business decisions of the companies developing the products. Nearly all of the business decisions for most licensed inventions concern potential markets in Europe, North America, Japan, Korea and Australia, or more generally, markets where the per capita incomes are greater than 30 percent of the United States, and where either public or private health insurance can pay for the products.

In cases where a technology will have significant use for persons living in lower-income countries, it will sometimes be the case that the U.S. government is among the countries providing donor funds, and in these cases, high prices will be a burden on US taxpayers, or limit the effectiveness of the US donor efforts.

Unnecessary exclusivity in United States

For some products that are already in clinical development, and even for some pre-clinical technologies, the exclusivity in other high-income countries is a sufficient incentive to bring products to the market. KEI has in the past asked the NIH to limit the exclusivity to other high-income countries, while permitting generic or biosimilar competition in the United States. To our knowledge, the NIH almost never (and perhaps never) considers this as an option, even though it is a very simple way to benefit U.S. residents while providing the incentive necessary to bring the products to market.

The period of time exclusivity applies (the term)

One of the more frustrating aspects of the NIH licensing practice concerns the period of time the exclusivity applies. In previous years, the licenses for NIH-owned patents sometimes limited the number of years of exclusivity, but more recently, apparently ALL of the NIH exclusive licenses run for the entire term of the patent.

One example of the earlier policy concerns the HIV drug didanosine (ddI), the subject of an NIH Office of Technology Transfer case study.

> “The technology transfer challenge was to negotiate a license that would provide a strong incentive for a drug company to make the significant investment necessary for the rapid development of a new drug while ensuring the long-term public health benefits. This balance was struck by offering a license that was initially exclusive, but which could became non-exclusive early, prior to the expiration of the NIH patents. Several companies competed for the license. Criteria for selecting the licensee included the

> company's technical ability to develop this compound into a drug and manufacture it in large quantities, its willingness to work cooperatively with the NIH, and its willingness to make development of this compound a priority. The BristolMyers Squibb plan was judged superior by the selection panel, and the license was signed in January 1988. NIH exercised its prerogative to have the license become nonexclusive in October 2001."
>
> *Videx® Expanding Possibilities: A Case Study, NIH, National Institutes of Health Office of Technology Transfer, September 2003,*

When asked recently about the NIH policy regarding the term of exclusivity, Mark Rohrbaugh said that the NTIS had negotiated licenses, including the ddI license, with shorter terms of exclusivity, but once the NIH took over responsibility for negotiations of licenses to the patents it owned, the agency has a policy of granting the life of the patent exclusivity in every license. This clearly runs counter to the requirements in § 209 to ensure that the "scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application."

KEI has made a number of proposals to the NIH regarding the term of exclusivity in license. One is to limit the exclusivity to a specific number of years, similar to the ddI license. In determining the number of years for exclusivity, KEI has asked the NIH to estimate the amount of money needed to bring a product through FDA approval, the anticipated market for the product, and to take into account other federal subsidies and incentives including but not limited to:

- Federal grants or contracts,
- Advance purchase agreements,
- Priority Review Vouchers,
- Orphan Drug Tax Credits,
- Orphan Drug Exclusivity,
- FDA test data exclusivity for both small molecules and biologic drugs, and
- Regulatory exclusivities and subsidies in Europe and other markets.

For some products, the existence of grants from the NIH or other federal agencies such as BARDA, DoD, etc, the eligibility for the FDA priority review voucher (worth around $100 million recently), and various regulatory exclusivities make the incentive of exclusivity in a patent license unnecessary once a product is approved by the FDA, therefore a much shorter patent exclusivity is appropriate. The NIH, however, makes no such distinction and grants life-of-patent exclusivity in all cases.

Another alternative to a specific shorter term for the license is to tie the term of exclusivity to the revenue generated by a product. For example, KEI has asked the NIH to set a benchmark revenue milestone, for example at $1 billion in global sales for a product, and then reduce the term of exclusivity by one year for every $500 million in additional global sales, or to consider different milestone targets. There are many advantages to tying the exclusivity to revenue

milestones, since the real world actual cash flow eliminates the need to guess about the size of the potential market.

The NIH has also rejected all of these proposals, and without any analysis of the feasibility.

Conditions on pricing

In the past, the NIH placed some conditions on product pricing. Both Taxol, a drug for cancer, and ddI, a drug for the treatment of HIV, are examples of products with such conditions.

More recently, during the COVID-19 pandemic, the US government has negotiated a number of contracts with pricing conditions, including in several cases, reference pricing clauses, such as most favored nation pricing conditions, or most favored customer clauses The Annex on Pricing Clauses in U.S. Government Contracts for COVID-19 Products illustrated that companies, including large ones, will agree to restrictions on pricing, including for products in development.

KEI has asked the NIH over a hundred times to include in its licenses a requirement that U.S. residents pay no more than the median price paid by residents in the seven countries with the largest GDP and at least 50 percent of US per capita income. The NIH has rejected every one of these requests, regardless of the stage of development of the technology.

The NIH Reasonable Pricing Clause experience

Following a controversy over the high price of the HIV drug zidovudine (AZT), President George Herbert Walker Bush (GHWB) put into practice the use of a reasonable pricing clause in NIH CRADA and patent license agreements. The first products to reach the market with the pricing clause were the unpatented cancer drug Taxol (approved by the FDA in 1992) and the HIV drug ddI (approved by the FDA in 1991).

Taxol

Taxol was an unpatented product for which the US government held the rights to all of the Phase 1, 2 and 3 clinical trials used for the FDA approval. The NIH entered into a CRADA agreement with Bristol Myers Squibb (BMS) to register the drug with the FDA and commercialize the drug. The CRADA gave BMS the exclusive rights to use the data from the NIH-funded and -conducted clinical trials for FDA approval, giving BMS what was effectively a five year monopoly. The language in the CRADA agreement with BMS was vague as regards the implementation of the obligation, but the NIH negotiated a 15-product reference pricing formula with BMS. The agreement allowed BMS to charge $4.87 a milligram for Taxol, a substantial increase over the $0.25 per milligram the NIH was paying a contractor to make the drug for clinical trials. This led to a controversy that is well documented in a Congressional hearing: US House of Representatives, Committee on Small Business, Subcommittee on Regulation, Business Opportunities, and Energy, *Exclusive Agreements between Federal Agencies and Bristol-Myers Squibb Co. for Drug Development*. Serial No. 102-35. July 29.

(https://babel.hathitrust.org/cgi/pt?id=pst.000019275802&seq=1), as well as other Congressional Hearings and GAO reports.

ddI

In addition to the shorter patent term, the NIH negotiated a reasonable pricing clause in its patent license with BMS for the HIV drug ddI, marked by BMS as Videx. BMS agreed to sell ddI at a price roughly 30 percent lower than the price that GSK was charging for AZT, a similar HIV drug.

The 1995 elimination of the NIH reasonable pricing clause

From 1991 to 1993, both Houses of Congress held hearings on the pricing of drugs developed with federal assistance, generating a number of news stories and commentary. Members of Congress also proposed additional measures to deal with high drug prices, including new concerns over the high prices for drugs for rare diseases, many of which had benefited from significant federal R&D subsidies. One supporter (at least publicly) of the reasonable pricing clause on NIH-funded drugs was Dr. Bernadine Healy, the Director of the NIH from April 9, 1991 to June 30, 1993.

From 1992 to 1994 the industry hardened its opposition to the reasonable pricing clause, and the NIH changed its policies following the election of President Bill Clinton and the appointment of Donna Shalala as Secretary of HHS in January 1993 and the appointment of Harold Varmus as NIH Director in November of 1993.

The biotech industry experienced a series of pricing swings from 1991 to 1995 which influenced the debate on the NIH reasonable pricing clause, even though the clause was rarely relevant to products approved by the FDA during that period.

In 1991, news reports about biotech share prices used terms like “soaring” or titles like “Biotech Firms' Stocks Dazzle Wall Street,”[1] By 1993 the tone had cooled, particularly for the venture market for biomedical stocks.

The NASDAQ Biotechnology (NBI) index was trading at 210 in early 1994, but fell below 145 in July. The NYSE Arca Biotechnology index (BTK) was started at 200 in October 1991 and peaked at 223.92 in January 1992, fell to 82 by 1994 and was as low as 78 in March 1995.

The declines in the biotech share prices were driven by various factors including concerns over possible Congressional imposed price controls, high profile failures of drugs in clinical trials and

[1] https://www.washingtonpost.com/archive/business/1991/04/15/biotech-firms-stocks-dazzle-wall-street/2459b873-cf27-4b58-8df7-f30fa21c029b/

court decisions in patent disputes. The NIH reasonable pricing clause became an accessible target of panicked biotech investors and drug company lobbyists.

In 1994, the NIH held two forums on the CRADA reasonable pricing clause. The first forum, held July 21, 1994, had panel members representing Pfizer, BMS, Upjohn and Eli Lilly, as well as the smaller firms Genetic Therapy Inc. and Mitotix, and Allan Fox, a lawyer for rights holders, as well as Brigham and Women's Hospital (a large recipient of NIH funding). and several government officials. At this meeting Lisa Raines, Vice President of Government Relations for Genzyme, the company created to commerize Ceredase, made a motion to eliminate the reasonable pricing clause. Ceredase was a drug developed at Tufts University on NIH grants, and at the time of the forum, it was at the time the most expensive drug in the world.

There was significant criticism of the first forum for its industry heavy representation, and the NIH was forced to hold a second forum on September 8, 1994. The published report on the CRADA forums is available here. I attended both forums, and spoke at the second. Among the arguments against the use of the reasonable pricing clause was that it had not been used effectively to benefit consumers, and was intensely disliked by investors and drug companies, so the net benefits of eliminating something that had no benefits favored its removal, an argument used today against the march-in rights clause in the Bayh-Dole Act.

In the 1994 midterm elections, the Republican Party captured unified control of Congress for the first time since 1952, elevating Representative Newt Gingrich as Speaker of the House and Senator Robert Dole as Senate President.

On April 11, 1995, the NIH published a Notice rescinding the reasonable pricing clause, including its enforcement in existing contracts. Dr. Varmus stated, “An extensive review of this matter over the past year indicated that the pricing clause has driven industry away from potentially beneficial scientific collaborations with PHS scientists without providing an offsetting benefit to the public.” I criticized the action as follows.

> James Love, an economist with the Center for Study of Responsive Law, a group founded by the consumer advocate Ralph Nader, said the decision abandoned efforts to protect consumers and taxpayers, and opened the door to high prices for pharmaceuticals developed through substantial Government investment. "Under today's actions, a drug company will be able to charge any conceivable price for any drug, no matter how small the private sector's role in the development of the drug," Mr. Love said, "and no matter how comprehensive and complete the Government's role in the drug's development."
> Warren E. Leary, U.S. Gives Up Right to Control Drug Prices, *New York Times*, April 12, 1995.

The misrepresentation of the data on NIH CRADAs

Following the elimination of the reasonable pricing clause in CRADAs, the NIH created a new type of CRADA for materials transfers. The original CRADA was then called a “Standard CRADA” and the new one a “Materials CRADA,” sometimes referred to later as a MCRADA. The new materials CRADA was initially widely used by the NIH, although over time much less so. But by combining the numbers of both the standard and the materials CRADAs, the critics of the reasonable pricing clause misleadingly claimed that the elimination of the clause led to a dramatic increase in industry engagement, and this became a standard talking point for critics of the reasonable pricing clause, particularly by the NIH OTT, AUTM members and drug companies.

Figure 1 illustrates how misleading it was to lump the numbers from the CRADAs and MCRADAs together. The average number of Standard CRADAs from 1989 to 1994 was 34. When the standard and materials CRADA numbers were added together, it appeared as if there were 87 agreements in 1996, and 153 in 1997, a huge increase. However, when standard CRADAs amounts are compared to each other, a different picture emerges. The 1996 number of standard CRADAs was 44, while the 1997 number of standard CRADAs was 32, the same or lower than four of the years when the reasonable pricing clause was in effect. By 2006, the number of standard CRADAs fell to 22, and was only 23 the following year, both amounts lower than any year when the reasonable pricing clause was in effect. From 1997 to 2010, the average number of standard CRADAs was slightly higher at 36, but only by 2, and during a period when the NIH budget per CRADA was far larger (see Table 1).

Figure 1: NIH Standard and Materials CRADAs, Reported by OTT as executive, by fiscal year

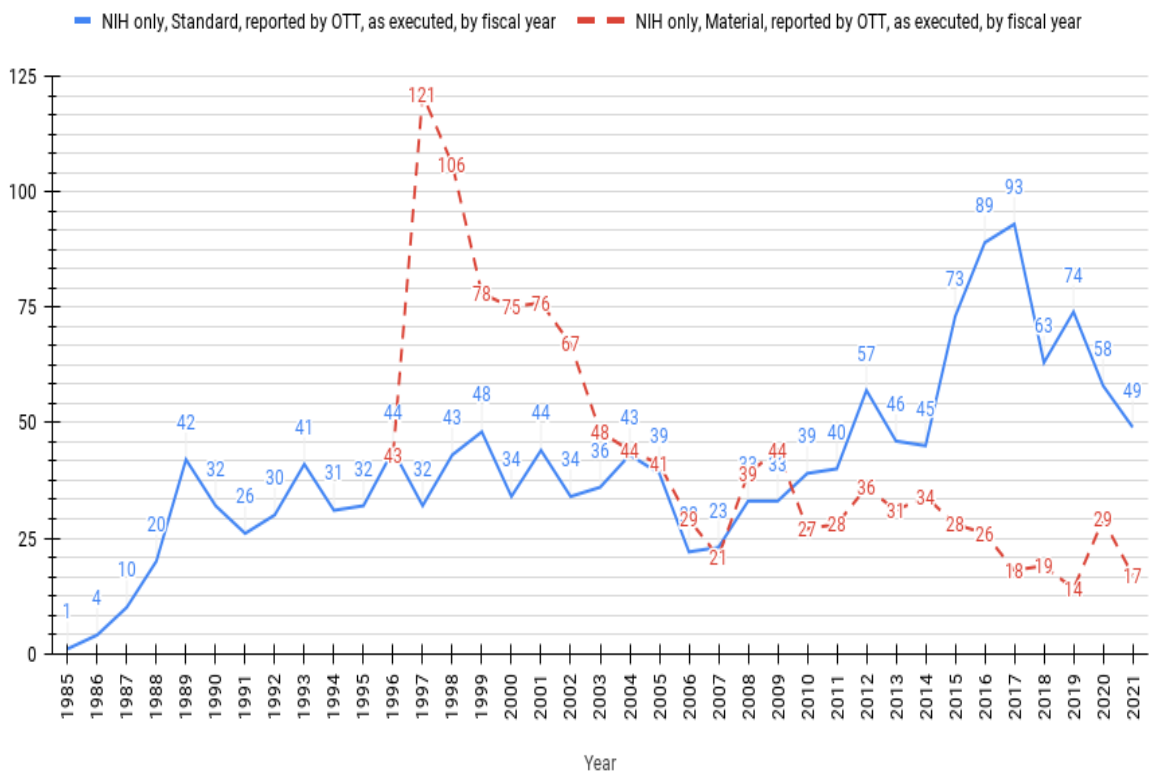


Table 1: Average number of standard CRADAS and NIH Budget per CRADA for different time periods

Period	Average number of standard CRADAs executed by fiscal year	Number of CRADAS	NIH Budget	NIH Budget / CRADA
1986 to 1988	11	34	$18,111,814,000	$532,700,412
1989 to 1994	34	202	$53,211,311,000	$263,422,332
1989 to 1995	33	234	$64,510,833,000	$275,687,321
1996 to 2002	40	279	$115,592,929,000	$414,311,573
2003 to 2009	33	229	$201,688,788,000	$880,737,066
2011 to 2020	64	638	$336,420,349,000	$527,304,622
1996 to 2010	36	547	$348,519,717,000	$637,147,563

Looking at the CRADA data over time, including the massive decline in the use of the materials CRADAs, it appears as though the number of CRADAs is driven by factors largely unrelated to the reasonable pricing clause, the national or global market for therapeutics or the NIH budget.

The data have been misused to mislead the general public and policymakers, not only by the rights holder lobby, including persons representing universities that have a putative mission to educate, but also frequently by NIH OTT officials to advance their anti-reasonable pricing agenda.

The NIH licenses of patents and data to Ridgeback for the Ebola Drug Ebanga

The NIH grants of an exclusive patent license and an exclusive license to US NIH clinical trial data for the Ebola drug Ebanga (ansuvimab-zykl, formerly referred to as mAb114) illustrates how the NIH can ignore the restrictions on exclusive license set out in § 209.

The research to develop mAb114 was carried out and supported by the NIH, BARDA, DARPA, and the clinical trials to support the registration of the drug were undertaken by the NIH in collaboration with public health authorities in Africa and MSF. According to one NIH release:

> “The National Institute of Allergy and Infectious Diseases (NIAID) Vaccine Research Center (VRC), part of NIH, developed the investigational treatment and conducted and sponsored the clinical trial. . . VRC scientists developed mAb114 in collaboration with scientists at the National Institute of Biomedical Research (INRB) in the DRC; the Institute for Research in Biomedicine and Vir Biotechnology, Inc.'s subsidiary Humabs BioMed, both based in Bellinzona, Switzerland; and the U.S. Army Medical Research

> Institute of Infectious Diseases at Fort Detrick, Maryland. The Defense Advanced Research Projects Agency funded the production of mAb114 for clinical testing." https://www.niaid.nih.gov/news-events/investigational-monoclonal-antibody-treat-ebola-safe-adults

Ridgeback Biotherapeutics, a firm headed by Wendy Holman, received two large grants from BARDA related to the drug, including Contract No. 75A50120C00009, wherein Ridgeback can be reimbursed up to $153,663,387.24 for "CMC efforts for mAB114 for the Development and Treatment of Ebola", and 75A50119C00059, wherein Ridgeback was awarded $13,988,547 for "Additional in-scope work for CMC efforts for mAB114 development for the treatment of Ebola"

The NIH initially provided a non-exclusive license to mAB144 inventions, but later would provide Ridgeback with exclusive rights to data from an NIH run clinical trial for purposes of drug registration. In September of 2020, NIAID told KEI the following regarding mAb114 clinical trial data via email:

> "NIAID filed two INDs related to mAb114 – one for the Phase 1 clinical trial of mAb114 and one for the PALM clinical trial in which the efficacy of mAb114, ZMapp, Remdesivir, and REGN-EB3 was evaluated. To enable expedited review of the BLA for mAb114 by the FDA, NIAID transferred the Phase 1 IND to Ridgeback Biotherapeutics. NIAID received no consideration for this transfer, and it was not conveyed under a license agreement. The transfer will accelerate access to this important therapeutic, enabling effective responses to ongoing Ebola outbreaks in Africa. NIAID remains the sponsor of the PALM clinical trial, and the data from this clinical trial has been shared with all of companies that supplied study products for this clinical trial."

By transferring the Phase 1 clinical data to Ridgeback, Ridgeback obtained a 12 year FDA regulatory monopoly on the test data.

The NIH could have retained the rights in the data, allowing the government to obtain generic or biosimilar versions of the drug from third parties. One consequence of the transfer of the data rights to Ridgeback is that for now, the US government now has to buy the drug from Ridgeback. Another consequence is that Ridgeback was able to claim a material threat medical countermeasure priority review voucher (PRV), as provided under section 565A of the Federal Food, Drug and Cosmetic Act (FDCA), which is currently worth about $100 million.

Ridgeback received FDA approval for Ebanga (mAb114) on December 21, 2020. But on March 15, 2021, the NIH apparently proposed making its patent license for the mAb114 inventions exclusive, despite the fact that Ridgeback had received significant funding from BARDA, had 12 years of exclusive FDA test data rights, has Orphan Drug marketing exclusivity through December 21, 2027 and received a priority review voucher worth about $100 million.

KEI's comments on the 2021 exclusive license notice is here. As usual, the NIH has not provided information to KEI on the final outcome of the proposed exclusive license.

ANNEX Pricing Clauses in U.S. Government Contracts for COVID-19 Products

In 2020 and 2021, several U.S. government contracts for the development of COVID-19 vaccines, therapeutics, diagnostic tests and other related products included provisions on pricing. Some contracts include a most favored nation pricing clause that specifically requires the company to provide the U.S. government with “a price lower” than the price offered to any centralized federal authority that is “a member of the Group of Seven plus Switzerland.” The non-US members of the G7 are Canada, France, Germany, Italy, Japan, the United Kingdom.

Table A-1, U.S. Government COVID-19 Contracts Containing Reference Price Constraints on Resultant Products

Contractor, Agency, and Contract Number	Subject	Page	Reference Price Term Excerpt
Pfizer DOD/Army W58P0522C0001 November 17, 2021	Paxlovid Purchase Agreement	33	**H.7 Most Favored Nation Clause** (a) If, at any time prior to, or during, the base term and any exercised options of this contract, Contractor enters into any agreement with a Covered Nation under which the Covered Nation commits to purchase (i) the same or a lesser volume of Product than the U.S. Government commits to purchase (ii) at a price lower than the price the U.S. Government is obligated to pay for Product under this contract, Contractor shall provide notice of such lower price to the U.S. Government within 30 days of the execution of the Contractor-Covered Nation agreement and the U.S. Government may elect, at its discretion, to receive the benefit of this provision and purchase the Product at that lower price.

ANP Technologies, Inc. DOD/Army W911QY20D0019 May 29, 2020	Development and Production of a Diagnostic	11	"MOST FAVORED CUSTOMER H.1 Most Favored Customer Awardee agrees that during the term of this contract and for a period of 5 years thereafter, that it shall not offer, sell or otherwise provide the production model of the CLIN 0001 end items (for the avoidance of doubt, CLIN 0001 end items in this clause shall mean a finished good of like material, like quality, to be used in a similar applications, and shall not include more general products to any entity at a price lower than that offered to the DoD. In the event that Awardee sells the production model at a lower unit price than that price sold to the DoD, Awardee shall immediately notify the Contracting Officer in writing of the lower price. For prior purchases, the Awardee shall reimburse the DoD, the difference between the lower price sold to the other customer(s) and the price sold to the DoD multiplied by the number of items sold. Such reimbursement shall occur within thirty days (30) of the Awardee discovering that the lower price was given to another customer. Notwithstanding the foregoing, the Parties may agree to apply the difference in price paid by the other customer(s) and DoD into additional quantities required by the DoD."
Becton, Dickson & Company DOD/Army W911SR2030001 July 1, 2020	Needle Production	17	**"9. Government Preference** 9.1 Pricing. During the term of the Agreement, the Recipient agrees that, in the event that it enters into a Group Purchasing Organization (GPO) contract with a Qualifying Third Party (as defined below) with respect to a Qualifying Product (as defined below) with a per unit GPO price lower than that offered for the same Qualifying Product to the Government, the Recipient shall (i) promptly notify the Agreements Officer in writing of the lower price and (ii) extend the lower price to all future sales of the Qualifying Product to the Government. . . . " For purposes of this section, "Covered Nation" shall mean a nation that is a member of the Group of Seven (Canada, France, Germany, Italy, Japan, the United Kingdom, and the United States) plus Switzerland.
Eli LIlly, DOD/Army W911QY21D0012 P0002 April 7, 2021	Monoclonal Antibody Treatment Production	7-8	**"H. 7 Sales to Covered Nations** (i) Due to the exceptional and unprecedented nature of the COVID-19 threat to global public health, as well as the investments made towards the development of a safe and effective therapeutic against COVID-19, Lilly agrees that it will not at any time prior to 30 September 2021 sell any COVID-19 bamlanivimab/etesevimab combination therapeutic supplied directly to the Government under this Agreement to any centralized federal authority (i.e., federal government or equivalent) of a nation that is a member of the Group of Seven plus Switzerland ('Covered Nation') at a lower price than the prices set forth in this contract. . . . "

Eli Lilly DOD/Army W911QY21C0016 October 26, 2020	Monoclonal Antibody Treatment Production	18	"**H.7 Sales to Covered Nations** (i) Due to the exceptional and unprecedented nature of the COVID-19 threat to global public health, as well as the investments made towards the development of a safe and effective therapeutic against COVID-19, Lilly agrees that it will not at any time prior to 30 June 2021 sell any COVID-19 therapeutic supplied directly to the Government under this Agreement to any centralized federal authority (i.e., federal government or equivalent) of a nation that is a member of the Group of Seven plus Switzerland ('Covered Nation') at a lower price than the prices set forth in this contract. . . ."
Emergent BioSolutions Canada Inc. DOD/Army W911QY2090013 June 24, 2020	"the research and development of an advanced human immune globulin manufactured from human plasma with antibodies to SARS-CoV-2 (COVID-HIG) for post-exposure prophylaxis (PEP) of Coronavirus Disease (COVID-190"	16	"**ARTICLE 9. Most Favored Customer** A. Awardee agrees that it shall not offer, sell, or otherwise provide the production model of the Prototype to any entity at a price lower than it offered to the DoD. In the event that Awardee sells the production model of the Prototype at a lower unit price than that price sold to the DoD, Awardee shall reimburse the DoD, the difference between the lower price sold to the other customer (S) and the price sold to the DoD multiplied by the number of items sold . . . ."
Immunome Inc DOD/Army W911QY2090019 July 3, 2020	"research and development of a standardizable and scalable [redacted] compromise of [redacted] antibodies . . . ."	16	"**ARTICLE 9. Most Favored Customer** A. Awardee agrees that it shall not offer, sell or otherwise provide the production model of the Prototype to any entity at a lower price than that offered to the DoD. In the event that Awardee sells the production model of the Prototype at a lower unit price than that price sold to the DoD, Awardee shall immediately notify the OTAO in writing of the lower price. . . ."
Inovio Pharmaceuticals, Inc. DOD/Army W911QY2090016 June 22, 2020	"the development of an FDA approved next generation electroporation device and array for DNA Vaccine delivery of INO-4800 against COVID-19, with demonstrated capability to be produced at a large scale, as well as full automation for production of the device arrays, (hereinafter referred to as the 'Prototype Project')."	17	"**ARTICLE 9. Most Favored Customer** A. For a period of six (6) years from the Effective Date, Awardee agrees that it shall not offer, sell or otherwise provide the production model of the Prototype to any entity at a price lower than that offered to the DoD. In the event that Awardee sells the production model of the Prototype at a lower unit price than that price sold to the DoD, Awardee shall immediately notify the OTAO in writing of the lower price. . . ."

Maxim Biomedical, Inc. DOD/Army W911QY20D0018 May 11, 2020	Diagnostic Production	10	"H.1 Most Favored Customer A. Awardee agrees that during the term of this contract and for a period of 5 years thereafter, that it shall not offer, sell or otherwise provide the production model of the CLIN 0001 end items (for the avoidance of doubt, CLIN 0001 end items in this clause shall mean a finished good of like material, like quality, to be used in a similar applications, and shall not include more general products to any entity at a price lower than that offered to the DoD. In the event that Awardee sells the production model at a lower unit price than that price sold to the DoD, Awardee shall immediately notify the Contracting Officer in writing of the lower price. . . ."
Murtech, Inc. DOD/Army W911QY20D0017 May 11, 2020	Diagnostic Production	15	"H.1 Most Favored Customer A. Awardee agrees that during the term of this contract and for a period of 2 years thereafter, it shall not offer, sell or otherwise provide the production model of the CLIN 0001 end items (herein the 'Items') (for the avoidance of doubt, CLIN 0001 production model end items in this clause shall mean a finished good of like material, like quality, to be used in a similar applications, and shall not include more general products) to any entity at a price lower than that offered to the DoD."
Novavax DOD/Army W911QY20C0077 P0002 June 4, 2020	"Vaccine Development and Production"	4	"The Contractor shall maintain a most favored customer provision for the product once authorized or licensed by the FDA, such that the Contractor shall not give any entity a better price than the DoD for a period of five (5) years from the award of this contract, limited to customers in the U.S. and purchases made in the U.S to include sale prices as compared to commercial clients with respect to quantity, location of delivery, fundamental differences in deliverable formulation, and material differences in terms and conditions for commercial contracts."
Sanofi DOD/Army W15QKN1691002; MCDC2011-005 July 30, 2020	Vaccine Research and Development (including Clinical Trials) and Production	28	"**5.1 Most Favored Nation Clause** (i) Due to the exceptional and unprecedented nature of the COVID-19 threat to global public health and in recognition of the long historical partnership between the U.S. Government and Sanofi Pasteur working on global pandemic solutions, as well as the investments made towards the development of a safe and effective vaccine against COVID-19, Sanofi Pasteur agrees that it will not sell any COVID-19 vaccine licensed under this Agreement to any nation that is a member of the Group of Seven plus Switzerland ('Covered Nation') at a price that is more favorable than those set forth in this Project Agreement."
SIO2 Medical Products, Inc. DOD/Army W911NF2030003 June 5, 2020	Vaccine Delivery Device Research and Development	13	"**9. Government Preference** 9.1 Pricing. During the period of performance and the exercised optional availability periods, the Recipient agrees that, in the event that it offers, sells or otherwise provides a Qualifying Product (as defined below) to any Qualifying Third Party (as defined below) at a per unit price lower than that offered for the same Qualifying Product to the Government or a third party purchasing Qualifying Product pursuant to a designation by the Government pursuant to Section 9.2 or 9.3 (an 'MCM Partner'), the Recipient shall (i) promptly notify the Agreements Officer in writing of the lower price and (ii) extend the lower price to all future sales of the Qualifying Product to the Government or an MCM Partner."

Merck Sharp & Dohme Contract DOD/Army W911QY21C0031 June 7, 2021	COVID 19 Therapeutic	21	H.7. Fully redacted including the title
Rigel Pharmaceuticals DOD/Army W911QY-21-9-0018 January 29, 2021	COVID-19 Therapeutic	29	"**Article 20. Most Favored Customer.** A. In the event that the Parties agree to a follow-on production agreement pursuant to 10 U.S.C. 2371b Awardee agrees that it shall sell to the U.S. Government up to [redacted] treatment courses of TAVALISSE at a price not greater than [redacted]. Any additional treatment course will be sold to the U.S. Government at a price to be negotiated and agreed by the Parties. B. If Awardee develops a like product (commercialized version or derivative of the production model of the Prototype) with similar capability and intended application, but at a lower unit price ("Like Product") regardless of quantity, Awardee shall make the DoD aware of that similar product and the technical and price differences between that product and the Prototype. Such notification shall be made to the °TAO in writing, of which email is an acceptable form, within thirty (30) days of such offering."

ANNEX: examples of NIH redactions regarding research collaboration agreement with Ridgeback

RESEARCH COLLABORATION AGREEMENT

This Agreement is between the **National Institute of Allergy and Infectious Diseases** ("NIAID"), which is a component of the National Institutes of Health ("NIH"), an agency of the U.S. Department of Health and Human Services, having offices located at 5601 Fishers Lane, Rockville, MD 20852, and **Ridgeback Biotherapeutics** ("Ridgeback") ("Collaborator"), having a principal place of business at (b) (6) (collectively, the "Parties"). This Agreement is neither a funding agreement as defined in 35 U.S.C. § 201(b) nor a cooperative research and development agreement authorized under the Federal Technology Transfer Act of 1986, as amended, 15 U.S.C. §§ 3710a *et seq.*, and Executive Order 12591 of April 10, 1987. NIAID enters into this Agreement pursuant to the authority of the Public Health Services Act of 1944, as amended (42 U.S.C. § 241).

BACKGROUND

1. (b) (4)
2.
2. NIAID and Collaborator want to transfer between the laboratories of their investigators, during the term of this Agreement, proprietary research materials (b) (4) required to conduct the research project (b) (4)

APPENDIX A

Research Project

I. **Abstract of the Research Project – for Public Release**
EITHER PARTY MAY, WITHOUT FURTHER CONSULTATION OR PERMISSION, RELEASE THIS ABSTRACT TO THE PUBLIC.

Ridgeback Biotherapeutics and the Vaccine Research Center (VRC), National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH) will collaborate to advance development of monoclonal antibodies against Ebola virus toward licensure for therapeutic and prophylactic use in control of outbreaks and prevention of epidemics.

II. **Goal(s) of Project**

(b) (4)

IV. Respective Contributions of the Parties

Ridgeback

(b) (4)

VRC/NIAID

(b) (4)

V. Material Contributed by VRC/NIAID

(b) (4)

VI. Material Contributed by Collaborator

(b) (4)

Submission Date: 8/18/2023

Name: James Love

Name of Organization: Knowledge Ecology International

Comment:

Additional Comment (attachment):

The NIH does not enforce the statutory requirement to restrict the scope of exclusive rights in a patent license as set out in 35 USC § 209(a)(1-2).

August 18, 2023
James Love
Knowledge Ecology International

Submitted to: SciencePolicy@od.nih.gov

The NIH does not enforce the statutory requirement to restrict the scope of exclusive rights in a patent license as set out in 35 USC § 209(a)(1-2).

Any reform of NIH licensing policy should address this failure.

Introduction

There are two aspects of the NIH's failure to enforce the 35 USC § 209 restrictions.

First, 35 USC § 209(a)(1) only allows the grant of an exclusive license on a federally-owned invention when, "granting the license is a **reasonable and necessary incentive** to call forth the investment capital and expenditures needed to (A) bring the invention to practical application; or (B) otherwise promote the invention's utilization by the public." (emphasis added).

Second, 35 USC 209(a)(2) requires that for an exclusive license, "the proposed scope of exclusivity is not greater than **reasonably necessary to provide the incentive** for bringing the invention to practical application, as proposed by the applicant, or otherwise to promote the invention's utilization by the public." (emphasis added).

The two conditions on the grant of an exclusive license on patents owned by the federal government are designed to protect the public from a private party obtaining a legally enforced monopoly on an invention owned by the federal government, except when the terms of the exclusive right are both reasonable and necessary to achieve commercialization, and the exclusive rights are limited to what is reasonably necessary.

The scope of rights that should be limited under § 209 may involve many issues, including most importantly these five issues:

1. The specific inventions,
2. The field of use,
3. The geographic territory,
4. The amount of time the exclusivity applies (the term), and
5. Conditions on pricing.

NIH Practice

The covered inventions

The specific inventions are often listed in the public notice for a license and are not limited to inventions with granted patents. The covered inventions may be inventions where applications for patents have been submitted, but not yet granted, and even inventions where applications may be filed in the future. For example, in the current prospective exclusive license to the mystery company EnZeta, the licensed inventions will include, in addition to four specific and named patent applications, "any and all other U.S. and ex-U.S. patents and patent applications

claiming priority to any one of the foregoing, now or in the future." Among the four named patent applications in the EnZeta license, two were filed 2023 and the most recent application was filed May 9, 2023, less than four months ago.

The field of use

In some cases, the NIH limits the field of use in a license, to some degree, and in others, the field of use is "commensurate in scope with the patent rights," or unlimited by the license itself.

The degree that a field of use is limiting can be important and varies by license. These are a few examples:

- EnZeta Immunotherapies, Inc. August 2023. "manufacture, distribution, sale and use of T-cell-based immunotherapies for solid tumors."

- Elgia Therapeutics, Inc., July 2023. "Development, manufacture, use and commercialization of Caspase Inhibitors disclosed and claimed in the prospective licensed patent rights, for the treatment of inflammatory diseases, such as hidradenitis suppurativa (HS) in humans and animals."

- Affini-T Therapeutics, Inc., December 2022. "Development, manufacture and commercialization of T or Natural Killer cell therapy products genetically engineered to express the P53 R175H-reactive T cell receptor claimed in the Licensed Patent Rights for the treatment of cancer in humans."

- Australian National University, May 2023. "commensurate in scope with the patent rights."

- University College London Business, Ltd. ("UCLB"), incorporated in England and Wales, May 2023. "commensurate in scope with the patent rights."

- The Progeria Research Foundation ("PRF"), July 2021. "commensurate in scope with the patent rights."

The geographic territory

The NIH most commonly grants worldwide rights to its patented inventions.

Concerns over developing country access

KEI often asks the NIH to exclude exclusivity in developing countries, or more generally, to not grant exclusive rights in countries with a per capita income of less than 30 percent of the United

States. As far as we know, the NIH has always rejected KEI's proposals to limit the exclusive rights in lower-income countries, even when the license covers treatments for HIV or other illnesses that often benefit from voluntary open licenses from big drug companies to the Medicines Patent Pool (MPP).

Just one of many examples of exclusive licenses in developing countries concerns the 2020 license to RNAceuticals, a firm without a web page. The technology is for N6, which is a "Novel, Broad, Highly Potent HIV-Specific Antibody and a Broadly Neutralizing Human Anti-HIV Monoclonal Antibody (10E8) Capable of Neutralizing Most HIV-1 Strains." Eleven health and patient NGOs and nine individuals wrote to Dr. Fauci on July 20, 2020 objecting to the territory of the license, stating:

> "For existing HIV drugs, most companies that currently hold patents on useful antiretroviral drugs have demonstrated a willingness to license on a non-exclusive basis in roughly 115 lower and middle income countries, including South Africa and India, via the Medicines Patent Pool. Instead this proposed license would extend exclusivity to this mystery firm to HIV antibodies already in clinical trials to Brazil, China, India, South Africa, and Russia, and apparently Serbia.
>
> The USAID is aware that most persons living with HIV reside in countries with lower incomes and scarce resources to purchase medicines, and that the role of donors in supporting such areas is constantly at risk and is declining relative to the number of persons needing treatments. While only a handful of developing countries are included in the proposed license, several have large populations of persons living with HIV, and five countries (India, China, Brazil, Russia and South Africa) can play an important role in manufacturing generic versions of products covered by the license. The exclusive license would allow the licensee to prevent that manufacture."

The United States Public Health Service Technology Transfer Policy Manual, Chapter No. 300, PHS Licensing Policy, 12/08/2010, includes this often ignored statement:

> "PHS seeks to promote commercial development of inventions in a way that provides broad accessibility for developing countries."

As the NIH is fully aware, there is massive evidence of disparities in access to new drugs by geography, and while the United States has repeatedly endorsed the norm "to promote access to medicines for all" in regard to intellectual property rights, the NIH routinely grants worldwide rights to licensed patents, knowing full well that in most cases this will lead to unequal access globally. Of particular concern are the licenses that include exclusivity in India and other countries with the capacity to manufacture and sell generic or biosimilar versions of treatments.

KEI has often asked HHS and the NIH to include, in licenses, a provision that permits the NIH to enable more competitive licensing in developing countries, either through the Medicines Patent

Pool or other arrangements. These requests are generally ignored by HHS and the NIH, and most NIH-issued exclusive licenses, with few exceptions, have provided for worldwide rights.

We have asked the NIH to take into account the fact that the inclusion of India and other developing countries in the geographic territory of the exclusive rights has almost no impact on the business decisions of the companies developing the products. Nearly all of the business decisions for most licensed inventions concern potential markets in Europe, North America, Japan, Korea and Australia, or more generally, markets where the per capita incomes are greater than 30 percent of the United States, and where either public or private health insurance can pay for the products.

In cases where a technology will have significant use for persons living in lower-income countries, it will sometimes be the case that the U.S. government is among the countries providing donor funds, and in these cases, high prices will be a burden on US taxpayers, or limit the effectiveness of the US donor efforts.

Unnecessary exclusivity in United States

For some products that are already in clinical development, and even for some pre-clinical technologies, the exclusivity in other high-income countries is a sufficient incentive to bring products to the market. KEI has in the past asked the NIH to limit the exclusivity to other high-income countries, while permitting generic or biosimilar competition in the United States. To our knowledge, the NIH almost never (and perhaps never) considers this as an option, even though it is a very simple way to benefit U.S. residents while providing the incentive necessary to bring the products to market.

The period of time exclusivity applies (the term)

One of the more frustrating aspects of the NIH licensing practice concerns the period of time the exclusivity applies. In previous years, the licenses for NIH-owned patents sometimes limited the number of years of exclusivity, but more recently, apparently ALL of the NIH exclusive licenses run for the entire term of the patent.

One example of the earlier policy concerns the HIV drug didanosine (ddI), the subject of an NIH Office of Technology Transfer case study.

> “The technology transfer challenge was to negotiate a license that would provide a strong incentive for a drug company to make the significant investment necessary for the rapid development of a new drug while ensuring the long-term public health benefits. This balance was struck by offering a license that was initially exclusive, but which could became non-exclusive early, prior to the expiration of the NIH patents. Several companies competed for the license. Criteria for selecting the licensee included the

> company's technical ability to develop this compound into a drug and manufacture it in large quantities, its willingness to work cooperatively with the NIH, and its willingness to make development of this compound a priority. The BristolMyers Squibb plan was judged superior by the selection panel, and the license was signed in January 1988. NIH exercised its prerogative to have the license become nonexclusive in October 2001."
>
> *Videx® Expanding Possibilities: A Case Study, NIH, National Institutes of Health Office of Technology Transfer, September 2003,*

When asked recently about the NIH policy regarding the term of exclusivity, Mark Rohrbaugh said that the NTIS had negotiated licenses, including the ddI license, with shorter terms of exclusivity, but once the NIH took over responsibility for negotiations of licenses to the patents it owned, the agency has a policy of granting the life of the patent exclusivity in every license. This clearly runs counter to the requirements in § 209 to ensure that the "scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application."

KEI has made a number of proposals to the NIH regarding the term of exclusivity in license. One is to limit the exclusivity to a specific number of years, similar to the ddI license. In determining the number of years for exclusivity, KEI has asked the NIH to estimate the amount of money needed to bring a product through FDA approval, the anticipated market for the product, and to take into account other federal subsidies and incentives including but not limited to:

- Federal grants or contracts,
- Advance purchase agreements,
- Priority Review Vouchers,
- Orphan Drug Tax Credits,
- Orphan Drug Exclusivity,
- FDA test data exclusivity for both small molecules and biologic drugs, and
- Regulatory exclusivities and subsidies in Europe and other markets.

For some products, the existence of grants from the NIH or other federal agencies such as BARDA, DoD, etc, the eligibility for the FDA priority review voucher (worth around $100 million recently), and various regulatory exclusivities make the incentive of exclusivity in a patent license unnecessary once a product is approved by the FDA, therefore a much shorter patent exclusivity is appropriate. The NIH, however, makes no such distinction and grants life-of-patent exclusivity in all cases.

Another alternative to a specific shorter term for the license is to tie the term of exclusivity to the revenue generated by a product. For example, KEI has asked the NIH to set a benchmark revenue milestone, for example at $1 billion in global sales for a product, and then reduce the term of exclusivity by one year for every $500 million in additional global sales, or to consider different milestone targets. There are many advantages to tying the exclusivity to revenue

milestones, since the real world actual cash flow eliminates the need to guess about the size of the potential market.

The NIH has also rejected all of these proposals, and without any analysis of the feasibility.

Conditions on pricing

In the past, the NIH placed some conditions on product pricing. Both Taxol, a drug for cancer, and ddI, a drug for the treatment of HIV, are examples of products with such conditions.

More recently, during the COVID-19 pandemic, the US government has negotiated a number of contracts with pricing conditions, including in several cases, reference pricing clauses, such as most favored nation pricing conditions, or most favored customer clauses The Annex on Pricing Clauses in U.S. Government Contracts for COVID-19 Products illustrated that companies, including large ones, will agree to restrictions on pricing, including for products in development.

KEI has asked the NIH over a hundred times to include in its licenses a requirement that U.S. residents pay no more than the median price paid by residents in the seven countries with the largest GDP and at least 50 percent of US per capita income. The NIH has rejected every one of these requests, regardless of the stage of development of the technology.

The NIH Reasonable Pricing Clause experience

Following a controversy over the high price of the HIV drug zidovudine (AZT), President George Herbert Walker Bush (GHWB) put into practice the use of a reasonable pricing clause in NIH CRADA and patent license agreements. The first products to reach the market with the pricing clause were the unpatented cancer drug Taxol (approved by the FDA in 1992) and the HIV drug ddI (approved by the FDA in 1991).

Taxol

Taxol was an unpatented product for which the US government held the rights to all of the Phase 1, 2 and 3 clinical trials used for the FDA approval. The NIH entered into a CRADA agreement with Bristol Myers Squibb (BMS) to register the drug with the FDA and commercialize the drug. The CRADA gave BMS the exclusive rights to use the data from the NIH-funded and -conducted clinical trials for FDA approval, giving BMS what was effectively a five year monopoly. The language in the CRADA agreement with BMS was vague as regards the implementation of the obligation, but the NIH negotiated a 15-product reference pricing formula with BMS. The agreement allowed BMS to charge $4.87 a milligram for Taxol, a substantial increase over the $0.25 per milligram the NIH was paying a contractor to make the drug for clinical trials. This led to a controversy that is well documented in a Congressional hearing: US House of Representatives, Committee on Small Business, Subcommittee on Regulation, Business Opportunities, and Energy, *Exclusive Agreements between Federal Agencies and Bristol-Myers Squibb Co. for Drug Development*. Serial No. 102-35. July 29.

(https://babel.hathitrust.org/cgi/pt?id=pst.000019275802&seq=1), as well as other Congressional Hearings and GAO reports.

ddI

In addition to the shorter patent term, the NIH negotiated a reasonable pricing clause in its patent license with BMS for the HIV drug ddI, marked by BMS as Videx. BMS agreed to sell ddI at a price roughly 30 percent lower than the price that GSK was charging for AZT, a similar HIV drug.

The 1995 elimination of the NIH reasonable pricing clause

From 1991 to 1993, both Houses of Congress held hearings on the pricing of drugs developed with federal assistance, generating a number of news stories and commentary. Members of Congress also proposed additional measures to deal with high drug prices, including new concerns over the high prices for drugs for rare diseases, many of which had benefited from significant federal R&D subsidies. One supporter (at least publicly) of the reasonable pricing clause on NIH-funded drugs was Dr. Bernadine Healy, the Director of the NIH from April 9, 1991 to June 30, 1993.

From 1992 to 1994 the industry hardened its opposition to the reasonable pricing clause, and the NIH changed its policies following the election of President Bill Clinton and the appointment of Donna Shalala as Secretary of HHS in January 1993 and the appointment of Harold Varmus as NIH Director in November of 1993.

The biotech industry experienced a series of pricing swings from 1991 to 1995 which influenced the debate on the NIH reasonable pricing clause, even though the clause was rarely relevant to products approved by the FDA during that period.

In 1991, news reports about biotech share prices used terms like “soaring” or titles like “Biotech Firms' Stocks Dazzle Wall Street,”[1] By 1993 the tone had cooled, particularly for the venture market for biomedical stocks.

The NASDAQ Biotechnology (NBI) index was trading at 210 in early 1994, but fell below 145 in July. The NYSE Arca Biotechnology index (BTK) was started at 200 in October 1991 and peaked at 223.92 in January 1992, fell to 82 by 1994 and was as low as 78 in March 1995.

The declines in the biotech share prices were driven by various factors including concerns over possible Congressional imposed price controls, high profile failures of drugs in clinical trials and

[1] https://www.washingtonpost.com/archive/business/1991/04/15/biotech-firms-stocks-dazzle-wall-street/2459b873-cf27-4b58-8df7-f30fa21c029b/

court decisions in patent disputes. The NIH reasonable pricing clause became an accessible target of panicked biotech investors and drug company lobbyists.

In 1994, the NIH held two forums on the CRADA reasonable pricing clause. The first forum, held July 21, 1994, had panel members representing Pfizer, BMS, Upjohn and Eli Lilly, as well as the smaller firms Genetic Therapy Inc. and Mitotix, and Allan Fox, a lawyer for rights holders, as well as Brigham and Women's Hospital (a large recipient of NIH funding). and several government officials. At this meeting Lisa Raines, Vice President of Government Relations for Genzyme, the company created to commerize Ceredase, made a motion to eliminate the reasonable pricing clause. Ceredase was a drug developed at Tufts University on NIH grants, and at the time of the forum, it was at the time the most expensive drug in the world.

There was significant criticism of the first forum for its industry heavy representation, and the NIH was forced to hold a second forum on September 8, 1994. The published report on the CRADA forums is available here. I attended both forums, and spoke at the second. Among the arguments against the use of the reasonable pricing clause was that it had not been used effectively to benefit consumers, and was intensely disliked by investors and drug companies, so the net benefits of eliminating something that had no benefits favored its removal, an argument used today against the march-in rights clause in the Bayh-Dole Act.

In the 1994 midterm elections, the Republican Party captured unified control of Congress for the first time since 1952, elevating Representative Newt Gingrich as Speaker of the House and Senator Robert Dole as Senate President.

On April 11, 1995, the NIH published a Notice rescinding the reasonable pricing clause, including its enforcement in existing contracts. Dr. Varmus stated, “An extensive review of this matter over the past year indicated that the pricing clause has driven industry away from potentially beneficial scientific collaborations with PHS scientists without providing an offsetting benefit to the public.” I criticized the action as follows.

> James Love, an economist with the Center for Study of Responsive Law, a group founded by the consumer advocate Ralph Nader, said the decision abandoned efforts to protect consumers and taxpayers, and opened the door to high prices for pharmaceuticals developed through substantial Government investment. "Under today's actions, a drug company will be able to charge any conceivable price for any drug, no matter how small the private sector's role in the development of the drug," Mr. Love said, "and no matter how comprehensive and complete the Government's role in the drug's development."
> Warren E. Leary, U.S. Gives Up Right to Control Drug Prices, *New York Times*, April 12, 1995.

The misrepresentation of the data on NIH CRADAs

Following the elimination of the reasonable pricing clause in CRADAs, the NIH created a new type of CRADA for materials transfers. The original CRADA was then called a “Standard CRADA” and the new one a “Materials CRADA,” sometimes referred to later as a MCRADA. The new materials CRADA was initially widely used by the NIH, although over time much less so. But by combining the numbers of both the standard and the materials CRADAs, the critics of the reasonable pricing clause misleadingly claimed that the elimination of the clause led to a dramatic increase in industry engagement, and this became a standard talking point for critics of the reasonable pricing clause, particularly by the NIH OTT, AUTM members and drug companies.

Figure 1 illustrates how misleading it was to lump the numbers from the CRADAs and MCRADAs together. The average number of Standard CRADAs from 1989 to 1994 was 34. When the standard and materials CRADA numbers were added together, it appeared as if there were 87 agreements in 1996, and 153 in 1997, a huge increase. However, when standard CRADAs amounts are compared to each other, a different picture emerges. The 1996 number of standard CRADAs was 44, while the 1997 number of standard CRADAs was 32, the same or lower than four of the years when the reasonable pricing clause was in effect. By 2006, the number of standard CRADAs fell to 22, and was only 23 the following year, both amounts lower than any year when the reasonable pricing clause was in effect. From 1997 to 2010, the average number of standard CRADAs was slightly higher at 36, but only by 2, and during a period when the NIH budget per CRADA was far larger (see Table 1).

Figure 1: NIH Standard and Materials CRADAs, Reported by OTT as executive, by fiscal year

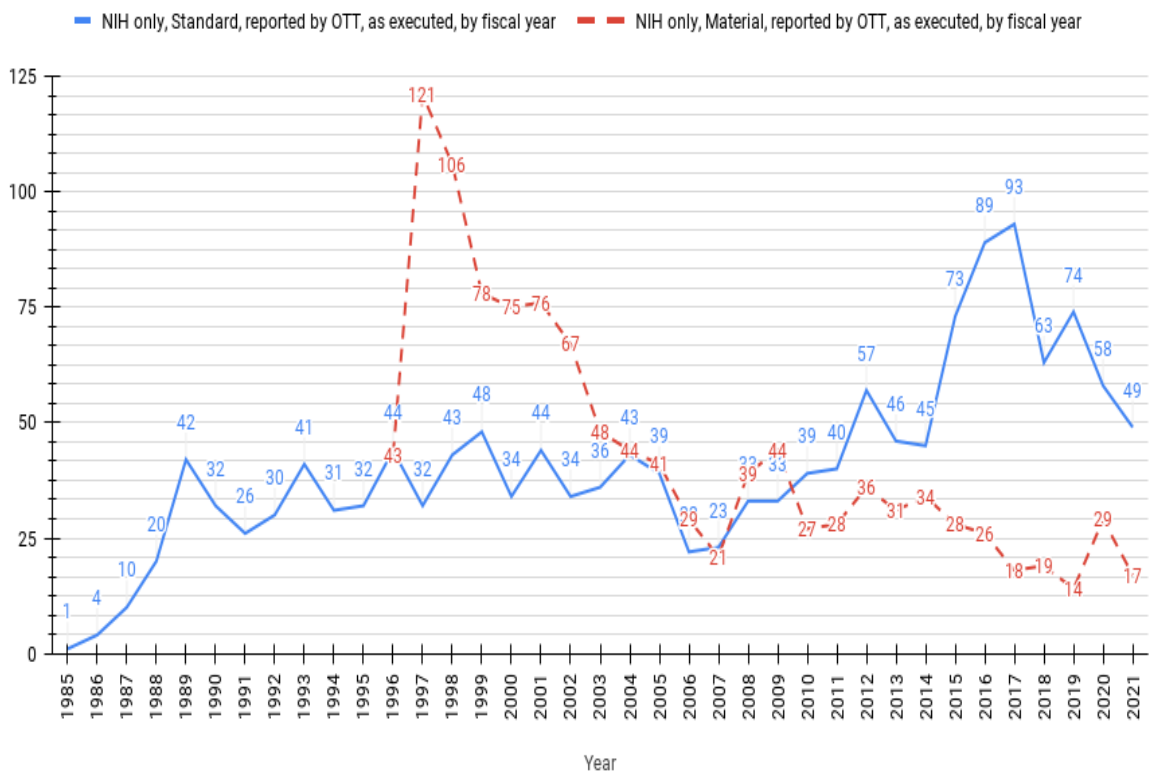


Table 1: Average number of standard CRADAS and NIH Budget per CRADA for different time periods

Period	Average number of standard CRADAs executed by fiscal year	Number of CRADAS	NIH Budget	NIH Budget / CRADA
1986 to 1988	11	34	$18,111,814,000	$532,700,412
1989 to 1994	34	202	$53,211,311,000	$263,422,332
1989 to 1995	33	234	$64,510,833,000	$275,687,321
1996 to 2002	40	279	$115,592,929,000	$414,311,573
2003 to 2009	33	229	$201,688,788,000	$880,737,066
2011 to 2020	64	638	$336,420,349,000	$527,304,622
1996 to 2010	36	547	$348,519,717,000	$637,147,563

Looking at the CRADA data over time, including the massive decline in the use of the materials CRADAs, it appears as though the number of CRADAs is driven by factors largely unrelated to the reasonable pricing clause, the national or global market for therapeutics or the NIH budget.

The data have been misused to mislead the general public and policymakers, not only by the rights holder lobby, including persons representing universities that have a putative mission to educate, but also frequently by NIH OTT officials to advance their anti-reasonable pricing agenda.

The NIH licenses of patents and data to Ridgeback for the Ebola Drug Ebanga

The NIH grants of an exclusive patent license and an exclusive license to US NIH clinical trial data for the Ebola drug Ebanga (ansuvimab-zykl, formerly referred to as mAb114) illustrates how the NIH can ignore the restrictions on exclusive license set out in § 209.

The research to develop mAb114 was carried out and supported by the NIH, BARDA, DARPA, and the clinical trials to support the registration of the drug were undertaken by the NIH in collaboration with public health authorities in Africa and MSF. According to one NIH release:

> “The National Institute of Allergy and Infectious Diseases (NIAID) Vaccine Research Center (VRC), part of NIH, developed the investigational treatment and conducted and sponsored the clinical trial. . . VRC scientists developed mAb114 in collaboration with scientists at the National Institute of Biomedical Research (INRB) in the DRC; the Institute for Research in Biomedicine and Vir Biotechnology, Inc.'s subsidiary Humabs BioMed, both based in Bellinzona, Switzerland; and the U.S. Army Medical Research

> Institute of Infectious Diseases at Fort Detrick, Maryland. The Defense Advanced Research Projects Agency funded the production of mAb114 for clinical testing." https://www.niaid.nih.gov/news-events/investigational-monoclonal-antibody-treat-ebola-safe-adults

Ridgeback Biotherapeutics, a firm headed by Wendy Holman, received two large grants from BARDA related to the drug, including Contract No. 75A50120C00009, wherein Ridgeback can be reimbursed up to $153,663,387.24 for "CMC efforts for mAB114 for the Development and Treatment of Ebola", and 75A50119C00059, wherein Ridgeback was awarded $13,988,547 for "Additional in-scope work for CMC efforts for mAB114 development for the treatment of Ebola"

The NIH initially provided a non-exclusive license to mAB144 inventions, but later would provide Ridgeback with exclusive rights to data from an NIH run clinical trial for purposes of drug registration. In September of 2020, NIAID told KEI the following regarding mAb114 clinical trial data via email:

> "NIAID filed two INDs related to mAb114 – one for the Phase 1 clinical trial of mAb114 and one for the PALM clinical trial in which the efficacy of mAb114, ZMapp, Remdesivir, and REGN-EB3 was evaluated. To enable expedited review of the BLA for mAb114 by the FDA, NIAID transferred the Phase 1 IND to Ridgeback Biotherapeutics. NIAID received no consideration for this transfer, and it was not conveyed under a license agreement. The transfer will accelerate access to this important therapeutic, enabling effective responses to ongoing Ebola outbreaks in Africa. NIAID remains the sponsor of the PALM clinical trial, and the data from this clinical trial has been shared with all of companies that supplied study products for this clinical trial."

By transferring the Phase 1 clinical data to Ridgeback, Ridgeback obtained a 12 year FDA regulatory monopoly on the test data.

The NIH could have retained the rights in the data, allowing the government to obtain generic or biosimilar versions of the drug from third parties. One consequence of the transfer of the data rights to Ridgeback is that for now, the US government now has to buy the drug from Ridgeback. Another consequence is that Ridgeback was able to claim a material threat medical countermeasure priority review voucher (PRV), as provided under section 565A of the Federal Food, Drug and Cosmetic Act (FDCA), which is currently worth about $100 million.

Ridgeback received FDA approval for Ebanga (mAb114) on December 21, 2020. But on March 15, 2021, the NIH apparently proposed making its patent license for the mAb114 inventions exclusive, despite the fact that Ridgeback had received significant funding from BARDA, had 12 years of exclusive FDA test data rights, has Orphan Drug marketing exclusivity through December 21, 2027 and received a priority review voucher worth about $100 million.

KEI's comments on the 2021 exclusive license notice is here. As usual, the NIH has not provided information to KEI on the final outcome of the proposed exclusive license.

ANNEX Pricing Clauses in U.S. Government Contracts for COVID-19 Products

In 2020 and 2021, several U.S. government contracts for the development of COVID-19 vaccines, therapeutics, diagnostic tests and other related products included provisions on pricing. Some contracts include a most favored nation pricing clause that specifically requires the company to provide the U.S. government with “a price lower” than the price offered to any centralized federal authority that is “a member of the Group of Seven plus Switzerland.” The non-US members of the G7 are Canada, France, Germany, Italy, Japan, the United Kingdom.

Table A-1, U.S. Government COVID-19 Contracts Containing Reference Price Constraints on Resultant Products

Contractor, Agency, and Contract Number	Subject	Page	Reference Price Term Excerpt
Pfizer DOD/Army W58P0522C0001 November 17, 2021	Paxlovid Purchase Agreement	33	**H.7 Most Favored Nation Clause** (a) If, at any time prior to, or during, the base term and any exercised options of this contract, Contractor enters into any agreement with a Covered Nation under which the Covered Nation commits to purchase (i) the same or a lesser volume of Product than the U.S. Government commits to purchase (ii) at a price lower than the price the U.S. Government is obligated to pay for Product under this contract, Contractor shall provide notice of such lower price to the U.S. Government within 30 days of the execution of the Contractor-Covered Nation agreement and the U.S. Government may elect, at its discretion, to receive the benefit of this provision and purchase the Product at that lower price.

ANP Technologies, Inc. DOD/Army W911QY20D0019 May 29, 2020	Development and Production of a Diagnostic	11	"MOST FAVORED CUSTOMER H.1 Most Favored Customer Awardee agrees that during the term of this contract and for a period of 5 years thereafter, that it shall not offer, sell or otherwise provide the production model of the CLIN 0001 end items (for the avoidance of doubt, CLIN 0001 end items in this clause shall mean a finished good of like material, like quality, to be used in a similar applications, and shall not include more general products to any entity at a price lower than that offered to the DoD. In the event that Awardee sells the production model at a lower unit price than that price sold to the DoD, Awardee shall immediately notify the Contracting Officer in writing of the lower price. For prior purchases, the Awardee shall reimburse the DoD, the difference between the lower price sold to the other customer(s) and the price sold to the DoD multiplied by the number of items sold. Such reimbursement shall occur within thirty days (30) of the Awardee discovering that the lower price was given to another customer. Notwithstanding the foregoing, the Parties may agree to apply the difference in price paid by the other customer(s) and DoD into additional quantities required by the DoD."
Becton, Dickson & Company DOD/Army W911SR2030001 July 1, 2020	Needle Production	17	**"9. Government Preference** 9.1 Pricing. During the term of the Agreement, the Recipient agrees that, in the event that it enters into a Group Purchasing Organization (GPO) contract with a Qualifying Third Party (as defined below) with respect to a Qualifying Product (as defined below) with a per unit GPO price lower than that offered for the same Qualifying Product to the Government, the Recipient shall (i) promptly notify the Agreements Officer in writing of the lower price and (ii) extend the lower price to all future sales of the Qualifying Product to the Government. . . . " For purposes of this section, "Covered Nation" shall mean a nation that is a member of the Group of Seven (Canada, France, Germany, Italy, Japan, the United Kingdom, and the United States) plus Switzerland.
Eli LIlly, DOD/Army W911QY21D0012 P0002 April 7, 2021	Monoclonal Antibody Treatment Production	7-8	**"H. 7 Sales to Covered Nations** (i) Due to the exceptional and unprecedented nature of the COVID-19 threat to global public health, as well as the investments made towards the development of a safe and effective therapeutic against COVID-19, Lilly agrees that it will not at any time prior to 30 September 2021 sell any COVID-19 bamlanivimab/etesevimab combination therapeutic supplied directly to the Government under this Agreement to any centralized federal authority (i.e., federal government or equivalent) of a nation that is a member of the Group of Seven plus Switzerland ('Covered Nation') at a lower price than the prices set forth in this contract. . . . "

Eli Lilly DOD/Army W911QY21C0016 October 26, 2020	Monoclonal Antibody Treatment Production	18	"**H.7 Sales to Covered Nations** (i) Due to the exceptional and unprecedented nature of the COVID-19 threat to global public health, as well as the investments made towards the development of a safe and effective therapeutic against COVID-19, Lilly agrees that it will not at any time prior to 30 June 2021 sell any COVID-19 therapeutic supplied directly to the Government under this Agreement to any centralized federal authority (i.e., federal government or equivalent) of a nation that is a member of the Group of Seven plus Switzerland ('Covered Nation') at a lower price than the prices set forth in this contract. . . ."
Emergent BioSolutions Canada Inc. DOD/Army W911QY2090013 June 24, 2020	"the research and development of an advanced human immune globulin manufactured from human plasma with antibodies to SARS-CoV-2 (COVID-HIG) for post-exposure prophylaxis (PEP) of Coronavirus Disease (COVID-190"	16	"**ARTICLE 9. Most Favored Customer** A. Awardee agrees that it shall not offer, sell, or otherwise provide the production model of the Prototype to any entity at a price lower than it offered to the DoD. In the event that Awardee sells the production model of the Prototype at a lower unit price than that price sold to the DoD, Awardee shall reimburse the DoD, the difference between the lower price sold to the other customer (S) and the price sold to the DoD multiplied by the number of items sold . . . ."
Immunome Inc DOD/Army W911QY2090019 July 3, 2020	"research and development of a standardizable and scalable [redacted] compromise of [redacted] antibodies . . . ."	16	"**ARTICLE 9. Most Favored Customer** A. Awardee agrees that it shall not offer, sell or otherwise provide the production model of the Prototype to any entity at a lower price than that offered to the DoD. In the event that Awardee sells the production model of the Prototype at a lower unit price than that price sold to the DoD, Awardee shall immediately notify the OTAO in writing of the lower price. . . ."
Inovio Pharmaceuticals, Inc. DOD/Army W911QY2090016 June 22, 2020	"the development of an FDA approved next generation electroporation device and array for DNA Vaccine delivery of INO-4800 against COVID-19, with demonstrated capability to be produced at a large scale, as well as full automation for production of the device arrays, (hereinafter referred to as the 'Prototype Project')."	17	"**ARTICLE 9. Most Favored Customer** A. For a period of six (6) years from the Effective Date, Awardee agrees that it shall not offer, sell or otherwise provide the production model of the Prototype to any entity at a price lower than that offered to the DoD. In the event that Awardee sells the production model of the Prototype at a lower unit price than that price sold to the DoD, Awardee shall immediately notify the OTAO in writing of the lower price. . . ."

Maxim Biomedical, Inc. DOD/Army W911QY20D0018 May 11, 2020	Diagnostic Production	10	"H.1 Most Favored Customer A. Awardee agrees that during the term of this contract and for a period of 5 years thereafter, that it shall not offer, sell or otherwise provide the production model of the CLIN 0001 end items (for the avoidance of doubt, CLIN 0001 end items in this clause shall mean a finished good of like material, like quality, to be used in a similar applications, and shall not include more general products to any entity at a price lower than that offered to the DoD. In the event that Awardee sells the production model at a lower unit price than that price sold to the DoD, Awardee shall immediately notify the Contracting Officer in writing of the lower price. . . ."
Murtech, Inc. DOD/Army W911QY20D0017 May 11, 2020	Diagnostic Production	15	"H.1 Most Favored Customer A. Awardee agrees that during the term of this contract and for a period of 2 years thereafter, it shall not offer, sell or otherwise provide the production model of the CLIN 0001 end items (herein the 'Items') (for the avoidance of doubt, CLIN 0001 production model end items in this clause shall mean a finished good of like material, like quality, to be used in a similar applications, and shall not include more general products) to any entity at a price lower than that offered to the DoD."
Novavax DOD/Army W911QY20C0077 P0002 June 4, 2020	"Vaccine Development and Production"	4	"The Contractor shall maintain a most favored customer provision for the product once authorized or licensed by the FDA, such that the Contractor shall not give any entity a better price than the DoD for a period of five (5) years from the award of this contract, limited to customers in the U.S. and purchases made in the U.S to include sale prices as compared to commercial clients with respect to quantity, location of delivery, fundamental differences in deliverable formulation, and material differences in terms and conditions for commercial contracts."
Sanofi DOD/Army W15QKN1691002; MCDC2011-005 July 30, 2020	Vaccine Research and Development (including Clinical Trials) and Production	28	"**5.1 Most Favored Nation Clause** (i) Due to the exceptional and unprecedented nature of the COVID-19 threat to global public health and in recognition of the long historical partnership between the U.S. Government and Sanofi Pasteur working on global pandemic solutions, as well as the investments made towards the development of a safe and effective vaccine against COVID-19, Sanofi Pasteur agrees that it will not sell any COVID-19 vaccine licensed under this Agreement to any nation that is a member of the Group of Seven plus Switzerland ('Covered Nation') at a price that is more favorable than those set forth in this Project Agreement."
SIO2 Medical Products, Inc. DOD/Army W911NF2030003 June 5, 2020	Vaccine Delivery Device Research and Development	13	"**9. Government Preference** 9.1 Pricing. During the period of performance and the exercised optional availability periods, the Recipient agrees that, in the event that it offers, sells or otherwise provides a Qualifying Product (as defined below) to any Qualifying Third Party (as defined below) at a per unit price lower than that offered for the same Qualifying Product to the Government or a third party purchasing Qualifying Product pursuant to a designation by the Government pursuant to Section 9.2 or 9.3 (an 'MCM Partner'), the Recipient shall (i) promptly notify the Agreements Officer in writing of the lower price and (ii) extend the lower price to all future sales of the Qualifying Product to the Government or an MCM Partner."

Merck Sharp & Dohme Contract DOD/Army W911QY21C0031 June 7, 2021	COVID 19 Therapeutic	21	H.7. Fully redacted including the title
Rigel Pharmaceuticals DOD/Army W911QY-21-9-0018 January 29, 2021	COVID-19 Therapeutic	29	"**Article 20. Most Favored Customer.** A. In the event that the Parties agree to a follow-on production agreement pursuant to 10 U.S.C. 2371b Awardee agrees that it shall sell to the U.S. Government up to [redacted] treatment courses of TAVALISSE at a price not greater than [redacted]. Any additional treatment course will be sold to the U.S. Government at a price to be negotiated and agreed by the Parties. B. If Awardee develops a like product (commercialized version or derivative of the production model of the Prototype) with similar capability and intended application, but at a lower unit price ("Like Product") regardless of quantity, Awardee shall make the DoD aware of that similar product and the technical and price differences between that product and the Prototype. Such notification shall be made to the °TAO in writing, of which email is an acceptable form, within thirty (30) days of such offering."

ANNEX: examples of NIH redactions regarding research collaboration agreement with Ridgeback

RESEARCH COLLABORATION AGREEMENT

This Agreement is between the **National Institute of Allergy and Infectious Diseases** ("NIAID"), which is a component of the National Institutes of Health ("NIH"), an agency of the U.S. Department of Health and Human Services, having offices located at 5601 Fishers Lane, Rockville, MD 20852, and **Ridgeback Biotherapeutics** ("Ridgeback") ("Collaborator"), having a principal place of business at (b) (6) (collectively, the "Parties"). This Agreement is neither a funding agreement as defined in 35 U.S.C. § 201(b) nor a cooperative research and development agreement authorized under the Federal Technology Transfer Act of 1986, as amended, 15 U.S.C. §§ 3710a *et seq.*, and Executive Order 12591 of April 10, 1987. NIAID enters into this Agreement pursuant to the authority of the Public Health Services Act of 1944, as amended (42 U.S.C. § 241).

BACKGROUND

1. (b) (4)
2.
2. NIAID and Collaborator want to transfer between the laboratories of their investigators, during the term of this Agreement, proprietary research materials (b) (4) required to conduct the research project (b) (4)

APPENDIX A

Research Project

I. **Abstract of the Research Project – for Public Release**
EITHER PARTY MAY, WITHOUT FURTHER CONSULTATION OR PERMISSION, RELEASE THIS ABSTRACT TO THE PUBLIC.

Ridgeback Biotherapeutics and the Vaccine Research Center (VRC), National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH) will collaborate to advance development of monoclonal antibodies against Ebola virus toward licensure for therapeutic and prophylactic use in control of outbreaks and prevention of epidemics.

II. **Goal(s) of Project**

(b) (4)

IV. Respective Contributions of the Parties

Ridgeback

(b) (4)

VRC/NIAID

(b) (4)

V. Material Contributed by VRC/NIAID

(b) (4)

VI. Material Contributed by Collaborator

(b) (4)

Submission Date: 8/18/2023

Name: Charles Sauer

Name of Organization: Market Institute

Comment:

More innovation is fairly easy – create the right incentives

For good or bad – people, businesses, investors, and society react to incentives. Incentives help drive entrepreneurs to take risks, investors to put their money behind an idea, and inventors to develop new things. The US patent system is what has provided that incentive to US innovators, and with strong patents as the reward what has driven our economy forward – since our founding.

However, often when we talk about innovation – inventors end up being considered the villians. When they make money from something that we need. When they profit from something that makes our lives' better. But, we are often only looking at the winners. The ones that took the risk – and succeeded. Many inventors never develop the next life saving vaccine, quality of life changing technology, or even a best selling toy. It takes lots of different innovations to get the few that end up changing our world. And, most of the time – these innovations are funding by the individuals. They take on this risk because we have a strong patent – maybe not as strong as it once was, but we have a good patent system. That is the incentive that is needed.

Incentives work, for instance, when training a puppy – you give them treats when they do something that is good. Eventually, that puppy starts doing the things that you like more often. People and businesses are not that different. If you want them to do something you give them a reward – and eventually you start getting more of that thing. In the case of innovation – their "treat" is a property right.

A property right for inventions – a right that is limited in time and only granted with disclosure – gives innovators the knowledge that if they risk their resources and develop the next big thing, then they can defend their right and profit from their idea.

At the recent workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer – many of the ideas discussed and some of the comments submitted would lessen the value of this incentive. Not allowing exclusive licenses weakens the incentives, adding a pricing caveat to March-In would weaken the incentive, referenced based prices would weaken the incentive, and adding more control would weaken the incentive. These ideas would weaken the incentive to innovate and therefore lessen the amount of innovation. These ideas wouldn't catalyze technology transfer – they would neutralize technology transfer.

So, if the NIH is asking to speed more innovation in order to spur competition, then the answer is simple – give the inventors, the investors, the businesses even more rights. Make technology transfer easier, give the developers more rights, and focus on the things that bring more people to the table instead of less.

Unlike a puppy that has a warm bed and cozy blanket at night– entrepreneurs have to take risks and aren't guaranteed a soft landing at any point in the process. They depend on knowing that their innovations won't be stripped from them.

In order to catalyze innovation and technology transfer – give the inventors some treats instead of the stick.

Charles Sauer

President

Market Institute

--
Charles Sauer
President
Market Institute

Additional Comment (attachment): None

Submission Date: 8/19/2023

Name: Jennifer Burke

Name of Organization: Partnership to Fight Chronic Disease

Comment:

Dear Director Jorgenson:

On behalf of the Partnership to Fight Chronic Disease (PFCD), we appreciate the opportunity to submit comments to the NIH in response to the topics covered in the workshop titled *"Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer."* PFCD is a national coalition of patients, providers, community organizations, business and labor groups, and health policy experts committed to raising awareness of the number one cause of death, disability, and rising health care costs: chronic disease.

PFCD is deeply concerned about the ongoing push to misuse the Bayh-Dole Act as a policy backdoor towards sweeping drug price controls that will hinder innovation, especially in addressing chronic diseases. We urge the NIH to uphold more than two decades of precedent by once again rejecting calls to twist Bayh-Dole into a price control mechanism.

Four decades ago, a bipartisan group of lawmakers realized that federally-funded research with commercialization potential was languishing on laboratory shelves. In fact, less than 5% of more than 28,000 inventions under the federal government's ownership ever reached the market -- a significant waste of R&D funding and potential breakthroughs.

To alleviate this problem, Congress passed the Bayh-Dole Act in 1980. This legislation decentralized IP management of federally-funded research and innovation to universities and other nonprofits that received research grants. The rationale was thattech transfer professionals would be more adept at recognizingpotentially-valuable innovations.

This straightforward solution sparked a surge of innovation across the United States, as universities began licensing promising research to private entities equipped with the resources and expertise to bring life-changing products to market.

Today, technology transfer under the Bayh-Dole Act sustainsover 6.5 million American jobs and contributes a trillion dollars to our GDP. This

framework efficiently channels the efforts of university researchers, entrepreneurs, and investors towards promising new technologies with the potential to benefit patients and drive our innovation economy. As a result, more than 200 lifesaving drugs and vaccines have reached the market.

Yet, for the past two decades, activists have targeted the Bayh-Dole Act as a potential lever to enact harmful price controls on any drug that receives federal funding in its earliest stage of research and development. They claim that so-called "march-in" rights include price as a criterion for agencies like the NIH to unilaterally relicense IP.

The NIH has routinely rejected this call for backdoor price controls, most recently in March 2023. While the Bayh-Dole Act includes four specific criteria for IP relicensing, price is not mentioned once, and the authors of the law have explicitly stated that the law was never intended to permit price controls.

In addition, during the July 31 workshop -- and in broader contexts -- march-in advocates began calling for NIH to revive the "reasonable pricing clause" in its Cooperative Research and Development Agreements (CRADAs) and other collaboration, funding, and licensing agreements. However, there is instructive precedent that the NIH must take into account when evaluating this request.

Back in the early 1990s, the NIH instituted a reasonable pricerequirement on drugs that stemmed from early-stage research conducted with federal laboratories and private partners. This requirement resulted in industry partners walking away from CRADA-controlled research without any "offsetting benefit" to be found in cheaper drugs. In 1995, then-NIH Director Harold Varmus rescinded the policy, stating:

> "An extensive review of this matter over the past year indicated that the pricing clause has driven industry away from potentially beneficial scientific collaborations with [federal laboratories] without providing an offsetting benefit to the public. Eliminating the clause will promote research that can enhance the health of the American people."

There is no evidence to suggest that the same decline in research partnerships could be avoided in this revived proposal. NIH should resist calls to repeat the mistakes of the past and focus on conducting and funding the research that patients -- including those with chronic diseases -- count on to provide new treatments and cures.

NIH is facing significant pressure to sacrifice innovation and investment in favor of short-term wins for price controls. However, NIH must not forget its core mission to seek "the application of…knowledge to enhance health, lengthen life, and reduce illness and disability." PFCD urges the agency to reject calls to misuse Bayh-Dole and NIH policies for ill-advised and undefined price restrictions that subvert legislative intent and hamper innovation.

PFCD appreciates the opportunity to provide comments to NIH for the purpose of strengthening our nation's technology transfer ecosystem. We stand ready to assist and answer any questions.

Sincerely,
Ken Thorpe on behalf of the Partnership to Fight Chronic Disease (PFCD)

***

Jennifer Burke
Communications Director
Partnership to Fight Chronic Disease
www.fightchronicdisease.org
@pfcd

Additional Comment (attachment):

August [XX], 2023

Lyric Jorgenson, Ph.D.
Acting Associate Director for Science Policy
National Institutes of Health Office of Science Policy
6705 Rockledge Dr #750
Bethesda, MD 20817

Dear Director Jorgenson:

On behalf of the Partnership to Fight Chronic Disease (PFCD), we appreciate the opportunity to submit comments to the NIH in response to the topics covered in the workshop titled *"Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer."*[12] PFCD is a national coalition of patients, providers, community organizations, business and labor groups, and health policy experts committed to raising awareness of the number one cause of death, disability, and rising health care costs: chronic disease.[13]

PFCD is deeply concerned about the ongoing push to misuse the Bayh-Dole Act as a policy backdoor towards sweeping drug price controls that will hinder innovation, especially in addressing chronic diseases. We urge the NIH to uphold more than two decades of precedent by once again rejecting calls to twist Bayh-Dole into a price control mechanism.

Four decades ago, a bipartisan group of lawmakers realized that federally-funded research with commercialization potential was languishing on laboratory shelves. In fact, less than 5% of more than 28,000 inventions under the federal government's ownership ever reached the market -- a significant waste of R&D funding and potential breakthroughs.[14]

To alleviate this problem, Congress passed the Bayh-Dole Act in 1980.[15] This legislation decentralized IP management of federally-funded research and innovation to universities and other nonprofits that received research grants. The rationale was that tech transfer professionals would be more adept at recognizing potentially-valuable innovations.[16]

This straightforward solution sparked a surge of innovation across the United States, as universities began licensing promising research to private entities equipped with the resources and expertise to bring life-changing products to market.

---

[12] https://osp.od.nih.gov/nih-to-host-workshop-on-transforming-discoveries-into-products-maximizing-nihs-levers-to-catalyze-technology-transfer/
[13] https://www.fightchronicdisease.org/public-policy-platform
[14] https://www.gao.gov/assets/rced-98-126.pdf pg 4
[15] https://drexel.edu/research/innovation/technology-commercialization/bayh-dole-act/#:~:text=The%20Bayh%2DDole%20Act%2C%20formerly,research%20programs%20within%20their%20organizations.
[16] https://www.law.cornell.edu/uscode/text/35/part-II/chapter-18

Today, technology transfer under the Bayh-Dole Act sustains over 6.5 million American jobs and contributes a trillion dollars to our GDP.[17] This framework efficiently channels the efforts of university researchers, entrepreneurs, and investors towards promising new technologies with the potential to benefit patients and drive our innovation economy. As a result, more than 200 lifesaving drugs and vaccines have reached the market.[18]

Yet, for the past two decades, activists have targeted the Bayh-Dole Act as a potential lever to enact harmful price controls on any drug that receives federal funding in its earliest stage of research and development.[19] They claim that so-called "march-in" rights include price as a criterion for agencies like the NIH to unilaterally relicense IP.[20]

The NIH has routinely rejected this call for backdoor price controls, most recently in March 2023.[21] [22] [23] While the Bayh-Dole Act includes four specific criteria for IP relicensing, price is not mentioned once, and the authors of the law have explicitly stated that the law was never intended to permit price controls. [24] [25]

In addition, during the July 31 workshop -- and in broader contexts -- march-in advocates began calling for NIH to revive the "reasonable pricing clause" in its Cooperative Research and Development Agreements (CRADAs) and other collaboration, funding, and licensing agreements.[26] [27] However, there is instructive precedent that the NIH must take into account when evaluating this request.

Back in the early 1990s, the NIH instituted a reasonable price requirement on drugs that stemmed from early-stage research conducted with federal laboratories and private partners.[28] This requirement resulted in industry partners walking away from CRADA-controlled research without any "offsetting benefit" to be found in cheaper drugs.[29] In 1995, then-NIH Director Harold Varmus rescinded the policy, stating:

> "An extensive review of this matter over the past year indicated that the pricing clause has driven industry away from potentially beneficial scientific collaborations with

---

[17] https://autm.net/AUTM/media/Surveys-Tools/Documents/AUTM-Infographic-22-for-uploading.pdf
[18] https://autm.net/AUTM/media/Surveys-Tools/Documents/AUTM-Infographic-22-for-uploading.pdf
[19]https://www.researchgate.net/publication/228173125_Why_Don't_We_Enforce_Existing_Drug_Price_Controls_The_Unrecognized_and_Unenforced_Reasonable_Pricing_Requirements_Imposed_Upon_Patents_Deriving_in_Whole_or_in_Part_From_Federally-Funded_Research
[20] https://www.washingtonpost.com/politics/2021/09/08/claim-that-us-government-already-has-power-lower-drug-prices/
[21] https://www.keionline.org/bayh-dole/bayh-dole-timeline
[22] https://www.washingtonpost.com/politics/2021/09/08/claim-that-us-government-already-has-power-lower-drug-prices/
[23] https://bayhdolecoalition.org/bayh-dole-coalition-statement-on-nih-rejection-of-xtandi-march-in-petition/
[24] https://www.law.cornell.edu/uscode/text/35/part-II/chapter-18
[25] https://www.washingtonpost.com/archive/opinions/2002/04/11/our-law-helps-patients-get-new-drugs-sooner/d814d22a-6e63-4f06-8da3-d9698552fa24/
[26] https://www.statnews.com/pharmalot/2023/06/13/sanders-biden-nih-drugs-medicine/
[27] https://www.sanders.senate.gov/in-the-news/sanders-vows-to-oppose-nih-nominee-until-biden-produces-drug-pricing-plan/
[28] https://bayhdolecoalition.org/wp-content/uploads/2023/06/CRADA-QA-Nov-2021-FINAL.pdf pg 4
[29] https://bayhdolecoalition.org/wp-content/uploads/2023/06/CRADA-QA-Nov-2021-FINAL.pdf pg 4

> [federal laboratories] without providing an offsetting benefit to the public. Eliminating the clause will promote research that can enhance the health of the American people."[30]

There is no evidence to suggest that the same decline in research partnerships could be avoided in this revived proposal. NIH should resist calls to repeat the mistakes of the past and focus on conducting and funding the research that patients -- including those with chronic diseases -- count on to provide new treatments and cures.

NIH is facing significant pressure to sacrifice innovation and investment in favor of short-term wins for price controls. However, NIH must not forget its core mission to seek "the application of…knowledge to enhance health, lengthen life, and reduce illness and disability."[31] PFCD urges the agency to reject calls to misuse Bayh-Dole and NIH policies for ill-advised and undefined price restrictions that subvert legislative intent and hamper innovation.

PFCD appreciates the opportunity to provide comments to NIH for the purpose of strengthening our nation's technology transfer ecosystem. We stand ready to assist and answer any questions.

Sincerely,

/s/

Partnership to Fight Chronic Disease

[30] https://www.techtransfer.nih.gov/sites/default/files/documents/pdfs/NIH-Notice-Rescinding-Reasonable-Pricing-Clause.pdf
[31] https://www.nih.gov/about-nih/what-we-do/nih-almanac/about-nih#:~:text=NIH%20is%20the%20steward%20of,and%20reduce%20illness%20and%20disability.