Commercialization of NIH-supported research

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Commercialization of NIH-supported research is incentivized both through allowing resulting inventions to be patented and licensed, and through direct funding for development efforts. Unfortunately, it's unclear whether the NIH currently invests "too little" in closing the gap between research advances and clinical applications, or "too much" in providing an unnecessary giveaway to the biopharmaceutical industry—much less which specific projects would or wouldn't benefit from additional commercialization incentives, or which policy mechanisms are most effective. Although past reform proposals have focused on patenting and licensing policies for NIH-funded inventions, the political and empirical challenges to improving these policies are daunting.

Instead, the NIH may have greater social impact through reforms to its direct funding of commercialization. First, the agency should design rigorous policy experiments to assess the impact of these programs for different kinds of inventions, such as whether some investments merely "crowd out" private-sector efforts. Second, Congress should increase NIH funding for late-stage biomedical development, following on the success of public-sector involvement in COVID-19 vaccine and drug development, with the goal of better aligning development efforts with social value rather than just market incentives.

1. What concerns exist with commercialization of NIH research?

The NIH is the world's largest funder of biomedical research, with a total budget around $45 billion (NIH, 2022a).[2] Over half of NIH funding is for basic science that is less likely to be funded by the private sector, such as understanding the biological mechanisms of disease. And commercialized products often build on NIH-funded advances; for example, one study found that NIH funding contributed to every one of the 210 new drugs approved by the FDA from 2010 to 2016, with 90% of this funding representing basic research (Cleary et al., 2018).

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[2] Over 84% of the NIH's budget supports extramural research, mostly by researchers at universities, hospitals, and independent research institutes; additionally, over 10% of the budget supports intramural research at NIH labs (NIH, 2022a).

The case for public R&D funding is well established (e.g., Lucking et al., 2020), but it is less clear what role the government should play in translating public research to more applied clinical settings. Some observers are concerned that there is too little commercialization of NIH-funded research, with many discoveries lingering in the "valley of death" between the lab and clinical applications (e.g., Seyhan, 2019). Closing this gap was the motivation for introducing patent and direct funding for commercialization, such as under the Bayh-Dole Act of 1980.[3] On the other hand, others are concerned that the government provides too much support for commercialization, allowing private firms to receive unnecessary profits from projects that have been "de-risked" with public funding. And both concerns can be true in different contexts—some inventions may have more-than-sufficient private-sector incentives for commercialization, while others remain underdeveloped.

2. What are the challenges with patent reform?

Past lobbying efforts for reform of NIH commercialization policy have primarily focused on restricting patents and their resulting pricing power out of a concern that patents often provide too much incentive for commercialization, imposing an unnecessary tax on consumers of patented products and on the firms that want to build on patented inventions. In response to these concerns, the NIH has taken limited steps to restrict patenting, but has generally declined to heavily police grantees' patenting choices.[4]

Unfortunately, it's unclear whether patents tend to help or hinder commercialization of publicly funded research. Perhaps surprisingly, innovation economists have not been able to determine whether patents *in general* have a net positive or negative effect on research investments (Ouellette and Williams, 2020), much less what their effect is for development of public research (Ouellette and Weires, 2019).

The NIH could take some steps to improve the evidence base for patent policy, including through better enforcement of reporting requirements on utilization of NIH-funded patents. The NIH could also use its control over what projects get funded to encourage grant recipients to provide evidence of what benefit patents on particular inventions might serve (Ayres and Ouellette, 2017). But given the political and empirical hurdles to any substantial reforms to the Bayh-Dole and Stevenson-Wydler frameworks, the NIH may have more social impact through reforms to commercialization efforts beyond patenting.

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[3] Currently, extramural grant recipients can patent inventions under the Bayh-Dole Act of 1980, and intramural inventions can be patented by the NIH under the similar Stevenson-Wydler Act of 1980.

[4] For example, the NIH abandoned its 1989-95 effort to put a "fair pricing" clause in its standard Cooperative Research and Development Agreements (CRADAs) with private firms because drug companies refused to sign the new CRADAs but kept collaborating with NIH scientists, complicating the resulting IP ownership (Contreras, 2020). The NIH has also rarely exercised its authority to restrict patenting where this would "better promote the policy and objectives" of Bayh-Dole, instead issuing nonbinding guidance to discourage patents in certain areas such as DNA segments and research tools (Rai and Eisenberg, 2003). Additionally, the NIH has declined every request to exercise "march-in" rights by granting additional licenses to Bayh-Dole patents (NIH, 2022b), although it has used the threat of march-in to encourage firms to voluntarily reduce prices (KEI, 2019).

3. How does the NIH directly fund commercialization?

Most of the NIH's 27 Institutes and Centers provide extramural funding for translational research and early-stage clinical trials (NIH, 2022c). The NIH also funds clinical trials through its intramural programs, often in coordination with the NIH Clinical Center (NIH, 2022d). The National Center for Advancing Translational Science (NCATS) was established in 2011 to address more systemic commercialization bottlenecks (Collins, 2011). And the Advanced Research Projects Agency for Health (ARPA-H) was created in 2022 to support "use-driven" research aimed at practical problems (NIH, 2022e).

In addition, the NIH directly funds commercialization efforts by private firms, primarily through the 1982 Small Business Innovation Research (SBIR) program and the 1992 Small Business Technology Transfer (STTR) program. By statute, federal grantmaking agencies are mandated to set aside not less than 3.2% of their extramural R&D budgets for SBIR and 0.45% for STTR, with coordination by the Small Business Administration (SBA).[5] SBIR/STTR programs are administered by 24 of the NIH Institutes and Centers, providing over $1.2 billion in annual funding (NIH, 2022f). Originally, agencies could only use SBIR funds for awards and technical assistance to small businesses, but since the 2011 SBIR and STTR Reauthorization Act, agencies may use up to 3% of their SBIR budgets on administrative costs, including quality control (SBA, 2020; SBA, 2012).

4. How could direct commercialization funding be improved?

Improving evidence about NIH commercialization funding through randomized policy experiments

Assessing the impact of NIH funding is challenging because researchers can't observe what would have happened in the absence of funding. If the NIH hadn't funded a clinical trial, would it have been funded by someone else, or not at all? Researchers can't just compare projects that were and weren't funded because NIH funding isn't distributed randomly—grant recipients are also likely to be "better" in other ways that are difficult to control for. But researchers have made progress in identifying plausible "counterfactual" scenarios, such as looking at firms that happen to fall on either side of an NIH funding cutoff.

For example, Azoulay et al. (2019) show that general NIH funding—not commercialization-focused funding—isn't merely "crowding out" private investment. Rather, each $10 million increase in NIH funding leads to 2.7 additional private-sector patents. Using funding cutoffs for SBIR grants from the Department of Energy (DOE)—not NIH—Howell (2017) concludes that receiving a grant doubled the probability that a firm would receive VC funding and positively impacted firm revenue and patenting. Myers and Lanahan (2022) also find that DOE SBIR grants had substantial spillovers for other firms.

[5] The SBIR requirement applies to agencies with R&D budgets over $100 million, and the STTR requirement applies to agencies with R&D budgets over $1 billion.

There is relatively little evidence, however, directly focused on NIH commercialization efforts. When a National Academies committee tasked with assessing the NIH SBIR/STTR programs requested review score information to conduct a similar analysis to Howell (2017), NIH would not provide this information (National Academies, 2022). But using a coarser measure, the National Academies (2022) found that after controlling for a firm's growth potential, "there was no statistically significant difference in outcomes [such as publications, patents, and clinical trials] between those firms that received an SBIR/STTR award on their first application and those that applied to the programs but were rejected during that application cycle." This result raises important questions about whether the SBIR/STTR mandate is actually effective at NIH, and whether Congress should provide the NIH with more flexibility in how to encourage private-sector commercialization.

For the same reason that the NIH funds randomized controlled trials (RCTs) to provide the best evidence of a medical intervention's clinical efficacy, the agency should consider RCTs to assess the efficacy of its policy interventions, as many scholars have suggested (e.g., Azoulay and Li, 2020; Watney and Williams, 2022). For example, to provide a better estimate of the impact of commercialization-focused funding, the NIH could randomize funding among all firms above a baseline quality threshold. Experimentation could also determine whether the separate NCATS and ARPA-H models are more effective commercialization funding models than centers within disease-focused institutes.

Importantly, randomization need not be at the level of funding decisions. Although randomizing funding would provide the clearest evidence of a program's impact, such an experiment may also be politically challenging to implement. Heard et al. (2017) describe a number of alternative experimental designs to accommodate real-world challenges in designing and implementing RCTs. For instance, the NIH could use a "randomized encouragement design" approach, in which potential grant applicants are randomly assigned to an opportunity or encouragement to apply for some funding opportunity.

Addressing market failures in biomedical commercialization

Private-sector firms commercialize products based on their expected market return, and thus underinvest in products with market failures—such as innovations that take a long time to commercialize, that generate positive externalities, that prevent rather than treat disease, or that are difficult to patent (Hemel and Ouellette, 2023a). Public funding can reduce this problem; for example, Budish, Roin, and Williams (2015) show that publicly funded clinical trials for cancer drugs are less distorted away from drugs with long commercialization lags.

Addressing these types of market failures should be a more explicit goal of existing NIH efforts to directly fund commercialization. In particular, when evaluating funding options for translational research and early-stage clinical trials, the NIH should prioritize projects that have high expected social value but that are unlikely to receive funding from private-sector sources. As just one example, research on biomarkers—medical indicators that can be used to shorten the length and cost of clinical trials—is difficult to patent and can have substantial benefits for other firms, and is thus likely to be underfunded by the private sector. Increasing NIH funding for both biomarker discovery and validating existing biomarkers would thus be worthwhile. Additional

research on pharmaceutical synthesis and manufacturing techniques could be similarly fruitful (Hemel and Ouellette, 2023b; National Academies, 2021).

Congress should also use the COVID-19 experience as an opportunity to dramatically rethink the role of the public sector in commercializing drugs and other medical products. A number of scholars have suggested that the public sector should be more directly involved in late-stage biomedical commercialization (e.g., Sampat, 2020; Hemel and Ouellette, 2019). The federal government not only could focus on social value rather than commercial value, but also may have a comparative advantage at navigating the federal regulations needed to bring a new product to market.

One option would be increased extramural funding for late-stage development. For example, Watney and Williams (2022) suggest a new $20 billion “biomedical innovation fund” housed within ARPA-H and given authority to use a range of policy tools, including large innovation prizes for high-value, low-profit drugs and patent buyouts to allow generic production of key medicines. Even more ambitiously, the federal government could manufacture some drugs itself, such as under the proposed Affordable Drug Manufacturing Act that was introduced in 2018 and 2020 (Hemel and Ouellette, 2023b).

To be sure, greater public-sector involvement in biomedical innovation would not be without challenges. Asking the NIH to more explicitly assess the social value of potential projects in addition to their scientific merit places a substantial informational burden on the agency, and it raises the risks of gaming and mismanagement (Hemel and Ouellette, 2023a). But the status-quo approach has its own challenges, and the payoff for society from facilitating development of lifesaving drugs that are neglected by the private sector would be well worth the costs.

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