

THE BIOPHARMACEUTICAL

RESEARCH ECOSYSTEM

— FIVE THINGS YOU NEED TO KNOW

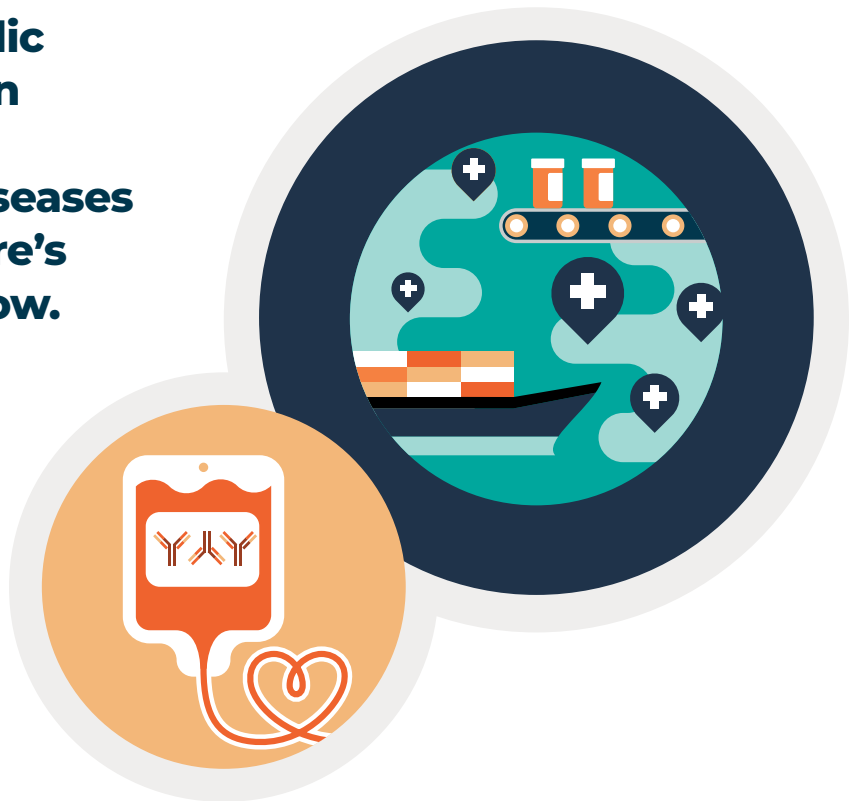
Five Things You Need to Know About the Biopharmaceutical Research Ecosystem During COVID-19



The American biopharmaceutical research ecosystem develops more innovative medicines than any other country in the world. Some critics have claimed that this success is because the National Institutes of Health (NIH) use public funds to discover new therapies which are then handed off to biopharmaceutical companies

to be manufactured, packaged and monetized. This misunderstanding of the way drug development actually works has led to policy proposals that could seriously harm the U.S. biopharmaceutical research ecosystem and jeopardize its longstanding success.

Now more than ever, it is critical that both public and private assets can be brought to bear in addressing critical diseases such as COVID-19. Here's what you need to know.



#1: Basic science research is conducted by both the public and private sectors and lays the foundation of our understanding of how the human body functions.



“Basic science research” – often called fundamental or bench research – typically focuses on understanding the functioning of the human body, both in health and in illness. It is performed to further scientific knowledge without an obvious or immediate benefit. The goal of basic science research is to understand the function of newly discovered molecular compounds and cells, strange phenomena in the body or little-understood disease processes. Many times, this new knowledge requires additional contributions from other scientists before it can lead to breakthrough methods or treatments years or decades later. For example, in 1945 two groups of physicists reported the detection of nuclear magnetic resonance (NMR) in condensed matter.ⁱ When it was developed, it had no obvious applications in medicine; however, multiple other researchers discovered other properties of NMR and in the 1970s scientists realized that the NMR machine could be hooked up to a computer

to make a magnetic resonance imaging (MRI) machine.ⁱⁱ The MRI is now a staple of medical diagnostics.

Every day, research conducted by scientists in the public and private sectors provides knowledge that leads to important advances in medicine. Consider the discovery of DNA (which has led to targeted therapies including cancer treatments) and neurotransmitters (leading to antidepressants and antiseizure medications). However, there are many other instances where basic science research has not yet resulted in any practical benefit to humans or animals. Academic, government and private industry scientists all contribute to the vast body of discoveries that result from basic science research, and that knowledge is shared and expanded upon by scientists through peer-reviewed publications, scientific meetings and licensing of intellectual property.

“Partnerships between labs at NIH and commercial entities usually begin in one of two ways. In one common scenario, a company may reach out to an investigator after reading their paper(s) or hearing a talk at a scientific meeting. For example, several companies approached NCI investigator Mitchell Ho after seeing posters presented by his postdocs during the 2018 American Association for Cancer Research meeting in Chicago. Ho’s lab develops antibody-engineering technologies that target and validate tumor antigens in solid tumors. He now collaborates with several commercial partners through three CRADAs and three licenses (with other agreements in the works). Collaborating with companies “helps our basic research move to the next step,” he said. Thanks to his commercial partnerships, antibodies to target two cell-surface proteins, glypican-3 (GPC3) on liver cancer cells and GPC2 on neuroblastoma cells, will likely begin in clinical trials this year.”

<https://irp.nih.gov/catalyst/v27i3/news-you-can-use-technology-transfer>

#2: Because the NIH does limited research related to drug development, without the investment of the biopharmaceutical industry the knowledge resulting from basic science research would generate many ideas for potential drugs and drug targets – but very few new medicines.



The biopharmaceutical industry's unique role in the research ecosystem is to utilize its scientific and industrial expertise to take the necessary risks to build on and further advance basic science research into safe and effective treatments that can be 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 technological platforms from private sector biopharmaceutical companies.

“We always need a pharmaceutical partner...I can't think of a vaccine, even one in which we've put substantial intellectual and resource input, that was brought to the goal line without a partnership with industry.”

— **DR. ANTHONY FAUCI** of National Institute of Allergy and Infectious Disease

The drug development process is commonly characterized as a “pipeline” where knowledge from basic science research is moved through a process that eventually becomes a new treatment in a straightforward path. In reality the process is a hugely complicated web of failure-prone iterative learnings that must be traversed by scientists, physicians, regulators, payers and patients.ⁱⁱⁱ

According to researchers at the Tufts Center for the Study of Drug Development, on average it costs \$2.6 billion to develop one new medicine, including the cost of the many failures. Only 12% of new molecular entities that enter clinical trials eventually receive U.S. Food and Drug Administration (FDA) approval.



There is a rich literature demonstrating the inter-connected contributions of NIH-supported research and the biopharmaceutical industry to the drug development process. This research also demonstrates the critical role of the private sector in advancing scientific ideas into drugs for patients.

- ▶ 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.^{iv}
- ▶ “Of the most prescribed drugs in 2007, the private sector was crucial for the discovery and development of virtually all [97 percent] of the 35 drugs and drug classes examined.” The authors went on to say; “All or almost all the drugs discussed (in the paper) would not have been developed – or, at best, would have been delayed significantly – in the absence of private-sector scientific discoveries.”^v
- ▶ A 2010 analysis of 252 drugs approved between 1998 and 2007 found that 76 percent originated in industry vs. 24 percent in academia.^{vi}
- ▶ A 2014 study of the most transformational drugs of the prior 25 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.^{vii}
- ▶ And 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.^{viii}

“Although NIH understands and contributes to the science of how to evaluate various therapeutic candidates, it does not have the expertise to develop individual products. The NIH enterprise is necessary [for the advancement of product development] but it is not sufficient.”

— **DR. JANET WOODCOCK**, Director of the Center for Drug Evaluation and Research at FDA

(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.)

#3: The U.S. biomedical research ecosystem is the envy of the world and leads the world in biopharmaceutical progress. Much of this success is due to the positive impact of the Bayh-Dole Act on public-private research collaboration.

Current policy debates have again called into question the correct balance of federal and industry contributions to biomedical innovation, with some stakeholders suggesting that NIH could take over the industry's current role and get the same level of innovation as we see today from the private industry. Rather than pitting critical sections of the biopharmaceutical research enterprise against each other, we should be focusing on strengthening the entire ecosystem and ensuring that the policies that have led to its success remain in place. The reason the U.S. is the global leader of biopharmaceutical innovation is because the IP system promotes competition by ensuring each player excels at their role and is incentivized to take risks and share information throughout the process.

Congress passed the Bayh-Dole Act in 1980 with bipartisan support to incentivize the private sector to make the substantial and risky investments needed to transform discoveries resulting from government-funded basic research into useful products. Bayh-Dole has helped

lay the foundation for the robust and entrepreneurial U.S. R&D ecosystem. Specifically, it allows grant recipients, such as universities, to retain the title to the patents covering such discoveries, enabling them to license the patents and right to use those discoveries to private sector partners who can then attempt to further develop them into useful products or medical treatments. Prior to enactment of the Bayh-Dole Act, the government retained the patents on federally-sponsored inventions – and only 5% of those patents were ever used in the private sector.^{ix}

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. In 1989, the NIH adopted a policy of requiring a “reasonable pricing” clause in CRADAs between NIH intramural laboratories and private sector partners. Under the policy, exclusive licenses to industry for inventions developed by the NIH required that there be “a reasonable relationship between the pricing of

“We are the place that supports the scientific innovations that lead to these breakthroughs, and ultimately, to new therapies,” Collins said in an interview.

“But we need to be part of an ecosystem that includes the private sector and philanthropy and advocates for that in order for that to come true.”

— **DR. FRANCIS COLLINS** Director of the National Institutes of Health

<https://news.bloomberglaw.com/pharma-and-life-sciences/research-not-heavy-hand-to-tamp-down-drug-costs-nih-collins>

a licensed product, the public investment in that product and the health and safety needs of the public.” Between 1986 and 1993, the NIH executed 206 CRADAs, most of them with industrial partners.^x

On September 8, 1994, NIH convened a panel of experts including academics, scientists, government administrators, patients and industry representatives to assess the impact of the so-called reasonable pricing clause on CRADAs. The expert panel concluded that the policy “did not serve the best interests of technology development” and recommended that the policy be rescinded. In 1995 NIH removed the clause and NIH Director Dr. Harold Varmus stated that, “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 [NIH] scientists without providing an offsetting benefit to the public. Eliminating this clause will promote research that can enhance the health of the American people.”^{xii} Removal of the clause resulted in a subsequent rebound in CRADAs. CRADAs are now a key vehicle for matching researchers with the industry to help get NIH inventions to patients. In 2018 alone, the NIH entered into 82 CRADAs, executed 298 licenses to NIH inventions and obtained 94 newly issued U.S. patents.^{xiii}

New companies, new jobs and ongoing royalty payments from industry back to universities are just some of the direct benefits of allowing licensing of inventions that benefitted from government-funded research.^{xiv} In fact, every biopharmaceutical sector job supports a total of five jobs across the economy, and the biopharmaceutical industry supported more than 4 million jobs across the U.S. economy in 2017.^{xv} Today, Bayh-Dole and other pro-innovation and intellectual property policies have encouraged collaboration and enabled America to become the leader in medical innovation.



“If you look through the success stories [of] the products that have come out of the intramural program [at NIH], most if not all of them involve a commercial partner,” said Tom Misteli the scientific director of NCI-CCR.

“NIH does not perform product development or commercialization. And unlike their counterparts at universities, NIH investigators cannot spin out a company around an invention. So, it’s essential that there be a way for intramural ideas and technology to be transferred to industry partners.”

<https://irp.nih.gov/catalyst/v27i3/news-you-can-use-technology-transfer>

#4: Even if policymakers were to funnel significantly more budget to NIH, it would not be able to produce medicines like we currently see today. NIH's mission is to uncover new knowledge that will lead to better health for everyone – and we should keep it that way.

The NIH budget (\$32.4 billion in FY17) is used to support their mission to “seek fundamental knowledge about the nature and behavior of living systems and to apply that knowledge to enhance health, lengthen life and reduce illness and disability.”^{xvi} Through the research grants it provides, NIH not only advances basic science but also has a critical role to play in training the future scientists that will drive the research enterprise. It is also responsible for the development and support of medical libraries, training of medical librarians and other health information specialists, and education about the importance of prevention for maintaining good health.^{xvii}

The NIH budget also supports efforts to improve the efficiency, quality and impact of the clinical trials infrastructure at academic medical centers across the U.S. By supporting clinical trials networks in HIV/AIDS,^{xviii} cancer,^{xix} lupus and rheumatoid arthritis^{xx} and rare diseases^{xxi} among others, NIH funding works to enhance investigator expertise and reduce bureaucracy by improving contract negotiation timelines for industry-sponsored clinical studies^{xxii} and creating harmonized institutional review board agreements.^{xxiii} The NIH-funded studies conducted through these networks are critical for

understanding the natural history of diseases, identifying critical biomarkers and establishing clinical guidelines for best standard of care. Private sector companies regularly collaborate with these networks by providing funding and drug supplies, contracting with the networks to run industry-sponsored clinical trials and providing scientific expertise to those networks through advisory committees.

Imagine the loss for the advancement of public health if the NIH was solely focused on developing new medicines.



According to Dr. Janet Woodcock, NIH's work is heavily geared toward the early stages of development, with a relatively small amount of expertise on bringing drugs to market. “The NIH enterprise is necessary and generates a huge knowledge machine to move the field ahead and generate scientists that work at FDA, industry and academia.”

<https://www.raps.org/news-and-articles/news-articles/2019/7/fdas-woodcock-weighs-in-on-role-of-nih-in-drug-de>

#5: In cases where public funding is provided, for example, to support clinical research or increase manufacturing capacity for potential new treatments and vaccines, some have called for the government to determine the price if the candidates are successful. This fails to recognize that reducing the incentives for the private sector to invest and take risks could have serious unintended consequences for future innovation.

We are in a new era of medicine where breakthrough science is rapidly transforming care and our approach to treating patients. The American biopharmaceutical research system's ability to reward collaboration and risk taking is resulting in advances and discoveries unlike anything we've seen before. The application of genomics to develop personalized medicines is enabling physicians to tailor treatments to the unique needs of the patient – minimizing side effects and maximizing the chances of successful treatment. Immunotherapy is harnessing patients' own immune systems to fight off diseases, including cancer and rare diseases, opening promising avenues of treatment for patients in need. Cell and gene therapies help our own bodies fight the actual root causes of disease at the cellular and genetic level. In 2018, the FDA approved a record 65 new medicines,^{xxiv} and there are about 4,500 medicines in development in the U.S. today, including 362 transformative cell and gene therapies.^{xxv}

During public health emergencies such as pandemics, the biopharmaceutical industry has a track record of responsible pricing and actively partnering with the government to ensure availability and affordability. In fact, Anthony Fauci, who leads the National Institute of Allergy and Infectious Diseases, has said, "I have not seen in my experience situations in which we were involved in the development of a vaccine, particularly for low- and middle-income countries that really needed it, where the pharmaceutical companies priced it out of their reach."

In the face of the COVID-19 crisis, PhRMA member companies have committed to working with governments to ensure that when new treatments and vaccines are approved they will be available and affordable for patients.^{xxvi} In addition, the government has a wide range of existing policies and programs to provide widespread, affordable access to diagnostics, treatments and vaccines as well as public-private partnerships to support the development and potential stockpiling of supplies needed to address COVID-19.^{xxvii}

Rather than harming the highly successful U.S. biopharmaceutical research ecosystem and the patients who need innovative treatments, we should look to policies that will support patient access and affordability without undermining the development of tomorrow's life-saving medicines. A primary goal of these policies should be to facilitate and support the continued collaboration between publicly funded and private sector research. Through thoughtful, market-based approaches we can continue to support a thriving ecosystem and allow the biopharmaceutical sector to continue to partner with the public sector to deliver innovative medicines and improve the lives of patients in unprecedented ways.

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