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Report to Congressional Requesters

October 2020

BIOMEDICAL RESEARCH

NIH Should Publicly Report More Information about the Licensing of Its Intellectual Property

GAO-21-52

GAO Highlights

Highlights of GAO-21-52, a report to congressional requesters

October 2020

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NIH Should Publicly Report More Information about the Licensing of Its Intellectual Property

Why GAO Did This Study

HHS labs conduct research that can contribute to the development of new life-saving drugs. HHS may grant rights to its inventions by licensing the patents to pharmaceutical companies that conduct the additional development activities and testing necessary to bring drugs to market. Public health experts and patients' rights advocates have raised concerns about the prices of drugs developed with federal support.

GAO was asked to review HHS's management of its intellectual property. This report examines (1) the extent to which HHS-owned intellectual property has contributed to the development of FDA-approved drugs, (2) what is known about the licenses associated with FDA-approved drugs, (3) factors NIH prioritizes when licensing its inventions and information about licensing it makes public, and (4) steps HHS has taken to protect its rights. GAO reviewed relevant laws and agency documents, analyzed patent and licensing data, and interviewed HHS officials, academic experts, industry representatives, and nongovernmental organizations.

What GAO Recommends

GAO is making two recommendations, including that NIH provide more information to the public about the licensing of its intellectual property. HHS concurred with GAO's recommendations.

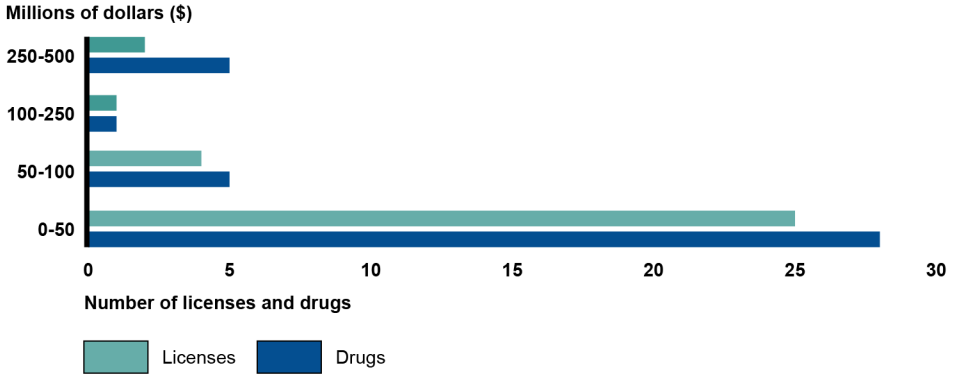
View GAO-21-52. For more information, contact John Neumann, (202) 512-6888, NeumannJ@gao.gov.

What GAO Found

Research conducted at Department of Health and Human Services (HHS) labs led to 4,446 U.S. patents owned by the agency covering a range of inventions from 1980 through 2019. During that period, the National Institutes of Health (NIH) had 93 patents—2 percent of the total—that contributed to the successful development of 34 drugs approved by the Food and Drug Administration (FDA) and brought to market, including vaccines and treatments for cancer.

These 34 drugs were developed by pharmaceutical companies and were associated with 32 licenses granted to them by NIH. As shown in the figure, these licenses have generated up to $2 billion in royalty revenue for NIH since 1991, when FDA approved the first of these drugs. Three licenses generated more than $100 million each for the agency.

Royalties from NIH Licenses of Inventions Associated with FDA-Approved Drugs, 1991 to February 2020



Source: GAO analysis of National Institutes of Health (NIH) data. | GAO-21-52

When licensing its inventions, NIH prioritizes the likelihood that the licensee can successfully develop a drug by considering such factors as technical expertise and the ability to raise capital. Consistent with federal interpretation of technology transfer statutory authorities, NIH does not consider the affordability of the resulting drug. NIH provides limited information to the public about its licensing activities. For example, the agency does not report which of its patents are licensed or release metrics that would enable the public to evaluate how licensing affects patient access to resulting drugs. Increasing the transparency of its licensing activities could improve the public's and policymakers' understanding of NIH's management of its intellectual property.

HHS monitors for unauthorized use of its inventions (infringement) and has taken steps to protect its rights. HHS relies primarily on inventors at its labs to monitor for potential infringement and generally encourages potential infringers to license the inventions. If cases proceed to litigation, HHS relies on the Department of Justice (DOJ) to protect its rights. Since 2009, HHS has worked with DOJ to defend its intellectual property in several cases in the U.S. and abroad and has referred one case to DOJ for litigation against an alleged infringer.

Contents

Tables

Figures

Abbreviations

ANDA	abbreviated new drug application
CDC	Centers for Disease Control and Prevention
CRADA	cooperative research and development agreement
Commerce	Department of Commerce
COVID-19	coronavirus disease 2019
DOJ	Department of Justice
FDA	Food and Drug Administration
FTC	Federal Trade Commission
HHS	Department of Health and Human Services
IPC	International Patent Classification
NIH	National Institutes of Health
NIST	National Institute of Standards and Technology
PhRMA	Pharmaceutical Research and Manufacturers of America
PrEP	pre-exposure prophylaxis
R&D	research and development
USPTO	United States Patent and Trademark Office

U.S. GOVERNMENT ACCOUNTABILITY OFFICE
441 G St. N.W.
Washington, DC 20548

October 22, 2020

The Honorable Carolyn B. Maloney
Chairwoman
Committee on Oversight and Reform
House of Representatives

The Honorable Debbie Stabenow
Ranking Member
Subcommittee on Health Care
Committee on Finance
United States Senate

The Department of Health and Human Services (HHS) has spent billions of dollars funding research and development (R&D), including at federal laboratories, which can directly or indirectly contribute to the development of new drugs used by the public.[1] For example, scientific discoveries from HHS labs have contributed directly to the creation of important medical treatments, such as vaccines against hepatitis A and human papillomavirus, both of which can cause cancer. More broadly, research funded by HHS contributes to general scientific knowledge that leads to new drug development.[2] As a critical input for private sector efforts to develop new drugs, such research can provide the basis for collaborative research between government labs and the private sector. Of the approximately $8 billion obligated for R&D at HHS federal labs in fiscal year 2018, the National Institutes of Health (NIH) accounted for about 90 percent of the funding, with the Centers for Disease Control and

[1]The term "drug" in this report includes small molecule drugs, therapeutic biological products, vaccines, in vivo diagnostic agents, and drug-device combinations approved by FDA. While we collectively refer to these products as FDA-approved drugs, these drugs can involve different FDA processes. For example, small molecule drugs are reviewed under different procedures than biological products, which have a larger and more complex chemical structure. We use the term lab in a broad sense to include all federally funded labs and R&D centers.

[2]See, for example, Cleary et al., "Contribution of NIH funding to new drug approvals 2010–2016," *Proceedings of the National Academy of Sciences*, vol. 115, no. 10 (2018).

Prevention (CDC) and the Food and Drug Administration (FDA) combined accounting for about 5 percent of the funding.[3]

Research at HHS's federal labs regularly leads to new intellectual property—including patented inventions owned by HHS—some of which has the potential to contribute directly to the development of new drugs.[4] To support such development, HHS engages in technology transfer, which is the process of transferring scientific findings and intellectual property to another organization for the purpose of further development and commercialization. This transfer can be accomplished through licensing rights to patented inventions owned by the government to other companies to develop. HHS has licensed patented inventions for decades and continues to license technology and engage in other types of actions to spur the development of vaccines and drugs to prevent and treat the Coronavirus Disease 2019 (COVID-19), including through collaborative research in its federal labs with private sector partners.

Since the 1980s, patients' rights and consumer advocates have raised concerns about the price of drugs that include contributions made by HHS-funded research, including that funded by the NIH and CDC. For example, the drug zidovudine was developed as a human immunodeficiency virus (HIV) treatment through joint efforts of NIH's National Cancer Institute and a pharmaceutical company to conduct clinical trials testing its safety and effectiveness. After receiving FDA approval in 1987, the manufacturer set the launch price of the drug at

[3]National Science Foundation, *Survey of Federal Funds for Research and Development, FYs 2018–19*. This funding includes obligations on intramural research, which includes costs associated with the administration of intramural R&D programs and extramural R&D procurements by federal personnel as well as actual intramural performance. Funding for external research, for example research done by universities and contractors, is known as extramural funding, and funding for R&D conducted by federal agencies in their own facilities is known as intramural funding. For the purposes of this report, we refer to these three agencies—NIH, CDC, and FDA—collectively as HHS since these agencies represent the vast majority of intramural research at HHS's federal labs.

[4]Section 4 of the Stevenson-Wydler Technology Innovation Act of 1980, as amended, defines "invention," in relevant part, as any invention or discovery that is or may be patentable or otherwise protected under title 35, United States Code (7 U.S.C. § 2321 et seq.). *See* Pub. L. No. 99-502, § 6(d)(9), 100 Stat. 1785, 1796 (1986), (amending Pub. L. No. 96-480, § 4 and codified as amended at 15 U.S.C. § 3703(7)). A patent is an exclusive right granted for a fixed period of time to someone who invents or discovers (1) a new and useful process, machine, manufacture, or composition of matter or (2) any new and useful improvement of such items. A patent owner can license or assign the patent rights as well as prevent others from making, using, importing, selling, or offering for sale the patented invention in the United States.

$10,000 per patient per year, which led to public backlash.[5] Similar concerns have been raised related to the contributions of HHS research to the anti-cancer drug Taxol and most recently with Truvada for HIV pre-exposure prophylaxis (PrEP).[6]

You asked us to review HHS's management of its intellectual property that has contributed to the development of new drugs. This report examines (1) the extent to which HHS-owned intellectual property has contributed to the development of FDA-approved drugs; (2) what is known about the licenses associated with FDA-approved drugs; (3) factors NIH prioritizes when licensing its patented inventions, and information about licensing it makes public; and (4) steps that HHS has taken to protect its intellectual property. In addition to this report, we are providing an online dataset of patents owned by HHS, which can be accessed on our website at https://www.gao.gov/products/GAO-21-52.

To address these objectives, we interviewed stakeholders with a range of perspectives, including academics, patient advocates, nonprofit organization representatives, industry representatives from trade associations and individual companies, officials from other federal agencies' technology transfer offices, and representatives of university technology transfer offices. In addition, we provided a written questionnaire to the nine technology transfer offices responsible for managing the intellectual property of NIH, CDC, and FDA federal labs to collect comparable information on technology transfer activities. We then conducted follow-up interviews with selected NIH technology transfer offices responsible for the majority of the FDA-approved drugs we identified or that had a research mission related to technology transfer.

To examine the contributions of HHS-owned intellectual property to the development of FDA-approved drugs, we obtained data from NIH's intellectual property management database on patents and licenses

[5]Ameet Sarpatwari, Alison K. LaPidus, Aaron S. Kesselheim. "Revisiting the National Institutes of Health Fair Pricing Condition: Promoting the Affordability of Drugs Developed with Government Support." *Annals of Internal Medicine*, vol. 172, no. 5 (2020), doi: 10.7326/M19-2576.

[6]For Taxol, see GAO, *Technology Transfer: NIH-Private Sector Partnership in the Development of Taxol*, GAO-03-829 (Washington, D.C.: June 4, 2003). For Truvada, see Amy Kapczynski and Christopher Morten, Yale Global Health Justice Partnership, "Letter to House Committee on Oversight and Reform, for May 16, 2019, Hearing on HIV Prevention Drug: Billions in Corporate Profits after Millions in Taxpayer Investments."

granted from 2000 through 2019.[7] We used U.S. Patent and Trademark Office (USPTO) PatentsView data for the period 1980 through 2019 to identify patents owned by HHS and examine selected patent characteristics. For example, we used PatentsView data on International Patent Classification (IPC) technology type to help describe the underlying technology of the patents, such as whether they involved pharmaceutical technology. The license data we obtained were for licenses associated with patents granted from 2000 through 2019, and we analyzed the types of licenses granted. NIH identified all FDA-approved drugs associated with HHS's licensed inventions, 34 in total.[8] We obtained and analyzed data on these FDA-approved drugs from IBM's Truven Health Analytics Red Book and the FDA's Orange Book to identify the medical uses and related patents and exclusivities, as of June 2020. We took various steps to assess the reliability of these data sources, including reviewing related documentation, interviewing knowledgeable officials, and reviewing data for errors, omissions, and outliers, among other steps. We found them reliable for the purposes of reporting the types of patents, identifying the use of drugs, and related patents associated with drugs in the Orange Book.

To examine what is known about licenses associated with FDA-approved drugs, we obtained and analyzed NIH data related to these licenses, including total royalties generated by licenses and exclusivity of the licenses, for each of the identified drugs. We also obtained and analyzed data from the Centers for Medicare and Medicaid Services' drug spending dashboard for the period 2014 through 2018 to determine total spending from Medicare Part B, Medicare Part D, and Medicaid on these drugs and, where available, the number of beneficiaries served.[9] We reviewed these data and found them reliable for the purposes of reporting program spending on these drugs. In addition, we interviewed agency staff with

[7]NIH managed intellectual property for CDC and FDA until a decentralization in fiscal year 2016. NIH's data contains the historical data for these agencies. FDA began to separately manage its intellectual property with the decentralization, and we coordinated with FDA to obtain any recent information not in the NIH database.

[8]These 34 FDA-approved drugs include two combination products—drug-coated stents for surgical procedures. This list excludes other medical devices with no drug component, drugs approved by national regulators of medical products in other countries but not approved by FDA, and veterinary drugs that may have been developed from NIH inventions.

[9]Spending from 2014 through 2018 represents the most recent data available on the dashboard for Medicare and Medicaid drug spending at the time we concluded our review.

knowledge of these licenses at select technology transfer offices affiliated with NIH's research institutes and at NIH's Office of Technology Transfer.

To examine what factors NIH prioritizes in licensing its patented inventions and what licensing information it makes public, we reviewed relevant statutes, regulations, and HHS guidance on technology transfer.[10] We also obtained and reviewed license agreements for all 34 FDA-approved drugs that involved HHS-owned patented inventions as well as standard license agreements used by NIH.[11] We reviewed information published by NIH on its technology transfer processes, including marketing information on its technologies, Federal Register notices, and publicly reported information in annual technology transfer reports. We also interviewed knowledgeable agency officials at NIH's Office of Technology Transfer, select NIH technology transfer offices, FDA, and the National Institute of Standards and Technology (NIST).

To examine the steps that HHS has taken to protect its intellectual property, we reviewed relevant statutes, regulations, and HHS guidance on technology transfer. We obtained and analyzed data from the NIH Office of Technology Transfer's intellectual property management database on cases of potential infringement for the period 2016 through 2019. We also obtained information on legal cases involving HHS-owned intellectual property from the Department of Justice (DOJ), for the period 2009 through 2019. DOJ helps HHS enforce its intellectual property rights both domestically and internationally.[12] After analyzing agency data, we selected closed civil action cases that provided examples of each type of action taken to protect HHS intellectual property. Although the results of these cases are not generalizable to all cases, they provide illustrative examples of actions taken to protect HHS intellectual property. We obtained and reviewed documentation on these cases, such as court filings and decisions. In addition, we interviewed HHS and DOJ officials

[10]Department of Health and Human Services, Public Health Service, *United States Public Health Service Technology Transfer Policy Manual*, (Rockville, Md.: September 2013).

[11]Standard license agreements refer to standardized templates used by technology transfer offices as a starting point to negotiate licenses, including licenses for rights to the government's patented inventions.

[12]DOJ officials identified examples of civil actions DOJ litigated related to HHS intellectual property from 2009 through 2019. DOJ officials explained that they compiled the information based on their knowledge of prior cases and related documentation. Therefore, the list of cases may not contain all cases where DOJ defended HHS intellectual property rights.

with knowledge of agency enforcement processes. For additional information on our scope and methodology, see appendix I.

We conducted this performance audit from September 2019 to October 2020 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Background

Legal Framework for Technology Transfer

A series of federal laws and executive orders enacted over a 40-year span have directed federal agencies to enhance their labs' beneficial impact on society by helping to ensure that new technology is transferred to the marketplace. One of the first technology transfer laws, the Stevenson-Wydler Technology Innovation Act of 1980, established technology transfer as a federal policy and required federal labs to devote budget and personnel resources to promoting the transfer of federal technologies to the private sector.[13] This law also required federal labs to set up Offices of Research and Technology Applications (which, for the purposes of this report, we refer to as technology transfer offices). HHS and other federal agencies transfer technology by, among other things, licensing patents on inventions created by federal labs. This is consistent with the requirements of the Bayh-Dole Act of 1980, another key law providing the foundation for federal technology transfer activities.[14] Such licensing aims to bring inventions developed by the federal government to practical application by putting them in the hands of those who can further develop them.

Since 1980, additional laws have been enacted to help further the development of federally owned inventions for commercial use. For example, in 1984, through amendments to the Bayh-Dole Act, the Department of Commerce (Commerce) became responsible for issuing

[13]Stevenson-Wydler Technology Innovation Act of 1980, Pub. L. No. 96-480, §§ 3, 11, 94 Stat. 2311, 2312, 2318-19 (codified as amended at 15 U.S.C. §§ 3702, 3710).

[14]Patent and Trademark Law Amendments Act, Pub. L. No. 96-517, 94 Stat. 3015 (1980) (codified as amended in 35 U.S.C. §§ 200-212), commonly referred to as the Bayh-Dole Act.

regulations to implement the act.[15] This responsibility is delegated to NIST. The Stevenson-Wydler Act was amended by the Federal Technology Transfer Act of 1986, which, among other things, empowered federal agencies to allow the directors of government-owned, government-operated labs to enter into cooperative research and development agreements (CRADA) and negotiate license agreements for inventions created in their agencies' labs.[16] In addition, the Technology Transfer Commercialization Act of 2000 required Commerce to provide Congress with summary reports on federal agencies' patent licensing and other technology transfer activities.[17] Since 2007, Commerce has delegated to NIST the role of providing to Congress an annual report summarizing technology transfer activities at federal agencies.[18]

HHS Agencies' Research, Missions, and Technology Transfer

HHS agencies provide substantial government funding to R&D conducted by scientists at federal labs and by scientists outside the federal government to meet agency missions.[19] NIH, FDA, and CDC obligated $36 billion for all federal lab and external R&D in fiscal year 2018, with 97 percent of that funding coming from NIH, according to the National Science Foundation. Of the $36 billion obligated in fiscal year 2018, $8 billion in intramural funding (for R&D conducted by federal agencies in their own facilities) supported biomedical research. According to NIH officials, all of the HHS federal labs generate inventions that can become intellectual property owned by the government. However, the intramural

[15]Pub. L. No. 98-620, § 501(10), 98 Stat. 3335, 3367 (amending 35 U.S.C. § 206).

[16]Pub. L. No. 99-502, § 2, 100 Stat. 1785, 1785 (1986) (amending Pub. L. No. 96-480, adding § 12, codified as amended at 15 U.S.C. § 3710a(a)).

[17]Pub. L. No. 106-404, § 10(a)(3), 114 Stat. 1742, 1748 (amending Pub. L. No. 96-480, codified at 15 U.S.C. § 3710(g)(2)).

[18]In 2007, the America Creating Opportunities to Meaningfully Promote Excellence in Technology Education and Science (COMPETES) Act eliminated Commerce's Technology Administration, which had been responsible for collecting information on all federal agencies' technology transfer activities and submitting the information to Congress and the Office of Management and Budget. Pub. L. No. 110-69, § 3002(a)(1), 121 Stat. 572, 586 (2007) (amending Pub. L. No. 96-480, § 5, codified at 15 U.S.C. § 3704).

[19]The Bayh-Dole Act generally has given extramural researchers, such as federal contractors and university-based grantees, the option to retain ownership rights to, and profit from, commercializing the inventions they create as part of federally sponsored research projects. In return for these rights, extramural researchers are required to take certain actions, such as to file for patent protection, pursue commercialization of the inventions, and provide a "nonexclusive, nontransferable, irrevocable, paid-up license" to practice these federally funded inventions for government purposes. Inventions owned by extramural researchers are out of the scope of this report.

programs focus on basic biomedical research to achieve agency missions rather than specifically on developing new drugs. Developing a commercial product from such inventions may necessitate the agency to partner with other entities, such as pharmaceutical companies.

Federal law states that it is Congress's policy and objective to use the patent system to, among other things, promote the commercialization and public availability of inventions,[20] and that technology transfer, consistent with [agencies'] mission responsibilities, is the responsibility of each laboratory science and engineering professional.[21] Each federal agency involved in technology transfer, including federal patent licensing, designs its own program to meet its own technology transfer objectives, consistent with its other mission responsibilities. Within HHS, federal labs are guided by their agency's underlying mission, specifically:

- **NIH.** NIH's mission is 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. As part of this mission, NIH's goal is to, among other things, expand the knowledge base in medical and associated sciences to enhance economic well-being and ensure a continued high return on public investment in research. For example, the National Cancer Institute—one of the 27 research institutes and centers at NIH—includes federal labs with a mission to enhance cancer research, prevention, treatment, and training by conducting basic, clinical, and other types of research. Researchers at these labs develop technologies related to the detection, diagnosis, and treatment of cancer, among other things.
- **FDA.** FDA's mission is to protect the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring the safety of the food supply, cosmetics, and products that emit radiation.
- **CDC.** CDC's mission is to, among other things, increase health security and fight disease. CDC aims to save lives and protect people from health threats by conducting critical science and providing health information that protects the public against expensive and dangerous health threats.

[20]35 U.S.C. § 200.

[21]15 U.S.C. § 3710(a)(2).

Each of these HHS agencies funds intramural research that can lead to new inventions and manages its inventions through technology transfer offices.[22] NIH divides the management of inventions among technology transfer offices affiliated with its research institutes and centers and NIH's Office of Technology Transfer. NIH's eight technology transfer offices manage patent prosecution and negotiate license agreements for specific research institutes and centers. NIH's Office of Technology Transfer manages active licenses and develops technology transfer metrics. FDA manages all of its technology transfer activities through its own technology transfer office. NIH's National Institute of Allergy and Infectious Diseases' technology transfer office has an interagency agreement with CDC to manage CDC's patenting and licensing.

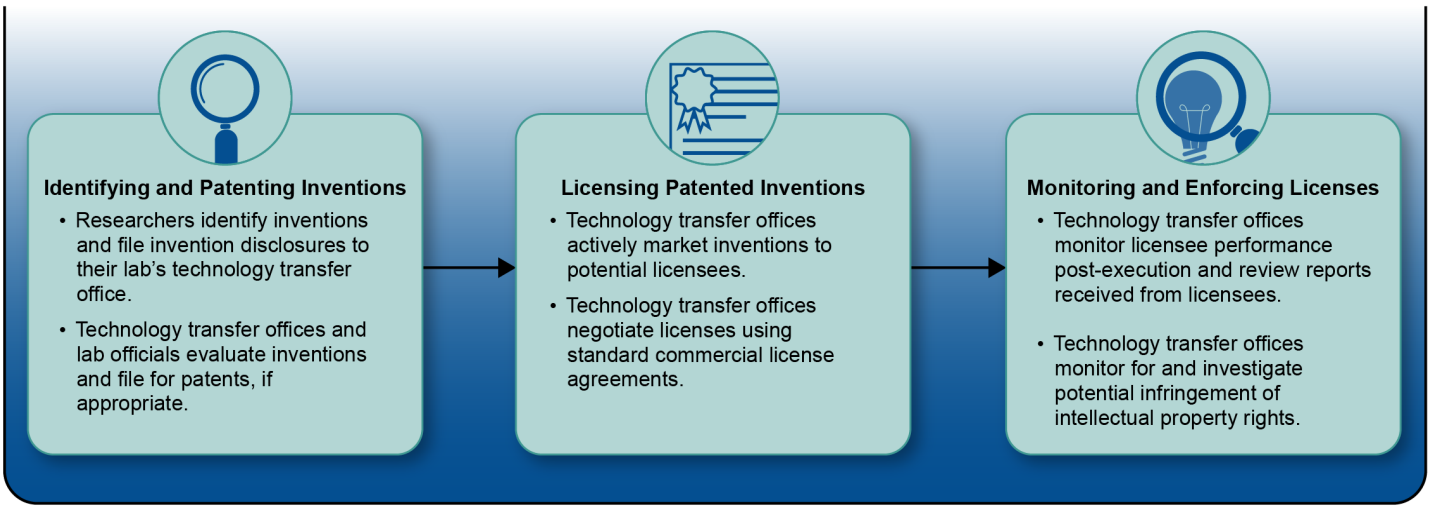
The Process for Managing HHS Intellectual Property

HHS labs generate intellectual property, such as inventions that can be patented. A patent is an exclusive right granted for a fixed period of time to an inventor, which can be assigned to other entities.[23] The process of managing patented inventions begins with scientists at HHS's federal labs submitting an invention disclosure to their lab's technology transfer office. Technology transfer and lab officials review the invention disclosure and consider whether it is patentable and supports the lab's mission. They also consider whether patenting the invention is likely to result in a successful commercialization or other practical application before deciding whether to pursue a patent in the United States and other countries (see fig. 1).

[22]The agency or office managing specific technology transfer responsibilities has changed over time. The National Technical Information Service, a unit of the Department of Commerce, managed marketing and licensing activities of HHS intramural inventions until 1992, when NIH's Office of Technology Transfer took over all licensing responsibilities, coordinating with institutes and centers that generated the inventions. Most recently, HHS agencies decentralized technology transfer, with each agency managing its own technology transfer activities.

[23]A patent owner can prevent others from making, using, selling, or offering for sale the patented invention in the United States, or importing it into the United States without authorization. A patent owner can license or assign the patent rights.

Figure 1: HHS Intellectual Property Management Process



Source: GAO analysis based on review of regulations and agency documentation. | GAO-21-52

HHS agencies seek to attract potential licensees, such as pharmaceutical companies, universities, and nonprofits, to develop their technologies.[24] Interested parties can submit an application to license patented inventions developed by federal labs. Technology transfer offices negotiate the terms of the patent license. They use standard commercial license agreements as a starting point for negotiating the terms and conditions of licensees' contractual obligations, such as financial compensation to the government in the form of royalties based on sales or the exclusivity of a license.[25] Laws and federal regulations require government-operated labs to incorporate certain terms in the license agreements, such as provisions that protect the government's interests in federally funded inventions and allow the government agency to terminate

[24]A licensee, in this context, is an entity that gains a legal right to use a patented invention owned by the federal government. We previously reported on the patent licensing process at several federal agencies, including NIH, in GAO, *Federal Research: Additional Actions Needed to Improve Licensing of Patented Laboratory Inventions*, GAO-18-327 (Washington, D.C.: Jun. 19, 2018).

[25]License agreements may grant to the licensee nonexclusive, partially exclusive, or fully exclusive rights to practice the invention. Federal agencies must publicly announce their intent to grant some exclusive and partially exclusive licenses for at least 15 days before the license is granted. After this period, the agency considers public comments and objections. Negotiations then begin with the license applicant.

or modify the agreements. These terms are reflected in standard license agreements. Agencies may include additional provisions so long as they do not run contrary to what is required by law. For example, NIH had a reasonable pricing clause from 1989 until 1995 for CRADAs and exclusive licenses related to CRADAs.[26] Negotiations are often an iterative process in which both the technology transfer office and the licensee request adjustments to the terms of the license, such as scope of the license, royalty rates, and drug development milestones.

Federal agencies are responsible for monitoring licenses post-execution. As part of such monitoring, NIH's Office of Technology Transfer reviews thousands of sales reports annually, which provide the basis for collecting royalty payments on sales of inventions that were successfully commercialized into products, according to NIH officials.[27] Federal agencies are authorized to undertake all suitable and necessary steps to protect the rights to federally owned inventions on behalf of the federal government, which could include monitoring intellectual property for potential infringement—the unauthorized use of patented inventions—and enforcing intellectual property rights.[28] HHS guidance states that the federal government's ability to use its intellectual property portfolio as a tool to develop technology is diminished by patent infringement. According to this guidance, patent infringement discourages the licensing and development of government inventions, reduces sales of licensed

[26]This clause stated there should be a reasonable relationship between the pricing of a product licensed under a CRADA, the public investment in that product, and the health and safety needs of the public. When NIH revoked the reasonable pricing clause in 1995, the NIH director cited an extensive review conducted over the preceding year, which indicated that the clause had driven away industry from potentially beneficial scientific collaborations with NIH scientists without providing an offsetting benefit to the public. The review included two panels of experts and industry representatives convened by NIH in July and September 1994, which presented their findings to the Director of NIH; see NIH, *Reports of the NIH Panels on Cooperative Research and Development Agreements: Perspectives, Outlook, and Policy Development* (December 1994). The second panel concluded that NIH needed to address a perception that the reasonable pricing clause was an impediment to achieving NIH's mission of promoting cooperative research and facilitating the transfer of technology to the private sector. Some scholars have called for a reinstatement of such a clause, see Sarpatwari, LaPidus, and Kesselheim. "Revisiting the National Institutes of Health Fair Pricing Condition."

[27]A portion of royalty income is paid to the inventor of the patent, per statute. 15 U.S.C. § 3710c(a)(1). The remaining royalty income is returned to the research institute where the invention was developed to support further research or patenting of other inventions.

[28]See 35 U.S.C. § 207(a)(3). All agencies must coordinate with DOJ for any litigation related to their intellectual property. See 28 U.S.C. §§ 515-519, which makes the Attorney General responsible for and the supervisor of all litigation.

products that have been commercialized, and reduces the incentives for federal inventors to report their inventions to the technology transfer office.

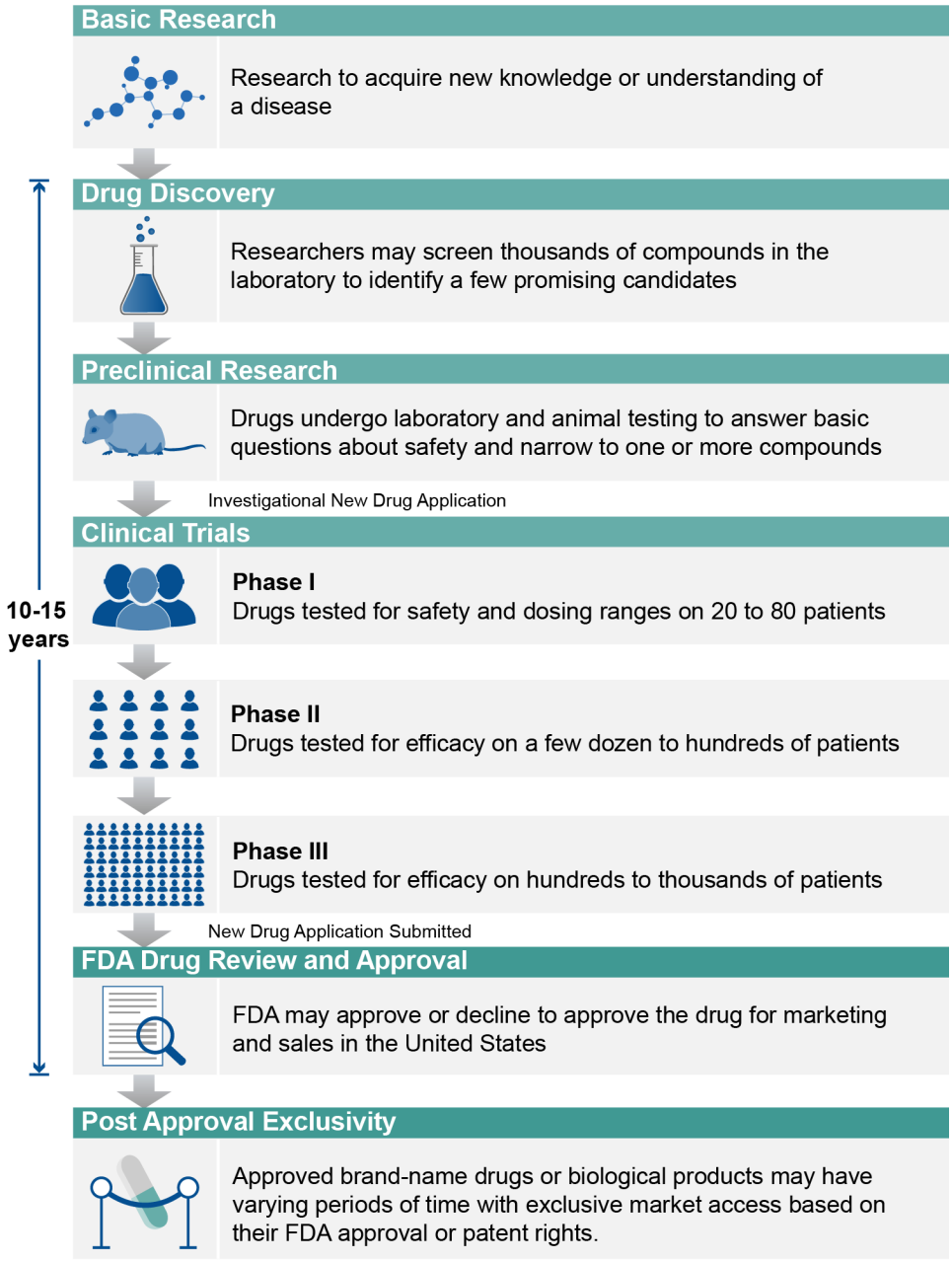
Incentives for Drug Development

The process of bringing a new drug from a laboratory invention to the market is long and costly and can involve multiple public and private entities that fund and perform R&D (see fig. 2.) For a new drug, the entire drug discovery, development, and FDA review and approval process can take 15 or more years, often accompanied by high development costs.[29] During this process, many new drug candidates fail to prove in clinical trials that they are safe and effective.[30]

[29]For more information on this process, see GAO, *Drug Industry: Profits, Research and Development Spending, and Merger and Acquisition Deals*, GAO-18-40 (Washington, D.C.: Nov. 17, 2017). This timeline refers to standard FDA approval processes and can be substantially shorter with accelerated processes.

[30]For more information on challenges in drug development and the use of artificial intelligence to address them, see GAO, *Artificial Intelligence in Health Care: Benefits and Challenges of Machine Learning in Drug Development*, GAO-20-215SP (Washington, D.C.: December 2019).

Figure 2: Drug Discovery, Development, and Approval Process



Source: GAO analysis of Food and Drug Administration FDA) and Pharmaceutical Research and Manufacturers of America (PhRMA) documentation. | GAO-21-52

Patent and market exclusivity periods provide opportunities for pharmaceutical companies to recoup their R&D investments in new drugs by limiting competition for specified periods of time. Typically, early in the R&D process, companies developing a new drug apply for patents on the active ingredient or a new combination of known ingredients. Pharmaceutical companies may also apply to USPTO for patents on other aspects of the drug, such as a method of use or method of manufacturing.[31] In addition, companies may license patents through agreements with other companies, universities, or federal agencies. Without the relevant patents needed to produce a drug or an agreement to license them, pharmaceutical companies may be unable to legally make, use, import, or sell the drug during the term of the patent. Patent terms generally expire after 20 years from the date of filing.[32] Federal law also authorizes certain periods of regulatory exclusivity, for eligible FDA-approved drugs, during which time FDA generally cannot approve a similar competing version of the drug for marketing.[33] These exclusivities are independent of the rights granted under a patent and may be granted for certain products such as those that relate to active ingredients never approved before by FDA (5 years), certain biological products (12 years), and orphan drugs (i.e., drugs designated to treat, diagnose, or prevent rare diseases or conditions) (7 years).[34] Patent protection time periods and exclusivity time periods are independent of each other and can run concurrently or not.

Pharmaceutical and biotechnology companies seek to maximize profits, in part by investing in the development of drugs that can command high prices. High prices pose challenges for the public in being able to afford

[31]Companies can continue to obtain patents on innovations to existing products, such as new methods of administering a drug.

[32]Since patents for new drugs are often granted prior to their approval for marketing, the useful patent life can be shorter than this amount, according to FDA. In some circumstances, patents can be extended under 35 U.S.C. § 156 to partially compensate for patent term lost during required U.S. regulatory review of a drug prior to approval.

[33]According to FDA officials, in some cases, the agency cannot accept an application for competing drugs.

[34]The exclusivity period for active ingredients never before approved by FDA runs from the time of new drug application approval. 21 U.S.C. § 355(c)(3)(E)(ii). The exclusivity period for certain biological products runs from the time of biologics license application approval. 42 U.S.C. § 262(k)(7). For orphan drugs, pharmaceutical companies must apply for orphan designation from FDA prior to submitting an application for the drug's approval. 21 U.S.C. §360cc. Upon approval, orphan drugs may quality for 7 instead of 5 years of exclusivity for the new active ingredient.

and receive access to drugs to treat diseases, according to scholars and public health advocates.[35] Our prior work found that some companies seek to extend patent protection or exclusivity periods for existing drugs as a means to extend revenue generation by delaying or limiting the effect of generic competition. This process is sometimes referred to as "evergreening" or "patent hopping."[36]

The Federal Trade Commission (FTC) and the DOJ enforce federal antitrust laws that prohibit activities, such as price fixing and mergers and acquisitions where the effect may be substantially to lessen competition or tend to create a monopoly.[37] Pharmaceutical companies are subject to these antitrust laws. FTC and DOJ each have authority and responsibilities under the antitrust laws. In addition, FTC has authority to investigate and take action against unfair methods of competition.[38]

When brand-name drug products' patents expire and exclusivity periods end, follow-on versions of the drug that have been approved by FDA can enter the market. These products are referred to as generics for small molecule drugs and as "biosimilars" for biological products.[39] Under the Drug Price Competition and Patent Term Restoration Act of 1984—commonly known as the Hatch-Waxman Amendments—a generic drug must generally be demonstrated to be equivalent to the brand-name drug product in active ingredient(s), performance characteristics, and intended

[35]Two bills introduced in 2019 seek to address the high prices of drugs in the United States. In the Senate, the Prescription Drug Pricing Reduction Act of 2019 (S. 2543, 116th Cong. (1st Sess. 2019)) was introduced in September 2019. The Elijah E. Cummings Lower Drug Costs Now Act (H.R. 3, 116th Cong. (1st Sess. 2019)), introduced in September 2019, was passed by the House of Representatives in December 2019. In addition, the President signed four executive orders to lower drug prices in July 2020. According to HHS's Centers for Medicare and Medicaid Services, total U.S. spending on retail prescription drugs reached $335 billion in 2018, and retail U.S. drug prices grew between 1973 and 2017, falling slightly in 2018.

[36]GAO-18-40.

[37]See 15 U.S.C. §§ 1, 18, 45. In addition, private parties and states may enforce state and federal antitrust laws by bringing suit for violations of these laws. See 15 U.S.C. §§ 15, 15c.

[38]See 15 U.S.C. § 45.

[39]Small molecule drugs are initially regulated and approved under section 505 of the Federal Food, Drug, and Cosmetic Act, codified at 21 U.S.C. § 355. Biological products are initially regulated and approved under the Biologics Price Competition and Innovation Act of 2009, codified at 42 U.S.C. § 262.

use, among other characteristics.[40] Pharmaceutical companies submit an abbreviated new drug application (ANDA) to FDA to market a generic drug. For biological products, the Biologics Price Competition and Innovation Act of 2009 provided an abbreviated pathway for companies to obtain approval of "biosimilar" biological products.[41]

A Small Portion of Licensed Inventions Contribute Directly to New Drugs

HHS patents inventions covering a range of technologies related to biomedical research. Of those inventions, about half are potentially relevant to pharmaceutical development, with a small portion being licensed and contributing directly to the development of FDA-approved drugs. According to our analysis of USPTO PatentsView data, HHS obtained a total of 4,446 U.S. patents covering a range of technologies from 1980 through 2019 (see table 1). Biotechnology patents, which include devices for growing microorganisms or animal tissues, were the most common primary technology type for a patent, followed by pharmaceuticals and organic fine chemistry.[42] Twenty-two percent of patents were identified as a pharmaceutical technology for their primary technology type and 42 percent included the pharmaceutical technology type as one of several identified technology types.[43] In that same time period, 2 percent of all HHS-owned U.S. patents were associated with licenses that contributed to FDA-approved drugs.

[40]Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified in pertinent part as amended at 21 U.S.C. § 355(j)).

[41]Pub. L. No. 111-148, tit. VII, subtit. A, 124 Stat. 119, 804 (2010) (codified in pertinent part as amended at 42 U.S.C. § 262(k), (l)).

[42]Organic fine chemistry is a multi-step process of producing pure, carbon-containing chemicals that serve as building blocks for different products, including pharmaceuticals.

[43]USPTO classifies patent technology types according to the Cooperative Patent Classification system codes and also provides the International Patent Classification (IPC) technology type codes. The IPC system is an international system administered by the World Intellectual Property Organization. Patents may be classified with a primary IPC technology type and can be classified with additional secondary technology types, as appropriate. For example, a biotechnology patent may also be identified as also relevant to pharmaceutical technology.

Table 1: U.S. Patents Granted to the Department of Health and Human Services (HHS) between 1980 and 2019 by Primary Technology Type

Primary IPC technology type[a]	U.S. patents granted		Licensed patents associated with drugs[c]
	Number	Percentage[b]	
Biotechnology	2,040	46	38
Pharmaceuticals	962	22	45
Organic fine chemistry	474	11	7
Analysis of biological materials	255	6	2
Medical technology	209	5	-
Measurement	207	5	-
Other technologies[d]	194	4	2
Computer technology	57	1	-
Chemical engineering	48	1	-
Total	**4,446**	**100**	**94**

GAO analysis of U.S. Patent and Trademark Office and National Institutes of Health data. | GAO-21-52

Notes: This table does not include pending applications or foreign patents assigned to HHS.

[a]Primary International Patent Classification (IPC) technology type in the U.S. Patent and Trademark Office's PatentsView dataset. The IPC system is an international classification system administered by the World Intellectual Property Organization. Some patents have multiple technology types in the data listed after the primary technology type.

[b]The sum of the percentages exceeds 100 due to rounding.

[c]This column refers to the number of HHS-owned U.S. patents that HHS licensed to pharmaceutical companies. These companies used the patents in developing 34 Food and Drug Administration approved drugs. The patents are classified in the table by the primary IPC technology type, but some patents included multiple technology type classifications.

[d]Other technologies include 24 types of technologies such as food chemistry, optics, civil engineering, and machine tools. The number of patents with these primary technology types ranged from one to 24. This category also included 27 patents missing a primary IPC technology type.

Of the 4,446 U.S. patents obtained by HHS, HHS licensed 94 patents—primarily involving NIH technology—to pharmaceutical companies, which used them in the development of 34 FDA-approved drugs.[44] For additional information on these drugs, see appendix II. USPTO classified 72 of the 94 patents as pharmaceutical technologies, either as the

[44]Thirty-two licenses covered these 94 U.S. patents, as discussed later in this report. This is because licenses are typically for related groups of patents covering the same or similar inventions—also called patent families. Of the 94 patents licensed to pharmaceutical companies which resulted in the development of FDA-approved drugs, 93 were based on inventions in NIH federal labs. The 34 FDA-approved drugs do not include drugs where general scientific research funded by HHS may have contributed to the development of the drug separately from government owned intellectual property.

primary or secondary technology type. The remaining 22 patents licensed to develop drugs were not classified as pharmaceutical technologies, but still had direct application to the development of a drug. According to NIH officials, agency research is typically at the early stages of the drug development process, and related inventions involve substantial uncertainty about whether they will result in FDA-approved products. One researcher we spoke with said that innovation is rare, and there is no accurate way to predict successful inventions from the number of patents.

Patented inventions that contributed to FDA-approved drugs came primarily from a few NIH research institutes. Of the 34 drugs associated with NIH's licensed inventions, the National Cancer Institute provided patented inventions for 21 drugs, and the National Institute of Allergy and Infectious Diseases contributed patented inventions for four.[45] Seven other NIH institutes had patented inventions that contributed to one or more of the 34 FDA-approved drugs.[46] In addition to NIH's patented inventions, FDA contributed a patented invention to one of the 34 drugs.[47] CDC did not identify any patented inventions that contributed directly to an FDA-approved product through licensing.[48] These 34 drugs cover a range of medical uses including vaccines for diseases, such as hepatitis and human papillomavirus, cancer treatments, and antiviral drugs to treat diseases such as HIV.

[45]The National Cancer Institute and National Institute of Allergy and Infectious Diseases are the two largest NIH institutes by appropriations. In some cases, collaborations occurred across NIH research institutes. For example, the National Cancer Institute collaborated with the National Institute of Neurological Disorders and Stroke to design a phase II clinical trial showing that the active ingredient daclizumab was effective in patients with multiple sclerosis.

[46]Technology transfer officials representing institutes that did not contribute to FDA-approved products described several factors that can affect the likelihood that an institute would contribute to an FDA-approved product including how recently the institutes were founded, smaller research budgets, and the research mission of the institute not aligning with technologies that contribute to drugs.

[47]FDA licensed a patented invention to ISIS Pharmaceuticals which contributed to the development of Vitravene, along with separately licensed patented inventions from the National Cancer Institute. FDA officials stated that their research program is primarily focused on regulatory science and does not typically develop inventions that would contribute to drugs.

[48]CDC officials stated that their patent portfolio consists more of public health diagnostics inventions. However, CDC also owns patents on a regimen for use of a drug for pre-exposure prophylaxis in HIV at-risk populations. Those patents were the subject of infringement litigation, as of September 2020.

HHS-patented inventions made different types of contributions to each of the 34 FDA-approved drugs, including providing methods of using drugs, processes for preparing drugs, or the active ingredient. For example, NIH licensed a method of using a drug—darunavir— which was associated with the product Prezista.[49] (The licensee owned patents on the active ingredient.) According to the HHS-owned patent, this method of using the drug reduced the likelihood of drug resistance. In several other cases, HHS patents involved chemical processes used to prepare a drug: for example, a patented invention licensed by NIH to develop Sporanox involved using chemicals to make an antifungal treatment more soluble and thus usable as an oral medication. NIH also licensed substances that provided the active ingredients for biological products, such as vaccine candidates that were developed by pharmaceutical companies into three FDA-approved vaccines: Havrix, Twinrix, and RotaShield.[50]

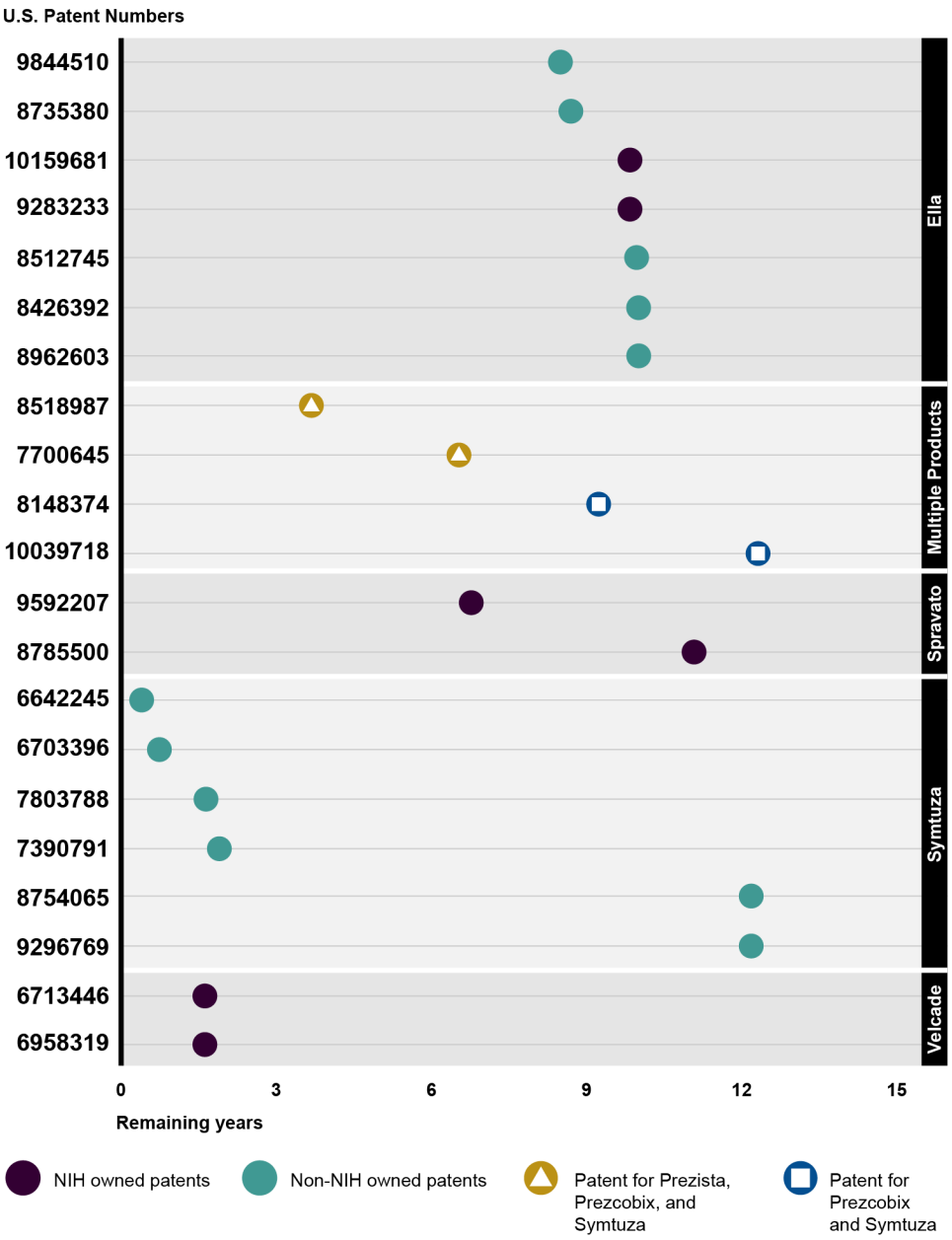
FDA-approved drugs can involve multiple patented inventions, with HHS-owned patents being one part of a portfolio of intellectual property used to commercialize a drug. According to our analysis of FDA's Orange Book patent data, as of June 2020, six of the 34 drugs associated with HHS's licensed inventions had active patents.[51] Each of the six drugs had multiple active patents listed in the Orange Book, which could include patents owned by NIH as well as patents owned by other organizations, such as the licensees (see fig. 3).

[49]Tibotec Therapeutics, which was later acquired by Janssen, owned the original rights to the darunavir compound. Janssen developed combination drugs using darunavir and other compounds which were associated with two other FDA-approved products: Prezcobix and Symtuza.

[50]According to FDA officials, Twinrix is a combination product that incorporates NIH intellectual property used in Havrix as well as the company's proprietary hepatitis B vaccine.

[51]Fifteen of the 34 were small molecule drugs approved through a new drug application and listed in the Orange Book, FDA's database for drugs approved under section 505 of the Food, Drug, and Cosmetics Act. The remaining drugs were approved by FDA under other statutory provisions and would not appear in the Orange Book. For additional information, see app. II. Patents that had expired at the time of our analysis were removed from the Orange Book; thus, this analysis does not represent all patents listed in the Orange Book for a given drug over time, nor does it capture patents of types not eligible for listing in the Orange Book.

Figure 3: Active Patents in FDA's Orange Book for Drugs with Contributions from NIH-Patented Inventions, as of June 2020



Source: GAO analysis of National Institutes of Health (NIH) and Food and Drug Administration (FDA) Orange Book data. | GAO-21-52

Note: FDA's Orange Book does not include expired patents. Several drugs involve additional patents that have expired. For example, the HHS-owned patents associated with a license for Prezista, Prezcobix, and Symtuza have expired and do not appear in the figure. This analysis only includes patents listed in FDA's Orange Book. Certain types of patents are not eligible for listing in the Orange

Book. This figure does not reflect regulatory exclusivities granted by FDA and only reflects expiration dates of patents listed in the Orange Book.

Collaborative research with scientists outside of NIH has led to some of the 94 patented inventions licensed to develop FDA-approved drugs. According to NIH data, 10 of the 34 FDA-approved drugs were jointly invented with researchers outside of HHS intramural programs. NIH officials stated that the vast majority of co-inventions are with universities. In addition, research conducted in CRADAs can lead to NIH-owned or jointly owned inventions. For example, NIH participated in a CRADA with GlaxoSmithKline that developed the vaccine candidate that led to the products Havrix and Twinrix. NIH officials noted that, while CRADAs can lead to inventions, only about 10 percent of agency CRADAs lead to new inventions.[52]

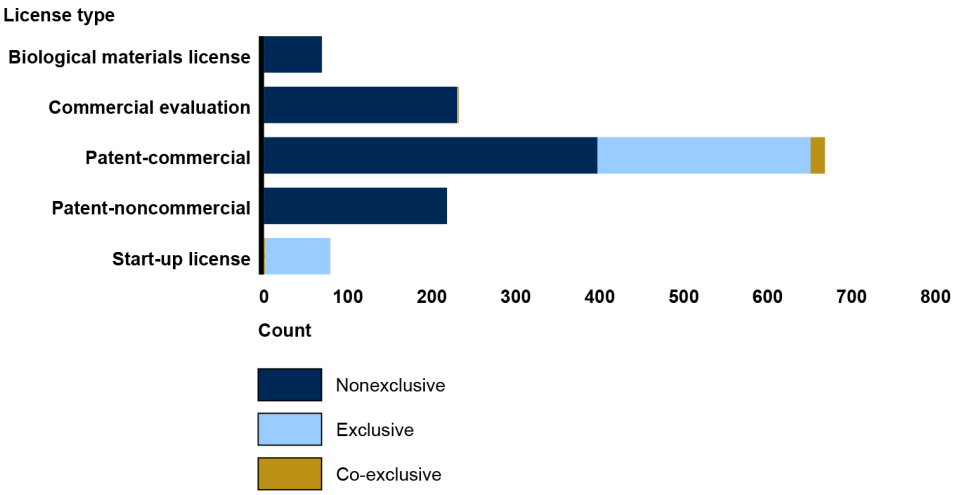
Our analysis of NIH licensing data also found that licenses granted for commercial development accounted for 53 percent of its licenses on inventions patented from 2000 through 2019.[53] Moreover, HHS granted more nonexclusive licenses than exclusive licenses, with exclusive licenses granted primarily for commercial development (see fig. 4).[54] NIH technology transfer officials stated that granting exclusivity can be necessary to incentivize the development of drugs through FDA approval and is the basis for decisions to grant exclusive licenses to agency-owned inventions.

[52]Intellectual property rights can vary based on the provisions of the CRADA agreement and what parties in the CRADA make the discovery. In the event of a joint invention, both the government and the other entity may be eligible for patent rights. That type of situation may also lead to additional agreements to consolidate the management of patent rights among the co-inventors.

[53]This analysis included licenses for patented inventions for commercial use, internal use (17 percent), commercial evaluation of an invention for development (18 percent), biological materials, and licenses to start-up companies.

[54]Licenses may be nonexclusive, partially exclusive, or fully exclusive, and may be limited to some fields of the invention's use or to specific geographic areas. An exclusive license is generally preferable to the private-sector party because it keeps the competition from using the invention. However, federal law establishes certain conditions which must be met to grant exclusivity. 35 U.S.C. § 209(a). In addition, HHS guidance establishes a preference for negotiating nonexclusive or co-exclusive licenses whenever possible.

Figure 4: HHS Licenses for Patented Inventions Granted from 2000 through 2019 by License Type and Exclusivity



Source: GAO analysis of National Institutes of Health (NIH) data. | GAO-21-52

Note: Department of Health and Human Services (HHS) licenses on patented inventions granted from 2000 through 2019 include NIH, Centers for Disease Control and Prevention (CDC), and Food and Drug Administration (FDA) licenses.

Licensing for commercial development of drugs poses challenges, and many inventions are never licensed for development, according to NIH technology transfer officials, who emphasized the risks and uncertainty involved in developing drugs from inventions. Our analysis of NIH licensing data found that from 2000 through 2019, about two-thirds of applications for exclusive licenses for commercial development of patented inventions did not result in a license (496 of 771 applications). Conversely, NIH granted 254 exclusive licenses for commercial development, about one-third of total applications during that period.[55] Representatives from industry associations of drug developers we interviewed stated that companies license technologies from (or acquire) privately held start-up companies more frequently than they license from federal labs. NIH officials noted that the agency may choose to stop making payments to maintain patents for different reasons, such as when

[55]Twenty-one applications were pending at the time of our analysis.

technologies appear unlikely to be licensed, become obsolete, or when federal laboratories discontinue research related to the invention.[56]

Licenses Associated with FDA-Approved Drugs Have Generated the Majority of NIH's Licensing Royalties

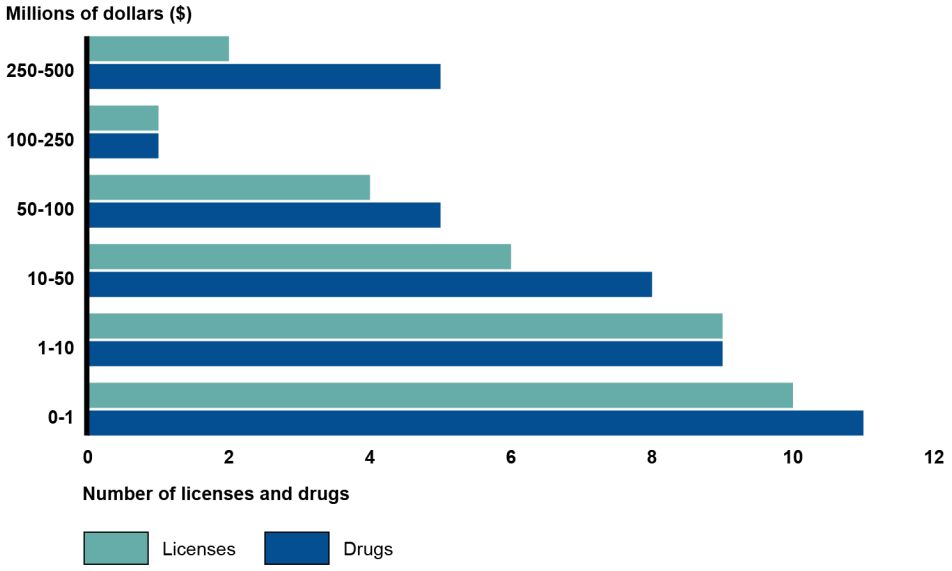
The small number of licenses for patented inventions that are associated with the 34 FDA-approved drugs generated the majority of NIH's licensing royalties since 1991, when the first of these drugs was approved. NIH has granted 32 such licenses, which involved 94 U.S. patents.[57] According to NIH, as of February 2020, these licenses had generated up to $2 billion in royalties, including three licenses that had generated more than $100 million each (see fig. 5). These licenses are associated with five drugs based on National Cancer Institute technologies (Gardasil, Gardasil 9, Prezcobix, Prezista, and Symtuza) and one drug based on National Institute of Allergy and Infectious Diseases technology (Synagis). Because royalties are typically based on sales, some of the licenses' high royalties reflect the commercial success of the drugs associated with these licenses.[58] According to NIH, the royalty rates for these 32 licenses ranged from less than 1 percent to over 10 percent of sales.

[56]Agencies are to pay maintenance fees to USPTO at 3.5, 7.5, and 11.5 years after the date of issue in order to keep the patent in force, with the associated fees increasing over the life of the patent.

[57]One of the 32 licenses involved an FDA patent granted in 1988 (the only non-NIH patent associated with an FDA-approved drug) that expired in 2009.

[58]The sales used to calculate royalties were the manufacturing company's sales of the drugs, not the final costs paid by patients, insurers, or federal programs, according to NIH officials. Several entities are involved with, and pay different prices for, prescription drugs as they move from the manufacturer to the patient. In general, manufacturers develop and sell their drugs to wholesalers, and wholesalers then sell the drugs to pharmacies.

Figure 5: Royalties Generated by NIH Licenses of Patented Inventions Associated with FDA-Approved Drugs, 1991–February 2020



Source: GAO analysis of National Institutes of Health (NIH) data. | GAO-21-52

Note: There are 32 NIH licenses associated with 34 drugs approved by the Food and Drug Administration (FDA). The number of licenses counted in the figure adds up to 32. The number of drugs counted in the figure exceeds 34 because some drugs are associated with more than one license and royalty range.

The commercial success of some of these drugs is reflected in the federal government's spending on them in several federal insurance programs. Our analysis of spending in three federal programs that provide insurance coverage for drugs to eligible beneficiaries—Medicare Part B, Medicare Part D, and Medicaid—identified four drugs that were associated with NIH licensed inventions with annual spending over $100 million in at least one of the three programs in 2018: Prezcobix, Prezista, Synagis, and Velcade.[59] (For additional information on spending in these programs, see app. III.) Prezista and Prezcobix—prescribed to HIV patients who do not respond to other antiviral medications—accounted for about $606 million

[59]Medicare Part B covers drugs typically administered by a physician or under a physician's supervision. Drugs covered under Part B include injectable drugs, some oral cancer drugs, and drugs infused or inhaled through durable medical equipment. Medicare Part D is the voluntary program that provides outpatient prescription drug coverage for Medicare beneficiaries who enroll in Part D drug plans. Medicaid is a joint federal-state health care program for low-income and medically needy individuals.

of Medicare Part D spending in 2018 (see fig. 6).[60] Prezista and Prezcobix were used to treat, respectively, about 23,000 and 18,000 patients enrolled in Medicare Part D in 2018.

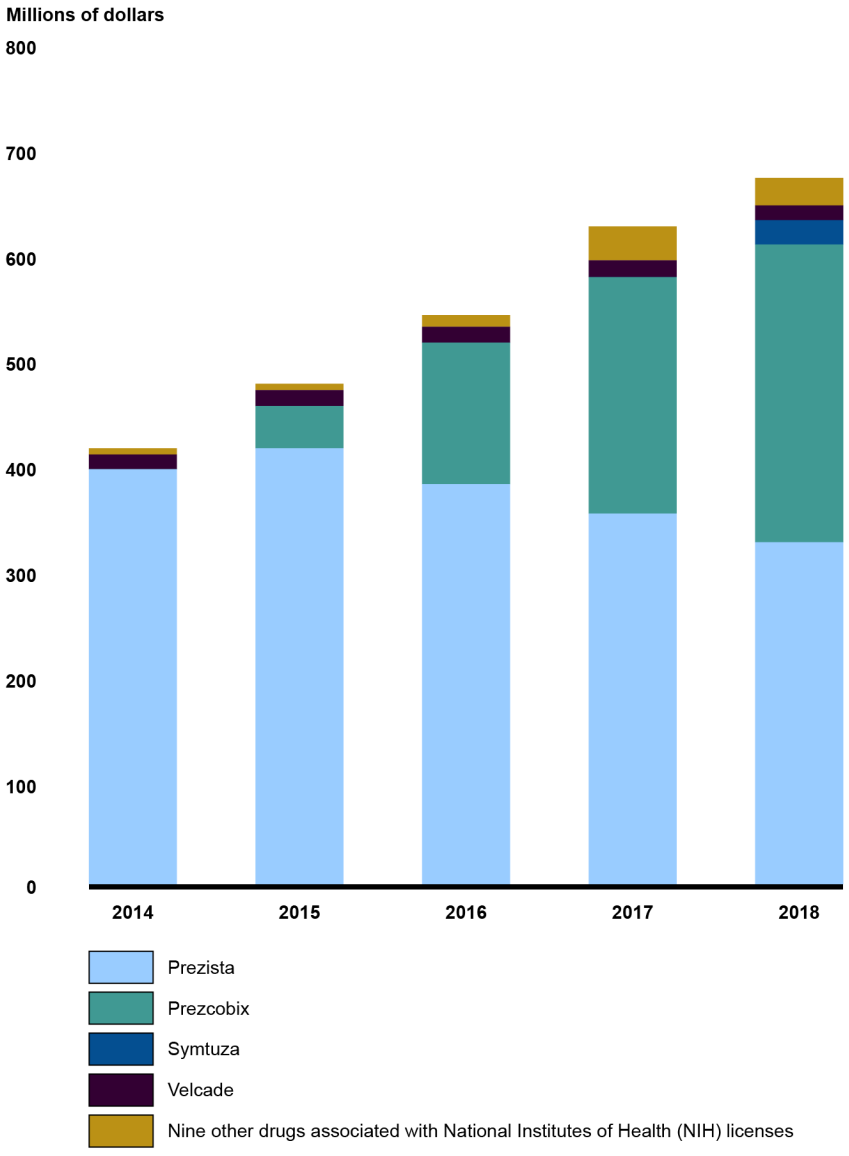
We found that 13 of the 34 drugs had Medicare Part D spending during the period from 2014 through 2018. These 13 brand-name drugs accounted for between $400 and $700 million dollars in Medicare Part D spending annually—about 0.4 percent of all Medicare Part D spending on drugs—from 2014 through 2018.[61] In addition to these 13 drugs, several other of the 34 drugs were commercially successful brand-name drugs before becoming available as generics. For example, the cancer drug Taxol's worldwide sales exceeded $9 billion from 1993 through 2002, covering a period from the year after FDA approval to when generic versions entered the market.[62]

[60]Medicare Part D spending reflects the total amount of expenditures for the prescription claim in the calendar year, including amounts paid by the Medicare Part D plan and beneficiary payments. These totals do not include manufacturer rebates or other price concessions.

[61]Net Medicare Part D spending on retail prescription drugs accounted for approximately $96 billion of $341 billion in total net retail sales of prescription drugs in 2016, approximately one-quarter of spending, according to the Pew Charitable Trusts' analysis of prescription drug spending. Susan K. Urahn et al., *The Prescription Drug Landscape, Explored* (Pew Charitable Trusts, March 2019).

[62]GAO-03-829.

Figure 6: Medicare Part D Expenditures for 13 Brand-Name Drugs Associated with NIH Licensed Patented Inventions, Calendar Years 2014–2018

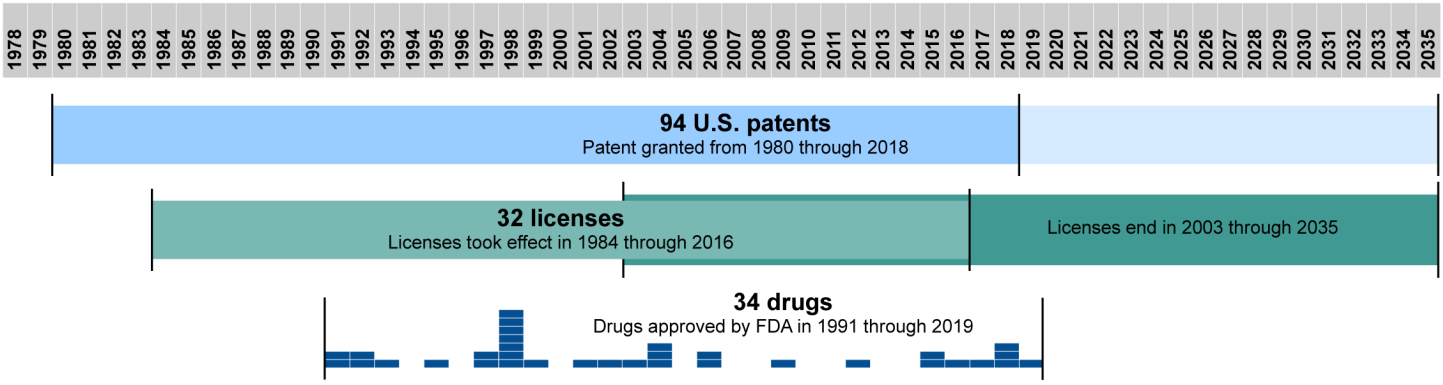


Source: GAO analysis of Centers for Medicare and Medicaid Services Dashboard data. | GAO-21-52

Note: This analysis does not include drugs that were available as generics or were not on the market at any time from 2014 through 2018. Medicare Part D spending reflects the total amount of expenditures for the prescription claim in the calendar year, including amounts paid by the Medicare Part D plan and beneficiary payments. These totals do not include manufacturer rebates or other price concessions.

The 34 drugs were approved by FDA between 1991 and 2019 (see fig. 7). The associated licenses, the first of which took effect in 1984 and the most recent in 2016, are active until the expiration of the last patent covered in the license.[63]

Figure 7: NIH Licenses and U.S. Patents Associated with 34 FDA-Approved Drugs, as of December 2019



Source: GAO analysis of National Institutes of Health (NIH) and United States Patent and Trademark Office (USPTO) data. | GAO-21-52

Note: The number of U.S. patents indicates issued patents and does not include patent applications pending with USPTO. The number of licenses reflects those granted by NIH that are associated with drugs approved by the Food and Drug Administration (FDA). Drugs may be associated with multiple applications for FDA approval and more than one approval (a drug can be initially approved to treat one condition and later another).

The majority of the NIH licenses associated with the FDA-approved drugs (26 of 32) are exclusive licenses on patented inventions.[64] By comparison, our analysis of NIH licensing data found that 72 percent of NIH licenses on patented inventions granted since 2000 were nonexclusive.[65] NIH officials explained that licenses associated with the development of FDA-approved drugs are typically exclusive because exclusive rights to use the inventions make the companies, and the

[63]Thirty-one of the 32 licenses involved patented inventions, and one license was a biological materials license that did not involve a patent.

[64]The 26 exclusive licenses comprise exclusive and co-exclusive licenses, where the license is split among several entities. The remaining six licenses were nonexclusive, including one biological materials license.

[65]The licenses for patented inventions comprise patent commercial licenses, internal use licenses, licenses to start-ups, commercial evaluation licenses, and biological materials licenses associated with patents granted in 2000 through 2019. Our analysis did not include licenses for unpatented inventions, such as research tools.

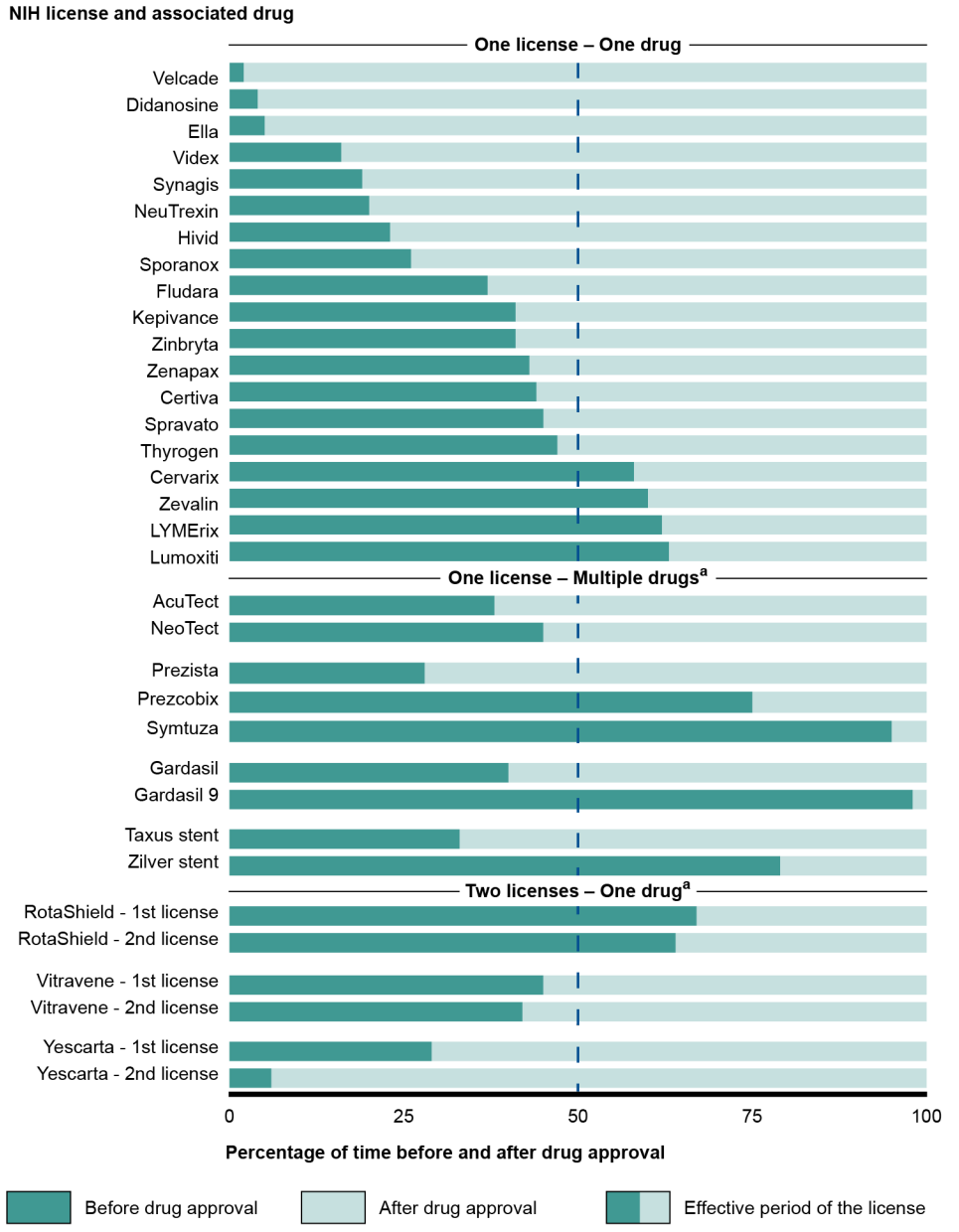
investors these companies work with, more likely to undertake the risks associated with new drug development.

There was variation in the timing of FDA approval during the life of the license for the 34 FDA-approved drugs. According to NIH officials, NIH inventions are typically licensed early in the drug development process, prior to clinical trials, when a substantial amount of additional development is required to get to FDA approval. Our analysis shows that in the case of the licenses associated with these drugs, FDA approval occurred on average 8 years after the licenses took effect, or less than half the time into the effective period of the licenses (see fig. 8). Because these licenses typically remain in effect until the expiration of the last licensed patent, licensees retained rights to use these inventions after FDA approval of the associated drug. Four drugs were approved within 2 years of the licenses taking effect.[66] In addition, two other drugs were approved before the licenses took effect (and are not reflected in fig. 8).[67]

[66]These are Didanosine Delayed-Release Capsules, Ella, Velcade, and Yescarta. The Didanosine Delayed-Release Capsules were the one generic drug among the 34. It is a generic version of the brand-name drug Videx, another of the 34. NIH licensed its inventions to develop the generic version before the patent expired. NIH granted two licenses associated with Yescarta: the first license took effect about 4 years and the second about 1 year before FDA approval.

[67]These are Havrix and Taxol. NIH granted two licenses associated with Havrix: the first license took effect about 10 years before FDA approval and the second about 1 year after FDA approval. Twinrix was developed under the same license as Havrix and is not reflected in fig. 8.

Figure 8: Percentage of the Effective Period before and after FDA Approval for NIH Licenses Associated with FDA-Approved Drugs



Source: GAO analysis of National Institutes of Health (NIH) data. | GAO-21-52

Notes: The effective periods of the 32 licenses ranged from 7 to 31 years. The figure does not reflect three licenses associated with drugs approved by the Food and Drug Administration (FDA) before NIH granted those licenses.

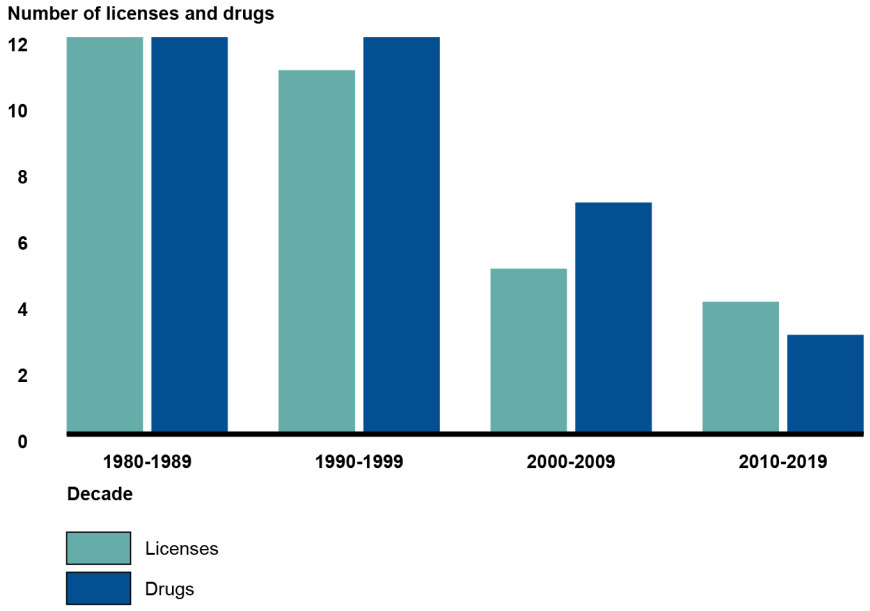
[a]A single license can be associated with multiple products and vice versa.

Our analysis of NIH data for the 32 licenses found that the number of licenses associated with FDA-approved drugs decreased over time (see fig. 9). Generally, NIH files patent applications soon after an invention is made to allow scientists to publish related research findings rather than at a later stage when the technology is more mature and closer to commercialization. This results in an earlier patent expiration date that reduces time for obtaining FDA approval during the term of the patent and the effective period of a license for that patent.[68] NIH officials suggested that a 1995 change in U.S. patent law in how patent terms are calculated reduced in some cases the period of time during which a product could be approved by FDA during the life of the license.[69] In addition, NIH's more recent licenses may involve products in development that may receive FDA approval in the future. NIH does not track the development of additional FDA-approved products that could result from its licensed patented inventions after licenses end. Other factors cited by NIH officials that could explain the decline in the number of the licenses associated with FDA-approved drugs over time include changes in FDA review standards and in the drug industry.

[68]NIH scientists disseminate information on scientific discoveries primarily through publications and presentations, only seeking patent protection when it is necessary for commercial development, according to HHS guidance on technology transfer. HHS policy is to rapidly publish results and not delay publication to patent. NIH officials stated that due to this policy, early publication and patenting means that there may be less time for commercialization under a license.

[69]This change resulted from U.S. obligations under the General Agreement on Tariffs and Trade. See Pub. L. No. 103-465, § 532, 108 Stat. 4984 (1994) (implementing the General Agreement on Tariff and Trade). As a result of this change, patent terms are calculated from the date of patent application filing, rather than the date of patent issuance. Thus, for products with long development times, this change had the potential to reduce the time period during which the patent was active after approval of the product.

Figure 9: NIH Licenses for Patented Inventions Associated with FDA-Approved Drugs, by Decade of Licenses Taking Effect, as of December 2019



Source: GAO analysis of National Institutes of Health (NIH) data. | GAO-21-52

Note: Some Food and Drug Administration (FDA)-approved drugs were associated with multiple licenses taking effect in more than one decade. In these cases, we counted the drug with the oldest license.

Some of NIH's 32 license agreements provided specific provisions related to product pricing or patient access. Six of the 12 licenses associated with FDA-approved products that took effect from 1988 through 1993, had a

reasonable pricing clause.[70] More recently, of the nine licenses that took effect since 2000, four had a patient assistance clause.[71]

Eight of the 32 licenses associated with FDA-approved products were active as of December 2019. They represented 4 percent of the total of 208 NIH licenses for patented inventions that were active at that time.[72] Six of the NIH's eight technology transfer offices told us in March 2020 that they had other licenses that were active or under negotiation that could lead to additional FDA-approved products in the future.

NIH Prioritizes Bringing New Drugs to Market When Licensing Inventions and Publicly Reports Limited Licensing Information

We found that NIH prioritizes the licensee's potential to bring a new drug to market when licensing its intellectual property. NIH does not consider the affordability of drugs that may result from the licensing of its inventions but considers competition implications before granting an exclusive license, which could have an effect on the number of competitors producing a drug and the drug's affordability. However, NIH has not incorporated a competition-related legal provision that is required by the Bayh-Dole Act in its standard commercial license agreements.[73] We also found that information about licensing that NIH makes public is limited to metrics, such as the number of patents and licenses, the Federal Register notices that NIH publishes to meet statutory requirements, and invention marketing information. As a result, the public

[70]An example of a reasonable pricing clause is: "[HHS] has responsibility for funding basic biomedical research, for funding medical treatment through programs such as Medicare and Medicaid, for providing direct medical care and, more generally, for protecting the health and safety of the public. Because of these responsibilities, and the public investment in the research that culminated in the Licensed Patent Rights, [NIH] may require licensee to submit documentation in confidence showing a reasonable relationship between the pricing of a licensed product, the public investment in that product and the health and safety needs of the public. This paragraph shall not restrict the right of licensee to price a Licensed Product or Licensed Process so as to obtain a reasonable profit for its sale or use."

[71]An example of a patient assistance clause is: "Licensee agrees after its first commercial sale, to make reasonable quantities of licensed product(s) or materials produced through its use of licensed processes available on a compassionate use basis to patients, either through the patient's physician(s) and/or the medical center treating the patient."

[72]The 208 active licenses for patented inventions comprise patent commercial licenses, internal use licenses, licenses to start-ups, commercial evaluation licenses, and biological materials licenses associated with patents issued in 2000 through 2019. Our analysis did not include licenses for unpatented inventions, such as research tools, or pending patent applications.

[73]35 U.S.C. § 209(d)(3)(D).

has little information about NIH's licensing to allow for an evaluation of its impact on patient access to resulting drugs.

NIH Prioritizes Bringing Drugs to Market without Considering Drug Affordability

NIH Prioritizes the Commercial Development of New Drugs

When NIH licenses its patented inventions, officials said it prioritizes the potential for commercial development of what is typically an early-stage technology into a medical product that would be available to the American public on the market. In evaluating an application for a license, NIH considers a company's technical expertise, ability to raise capital, market analysis, as well as research, development, and marketing plan to determine the company's potential to develop a medical product that will be approved by FDA. NIH officials stated that the public interest is served best when commercial entities develop the medical knowledge transferred from NIH laboratories into medical products.[74]

According to NIH officials, the agency's technology transfer offices do not consider the price or affordability of a drug based on the agency's intellectual property for several reasons:

- **Emphasis on practical application.** The prioritization of the commercial development of inventions made at federal labs is captured in the definition of "practical application" in the Bayh-Dole Act and is consistent with its interpretation across the federal government, according to agency officials. Officials at NIST, the agency responsible for developing the federal regulations based on the Bayh-Dole Act, stated that NIST's prior analysis supports the conclusion that "reasonable terms" in the regulations' definition of

[74]In its strategic plan, NIH defines the agency's central mission as seeking "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"; see National Institutes of Health, *NIH-wide Strategic Plan Fiscal Years 2016-2020: Turning Discovery Into Health* (Dec. 16, 2015). NIH's Office of Technology Transfer describes its role as supporting that mission by transferring medical knowledge from NIH laboratories to other organizations for the purpose of developing that knowledge into medical products. According to NIH's most recent technology transfer report, "the full potential of [NIH] inventions would not be realized, and the public would not receive the full benefit of these biomedical discoveries" without technology transfer; see National Institutes of Health, *NIH Technology Transfer Annual Report FY2019*.

practical application refers to incentives for public-private collaboration and not to considerations of affordability or price (see text box).[75] NIH officials stated that performance milestones in the license agreement enable NIH to terminate the license if a licensee does not make reasonable progress toward practical application. Officials at NIH expressed a concern that attaching price-related conditions to licenses would deter companies from licensing government-owned intellectual property and deter innovation. Representatives from one drug industry association we interviewed confirmed that such conditions would make it riskier for companies to license intellectual property from NIH, but that each company would make its own calculation of the risk and reward.

Debate about the Meaning of "Reasonable Terms" in the Bayh-Dole Act

The concept of "reasonable terms" is included in the definition of practical application in the federal regulations for the Bayh-Dole Act that are used in the licensing of government-owned intellectual property. The definition states that practical application means, among other things, "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." 37 C.F.R. § 404.3(d). According to officials at the National Institute of Standards and Technology, the agency responsible for writing the regulations, and the National Institutes of Health (NIH), "reasonable terms" does not include price.

Scholars and public interest advocates working in the areas of intellectual property and public health have raised concerns about the high prices of drugs in the United States, including drugs that result from NIH inventions and other NIH contributions. Some of them say that "available to the public on reasonable terms" in the definition of practical application means that NIH must consider the price of the resulting product when licensing its intellectual property. Others suggest that the intended meaning of "available to the public on reasonable terms" in the Bayh-Dole Act is subject to debate, particularly over who is considered "the public" (e.g., the licensee, the payer, the end user) and whether the plain meaning of "reasonable terms" is apparent and includes pricing.[a]

Source: GAO. | GAO-21-52

[a]For a summary of key arguments, see National Academies of Sciences, Engineering, and Medicine, *The Role of NIH in Drug Development Innovation and Its Impact on Patient Access: Proceedings of a Workshop* (Washington, D.C.: The National Academies Press, 2019). https://doi.org/10.17226/25591.

- **Lack of mandate and expertise.** NIH's current position is consistent with the agency's 2004 report to Congress stating that NIH did not have the mandate or authority to be the arbiter of drug affordability.[76]

[75]NIST officials directed us to a 2002 public letter from Birch Bayh and Bob Dole written after they left the Senate. In the letter, they stated that the law, enacted in 1980, had not intended for the government to determine price. Birch Bayh and Bob Dole, "Our Law Helps Patients Get New Drugs Sooner," letter to the *Washington Post* (Apr. 11, 2002).

[76]National Institutes of Health, Department of Health and Human Services, *Report to Congress on Affordability of Inventions and Products* (July 2004).

NIH officials also told us that consideration of affordability is outside the scope of technology transfer activities and that NIH technology transfer offices and NIH more broadly lack expertise to determine reasonable price provisions.[77]

- **Most licensed inventions are licensed at an early stage.** NIH officials told us that most NIH-patented inventions are licensed at an early, preclinical, stage, and are therefore typically years away from being developed into a drug. In addition, few licenses lead to the commercial development of an FDA-approved drug. Therefore, consideration of affordability of the final product that may result from a license is not only difficult but is also irrelevant for the majority of licenses granted by NIH. Generally, according to NIH officials, they negotiate license terms and sign agreements with licensees at a stage when there is little certainty whether the licensed inventions may lead to a drug that gains FDA approval and is commercially successful during the lifetime of the license.

In addition, NIH officials told us, the odds of finding a company interested in licensing an NIH technology are low to begin with. The situation is similar for universities, which often have few license applicants for their inventions, putting them in a weaker negotiation position, according to a representative from a university technology transfer organization we interviewed. According to NIH officials, NIH makes a strong effort to ensure that the license application results in a license because this could be the agency's only chance to set that invention on a path to commercialization.[78]

NIH Considers Competition Before Granting Some Exclusive Licenses

While NIH does not consider the affordability of drugs that may result from the licensing of its inventions, the agency does consider whether to grant an exclusive license, which would have an effect on the number of competitors producing a drug and ultimately affordability.[79] Federal law

[77]Some scholars who argue in favor of a new reasonable pricing clause suggested that a different agency at HHS could take on that responsibility. See, for example, National Academies, *The Role of NIH in Drug Development Innovation*.

[78]NIH officials explained that because maintaining patents is costly, they expect the licensees to take over those costs and that NIH abandons patents for which the likelihood of licensing does not justify the costs. In our analysis of HHS U.S. patents granted from 2000 through 2019, we found that HHS abandoned 26 percent of these patents.

[79]Although federal technology transfer favors nonexclusive licensing, and most licenses granted by NIH are nonexclusive, exclusive licensing is more common in cases where NIH intellectual property leads to drugs and vaccines, according to NIH officials.

requires NIH to consider whether granting an exclusive license would "tend substantially to lessen competition or create or maintain a violation of the Federal antitrust laws."[80] Vigorous competition among sellers in an open marketplace gives the American public the benefits of lower prices, higher quality products and services, more choices, and greater innovation, according to FTC guidance.[81]

As part of the evaluation of applications for exclusive licenses (see text box), a technology transfer office prepares a preliminary determination of suitability memorandum, which contains a description of the technology and disease, market assessment of the need associated with the disease, overview of the company's potential to commercialize the technology, and how the application meets the criteria for exclusive licensing. These memoranda are typically reviewed by the Exclusive License Consultation Group—an NIH-wide body that manages exclusive licensing and includes CDC and FDA officials—before the technology transfer office submits a notice of intent to grant an exclusive license for publication in the Federal Register.[82]

NIH Criteria for Evaluating Exclusive License Applications

Based on statutory requirements (35 U.S.C. § 209(a)), before granting an exclusive license, NIH must determine, among other things, that

1. exclusive licensing serves the best interests of the public;
2. an exclusive or partially exclusive license is a reasonable and necessary incentive to promote the investment of risk capital to bring the invention to practical application;
3. exclusive license terms and conditions are not broader than necessary; and
4. exclusive licensing will not lessen competition.

Source: GAO presentation of National Institutes of Health (NIH) information. | GAO-21-52

In addition, according to NIH officials, they address competition concerns when negotiating field of use provisions for exclusive licenses. A field of use provision limits the licensee's rights to use the licensed technology to specified applications and provides NIH, as the licensor, greater control over the use of its intellectual property. As licensor, NIH can set a general or very specific field of use. NIH officials stated that when negotiating

[80]35 U.S.C. § 209(a)(4) and 37 C.F.R. § 404.7(iii).

[81]U.S. Federal Trade Commission, *Guide to Antitrust Laws*. Available online at: https://www.ftc.gov/tips-advice/competition-guidance/guide-antitrust-laws.

[82]The statute requires NIH to publish a notice of intent to grant an exclusive license for some exclusive licenses. 35 U.S.C. § 209(e).

licenses they generally seek a field of use that is not greater than what a company needs to develop a product under a license and that would allow NIH to separately license the same technology for different uses, conditions, or combinations with other products, which minimizes detriment to competition.[83]

NIH technology transfer officials told us that they do not consider competition after the license agreement has been signed and did not know about an FTC complaint that a company had engaged in anticompetitive behavior while holding an NIH license. The license was granted to Bristol-Myers Squibb to explore new methods of using the cancer drug Taxol, which was initially approved by FDA to treat ovarian cancer. In 2003, while Bristol-Myers Squibb was holding this exclusive license, FTC found that the company had engaged in anticompetitive behavior that delayed the entry of a generic drug capable of competing with Bristol-Myers Squibb's lucrative monopoly on Taxol.[84] The drug had become the best-selling brand-name cancer drug by 2001.

When we asked NIH officials about FTC's 2003 Taxol-related complaint against Bristol-Myers Squibb (see text box), they stated that they did not know about it and that they do not track FTC complaints. According to them, the company's behavior, as characterized in the FTC complaint, would not be concerning to NIH's Office of Technology Transfer as long as Bristol-Myers Squibb was complying with the terms of its NIH license. NIH officials stated that review of competition issues is the responsibility of agencies with authority to enforce competition law, such as DOJ and FTC.

[83]NIH officials explained that NIH avoids granting an exclusive license to a company that already has a related or potentially competing product to the NIH technology, which reduces the risk that the company would "shelve" the licensed technology and potentially increases competition.

[84]U.S. Federal Trade Commission, Complaint in the Matter of Bristol-Myers Squibb, Docket No. C-4076, Apr. 14, 2003. See also *Overview of FTC Actions in Pharmaceutical Products and Distribution* (Washington, D.C.: September 2019). The FTC complaint was not covered in GAO-03-829.

The Taxol Case

In October 1996, the National Institutes of Health (NIH) granted an exclusive license to pharmaceutical company Bristol-Myers Squibb (BMS) on three NIH patents related to cancer drug paclitaxel, known at the time under its brand-name Taxol. The Food and Drug Administration (FDA) approved Taxol to treat advanced ovarian cancer in 1992.

The license represented a continuation of a prior NIH-BMS collaboration, which provided the company with research results that enabled paclitaxel to be commercialized as Taxol and made available as a treatment—initially for ovarian cancer patients, and later for other cancer patients. In 1991, NIH and BMS signed a cooperative research and development agreement (CRADA), and, during the first 2 years of the CRADA, NIH conducted most of the clinical trials associated with paclitaxel. The results of NIH's clinical trials were critical for BMS to secure FDA's initial approval in 1992 to market Taxol for the treatment of advanced ovarian cancer. As a CRADA partner, BMS had an option to apply for an exclusive license on related inventions from NIH. NIH did not have a patent on paclitaxel.

The three patents that BMS licensed from NIH resulted from the CRADA and were for new methods of using paclitaxel in cancer treatment. The license was in effect from October 1996 through September 2013. BMS officials previously told GAO that BMS did not use these inventions in any of BMS's applications to FDA to expand the approved uses of Taxol (GAO-03-829).

In 2003, while the license was in effect, BMS was found by the Federal Trade Commission (FTC) to have engaged in a pattern of anticompetitive activity over a decade in order to delay generic competition and maintain its monopoly over three highly profitable branded drugs, including Taxol, with total net annual sales of $2 billion. The conduct described by FTC included BMS entering into an unlawful agreement with a generic competitor in order to obtain an additional 30-month stay on FDA approval of a generic equivalent to Taxol. According to FTC's complaint, BMS acted in a predatory fashion to forestall competitive threats and knew that generic entry would decimate its sales, and that any delay in such entry would be highly profitable for BMS but very costly for consumers. FTC stated that as a result of BMS's illegal conduct, consumers paid hundreds of millions of dollars in additional costs for these drugs. By 2001, Taxol had become the best-selling cancer drug in history, and worldwide sales of Taxol had totaled $9 billion through 2002 (GAO-03-829).

Source: GAO, *Technology Transfer: NIH-Private Sector Partnership in the Development of Taxol*, GAO-03-829 (Washington, D.C.: June 4, 2003) and U.S. Federal Trade Commission, Complaint in the Matter of Bristol-Myers Squibb, Docket No. C-4076 (Apr. 14, 2003). | GAO-21-52

Standard License Agreements Do Not Include a Requisite Competition-Related Provision

During our review, we found that NIH has not incorporated into its standard commercial license agreements a competition-related provision that is required by statute.[85] This provision, which was added to the statute in 2000, would empower NIH to terminate the license in whole or in part if NIH determines that the licensee has been found by a court of

[85]35 U.S.C. § 209(d)(3)(D); 37 C.F.R § 404.5(b)(8)(v).

competent jurisdiction to have violated the federal antitrust laws in connection with its performance under the license agreement.[86]

NIH's standard commercial license agreements do not include this requisite provision. In our analysis of the nine licenses associated with FDA-approved products that were granted after 2000, we found that none included the provision. NIH officials acknowledged that this provision was required and that NIH should have updated its standard license agreements following the change to the statute. They noted, however, that even if this provision were included, its scope would not extend to a finding of anticompetitive behavior by FTC, such as the 2003 FTC complaint against Bristol-Myers Squibb related to Taxol, because the statute specifies that the finding must be by a court of competent jurisdiction. Nonetheless, incorporating this requisite provision would be important for cases where a court of competent jurisdiction finds that a licensee has engaged in anticompetitive behavior and would provide NIH with a stronger tool for addressing such behavior.[87]

According to NIH officials, in response to our review the agency is taking steps to add this provision to its standard license agreements. Specifically, NIH officials stated that new exclusive and partially exclusive licenses would have a provision consistent with the statutory requirement beginning on October 8, 2020. The Public Health Service Technology Transfer Policy Board will be asked to formally approve exclusive and partially exclusive standard license agreements with the new provision at its next meeting. Taking steps to ensure that the standard commercial license agreements contain sufficient information about the terms required by statute—including certain actions that can lead to termination of the licenses—can help reduce the risk that licensees of government-

[86]Officials at NIST, the agency responsible for developing the federal regulations based on the Bayh-Dole Act, stated that this provision would apply to exclusive and nonexclusive licenses. While the statute applies to licenses with different degrees of exclusivity, an exclusive license can raise antitrust concerns under certain conditions, whereas a nonexclusive license generally does not present such concerns, according to FTC and DOJ guidelines. Department of Justice and U.S. Federal Trade Commission, *Antitrust Guidelines for the Licensing of Intellectual Property* (January 2017).

[87]NIH officials explained that adding this provision would not involve monitoring by NIH of decisions by courts of competent jurisdiction for two reasons. First, such a monitoring would require human resources that NIH's technology transfer offices lack. Second, it is not necessary because a licensee found by a court of competent jurisdiction to have violated the federal antitrust laws in connection with its performance under the license agreement would be required by the court to report the violation to NIH.

owned intellectual property will engage in anticompetitive behavior. Such behavior can lessen the benefits of technology transfer to the public. For example, we have previously reported that less competition in a relevant market is associated with higher drug prices and can negatively affect innovation.[88]

NIH Makes Limited Licensing Information Available to the Public

NIH Is Required by Statute to Report Some Licensing Metrics and Information

Consistent with statutory requirements, NIST reports annually on technology transfer activities across the federal government.[89] Its most recent annual report provided metrics for licensing and other technology transfer activities during fiscal year 2016 at 11 federal agencies, including HHS (see table 2).[90] In addition to providing data to NIST for its required annual report, NIH reports similar aggregate metrics online, including for more recent years not covered in the NIST annual report.[91]

Table 2: Federal Technology Transfer Metrics Reported by NIST for Fiscal Year 2016

Metric	Unit	HHS metrics[a]
Licensing metrics		
Licenses, total active	Number	1,750
New licenses		278
Invention licenses, total active[b]	Number	1,721
New invention licenses		221
Income-bearing licenses, total active	Number	837

[88]GAO, *Drug Industry: Profits, Research and Development Spending, and Merger and Acquisition Deals*, GAO-18-40 (Washington, D.C.: Nov. 17, 2017).

[89]Pub. L. No. 106-404, § 10(a)(3), 114 Stat. 1742, 1748 (amending Pub. L. No. 96-480, § 11 and codified at 15 U.S.C. § 3710(g)(2)). This law required Commerce to report to Congress on technology transfer activities, a function delegated to NIST in 2007.

[90]National Institute of Standards and Technology, *Federal Laboratory Technology Transfer Fiscal Year 2016: Summary Report to the President and the Congress* (September 2019). For HHS, NIST reported on technology transfer activities conducted by NIH, CDC, and FDA. The other 10 agencies were the Departments of Agriculture, Commerce, Defense, Energy, Homeland Security, the Interior, Transportation, and Veteran Affairs; the Environmental Protection Agency; and the National Aeronautics and Space Administration.

[91]As of September 1, 2020, technology transfer metrics published by NIH online at https://www.ott.nih.gov/reportsstats/ott-statistics covered fiscal years 1995 through 2019.

Metric	Unit	HHS metrics[a]
Income-bearing exclusive licenses	Number	23
Total income, all active licenses	Dollars	$ 133 million
Invention licenses		$ 131 million
Total earned royalty income	Dollars	$ 110 million
Patenting metrics		
New inventions disclosed	Number	320
Patent applications filed	Number	269
Patents issued	Number	579
Other metrics		
Cooperative research and development agreements (CRADAs), total active	Number	590
New CRADAs		134
Traditional CRADAs, total active	Number	391
Other collaborative research and development relationships	Number	147

Source: GAO presentation of information from the "Federal Laboratory Technology Transfer: Fiscal Year 2016" report by the National Institute of Standards and Technology (NIST). | GAO-21-52

Note: The NIST report for fiscal year 2016 is the most recent available annual report as of September 2020.

[a]The Department of Health and Human Services (HHS) metrics reflect information for the National Institutes of Health, Centers for Disease Control and Prevention, and the Food and Drug Administration.

[b]Invention licenses are licenses for patented inventions.

Although the aggregate metrics measuring outputs are useful—for example, for understanding the overall level of patenting and licensing activities by agency over time—they do not allow either the agencies themselves or external observers to measure and analyze the impact of technology transfer activities. As an example, using these metrics would not allow the public to conduct a data-driven analysis of differences between technologies and patent portfolios that are more and less likely to be licensed or compare how exclusive and nonexclusive licensing affects patient access to the resulting drugs. A recent effort led by NIST to identify and promote approaches to enhance U.S. innovation concluded

that the existing metrics used by federal agencies are inadequate for evaluating the impact of federal technology transfer.[92]

In addition, NIH is required by the Bayh-Dole Act to publish notices of intent to grant exclusive licenses, except as otherwise specified in the statute.[93] The notices published by NIH and other HHS agencies in the Federal Register may identify the name of a company or companies applying for an exclusive license, inventions or patents associated with those inventions, and field of use of the proposed license.[94] However, the public does not receive notice of the majority of licenses that NIH considers granting and does not know what companies hold those that are granted. This is because there is no statutory requirement to publish notice for the most common type of license granted, nonexclusive licenses. Moreover, exclusive licenses granted under CRADAs are exempt from the Bayh-Dole Act requirement to publish notices for exclusive licenses.

NIH Makes Some Information Public to Market Inventions for Licensing

NIH maintains a website of marketing abstracts for inventions that are available for licensing, including those for which USPTO has issued a patent or is examining a patent application.[95] As of September 2020, the website listed more than 1,600 marketing abstracts for patented and unpatented technologies that were available for licensing.[96] Some of these technologies go back decades, and NIH continues to market them on the website as long as they are deemed viable candidates for licensing. The marketing abstract for a technology does not mention if the

[92]The specific finding based on consultations with government and external stakeholders was that "current metrics to capture, assess, and improve the broad technology transfer outcomes and impacts of federally funded R&D as well as operational processes underpinning technology transfer within the context of benchmarking with global science and technology trends and metrics are inadequate." See Department of Commerce, National Institute of Standards and Technology, *Return on Investment Initiative Final Green Paper: Unleashing American Innovation*, NIST Special Publication 1234 (April 2019).

[93]35 U.S.C. § 209(e).

[94]Our analysis of Federal Register notices shows that during the 20-year period from 2000 through 2019, NIH published 534 notices of intent to grant an exclusive license and CDC published 24, a combined average of 28 per year.

[95]See https://www.ott.nih.gov/opportunities.

[96]The information about NIH licensing opportunities published on the website is also available in the public FLC Business database maintained by the Federal Laboratory Consortium for Technology Transfer. See https://federallabs.org/flcbusiness.

technology has already been licensed. Moreover, NIH officials told us that the website is not a comprehensive source of information about NIH inventions available for licensing.[97] These limitations make the website less useful to researchers and members of the public who may want to gather information about the overall portfolio of technologies that are actively licensed or compare them to technologies that are available for licensing but have not been licensed.

NIH also publishes its own annual technology transfer report, which, as NIH officials told us, is used for marketing purposes.[98] The bulk of the most recent report, for fiscal year 2019, showcased inventions at several research institutes, described marketing outreach activities, and provided examples of collaborations, awards, and publications.[99]

NIH Does Not Publicly Report Enough Information about Licensing to Allow Evaluation of Its Impact

NIH makes some general information on inventions and licensing publicly available: in addition to the information described above, NIH provides standard license agreements and a description of the licensing process on its website.[100] However, the public has little information about NIH's licensing to allow for an evaluation of its impact on public health.[101] As we have reported in the past, federal laws generally prohibit agencies from disclosing information that concerns or relates to trade secrets, processes, operations, statistical information, and related information.[102] Therefore, aspects of the federal technology transfer process that NIH engages in with the private sector may not be disclosed to the general public. Similarly, the details of the negotiations and agreements that NIH

[97]According to NIH officials, scientific publications and conference presentations by NIH scientists may be more important sources of information about new inventions. Published patent applications and issued patents, which are generally public, also contain such information.

[98]An archive of NIH's past annual technology transfer reports is available at https://www.ott.nih.gov/reportsstats/annual-reports.

[99]National Institutes of Health, *NIH Technology Transfer: Annual Report FY2019*. The NIH report includes several output metrics, such as numbers of exclusive and nonexclusive licenses for fiscal years 2006 through 2018 that are not published in the NIST annual technology transfer report.

[100]See https://www.ott.nih.gov.

[101]For example, NIH's strategic plan does not mention technology transfer, of which licensing is an important element, or explain how technology transfer contributes to NIH's stewardship of public investment in biomedical research; see National Institutes of Health, *NIH-Wide Strategic Plan Fiscal Years 2016-2020*.

[102]GAO-03-829.

makes with industry partners may not be disclosed. However, those laws do not protect other information about NIH's licensing activities from public disclosure.

Examples of licensing information NIH does not provide to the public include:

- NIH published online the list of the 34 FDA-approved products associated with the licenses of NIH intellectual property, but it has not provided information on what NIH inventions or patents were licensed for each drug or the number of licenses associated with each drug.
- More broadly, NIH does not provide information on what technologies—and patents associated with them—have been licensed in a given year or on what companies hold NIH licenses.
- NIH does not report on how many of the licenses it grants originate from CRADAs.

Moreover, information available in the public domain—such as the data for patents owned by HHS, which we analyzed and cited earlier in this report—is not accessible without considerable expertise and effort, according to knowledgeable experts we interviewed.[103] The lack of such information and of access to it in a user-friendly, searchable, and machine-readable format impedes the public's and policymakers' ability to understand and evaluate the nature, significance, and impact of publicly owned inventions on the development of drugs and other biomedical products. Although patents and related data on patent owners and types of patented technology are public, linkages between patents and products are not. For example, inventions of active ingredients, which provide the foundation for the discovery and development of new drugs, are more likely to be associated with strong patents that are appealing to potential licensees than inventions of chemical processes for manufacturing a drug. Our analysis of the 94 U.S. patents that were licensed by NIH for

[103]As a recent government report found, the lack of a searchable database for federal technology transfer activities is not unique to HHS. Specifically, "a modern, secure, and interoperable platform that is easy to access, analyze, and use is not available for reporting data on intellectual property resulting from extramural and intramural [federal research and development government-wide]"; see NIST, *Return on Investment Initiative*.

Moreover, we used publicly available USPTO data from the PatentsView database to conduct an independent search for patents owned by HHS. Our review matched 2,760 of these patents to 3,096 patents listed in data provided to us by NIH, leaving a total of 336 HHS-owned patents not identifiable in the publicly available data. For more information, see appendix I. Our data set of HHS-owned patents can be accessed on our website at https://www.gao.gov/products/GAO-21-52.

the development of the 34 FDA-approved drugs shows that 45 of these patents involved an invention related to an active ingredient of a drug whereas 47 were related to a method of using or producing a drug. Information of this kind is necessary for a better understanding of NIH's role in drug development and, more broadly, of the impact of various facets of NIH's management of its intellectual property on public health.

Greater transparency about licenses that originate from NIH CRADAs with pharmaceutical companies and other nongovernmental entities could also increase accountability. We found that licenses associated with at least seven of the 34 FDA-approved drugs grew out of CRADAs, including Taxol and two recently approved drugs.[104] In addition, university technology transfer representatives and a pharmaceutical company representative we interviewed noted that drug development research is becoming increasingly collaborative. While NIH officials told us that such licenses are uncommon, there is a public benefit in knowing, at a minimum, how many of them there are, and in what ways the inventions associated with them are similar to or different from those in other licenses granted by NIH.

NIH officials cited two main reasons for the current level of licensing information that is made public. First, as noted earlier, they cited legal constraints on public disclosure of commercial confidential and other privileged information. However, the examples above illustrate that NIH can provide more information while adhering to these constraints.[105] In addition, if NIH were to develop a searchable public database of licensing and related patenting activities, the agency could employ data techniques

[104]The seven drugs are Ella, Havrix, Taxol, Twinrix, Thyrogen, Velcade, and Yescarta. See table 6 in app. II for their years of FDA approval.

[105]Some legal scholars argue that the pharmaceutical industry has adopted overly broad claims of what information constitutes a trade secret, including information about drug prices. According to them, trade secret law is not merely a contest of private commercial interests but should instead be embedded in the broader consideration of key societal interests; see Robin Feldman and Charles Tate Graves, "Naked Price and Pharmaceutical Trade Secret Overreach," *Yale Journal of Law and Technology*, vol. 22, no. 61 (2020). One scholar we interviewed told us that licensing information that NIH does not make routinely transparent (such as royalty rates, geographical limitations on licensing, and other conditions) is likely well known among those in the field. As a result, this scholar suggested, the lack of transparency mostly serves to deny the general public, public interest groups, and researchers information that is necessary for evaluating such issues as fair returns on publicly funded innovation.

and methods to anonymize and redact commercial confidential information.

Second, NIH officials stated that providing additional information about licensing and related patenting activities would involve a significant effort that would further strain the agency's technology transfer resources. While increasing the quantity, quality, and granularity of information would likely increase some costs, it could reduce other costs. One example is the cost of resources NIH dedicates to reviewing requests submitted under the Freedom of Information Act by members of the public, who may seek information about licensing that NIH does not make publicly available.[106] It is possible that this cost could decrease if NIH were to put more and better quality information in the public domain. It is also possible that providing such information in a user-friendly format could benefit NIH's marketing outreach to start-ups and other companies unfamiliar with federal technology transfer by improving their understanding of it.[107] In this way, increased transparency could be beneficial to innovation as well as accountability.

One of the principles of federal internal control is that management of a federal government entity should externally communicate quality information to an audience that encompasses the President, Congress, and the general public.[108] According to this principle, federal program managers should communicate quality information so that external parties

[106]According to HHS, in fiscal year 2019 NIH processed 1,686 Freedom of Information Act (5 U.S.C. § 552) requests and dedicated more than 37 full-time staff and almost $5 million to processing and related litigation. Department of Health and Human Services, *HHS Fiscal Year 2019 Freedom of Information Annual Report*, available at https://www.hhs.gov/foia/reports/annual-reports/2019/index.html. We did not analyze the extent to which information related to NIH's management of its intellectual property accounts for the number of FOIA requests and corresponding resources to process them.

[107]Although federal technology transfer has been in place for about 40 years, it continues to be hampered by low demand and low levels of knowledge about it in the private sector, according to NIST officials. One knowledgeable stakeholder told us that companies generally struggle to find or understand the information related to federal technology transfer opportunities, including licensing. We addressed the need for better communication of federal technology transfer to potential customers, including small businesses and entrepreneurs in prior work; see GAO, *Technology Transfer: Federal Laboratory Consortium Should Increase Communication with Potential Customers to Improve Initiatives*, GAO-15-127 (Washington, D.C.: Oct. 3, 2014). According to a more recent government report about federal technology transfer, companies value consistent, discoverable, and easily accessible information; see NIST, *Return on Investment Initiative*.

[108]GAO, *Standards for Internal Control in the Federal Government*, GAO-14-704G (Washington, D.C.: September 2014).

can help the government achieve its objectives and address related risks. Federal program managers are expected to periodically evaluate methods of communication so that the organization has the appropriate tools for timely external reporting. Consistent with the internal control standards, increasing the transparency of NIH's licensing decisions and activities would improve the taxpayers' and policymakers' understanding of how the management of NIH's intellectual property supports its mission to improve the nation's health. The level of information that NIH publicly reports at present does not allow researchers or members of the public to evaluate the effectiveness of licensing, an important element of NIH's broader intellectual property management practices. Opportunities exist for NIH to improve accountability by increasing the transparency of its licensing activities and demonstrating how they advance the public interest.

HHS Monitors for Potential Infringement and May Take Several Actions to Protect Its Intellectual Property Rights

HHS protects its intellectual property by monitoring for unauthorized use of its inventions (infringement) and by taking steps to enforce its rights. From 2016 through 2019, HHS relied primarily on inventors at its labs to monitor for potential infringement. When aware of infringement, HHS generally encourages potential infringers to take a license for the infringed inventions and, if matters proceed to litigation, relies on DOJ to enforce its rights. For exclusively licensed inventions, HHS grants licensees the power of enforcement. From 2009 through 2019, HHS coordinated with DOJ on 24 cases involving its intellectual property, primarily acting to defend its intellectual property against challenges in the United States and abroad.

HHS Relies Primarily on Inventors at Its Federal Labs to Monitor for Potential Infringement

HHS relies primarily on inventors to detect and report potential infringement, but can learn about infringement from other sources (see table 3). Inventors at NIH and CDC federal labs can identify potential infringement through scientific channels, such as conferences, meetings, and publications. However, NIH Office of Technology Transfer officials stated that determining whether agency intellectual property is being infringed is a legal determination and is not the responsibility of inventors. These types of potential infringement typically involve research materials or tools, according to NIH Office of Technology Transfer officials. For example, in fiscal year 2017, an inventor reported to the NIH Office of

Technology Transfer that a company was potentially infringing intellectual property related to antibodies for cancer immunology research.[109]

FDA has not received a report of potential infringement since assuming responsibility for monitoring for infringement of its intellectual property, but stated that such reports would most likely come from an inventor.[110] FDA officials stated that FDA's portfolio of intellectual property consists primarily of methods and process improvements related to regulatory science, which makes detecting potential infringement difficult. For example, FDA-owned intellectual property includes a method which allows for vaccine manufactures to produce a meningitis vaccine more efficiently; FDA officials noted that it would be difficult to determine if that particular method was used to produce a company's meningitis vaccine, which in turn would make it difficult to prove infringement.

Table 3: Sources of Information on Reported Potential Infringement at the NIH Office of Technology Transfer, Fiscal Years 2016–2019[a]

Source	Description	Number of reports of potential infringement
Inventor	An inventor at an NIH institute or center learns about potential infringement and informs the NIH Office of Technology Transfer.	17
Other[b]	Includes active monitoring, as well as allegations that go through technology transfer offices or the NIH Office of Technology Transfer.	3
Paragraph IV notifications[c]	The NIH Office of Technology Transfer learns that its intellectual property rights are being infringed when it receives a notice letter from a generic pharmaceutical company that is filing an abbreviated new drug application (ANDA) with a paragraph IV challenge.	3
Licensee	A licensee learns about potential infringement and informs NIH.	1
Total		**24**

Source: GAO analysis of National Institutes of Health (NIH) infringement data. | GAO-21-52

[a]This table does not include instances where the NIH Office of Technology Transfer learned about infringement because a licensee exercised its right of enforcement and took action against an alleged infringer; these instances were not included because NIH does not track this information. The time frame of 2016-2019 was selected because NIH's technology transfer program was decentralized effective in fiscal year 2016.

[b]NIH's Office of Technology Transfer officials stated that, for some entries in its technology transfer database, it would not be possible to determine the original source of the allegation.

[109]NIH investigated this case and closed it because of the intellectual property's low value, among other reasons.

[110]The NIH Office of Technology Transfer was responsible for protecting FDA-owned intellectual property before NIH's technology transfer program was decentralized in fiscal year 2016.

[c]These notice letters fall under the legal framework of the Hatch-Waxman Act, whereby the infringer claims that the patent is invalid or will not be infringed by the generic product. See Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified in pertinent part as amended at 21 U.S.C. § 355(j)). HHS Office of General Counsel coordinates with the DOJ on related litigation.

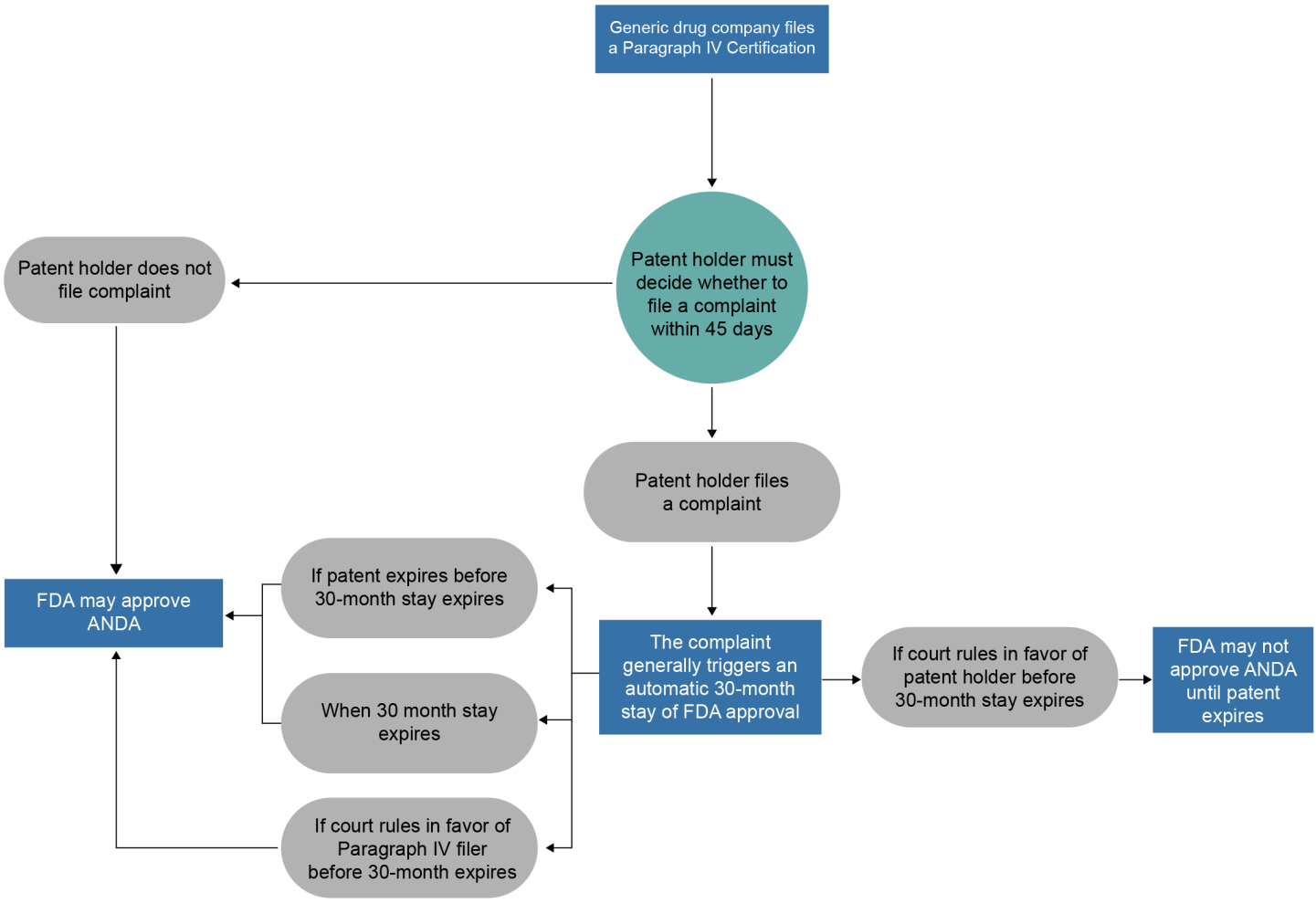
NIH's Office of Technology Transfer's monitoring and enforcement unit, as well as the individual technology transfer offices that manage patenting and licensing, may actively monitor for infringement in specific technology areas where the agency holds a significant portfolio, such as HIV diagnostics. NIH will only actively monitor a specific technology area when it makes sense from a cost-benefit standpoint. Moreover, NIH Office of Technology Transfer officials stated that they typically identify potential infringement as part of other ongoing work. For example, the Office of Technology Transfer opened an investigation into whether a particular company's technology infringed upon NIH intellectual property after an NIH official attended a scientific conference and noticed that the technologies were similar.[111] Likewise, technology transfer staff at the federal labs are generally aware of the technologies in their portfolios and can use this knowledge to help detect potential infringement.

HHS also receives notifications, as part of some court proceedings, when its intellectual property is challenged. For instance, under the Hatch-Waxman Act, a generic pharmaceutical manufacturer seeking FDA approval to market a generic version of a drug for which patents are listed in the Orange Book may submit an abbreviated new drug application (ANDA) with a paragraph IV certification claiming that the drug's patents are invalid or that it will not be infringed by the ANDA.[112] If an ANDA contains a paragraph IV certification, then the ANDA applicant is required to send a notice letter to the patent owner. In turn, the patent owner has a 45-day window to sue for patent infringement (see fig. 10). NIH officials stated that HHS can receive similar types of notifications related to generic pharmaceutical manufacturers entering the market through foreign courts or patent offices.

[111]The NIH Office of Technology Transfer closed this case after its investigation revealed that the technical specifications of the technologies were different.

[112]Pharmaceutical companies submit an ANDA to FDA to market a generic drug. A new drug application submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act also may rely on a listed drug and contain a paragraph IV certification. See Pub. L. No. 98-417, § 103, 98 Stat. 1585, 1593-94 (1984) (amending section 505(b) of the Federal Food, Drug, and Cosmetic Act).

Figure 10: FDA Review Process for an ANDA[a] with a Paragraph IV Certification[b]



Source: GAO analysis of relevant statutes, Food and Drug Administration (FDA) and Abbreviated New Drug Application (ANDA) documentation. | GAO-21-52

[a]A company files an ANDA when it wants to sell a generic version of a brand-name drug listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, also known as the Orange Book. ANDAs must demonstrate that the generic drug is bioequivalent to a listed brand-name drug in the Orange Book.

[b]When a company files an ANDA, it must certify against a reference listed drug in the FDA's Orange Book. A paragraph IV filing is a certification that the patents in question are invalid or not enforceable, or are not infringed by the proposed generic product.

Licensees may also bring reports of potential infringement to the Office of Technology Transfer's attention. For example, in fiscal year 2016, a licensee notified the NIH Office of Technology Transfer of potential infringement of a method for the production of vaccines. The investigation

was closed because the licensee did not identify the name of the alleged infringer.

HHS guidance states that the NIH Office of Technology Transfer shall be responsible for the initial investigation of an alleged instance of infringement for technologies it manages.[113] Our analysis of NIH potential infringement data shows that, since fiscal year 2016, 23 of 24 investigations of potential infringement have been closed without completing a license agreement. NIH closed investigations without a license agreement for several reasons, including that the cost of enforcing the intellectual property outweighed the value that would have been gained from pursuing further action. For example, in fiscal year 2016 the NIH Office of Technology Transfer closed an investigation into a company potentially infringing intellectual property related to a laboratory reagent used in cancer research, in part because of the low value of the intellectual property. NIH officials also end investigations when they determine that infringement has not occurred. For example, in 2017, the NIH Office of Technology Transfer ended an investigation involving a method of use patent for an anti-cancer compound because the potential infringer was only selling it as a lab reagent, which did not infringe NIH's patent.

HHS Encourages Infringers to License Technologies, Relies on Licensees to Enforce Exclusively-Licensed Intellectual Property Rights, and Defends HHS Patents When Challenged

HHS guidance states that agencies should take one or more of the following actions to protect agency intellectual property rights: (1) encourage alleged infringer(s) to license or sublicense the technology, (2) grant its exclusive licensees the right of enforcement, or (3) engage in a legal proceeding through DOJ. NIH officials stated that the agency has a responsibility to seek a reasonable return on the use of its intellectual property, but that this responsibility has to be balanced against the broader technology transfer goal of supporting public health.[114] Table 4 shows the types of protection strategies HHS and DOJ use to protect agency intellectual property rights.

[113]The NIH Office of Technology Transfer does not conduct an investigation when it learns that an ANDA with a paragraph IV certification has been filed. Under 35 U.S.C. § 271(e)(2)(A), it is considered an act of infringement to submit an ANDA. For this reason, an investigation as to whether infringement occurred is unnecessary. With other types of cases, NIH OTT has to investigate to determine if infringement occurred.

[114]This balancing can affect what steps the agency takes to protect its intellectual property. For example, NIH officials stated that if an infringed product were benefiting the public, it would not benefit public health to force the product to be removed from the market.

Table 4: Strategies Used to Protect HHS-Owned Intellectual Property Rights

Type of protection strategy	Description
Encourage alleged infringer to license or sublicense technology	If the technology allegedly infringed is claimed in a pending patent application, the National Institutes of Health (NIH) Office of Technology Transfer will offer the prospective infringer a license to the technology. If the technology is claimed in an issued patent, the NIH Office of Technology Transfer will make a determination whether the patent has been infringed and, if it is, may demand that the infringer take a license.
Grant exclusive licensees the right of enforcement	NIH may allow licensees to defend HHS-owned intellectual property on behalf of the agency.
Engage in legal proceeding through DOJ	DOJ may engage in legal proceedings on behalf of HHS. The types of legal proceedings include, but are not limited to, filing complaints in response to abbreviated new drug applications with paragraph IV certifications,[a] affirmative and defensive patent litigation[b], and defending HHS during proceedings at the Patent Trial and Appeal Board.[c]

Source: GAO analysis of the *Public Health Service Technology Transfer Policy Manual* and interviews with Department of Health and Human Services (HHS) and Department of Justice (DOJ) officials. | GAO-21-52

[a]These complaints are domestic proceedings under the legal framework of the Hatch-Waxman Act, whereby the infringer claims that the patent is invalid, unenforceable, or will not be infringed by the generic product. See Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified in pertinent part as amended at 21 U.S.C. § 355(j)). The patent owner then has a limited time in which to bring suit for an infringing act in filing the disclosure.

[b]Affirmative litigation involves a complaint filed by DOJ in response to a request from HHS whereby the government claims that its patents are being infringed. Defensive litigation involves DOJ responding on behalf of HHS to a complaint against the government.

[c]Proceedings at the U.S. Patent and Trademark Office include inter partes review, which is an administrative trial proceeding to review the patentability of one or more claims in a patent. While government agencies may be respondents before the Patent Trial and Appeals Board, government agencies cannot petition for inter partes review. See Return Mail, Inc. v. United States Postal Service, 139 S. Ct. 1853 (2019).

NIH officials reported that they will generally encourage potential infringers to license or sublicense technology when they have determined that an instance of potential infringement is supported by evidence. For instance, when NIH learned that a company was potentially infringing on an NIH technology, the Office of Technology Transfer opened an investigation and sent a warning letter, which led to the successful completion of a license agreement for use of the technology in fiscal year 2019. Since fiscal year 2000, 71 (20 percent) of NIH's closed infringement investigations resulted in the alleged infringer completing a license agreement. As of February 2020, NIH had 44 active infringement investigations.

NIH officials stated that they typically rely on licensees to enforce agency intellectual property rights when they are licensed exclusively. Licensees are required to notify HHS if they want to exercise their right of enforcement through litigation because DOJ has the first right of enforcement for government-owned intellectual property. Typically, the

Office of Technology Transfer's monitoring and enforcement unit is the contact point for official notices. However, these notices are not tracked by NIH because they are relatively rare events, according to NIH officials. NIH officials stated that the value of having exclusive licensees enforce the agency's intellectual property rights is that licensees are very motivated to enforce their rights and make risk assessments based on the value of the intellectual property. NIH officials stated that the decisions licensees make regarding whether to enforce intellectual property give NIH a better idea of how valuable its intellectual property is. Moreover, NIH officials stated that having licensees enforce the agency's intellectual property rights saves the government time and money.

HHS guidance states that technology transfer officials should weigh the cost of litigation against the value of the intellectual property when determining whether to enforce patent rights by referring an action to DOJ. DOJ has responsibility for enforcing intellectual property rights across the federal government. DOJ officials reported that there were 42 instances of litigation involving government intellectual property from all agencies between 2009 and 2019. DOJ officials identified 24 U.S. and foreign civil actions related to HHS-owned intellectual property referred in the same period.[115] Of these cases, 22 involved infringement of FDA-approved products associated with HHS intellectual property by generic drug manufacturers seeking to market generic versions of Prezista, a drug used to treat HIV, or Velcade, an anti-cancer medication. NIH officials stated that most of the cases involved Prezista and Velcade because of their success around the world.

The majority of civil actions identified by DOJ involved defending HHS-owned intellectual property rights. Most domestic cases went through Hatch-Waxman proceedings, which are a standardized process for a generic drug manufacturer to challenge patents associated with a brand-name drug and enter the market. In some cases, HHS declined to file a complaint against an ANDA filer, such as in fiscal year 2019 when a company filed an ANDA to market dexamethasone to be used in combination with Velcade. In other cases, HHS filed a complaint, such as in fiscal year 2014 when it defended its Prezista patents against

[115]According to DOJ officials, they do not track cases by agency since the agency is responsible for all litigation involving intellectual property rights. DOJ officials in the Intellectual Property Division identified cases based on their knowledge of the cases and review of records.

challenges from several generic pharmaceutical companies.[116] Likewise, all examples of international litigation provided by DOJ were defensive. Affirmative patent infringement cases, where HHS initiates litigation related to infringement outside of Hatch-Waxman proceedings, such as United States v. Gilead Sciences, Inc., are rare (see text box).[117]

Pre-Exposure Prophylaxis (PrEP)

In February 2006, the Centers for Disease Control and Prevention (CDC) filed a patent application with the U.S. Patent and Trademark Office for an HIV pre-exposure prophylaxis (PrEP) regimen to prevent HIV infection. From 2007-2012, the National Institutes of Health (NIH) funded extramural research that resulted in successful clinical trials that demonstrated positive results for CDC's invention. In July 2012, the Food and Drug Administration (FDA) approved Gilead Science's application to use Truvada—an antiviral drug used to treat HIV—for PrEP. In its application, Gilead Sciences used publicly available clinical trial data from the extramural research funded by NIH.

In 2014, CDC issued comprehensive clinical guidelines recommending that daily PrEP be considered for HIV prevention in all people who are at substantial risk. The World Health Organization issued similar recommendations in 2015. After these guidelines were issued, sales for Truvada for PrEP increased substantially, both in the United States and worldwide. In 2016, there were 77,120 PrEP users in the United States, compared to 8,768 in 2012. Gilead Sciences increased the price of Truvada for PrEP from $1,250 per month in 2012 to $1,800 per month in 2019. In addition, Gilead sought, and received in 2019, FDA approval to sell Descovy—a combination antiviral drug for HIV treatment—for PrEP for men and transgender women who have sex with men.

From 2014 through 2017, NIH, on behalf of CDC, encouraged Gilead Sciences to take a worldwide license for PrEP. However, NIH was unable to negotiate a license agreement. During this time, CDC's European PrEP patents were challenged at the European Patent Office. CDC prevailed in this case, and the challenger accepted a worldwide nonexclusive license to the PrEP patents.

In August 2019, Gilead Sciences submitted four petitions for inter partes review, which is an administrative trial proceeding to challenge the patentability of one or more claims in a patent, to the Patent Trial and Appeal Board for CDC's PrEP patents. In February 2020, the Patent Trial and Appeal Board denied institution of the inter partes reviews for the patents-in-suit because Gilead did not demonstrate a reasonable likelihood of prevailing on any grounds it argued in its petition.

In November 2019, the Department of Justice filed a complaint on behalf of the Department of Health and Human Services (HHS) against Gilead for willful infringement of CDC's PrEP patents. HHS claimed that both Truvada and Descovy for PrEP infringed on CDC's PrEP patents. As of September 2020, the litigation is ongoing.

Source: Complaint, United States v. Gilead Sciences, Inc., No. 1:19CV02103 (D. Del. Nov. 6, 2019); Gilead Science, Inc. v. United States, No. IPR2019-01455, No. IPR2019-01456 (P.T.A.B. Feb. 5, 2020); Gilead Science, Inc. v. United States, No. IPR2019-01453, No. IPR2019-01454 (P.T.A.B. Feb. 20, 2020). | GAO 21 52

[116]Three generic pharmaceutical manufacturers filed separate ANDAs over the course of 2010 and 2011 challenging HHS's Prezista patents. All of these cases were successfully settled with license agreements.

[117]Hatch-Waxman proceedings are technically affirmative cases because DOJ has to file a complaint in response to the infringer's ANDA. The complaint makes the government the plaintiff and the infringer the defendant. However, these cases are defensive in nature because the infringer is taking the first action by filing the ANDA with a paragraph IV certification.

Of the civil actions identified by DOJ, the majority of cases involved international patent infringement. From 2009 through 2019, DOJ reported that 14 of 24 civil actions involved litigation in foreign patent jurisdictions, including Australia, Canada, and Portugal. DOJ officials stated that international cases involving HHS intellectual property tend to be initiated through legal proceedings similar to those found under the Hatch-Waxman Act, where a generic drug manufacturer sought entry into a country's market by challenging the intellectual property owned or licensed by a brand-name drug manufacturer.[118] DOJ reported that all international cases between 2009 and 2019 involved DOJ defending HHS intellectual property from patent challenges rather than suing an alleged infringer for patent infringement. For example, in 2018, DOJ unsuccessfully defended one of HHS's Canadian Velcade patents when Teva Canada Limited claimed, among other things, that one of HHS's Velcade patents was invalid. A federal Canadian court ruled that the patent was invalid, and this decision was upheld by a Canadian appellate court.[119]

Conclusions

Since 1980, HHS's research has generated over 4,000 U.S. patents owned by the government and 32 licenses that contributed to the development of 34 FDA-approved drugs. While these represent a small portion of drugs approved by FDA, they include new treatments for life-threatening diseases, such as cancer and HIV-caused acquired immunodeficiency syndrome, and have generated substantial revenues for the drug industry.

NIH must demonstrate to the public that it uses the statutory tools available for managing its intellectual property to benefit the American people. Technology transfer laws direct the federal government to license its intellectual property in ways that do not lessen competition, thereby encouraging lower prices, high-quality products, and greater innovation. While NIH considers competition before granting exclusive licenses, it has not incorporated a statutory provision related to federal antitrust laws into its standard license agreements.

[118]Foreign litigation is handled by DOJ's Office of Foreign Litigation. However, this office is not licensed to practice law in foreign courts, so it instead functions as an in-house counsel coordinating with foreign counsel on behalf of federal agencies.

[119]DOJ reported that, as of February 18, 2020, the case is still pending a response to a petition made to the Supreme Court of Canada.

NIH publicly reports limited licensing information. For example, NIH does not currently provide to the public a list of technologies or patents it has licensed. This limits the public's and policymakers' ability to evaluate the impact of licensing on NIH's core mission of improving health. According to internal control standards, access to quality information enables external parties to help the government achieve its objectives and address related risks. Reporting licensing information that is not protected from public disclosure by federal laws in a format that facilitates its accessibility and usability, such as a searchable public database, would improve transparency and enable the public and policymakers to evaluate how NIH's management of government-owned intellectual property improves the nation's health.

Recommendations for Executive Action

We are making the following two recommendations to NIH:

The Director of NIH should revise NIH's standard commercial license agreements to incorporate a provision consistent with 35 U.S.C. § 209(d)(3)(D) to put licensees on notice that the agency can terminate the license in whole or in part if the licensee has been found by a court of competent jurisdiction to have violated the federal antitrust laws in connection with its performance under the license agreement. (Recommendation 1)

The Director of NIH should determine—in collaboration with outside stakeholders as appropriate—what licensing information is most useful to enable the public's and policymakers' understanding of licensing outcomes and impacts and, to the extent permitted by law, publicly report such information in an accessible and searchable format to the maximum extent possible. (Recommendation 2)

Agency Comments and Our Evaluation

We provided a draft of this report to HHS for review and comment. We also provided a draft for review and technical comment to DOJ, NIST, and USPTO. We incorporated technical comments, as appropriate. Overall, HHS agreed with our findings and concurred with both of our recommendations. In HHS's response, which is reproduced in appendix IV, HHS said it would begin addressing our first recommendation by October 8, 2020, by inserting a new provision into exclusive and partially exclusive license agreements and would seek a formal approval of updated standard license agreements from the Public Health Service Technology Transfer Policy Board. The actions HHS identifies, if implemented, would satisfy the intent of our recommendation. We note, however, that HHS's response—by specifically addressing exclusive and partially exclusive licenses—suggests it may not add this provision to

nonexclusive licenses. We would encourage HHS to consider whether it is necessary under the law to include such a provision in its nonexclusive license agreements even if as a practical matter doing so may not be necessary. For the second recommendation, HHS said that it would develop a plan in the first quarter of fiscal year 2021 outlining how it would provide more information on patents and licenses on an agency website.

NIH noted in its general comments that our approach to using data in different time periods may be misleading, but the agency provided no technical comments on our objectives, scope, and methodology raising specific concerns. Our use of these data was intended to illustrate the scope of NIH's contributions to drug development over a period for which data were available and to account for both the early stage of government-owned patented inventions and long lead times required for drug development. We did not use these data to make any critiques or commentary on NIH's past licensing or technology transfer practices. We acknowledge that NIH intellectual property management has changed over time, and our recommendations are based on current agency practices. In addition, we have provided information on relevant changes to patent law and agency practices to provide such context in our report.

As agreed with your offices, unless you publicly announce the contents of this report earlier, we plan no further distribution until 30 days from the report date. At that time, we will send copies to appropriate congressional committees, the Secretary of Health and Human Services, and other interested parties. In addition, this report will be available at no charge on the GAO website at http://www.gao.gov.

If you or your staff have questions about this report, please contact John Neumann, Managing Director, at (202) 512-6888 or neumannj@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. Key contributors to this report are listed in appendix V.

John Neumann
Managing Director,
Science, Technology Assessment, and Analytics

Appendix I: Objectives, Scope, and Methodology

We reviewed the Department of Health and Human Services' (HHS) management of its intellectual property that has contributed to the development of new drugs. Specifically, this report examines (1) the extent to which HHS-owned intellectual property has contributed to the development of Food and Drug Administration (FDA)-approved drugs; (2) what is known about the licenses associated with FDA-approved drugs; (3) factors National Institutes of Health (NIH) prioritizes when licensing its patented inventions, and information about licensing it makes public; and (4) steps that HHS has taken to protect its intellectual property. In addition to this report, we are providing an online dataset of patents owned by HHS, which can be accessed on our website at https://www.gao.gov/products/GAO-21-52.

To address all of these objectives, we interviewed stakeholders with a range of perspectives. We identified these stakeholders using a non-generalizable snowball sampling approach. This approach started with reviewing prior GAO work, background reading, and preliminary interviews with stakeholders. Our sample expanded based on suggestions from interviewees on how to obtain different perspectives on the management of federal intellectual property and drug development. These stakeholders included academics; patient advocates; representatives from nonprofit organizations, trade associations, and private companies; and officials from technology transfer offices at non-HHS agencies and universities. As appropriate, we obtained related documentation, such as published studies or relevant academic articles, or followed up with additional questions to clarify our understanding of their perspectives.

We developed a questionnaire for HHS's nine technology transfer offices to collect comparable information on the portfolio of inventions developed by each research institute, the roles of different organizations in managing intellectual property, and processes related to managing patenting, licensing, and the enforcement of intellectual property rights, among other issues. In addition, we identified which technology transfer offices had licensed inventions associated with FDA-approved products and developed questions targeted to the products of each, such as the rationale for exclusively licensing certain inventions. To confirm that these questions provided appropriate information, we conducted a pre-test with two of the technology transfer offices— one with a licensed invention associated with an FDA-approved product and one without.[1] We provided

[1]Based on our results, we added an additional question to the questionnaire.

the written questionnaire to the remaining seven technology transfer offices responsible for managing the intellectual property of NIH, Centers for Disease Control and Prevention (CDC), and FDA federal labs. We then conducted follow-up interviews with select technology transfer offices responsible for the majority of the drugs we identified or that had a research mission related to technology transfer.

To examine the contributions of HHS-owned intellectual property to the development of FDA-approved drugs, we obtained data from NIH's intellectual property management database, including patents granted for the period 2000 through 2019 and licenses associated with patents granted during that time period.[2] In addition, we obtained data from the U.S. Patent and Trademark (USPTO) PatentsView database to identify patents owned by HHS and examine selected patent characteristics.[3]

Specifically, we used data from PatentsView to find patents granted from 1980 through 2019 that were originally assigned to HHS, NIH, FDA, CDC, or individual research institutes or centers. According to USPTO officials, patent assignee names are taken directly from required patent application documentation and can contain typographical errors and omissions. For example, HHS may be listed as the "Department of Human Services" or other variations of the name instead of its proper name of "Department of Health and Human Services." We developed an algorithm to detect combinations of characters with these names and identify patents assigned to HHS or its sub agencies, such as NIH, in PatentsView data. We then compared NIH data on U.S. patents granted from 2000 through 2019 with PatentsView data from the same period, as well as the 94 licensed U.S. patents associated with FDA-approved drugs. Ninety-two of the 94 patents were successfully matched, and we matched 2,760 of the

[2]NIH managed intellectual property for CDC and FDA until a decentralization in fiscal year 2016. NIH's data contains the historical data for these agencies and NIH has continued to manage CDC's intellectual property. FDA began to separately manage its intellectual property with the decentralization, and we coordinated with FDA to obtain any recent information not in the NIH database.

[3]PatentsView is a patent data visualization and analysis platform for U.S. patent data. PatentsView uses data derived from USPTO bulk data files for research purposes.

3,096 patents granted to HHS in NIH's data from 2000 through 2019 with PatentsView data.[4]

We analyzed patents that did not match across the two data sources and found the following:

- We found 155 patents assigned to HHS agencies in the PatentsView data did not appear in the NIH data. We provided a sample of 20 patents to NIH officials to identify potential causes. According to NIH officials, these patents included nine patents involving extramural funding where the government retained limited rights and nine patents that were confirmed as HHS-owned patents.[5] NIH officials also stated that there can be lag in the data entry of patents at NIH when third parties are involved. We kept the nine patents that NIH confirmed it owned and excluded the remaining 146 patents from our analysis, to avoid potentially including patents involving extramural funding.[6]
- We found that 336 of 3,096 patents listed in the NIH data did not appear in the PatentsView data. We provided a sample of 20 patents to NIH officials to identify potential causes. According to NIH officials, 15 of these patents involved errors made by NIH contract law firms, co-inventors managing joint inventions, or licensees provided with authority to prosecute patents on NIH's behalf. Specifically, NIH was excluded or named incorrectly on the patent in these cases, but the patents did include NIH inventions.[7] In addition, four of the 20 patents involved the government receiving rights to intellectual property

[4]The two patents that did not match of the 94 patents associated with FDA-approved products included one with no assignee in the PatentsView data and another that listed another entity as the assignee.

[5]Six lapsed patents had previously been managed by CDC, and three were co-inventions with outside parties that were being managed by the outside party and had not been reported to NIH. CDC managed its own patenting and licensing until 2013, and some patents that lapsed before 2013 were not reported to NIH when management changed hands. HHS agencies may enter into agreements with co-inventors—called inter-institutional agreements—providing authority to manage patent prosecution and licensing. In these cases, co-inventors had not informed HHS of a patent being issued. In addition, two of the 20 patents were FDA patents managed by FDA after its decentralization and confirmed by FDA from their intellectual property management database.

[6]This 146 includes the nine patents NIH identified as involving extramural funding and the remaining 137 patents that they did not review.

[7]Errors in assignment and inventorship can be corrected administratively so long as there is agreement between the relevant parties. If the relevant parties are not in agreement on the material facts of the error, litigation could be necessary.

through a legal settlement, such as a patent interference.[8] Based on these results, we included all 336 patents in our analysis of technology types.

After developing this dataset, we identified the International Patent Classification (IPC) technology type for each patent. For the patents owned by HHS from 1980 through 2019, we used the IPC code to determine the underlying technologies associated with the patent. To analyze NIH licensing data, we analyzed the types of licenses on patented inventions granted from 2000 through 2019 by their type and exclusivity. To assess the reliability of USPTO and NIH data on patents, we reviewed documentation from both agencies; interviewed knowledgeable officials; reviewed the data for potential errors, omissions, and outliers; and validated select observations against underlying patent documents. Based on our review, we determined these data were sufficiently reliable for the purposes of reporting the technology types of patents and license type and exclusivity.

NIH identified all FDA-approved drugs associated with HHS's licensed inventions, 34 in total.[9] We matched these 34 drugs with data from IBM's Truven Health Analytics Red Book using drug name and obtained the Red Book's associated therapeutic class codes to identify the medical uses of these drugs.[10] To assess the reliability of these data, we reviewed Red Book documentation and compared Red Book therapeutic class codes against FDA documentation. We found these data reliable for the purposes of identifying the therapeutic use of these drugs. For more information, see appendix II.

We reviewed the 34 FDA-approved products against FDA data and documents to determine the type of regulatory approval and patents listed

[8]The remaining patent in this sample included intellectual property rights granted through a cooperative research and development agreement.

[9]These 34 FDA-approved drugs include two combination products—drug-coated stents for surgical procedures. This list excludes other medical devices with no drug component, drugs approved by national regulators of medical products in other countries but not approved by FDA, and veterinary drugs that may have been developed from NIH inventions.

[10]Five of the 34 products could not be matched because they were not in the version of the Red Book available to GAO, which was up to date as of March 2018, or they were combination drugs and devices. We reviewed NIH data and FDA documentation on these drugs to classify them by therapeutic use. We also verified therapeutic class codes of select drugs against FDA documentation.

by FDA in the Orange Book as of June 2020. Specifically, we compared the 34 FDA-approved drugs with the Orange Book product file, the Purple Book, and other FDA documentation, matching them on product name and verifying matches with other information, such as FDA approval date, as necessary.[11] For the 16 products identified in the Orange Book data, we merged the Orange Book product file with its patent and exclusivity files to identify Orange Book listed patents and exclusivities current as of June 2020.[12] We merged these patents with the list of 94 U.S. patents provided by NIH to identify patents owned by HHS and those not owned by HHS. To assess the reliability of these data, we reviewed Orange Book documentation, obtained information about the data from FDA officials, and validated the results against the data provided by NIH. Based on our review, we determined these data were reliable for the purposes of identifying current patents and exclusivities associated with these drugs. We also reviewed documentation related to these drugs and obtained testimonial evidence from HHS technology transfer offices responsible for licensing the intellectual property to help develop these drugs.

To examine what is known about licenses associated with FDA-approved drugs, we obtained and analyzed NIH data related to these licenses, including total royalties generated by licenses and exclusivity of the licenses. In addition, we obtained license agreements for the 32 licenses identified by NIH as associated with FDA-approved products.[13] We used a data collection instrument to analyze all agency license agreements associated with FDA-approved drugs, and to collect information on: (1) provisions related to pricing and availability of products in license agreements, (2) provisions related to competition and antitrust issues, and (3) general information about the license agreement, such as the federal agency that signed it. To confirm that these questions provided the appropriate information, we conducted a pre-test using 12 of the

[11]FDA's Orange Book identifies drug products approved on the basis of safety and effectiveness by the FDA under the Federal Food, Drug, and Cosmetic Act. FDA's Purple Book identifies drug products approved on the basis of safety and effectiveness under the Biologics Price Competition and Innovation Act of 2009.

[12]According to FDA officials, the Orange Book patent data only list currently active patents and only those reported to FDA by the company applying for FDA approval. Therefore, the results of our analysis do not include expired patents listed in earlier versions of the Orange Book or unlisted patents. Patent data were not available from FDA's Purple Book for analysis.

[13]We also obtained available license applications and amendments.

license agreements. Our review of license agreements associated with FDA-approved drugs also involved comparing actual agreement provisions to provisions listed in NIH's standard license agreements.

We obtained and analyzed the most recent available Centers for Medicare and Medicaid Services' dashboard data for the period 2014 through 2018 to provide information on the total program spending for these drugs, and where available beneficiaries served. Specifically, we matched the 34 FDA-approved products to the Medicare Part B, Medicare Part D, and Medicaid dashboard datasets.[14] We reported total spending for each drug in each program as well as total beneficiaries when those data were available. We reviewed our prior work using these data, current methodological documentation, and reviewed the data for potential errors and found them reliable for the purposes of reporting total program spending on these drugs. For more information, see appendix III. In addition, we interviewed agency staff at select technology transfer offices affiliated with NIH's research institutes and at NIH's Office of Technology Transfer.

To examine what factors NIH considers in licensing its patented inventions and what licensing information it makes public, we reviewed relevant statutes, regulations, and HHS guidance on technology transfer. We compared NIH's public reporting to the relevant statutes, regulations, and guidance, as well as to the Standards for Internal Control in the Federal Government. In applying the internal control standards, the information and communication component—that management uses quality information to support the internal control system—was significant to this objective, along with the related principle that management should communicate information externally. We also obtained and reviewed license agreements associated with FDA-approved drugs that involved HHS-owned patented inventions, as well as standard license agreements used by NIH.[15] We reviewed information published by HHS on its technology transfer processes, including marketing information on its technologies, Federal Register notices, and publicly reported information

[14]We matched the 34 FDA-approved drugs to the dashboard data by brand-name. When a brand-name did not exist, we matched the generic name. Each program had a different number of matches, and none included all of the 34 FDA-approved drugs. In some cases, drugs were withdrawn from the market prior to 2014, such as the vaccines LYMErix and RotaShield.

[15]Standard license agreements refer to standardized templates used by technology transfer offices as a starting point to negotiate licenses, including licenses for rights to the government's patented inventions.

in annual technology transfer reports. We also interviewed knowledgeable agency officials at NIH's Office of Technology Transfer, select NIH technology transfer offices, FDA, and NIST.

To examine the steps that HHS has taken to protect its intellectual property, we reviewed relevant statutes, regulations, and HHS guidance on technology transfer. We obtained and analyzed data from the NIH Office of Technology Transfer's intellectual property management database on cases of potential infringement for the period 2016 through 2019. For example, based on interviews with agency officials and NIH data, we categorized and aggregated the sources that reported potential infringement to determine how the Office of Technology Transfer learns about potential infringement. We also obtained information from DOJ on civil actions for the period 2009 to 2019 where it defended or asserted HHS intellectual property rights, either domestically or internationally.[16]

After analyzing agency data, we identified and selected closed civil action cases that provided examples of each type of action taken to protect HHS intellectual property. We selected our cases using a non-random, stratified purposeful sampling approach based on selection criteria such as relevance to existing law, intellectual property associated with FDA-approved products, and regional variation. We obtained and reviewed documentation on these cases, such as court filings and decisions. Although the results of these cases are not generalizable to all cases, they provide illustrative examples of actions taken to protect HHS intellectual property. In addition, we interviewed agency staff with knowledge of HHS and DOJ enforcement processes.

We conducted this performance audit from September 2019 to October 2020 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

[16]DOJ officials identified examples of civil actions DOJ litigated related to HHS intellectual property from 2009 through 2019. DOJ officials explained that they compiled the information based on their knowledge of prior cases and related documentation. Therefore, the list of cases may not contain all cases where DOJ defended HHS intellectual property rights.

Appendix II: Information on Drugs Associated with National Institutes of Health (NIH) Licensed Inventions

NIH inventions licensed by pharmaceutical companies contributed to 34 drugs that were approved by the Food and Drug Administration (FDA) and cover a range of medical uses. NIH granted 32 licenses that are associated with these drugs, which were approved between 1991 and 2019. NIH licensed these inventions primarily to drug manufacturers. Of the 34 products, 32 have been approved by FDA as small molecule drugs or biological products, with the remaining two approved as drug-device combinations.

Therapeutic Uses of Drugs Associated with NIH Licensed Inventions

Of the 34 drugs approved by FDA that are associated with licenses of NIH-owned inventions, 22 are antiviral treatments, anti-cancer treatments, or vaccines. The remaining 12 products cover a range of medical uses including mental health treatment, drugs to aid in disease diagnosis, and stents combined with drugs to aid in surgery. See table 5.

Table 5: FDA-Approved Drugs Associated with Licenses of NIH Inventions by Therapeutic Class

Therapeutic class	Number of products	Product name (generic name)
Anti-cancer	6	Fludara (fludarabine)
		Lumoxiti (moxetumomab pasudotox-tdfk)
		Taxol (paclitaxel)
		Velcade (bortezomib)
		Yescarta (axicabtagene ciloleucel)
		Zevalin (ibritumomab tiuxetan)
Antidepressant	1	Spravato (esketamine)
Antifungal	2	NeuTrexin (trimetrexate glucoronate)
		Sporanox (itraconazole oral solution)
Antiviral	8	Didanosine[a] (Didanosine)
		Hivid (zalcitabine)
		Prezcobix (darunavir/cobicistat)
		Prezista (darunavir)
		Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide)
		Synagis (palivizumab – injection)
		Videx (Didanosine)
		Vitravene (fomivirsen (Intraocular route))
Diagnostic agent	3	Acutect (technetium-99m apcitide)
		NeoTect (technetium Tc 99m depreotide Injection)
		Thyrogen (thyrotropin alfa for injection)

Therapeutic class	Number of products	Product name (generic name)
Drug-device combination[b]	2	Taxus Express2 Monorail Paclitaxel-Eluting Coronary Stent System (paclitaxel-coated coronary stent)
		Zilver PTX Drug-Eluting Peripheral Stent (paclitaxel-coated peripheral stent)
Emergency contraceptive	1	Ella (ulipristal acetate)
Immunosuppressant	2	Zenapax (daclizumab)
		Zinbryta (daclizumab)
Protectant dental	1	Kepivance (palifermin)
Vaccine	8	Certiva (diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed)
		Cervarix (human papillomavirus bivalent vaccine)
		Gardasil (recombinant human papillomavirus quadrivalent vaccine)
		Gardasil 9 (human papillomavirus 9-valent vaccine, recombinant)
		Havrix (hepatitis A vaccine, inactivated)
		LYMErix (Lyme disease vaccine (recombinant OspA))
		RotaShield (rhesus rotavirus vaccine-tetravalent)
		Twinrix (hepatitis A inactivated & hepatitis B (recombinant) vaccine)
Total	**34**	

Source: GAO analysis of IBM's Red Book and National Institutes of Health (NIH) data and Food and Drug Administration (FDA) documentation. | GAO-21-52

[a]Didanosine is the only one of the 34 drugs approved by FDA associated with licenses of NIH inventions to have been approved under an abbreviated new drug application. It is a generic version of the drug Videx, also listed in the table. According to NIH officials, this was a unique case where the agency licensed a patented invention to a generic drug manufacturer. NIH had a license with one company and not all manufacturers of generic didanosine.

[b]Drug-device combination refers to a product made up of two or more regulated components, i.e., drug/device, biologic/device, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity, among other products. In the case of the two products with contributions from NIH patented inventions, these two products were drug eluting stents, a combination of a medical device (stent) and a drug that supports the use of the device (paclitaxel).

NIH Licenses Associated with FDA-approved Drugs

NIH granted 32 licenses that are associated with 34 FDA-approved drugs that were approved between 1991 and 2019. NIH granted many of these

licenses to drug companies (see table 6).[1] This is because NIH inventions are typically licensed early in the drug development process, before clinical trials which require greater resources for development through FDA approval, according to NIH officials. Drug companies bring the expertise and resources to invest in clinical trials necessary to achieve FDA approval and sometimes license NIH inventions following a research collaboration. In our analysis of the license agreements, we found that six of the 32 licenses originated from NIH's cooperative research and development agreements (CRADAs) with drug manufacturers.[2]

Table 6: FDA-Approved Drugs Associated with 32 Licenses of NIH Inventions and Related Information

	Product name	Therapeutic class	Year of FDA approval[a]	Number of NIH licenses	Licensee[b]
1	AcuTect	Diagnostic agent	1998	1	Berlex Laboratories
2	Certiva	Vaccine	1998	1	Baxter Pharmaceuticals
3	Cervarix	Vaccine	2009	1	MedImmune/GlaxoSmithKline
4	Didanosine Delayed-Release Capsules	Antiviral	2004	1	Barr Laboratories
5	Ellac	Emergency contraceptive	2015	1	Laboratoire HRA Pharma
6	Fludara	Anti-cancer	1991	1	Berlex Laboratories
7	Gardasil	Vaccine	2006	1	Merck
8	Gardasil 9	Vaccine	2018	1	Merck
9	Havrixc	Vaccine	1995	2	GlaxoSmithKline
10	Hivid	Antiviral	1992	1	Hoffmann-LaRoche
11	Kepivance	Protectant dental	2004	1	Amgen Inc.
12	Lumoxiti	Anti-cancer	2018	1	AstraZeneca
13	LYMErix	Vaccine	1998	1	GlaxoSmithKline
14	NeoTect	Diagnostic agent	1999	1	Berlex Laboratories
15	NeuTrexin	Antibiotic	1993	1	MedImmune
16	Prezcobix	Antiviral	2015	1	Janssen Therapeutics
17	Prezista	Antiviral	2006	1	Tibotec Pharmaceuticals

[1]The majority of these licenses were granted in the 1980s and 1990s. Over time, the model for drug development has evolved to focus on the importance of small companies doing early development and then licensing to or being acquired by large pharmaceutical companies. For more information, see GAO-18-40.

[2]These agreements allow federal labs to conduct research in cooperation with other entities, such as pharmaceutical companies. The primary purpose of CRADA legislation is to allow laboratories to enter into collaborative agreements for technology transfer with all types of organizations. Pub. L. No. 99-502, § 2, 100 Stat. 1785, 1785 (1986) (amending Pub. L. No. 96-480, adding § 12, codified as amended at 15 U.S.C. § 3710a).

	Product name	Therapeutic class	Year of FDA approval[a]	Number of NIH licenses	Licensee[b]
18	RotaShield	Vaccine	1998	2	Wyeth Laboratories
19	Sporanox Oral Solution	Antifungal	1997	1	Janssen Pharmaceuticals
20	Spravato	Antidepressant	2019	1	Mount Sinai/Janssen Therapeutics
21	Symtuza	Antiviral	2018	1	Janssen Therapeutics
22	Synagis	Antiviral	1998	1	MedImmune
23	Taxolc	Anti-cancer	1992	1	Bristol-Myers Squibb
24	Taxus Express2 Monorail Paclitaxel-Eluting Coronary Stent System	Drug-device combination	2004	1	Angiotech/Boston Scientific
25	Thyrogenc	Diagnostic agent	1998	1	Genzyme Corporation
26	Twinrixc	Vaccine	2001	2	GlaxoSmithKline
27	Velcadec	Anti-cancer	2003	1	Millennium Pharmaceuticals
28	Videx	Antiviral	1991	1	Bristol-Myers Squibb
29	Vitravene	Antiviral	1998	2	Isis Pharmaceuticals
30	Yescartab,[c]	Anti-cancer	2017	2	Cabaret Biotech/Kite Pharmab
31	Zenapax	Immunosuppressant	1997	1	Protein Design Laboratory/Hoffman-LaRoche
32	Zevalin	Anti-cancer	2002	1	IDEC Pharmaceuticals
33	Zilver PTX Drug-Eluting Peripheral Stent	Drug-device combination	2012	1	Angiotech/Cook Medical
34	Zinbryta	Immunosuppressant	2016	1	Abbott Biotherapeutics/Biogen

Source: GAO analysis of National Institutes of Health (NIH) data, and IBM's Red Book data. | GAO-21-52

Notes: The total number of drugs is 34. The number of licenses listed in the table exceeds 32 because some drugs are associated with more than one license and some licenses are associated with more than one drug.

[a]Food and Drug Administration (FDA) approval year is based on NIH information and is associated with the relevant NIH license. Drugs can have multiple approvals from FDA and multiple years and the approval year in this table may not be the first approval year of the drug. Subsequent acquisitions or licensing arrangements may lead to a different entity with FDA approval.

[b]Licensee information is from public NIH information, see https://www.ott.nih.gov/reportsstats/hhs-license-based-vaccines-therapeutics.

[c]At least one NIH license associated with this drug originated from an NIH cooperative research and development agreement with the licensee.

FDA Approvals and Exclusivities for the 34 Drugs Associated with NIH Licenses

The 34 FDA-approved drugs associated with NIH licenses include both small molecule drugs approved under section 505 of the Federal Food, Drug, and Cosmetic Act and biological products regulated under the Public Health Service Act, according to our analysis of FDA data and

documents.[3] NIH licensed inventions contributed to 16 small molecule drugs, 15 products under a new drug application and one generic product under an abbreviated new drug application (ANDA), according to our analysis of Orange Book data.[4] These products receiving approval under a new drug application can maintain market exclusivity for their product until the last patent expires. In addition to protection granted by the patent system, federal law can also provide periods of exclusivity after FDA approves a drug. For example, a new drug application receives 5 years of exclusivity from FDA when the drug comprises a new chemical entity—a drug that incorporates a new active ingredient.[5] In addition, products may be eligible for additional exclusivities from FDA. According to our analysis, three of the 16 Orange Book drugs had unexpired exclusivities listed in FDA's Orange Book as of June 2020.

- Spravato: FDA approved Spravato for use on March 5, 2019.This product has a new chemical entity exclusivity effective for 5 years, which expires in March 5, 2024.
- Symtuza: FDA approved Symtuza on July 17, 2018, and it is protected by a new chemical entity exclusivity until November 5, 2020, covering one of the active ingredients, tenofovir alafenamide. It is also protected by 3-year exclusivity until July 17, 2021, because a new clinical investigation was essential to approval of the application.
- Velcade: Velcade had both orphan drug exclusivity and pediatric exclusivity.[6] Velcade's owner requested and was granted orphan drug

[3]We analyzed information from the Orange Book, which identifies drug products approved on the basis of safety and effectiveness by the FDA under the Federal Food, Drug, and Cosmetic Act, as well as the Purple Book, which identifies biological products licensed on the basis of safety, purity, and potency by the FDA under the Public Health Service Act.

[4]The generic product is a unique case, according to NIH officials, where NIH exclusively licensed patented inventions that contributed to a new drug application for Videx. NIH then nonexclusively licensed the inventions to Barr Laboratories in August 2004, which released didanosine, a generic version of Videx.

[5]A new chemical entity exclusivity is to encourage the development of innovative drug products that include an entirely new active ingredient, as opposed to new formulations of previously approved active ingredients.

[6]Orphan drug exclusivity: To be eligible pharmaceutical companies must apply for orphan designation from FDA prior to a drug's approval. Orphan drugs may receive 7 years of exclusivity. 21 U.S.C. § 360cc. Pediatric exclusivity: When pediatric exclusivity is obtained, a 6-month period of exclusivity is added to all existing patents and exclusivity on all applications held by the sponsor for that active ingredient. 31 U.S.C. § 355a. Pediatric exclusivity does not stand alone, but attaches to existing exclusivity.

designations for its product for multiple myeloma and mantle cell lymphoma, which provided related exclusivities.[7] Of those orphan drug exclusivities, an exclusivity for mantle cell lymphoma is still in effect until October 8, 2021. Velcade also received pediatric exclusivity because it completed clinical trials assessing the effectiveness in children.[8] Since Velcade has both active patents and active exclusivities, each has received an additional period of 6 months exclusivity. For example, the orphan drug exclusivity extends to April 8, 2022, and the patent exclusivity extends from January 25, 2022, to July 25, 2022.

NIH-licensed inventions contributed to 16 biological products, according to our analysis of FDA data and documents. Most biological products are relatively large, structurally complex molecules, generally derived from living sources (such as humans, animals, and microorganisms).[9] A biological product licensed under section 351(a) of the Public Health Service Act may be eligible for exclusivities. Specifically, the Biologics Price Competition and Innovation Act of 2009, amending the Public Health Service Act, established two periods of exclusivity applicable to certain biological products, one with a duration of 4 years and the other with a duration of 12 years.[10] None of the 34 products with contributions from NIH licensed inventions were biosimilar products.[11] The remaining two products were drug-device combinations, which were approved as

[7]Orphan drug designations were also requested for acute lymphoblastic leukemia, neurofibromatosis type 2 (NF2), and follicular non-Hodgkin lymphoma. FDA did not approve Velcade for these orphan drug designations.

[8]According to FDA officials, pediatric exclusivity attaches a period of 6 months' exclusivity to the existing patents and exclusivities listed in the Orange Book for any drug product containing the same active ingredient as the drug studied.

[9]We did not analyze the current patents or exclusivities of biological products because FDA's data source, the Purple Book, did not contain information on current patents and exclusivities at the time of our analysis. FDA is in the process of updating the Purple Book to include exclusivity information, according to FDA officials.

[10]42 U.S.C. § 262(k)(7). Specifically, a new application may not be submitted until 4 years after the date the original biological product was approved by FDA, and a new product may not be approved until 12 years after the date of approval of the original biological product.

[11]Under section 351(i)(2) of the Biologics Price Competition and Innovation Act, "biosimilar" or "biosimilarity" means that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components, and there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.

medical devices but contained drug components also reviewed by FDA for safety and efficacy.

Appendix III: Spending Information on Drugs with Contributions from National Institutes of Health (NIH)-Licensed Inventions

We analyzed spending and usage of Food and Drug Administration (FDA)-approved drugs associated with inventions licensed by the NIH in three federal programs: Medicare Part B, Medicare Part D, and Medicaid. Specifically, we identified brand-name drugs with spending reported by the Centers for Medicare & Medicaid Services from 2014 through 2018 that had contributions from NIH intellectual property, the most recent data available at the time of our analysis. For each identified drug, we used publicly available spending information from the Centers for Medicare & Medicaid Services Drug Spending Dashboards to determine the total spending for each year in the program and the percentage of total program spending (see table 7). FDA-approved drugs can involve multiple patented inventions, with NIH licensed patents being a part of the portfolio of intellectual property used to commercialize a drug. Contributions from NIH licensed patents may be a small or a significant aspect of the product depending on the individual technology. The number of brand-name drugs identified in each program varies.

Table 7: Total Spending for Drugs Associated with NIH-Licensed Inventions by the Medicare Part B, Medicare Part D, and Medicaid Programs, Calendar Year 2018

Federal program	Number of identified brand-name drugs	Total program spending	Percent of total program spending
Medicare Part B	4	$456,518,140	1.0 %
Medicare Part D	13	$669,346,756	0.4%
Medicaid	13	$687,996,417	1.0%

Source: GAO analysis of Centers for Medicare & Medicaid Services Drug Spending Dashboard data. | GAO-21-52

Note: We matched brand-name drugs with spending in Medicare Part B, Medicare Part D, and Medicaid with a list of 34 drugs associated with National Institutes of Health (NIH) licenses to identify the number of brand-name drugs, total spending, and percent of program spending. Total reported spending differs across programs: Medicare Part B spending includes the effects of rebates and other discounts of spending, whereas Medicare Part D and Medicaid spending does not.

Our analysis did not include all 34 FDA-approved products with contributions from NIH intellectual property because some products were not on the market. For example, some products were

- Withdrawn prior to 2014. These include LYMErix and RotaShield.
- Approved after 2018. Spravato was approved for use by FDA in 2019; 2018 was the most recent year of available data.
- On the market as generics. Some products, such as Fludara and Taxol, have had generic versions enter the market, and the brand-

name versions are no longer available. Generic versions of Fludara (fludarabine) were purchased in all three programs. According to NIH officials, only one of the 34 drugs with contributions from NIH intellectual property was a generic drug, and this was a unique example. Generic drugs are not included in the tables below.

Program information is presented for each program separately because each program reports spending information differently. For example, Medicare Part B spending is reported after rebates on drug prices are provided, whereas Medicare Part D and Medicaid spending do not include the effects of rebates and other discounts on drug prices. Therefore, spending totals across programs are not directly comparable.

Medicare Part B Spending and Beneficiaries from 2014 through 2018

Medicare Part B covers drugs that are typically administered by a physician or under a physician's supervision. Drugs covered under Part B include injectable drugs, some oral cancer drugs, and drugs infused or inhaled through durable medical equipment. Due to the high prices of some Part B drugs, Medicare beneficiaries treated with these drugs may face significant financial responsibilities, since they are responsible for 20 percent of the cost.[1] Total spending on drugs reported for Medicare Part B reflects the payments by Medicare and the beneficiaries, net of discounts and rebates, referred to as the average sales price.[2]

In 2018, total Medicare Part B spending for 4 brand-name drugs associated with inventions licensed from NIH accounted for $457 million, approximately 1 percent of total program spending. Total program spending on these drugs varied substantially in 2018, ranging from about $98,000 on Havrix to about $443 million on Velcade (see table 8). In some cases, these drugs were used to treat a small number of beneficiaries, such as Kepivance, which treated 107 Medicare Part B beneficiaries in 2018. By contrast, the drug Velcade treated more than 20,000 beneficiaries in 2018.

[1]Medicare Part B pays 80 percent of the expenditures for drugs, and the beneficiary is responsible for the remaining 20 percent, which may be covered by a Medicare supplemental health insurance policy, an employer-sponsored retiree health plan, or Medicaid.

[2]Rebates are price concessions by manufacturers that are given to purchasers after the drug is delivered, and discounts are price concessions by manufacturers that are reflected in the price purchasers pay for a drug at the time of delivery.

Table 8: Total Spending and Number of Beneficiaries in the Medicare Part B Program for Brand-Name Drugs Associated with NIH's Licensed Inventions in Calendar Years 2014–2018, by Drug

	Spending[b] (beneficiaries)				
Brand name[a]	**2014**	**2015**	**2016**	**2017**	**2018**
Havrix (hepatitis A vaccine, inactivated)	$ 14,000 (249)	$ 13,000 (252)	$ 12,000 (216)	$ 21,000 (409)	$ 98,000 (1,765)
Kepivance (palifermin)	$ 417,000 (104)	$ 458,000 (107)	$ 507,000 (113)	$ 543,000 (107)	$ 412,000 (107)
Thyrogen (thyrotropin alfa for injection)	$ 13,643,000 (5,314)	$ 14,306,000 (5,086)	$ 14,325,000 (4,872)	$ 14,484,000 (4,636)	$ 12,634,000 (4,299)
Velcade (bortezomib)	$ 471,323,000 (20,351)	$ 505,044,000 (21,021)	$ 490,073,000 (20,652)	$ 483,709,000 (20,553)	$ 443,374,000 (20,262)

Source: GAO analysis of Centers for Medicare & Medicaid Services Drug Spending Dashboard data. | GAO-21-52

[a]This analysis identified brand-name drugs associated with the National Institutes of Health's (NIH)'s licensed intellectual property. Of the 33 brand-name drugs associated with NIH's licensed intellectual property, Medicare Part B covered the four listed in the table.

[b]Medicare Part B expenditures include the total amount of spending for the claim, including amounts paid by the Medicare Part B plan and beneficiary payments in the calendar year. These totals are net of manufacturer's rebates or other price concessions. Spending is rounded to the nearest thousand. This table includes brand-name drugs associated with expired NIH license agreements.

Medicare Part D Spending and Beneficiaries from 2014 through 2018

Medicare Part D is the voluntary program that provides outpatient prescription drug coverage for Medicare beneficiaries who enroll in Part D drug plans. Total spending on drugs reported for Medicare Part D reflects the amount paid by Part D plans and beneficiaries and do not reflect rebates or other price concessions received from manufacturers and others. In 2018, total Medicare Part D spending for 13 brand-name drugs associated with inventions licensed from NIH accounted for about $669 million, approximately 0.4 percent of total program spending.[3] Total program spending on these drugs varied substantially in 2018, ranging from $9,000 on Gardasil to about $324 million on Prezista (see table 9). In some cases, these drugs were used to treat a small number of beneficiaries, such as Videx EC, which treated 16 Medicare Part D beneficiaries in 2018. In other cases, vaccines, such as Havrix and Twinrix, and antiviral drugs, such as Prezista and Prezcobix, were used to treat more than 10,000 beneficiaries each in 2018.

[3]We identified three generic versions of drugs purchased by Medicare Part D that had contributions to the original brand-name version from NIH licensed inventions.

Table 9: Total Spending and Number of Beneficiaries in the Medicare Part D Program for Brand-Name Drugs Associated with NIH's Licensed Inventions in Calendar Years 2014–2018, by Drug

	Spending[b] (beneficiaries)				
Brand name[a]	**2014**	**2015**	**2016**	**2017**	**2018**
Ella (ulipristal acetate)	—	$ 5,000 (87)	$ 11,000 (202)	$ 18,000 (235)	$ 21,000 (271)
Gardasil (recombinant human papillomavirus quadrivalent vaccine)	$ 112,000 (429)	$ 90,000 (351)	$ 61,000 (215)	$ 19,000 (85)	$ 9,000 (33)
Gardasil 9 (human papillomavirus 9-valent vaccine, recombinant)	-	$ 15,000 (48)	$ 76,000 (237)	$ 131,000 (396)	$ 185,000 (537)
Havrix (hepatitis A vaccine, inactivated)	$ 1,065,000 (13,576)	$ 1,168,000 (14,740)	$ 3,152,000 (39,481)	$ 3,853,000 (49,555)	$ 12,324,000 (125,772)
Prezcobix (darunavir/cobicistat)	-	$ 40,283,000 (5,694)	$ 134,294,000 (12,279)	223,824,000 (16,153)	$ 282,038,000 (18,357)
Prezista (darunavir)	$ 393,063,000 (38,057)	$ 412,709,000 (38,311)	$ 379,269,000 (33,128)	$ 350,751,000 (27,212)	$ 323,744,000 (23,253)
Sporanox (itraconazole oral solution)	$ 3,312,000 (722)	$ 3,424,000 (687)	$ 3,626,000 (651)	$ 3,926,000 (680)	$ 3,871,000 (634)
Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide)	-	-	-	-	$ 22,705,000 (2,500)
Thyrogen (thyrotropin alfa for injection)	-	-	-	$ 388,000 (120)	$ 323,000 (94)
Twinrix (hepatitis A inactivated & hepatitis B (recombinant) vaccine)	$ 1,399,000 (8,025)	$ 1,736,000 (9,674)	$ 2,539,000 (13,727)	$ 3,589,000 (19,295)	$ 5,393,000 (27,981)
Velcade (bortezomib)	$ 13,685,000 (491)	$ 14,692,000 (537)	$ 15,264,000 (544)	$ 16,207,000 (566)	$ 14,455,000 (515)
Videx EC (didanosine)	$ 64,000 (56)	$ 46,000 (59)	$ 68,000 (68)	$ 19,000 (17)	$ 20,000 (16)
Zinbryta (daclizumab)	-	-	$ 1,781,000 (121)	$ 19,663,000 (466)	$ 4,259,000 (310)

Source: GAO analysis of Centers for Medicare & Medicaid Services Drug Spending Dashboard data. | GAO-21-52

[a]This analysis identified brand-name drugs associated with the National Institutes of Health's (NIH)'s licensed intellectual property. Of the 33 brand-name drugs associated with NIH's licensed intellectual property, Medicare Part D covered the 13 brand-name drugs listed in the table.

[b]Medicare Part D expenditures include the total amount of spending for the prescription claim, including amounts paid by the Medicare Part D plan and beneficiary payments in the calendar year. These totals do not include any manufacturer's rebates or other price concessions. Spending is rounded to the nearest thousand. This table includes brand-name drugs associated with expired NIH license agreements.

Medicaid Spending from 2014 through 2018

Medicaid is a joint federal-state health care program for low-income and medically needy individuals. Total spending on drugs reported for Medicaid reflects the amount paid by the federal and state governments and do not reflect rebates. In 2018, total Medicaid spending for 13 brand-name drugs associated with inventions licensed from NIH accounted for about $688 million, approximately 1 percent of total program spending.[4] Total program spending on these drugs varied substantially in 2018, ranging from about $5,000 on Gardasil to about $250 million on Synagis (see table 10). Individual beneficiary counts are not available for Medicaid in the dashboard data.

Table 10: Total Spending in the Medicaid Program for Brand-Name Drugs Associated with NIH's Licensed Inventions in Calendar Years 2014–2018, by Drug

	Spending[b]				
Brand name[a]	**2014**	**2015**	**2016**	**2017**	**2018**
Ella (ulipristal acetate)	$ 122,000	$ 427,000	$ 614,000	$ 1,029,000	$ 1,160,000
Gardasil (recombinant human papillomavirus quadrivalent vaccine)	$ 3,000	$ 15,000	$ 10,000	$ 3,000	$ 5,000
Gardasil 9 (human papillomavirus 9-valent vaccine, recombinant)	-	$ 71,000	$ 187,000	$ 285,000	$ 303,000
Kepivance (palifermin)	$ 179,000	$ 187,000	$ 211,000	$ 248,000	$ 245,000
Prezcobix (darunavir/cobicistat)	-	$ 29,688,000	$ 115,035,000	$ 182,724,000	$ 188,200,000
Prezista (darunavir)	$ 308,085,000	$ 324,578,000	$ 293,325,000	$ 238,408,000	$ 173,585,000
Sporanox (itraconazole oral solution)	$ 1,619,000	$ 2,014,000	$ 2,280,000	$ 2,125,000	$ 1,848,000
Symtuza (darunavir/cobicistat/ emtricitabine/tenofovir alafenamide)	-	-	-	-	$ 16,580,000
Synagis (palivizumab – injection)	$ 306,967,000	$ 221,488,000	$ 249,357,000	$ 260,924,000	$ 250,031,000

[4]We identified three generic versions of drugs purchased by Medicaid that had contributions to the original brand-name version from NIH licensed inventions.

	Spending[b]				
Brand name[a]	**2014**	**2015**	**2016**	**2017**	**2018**
Thyrogen (thyrotropin alfa for injection)	$ 3,305,000	$ 3,940,000	$ 4,663,000	$ 6,719,000	$ 4,421,000
Velcade (bortezomib)	$ 39,797,000	$ 47,410,000	$ 55,513,000	$ 58,516,000	$ 50,496,000
Videx[c] (didanosine)	$ 172,000	$ 140,000	$ 94,000	$ 49,000	$ 31,000
Zinbryta (daclizumab)	-	-	$ 452,000	$ 5,603,000	$ 1,090,000

Source: GAO analysis of Centers for Medicare & Medicaid Services Drug Spending Dashboard data. | GAO-21-52

[a]This analysis identified brand-name drugs associated with the National Institutes of Health's (NIH)'s licensed intellectual property. Of the 33 brand-name drugs associated with NIH's licensed intellectual property, Medicaid covered the 13 brand-name drugs listed in the table.

[b]Medicaid expenditures include the total amount of spending for both the federal and state reimbursements and is inclusive of any applicable dispensing fees in the calendar year. These totals do not include Medicaid rebates paid to states. Spending is rounded to the nearest thousand. This table includes brand-name drugs associated with expired NIH license agreements.

[c]Medicaid included both Videx and Videx EC, which are formulations of didanosine to treat HIV. Videx EC is an enteric coated formulation allowing for delayed release of didanosine. For the purposes of this report, these products were counted together.

Appendix IV: Comments from the Department of Health and Human Services

DEPARTMENT OF HEALTH & HUMAN SERVICES — OFFICE OF THE SECRETARY

Assistant Secretary for Legislation
Washington, DC 20201

October 2, 2020

John Neumann
Director
Science, Technology Assessment, and Analytics
U.S. Government Accountability Office
441 G Street NW
Washington, DC 20548

Dear Mr. Neumann:

Attached are comments on the U.S. Government Accountability Office's (GAO) report entitled, *"BIOMEDICAL RESEARCH: NIH Should Publicly Report More Information about the Licensing of Its Intellectual Property"* (Job code 103776/GAO-21-52).

The Department appreciates the opportunity to review this report prior to publication.

Sincerely,

Sara N. Morse
Principal Deputy Assistant Secretary for Legislation

Attachment

GENERAL COMMENTS OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE GOVERNMENT ACCOUNTABILITY OFFICE'S DRAFT REPORT ENTITLED: BIOMEDICAL RESEARCH: NIH SHOULD PUBLICLY REPORT MORE INFORMATION ABOUT THE LICENSING OF ITS INTELLECTUAL PROPERTY (GAO-21-52)

The U.S. Department of Health and Human Services (HHS) appreciates the opportunity from the Government Accountability Office (GAO) to review and comment on this draft report.

The National Institutes of Health (NIH) notes that combining patent data and royalties from the last 30 years and licensing from a shorter period, the last 20 years, may be misleading. NIH did not manage licensing in the early 1990s, and since NIH began to manage licensing, technology transfer practice has continued to mature. NIH patent licenses, and licenses from non-profit institutions more broadly, include more robust diligence terms and better monitoring and enforcement than licenses from the 1990s. Other significant aspects of technology transfer have changed: legal standards for patentability of inventions are more stringent, the patent protection period for technologies is shorter as a result of patent term changes on June 8, 1995 (e.g. NIH has a few patents still active based on applications filed before 1995, but none still active based on applications filed after June 7, 1995), small companies are more likely to develop early-stage biomedical technologies, and five years ago the patenting and licensing authority at NIH was delegated to each Institute/Center (IC) rather than managed by the central NIH Office of Technology Transfer. Assessing technology transfer at NIH by combining 20 or 30 years of practice without taking these changes into account does not properly reflect the extant operations.

Recommendation 1
The Director of NIH should revise NIH's standard commercial license agreements to incorporate a provision consistent with 35 U.S.C § 209(d)(3)(D) to put licensees on notice that the agency can terminate the license in whole or in part if the licensee has been found by a court of competent jurisdiction to have violated the federal antitrust laws in connection with its performance under the license agreement.

HHS Response
HHS concurs with GAO's recommendation. NIH will develop a clause consistent with 35 U.S.C. sec 209(d)(3)(D) to be inserted into exclusive or partially exclusive commercial patent license agreements. This new clause will be added by October 8, 2020, to new PHS exclusive or partially exclusive patent license agreements. At the next meeting of the PHS Technology Transfer Policy Board (TTPB), the Board will be asked to formally approve PHS model exclusive and partially exclusive commercial patent license agreements with the new clause.

Recommendation 2
The Director of NIH should determine – in collaboration with outside stakeholders as appropriate – what licensing information is most useful to enable the public's and policymakers' understanding of licensing outcomes and impacts and, to the extent permitted by law, publicly report such information in an accessible and searchable format to the maximum extent possible.

HHS Response

GENERAL COMMENTS OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE GOVERNMENT ACCOUNTABILITY OFFICE'S DRAFT REPORT ENTITLED: BIOMEDICAL RESEARCH: NIH SHOULD PUBLICLY REPORT MORE INFORMATION ABOUT THE LICENSING OF ITS INTELLECTUAL PROPERTY (GAO-21-52)

HHS concurs with GAO's recommendation. By October 8, 2020, NIH will add U.S. patent information to its list of Food and Drug Administration (FDA) approved products on the Office of Technology Transfer (OTT) website. NIH will develop a plan in Quarter 1 of fiscal year 2021 outlining the process for providing more information about patents and licenses on a website. The plans will take into account IT and database capabilities, the scope of patent and license information, the timing of updates, any concerns by commercial stakeholders, and the public's need for greater transparency of technology transfer activities.

Appendix V: GAO Contact and Staff Acknowledgments

GAO Contact

John Neumann, (202) 512-6888 or neumannj@gao.gov

Staff Acknowledgments

In addition to the contact named above, the following individuals made contributions to this report: Robert J. Marek (Assistant Director), Eric Charles (Analyst-in-Charge), Sada Aksartova, Adam J. Brooks, John E. Dicken, Robert Copeland, William A. Crafton, Patrick Harner, Virginia A. Chanley, Ardith A. Spence, Louise Fickel, Anika McMillon, Cindy Korir-Morrison, and Dan Lee.