What Are The Respective Roles Of The Public And Private Sectors In Pharmaceutical Innovation?

ABSTRACT What are the respective roles of the public and private sectors in drug development? This question is at the heart of some policy proposals, such as those that would give the government a share of profits from drugs at least partly developed with federal research dollars. This paper provides empirical data on these issues, using information included in the patents on drugs approved between 1988 and 2005. Overall, we find that direct government funding is more important in the development of "priority-review" drugs—sometimes described as the most innovative new drugs—than it is for "standard-review" drugs. Government funding has played an indirect role—for example, by funding basic underlying research that is built on in the drug discovery process—in almost half of the drugs approved and in almost two-thirds of priority-review drugs. Our analyses should help inform thinking about the returns on public research funding—a topic of long-standing interest to economists, policy makers, and health advocates.

The US public and private sectors are both involved in producing innovative drug products. Although industry supplies the bulk of the funds devoted to research and development, the public sector—primarily the National Institutes of Health (NIH)—supports most of the nation’s basic biomedical research.1,2

The question of what roles the different sectors play has recently become central to discussions of pharmaceutical policy. Several recent books and articles argue that the public sector is the main source of innovative drugs.3-5 The issue has been the subject of congressional debate and even made an appearance as a talking point during the 2008 presidential campaign, when then-candidate Hillary Clinton argued that various proposals for regulating drug prices were reasonable “because ultimately, the American tax payer pays for the development of a lot of these drugs through NIH grants and other kinds of research grants.”6

Background

Recoupment of Royalties and March-In Rights The belief that the public sector is responsible for a large share of drug development has fueled proposals to recoup profits from government-funded drugs—that is, to return to government coffers a share of the profits from drugs that have government-owned patents, or from drugs developed under federally funded research and development. Provisions to allow the government to recoup profits from patented drugs that are at least partly developed under federally funded research and development were considered in, but ultimately removed from, the legislation governing public-sector patenting known as the Bayh-Dole Act of 1980.7

But the idea has resurfaced periodically since then, including in proposals in 2001 from Sen. Ron Wyden (D-OR) and in 2003 from then-Rep. Rahm Emanuel (D-IL).8 And the director of the NIH, Francis Collins, recently suggested exploring licensing agreements that include “payback”
terms for drugs that are developed based on NIH technologies. Should these patented products make any money, these arrangements would steer a share of royalties back to the government to help fund future research.\textsuperscript{9} Congress has also noted “the public interest in securing an appropriate return” on NIH-funded drugs, in light of the “mounting concern over the cost to patients of therapeutic drugs.”\textsuperscript{10}

In addition to proposing recoupment of royalties, some advocates have urged the public sector to exercise its “march-in” rights to reduce drug prices, which, they argue, would also expand access to medicines. The Bayh-Dole Act established the government’s “march-in” right, saying, in part, that a government funding agency can ignore the exclusivity of a drug patent awarded under the terms of the act and grant additional licenses to produce the drug if certain criteria are met.

One of those criteria is the failure of the entity that receives the patent to satisfy what section 203 of the act calls the “health and safety needs” of consumers. Thus, scholars have urged the NIH to use this “march-in” authority to ensure that generic versions of drugs are available when patented versions are not being sold at reasonable prices.\textsuperscript{11} Health advocacy groups have filed petitions requesting the NIH to do so for a number of important drugs.\textsuperscript{12} To date, the NIH has not granted any of these requests.

The basic argument for recoupment is that private firms should not receive the bulk of the profits from drugs that resulted in significant part from public funding. Similarly, the logic behind using the march-in authority is that taxpayers should not have to pay twice for publicly funded research—once through taxes, and once through monopoly prices or restricted access to drugs.

Previous academic research—including case studies,\textsuperscript{13} surveys,\textsuperscript{14,15} and bibliometric analyses—\textsuperscript{16} which combine analyses of contents and citations—provide support for these arguments. The results show that public-sector research has an important impact on drug development. Government reports also indicate that the public sector has played a role in the development of particular drugs.\textsuperscript{17} Other analyses relate variations in public-sector funding across classes of drugs to patterns of Food and Drug Administration (FDA) approval of new drugs, with medicines more likely to be approved if the government supported their development.\textsuperscript{2,18} These previous studies generally focused on the overall role of public-sector funding in drug development, including both direct and indirect influences.

**Intellectual Property Rights** For recoupment and march-in proposals to be feasible, the government must have intellectual property rights—a form of ownership—to a drug. There are two ways for this to happen.

The first is that the government agency involved—typically the NIH—holds the patent. This has happened on a few occasions, when research conducted at the NIH has produced a marketable drug. A second, more common scenario is when the government funds external researchers—usually at a nonprofit research organization, such as a university—and the patent on the resulting invention acknowledges government support in what is called a “government interest statement.”\textsuperscript{19}

Government ownership of patents occurs when the government directly supports the research underlying these patents. Public-sector research can also have important indirect effects on drug development, including the creation of research tools used in drug development and the production of biological knowledge that helps guide research toward productive pathways. Even industry representatives agree with the widely held belief that such informational results of basic research are important for drug development.\textsuperscript{20}

**Scope of Paper** In this paper we provide new data to assist policy makers who are considering expanding recoupment or march-in measures. Our analyses also should help inform thinking about the returns on public research funding—a topic of long-standing interest to economists, policy makers, and health advocates. How large is the government’s direct impact on, and thus the scope for, the recoupment and march-in policies discussed above? How does this direct impact compare in magnitude to the government’s indirect impact? What roles do the public and private sectors play in pharmaceutical innovation? We examine these questions below, linking data on drug approval, patents, and consumers’ drug spending to information on publications and patents emanating from public-sector research.

**Study Data And Methods**

**Drug Data** Our analysis brings together a range of publicly available data from such federal agencies as the Patent and Trademark Office,\textsuperscript{21} the National Library of Medicine,\textsuperscript{22} the FDA,\textsuperscript{23,24} and the Agency for Healthcare Research and Quality (AHRQ).\textsuperscript{25}

We started with all new drugs—in FDA parlance, new molecular entities (NMEs)—approved between 1988 and 2005, using data from the Drugs@FDA database.\textsuperscript{23} This resulted in a sample of 478 newly approved drugs. We col-
lected patent information for these drugs using information from the FDA’s Orange Book, including hand-coded data from hard-copy versions of the book from 1988 to 2001 and information from electronic versions thereafter.

Focusing on new drug applications allowed us to capture most drugs approved over this period. To our knowledge, ours is the most comprehensive study to date of the public sector’s role in pharmaceutical innovation. However, the sample did exclude some large-molecule (biotechnology) drugs, for reasons we discuss below.

To examine potential differential roles of public-sector patents across different types of drugs, we also determined whether each of the new drugs was given “priority review”—which means that the review takes less time—by the FDA. Priority review is “given to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists.” One example is imatinib (marketed as Gleevec), a cancer-fighting drug, which was granted priority review in 2002 to treat a form of leukemia. Experts such as Michie Hunt have argued that priority-review drugs represent higher levels of innovativeness than other drugs.

We also collected information on sales of the drugs in 2006, using information from the Prescribed Medicines File of the Medical Expenditure Panel Survey (MEPS).

Finally, because the policy discussion about the roles of the public and private sectors in pharmaceutical innovation has received special attention in the context of HIV/AIDS drugs, we flagged these drugs for separate analyses, using information from the FDA to identify them. Of the 478 drugs in our sample, 379 were covered by at least one patent. These 379 drugs had 1,073 distinct patents associated with them. Because our measures of public-sector influence were based on information in the patents associated with drugs, we focused our analyses on these 379 drugs. For each of the patents on these drugs, we collected information about the primary holder of the patent; information contained in the government interest statements, discussed in the following paragraph; and all citations in these patents to previous patents and scientific publications.

**INDICATORS OF PUBLIC-SECTOR INVOLVEMENT**

We defined as public-sector patents all of those that were assigned to a government agency (which generally resulted from research conducted inside that agency) and all of those with government interest statements (most of which came from academic laboratories that had received government funding, generally through extramural research grants). The recipients of federal research grants are required to acknowledge government funding in their patent applications. These public-sector patents are the target of the recoupment and march-in strategies discussed above.

We used citation data in the patents associated with approved drugs as a proxy for the indirect impact of public-sector funding. Patent applicants are required to disclose any previous patents and publications that are related to their research. At least in theory, failure to do so can result in strong penalties for the applicant and his or her attorney, and invalidation of the patent.

A number of previous studies have used citation data to measure intellectual influence or knowledge flows between public- and private-sector researchers. We discuss our citation data in detail in the Appendix.

**LIMITATIONS**

▸ **SAMPLING FRAME:** Our reliance on drugs with patent data in the Orange Book potentially excluded some biotechnology drugs. Many of these drugs receive biological licenses rather than patents, so they are not subject to Orange Book listing requirements.

To examine the extent of this underrepresentation, we consulted a list of biotechnology drugs approved between 1982 and 2005. Overall, 57 percent of the drugs on that list were the subject of patents and thus would be included in our sample. Biotechnology drugs are generally believed to be more influenced by public-sector research than traditional pharmaceuticals are. Thus, any exclusion of these drugs probably understates the importance of the public sector.

Although we don’t have data for the entire period, in 2004–05—the last two years covered by our data—the FDA approved seven biological licenses, compared to forty-nine licenses for new molecular entities.

▸ **PATENT CITATION DATA:** Our assessment of the government’s indirect role in pharmaceutical innovation relies on patent citation data. Although citation analyses have long been used in policy and academic research, recently econ-
omists have expressed two concerns: that not all citations represent real knowledge flows, in which case we would be overstating the indirect public-sector role; and that not all real knowledge flows are represented in citations, in which case we would be understating it.

Strategic citation—that is, deliberately not citing “prior art,” or all public information relevant to a patent’s claim of originality—is a particular concern. Although strategic citation appears to be less prevalent in drug research and development than in other fields—such as information technology—this practice could also undervalue the magnitude of the government’s indirect effect.

**Study Results**

**Drugs With Public-Sector Influence** Exhibit 1 shows the different types of public-sector influence on the drugs in our sample. The drugs that received a public-sector patent (34 out of 379) are the ones in which the government could theoretically exercise march-in authority or use a recoupment policy.

The data reveal striking differences between priority-review drugs and standard-review drugs in terms of the proportion receiving a public-sector patent. This direct government role is much more pronounced for the most innovative drugs—those receiving priority review.

The data also show that the indirect impact of government funding is much larger than the direct effect. Although fewer than 10 percent of drugs had a public-sector patent, far larger proportions of drugs had patents that cited a public-sector patent, a government publication, or both. In all cases, the public-sector influence was much greater on priority-review drugs than on those receiving a standard review.

The indirect public-sector effect also dominated the direct effort when we examined the sales of the drugs, as reported in MEPS. The 478 drugs in our sample were associated with $132.7 billion in prescription drug sales in 2006. Drugs with public-sector patents accounted for 2.5 percent of these sales, while drugs whose applications cited federally funded research and development or government publications accounted for 27 percent (data not shown).

Exhibit 2 shows that the difference between standard-review and priority-review drugs is not limited to the proportion with public-sector patents. In their patents, priority-review drugs on average cited more public-sector patents and government publications.

**Drugs For HIV And Other Conditions** The nineteen HIV/AIDS drugs we studied were exceptional in terms of all our indicators of direct or indirect government influence (Exhibit 3). Nearly a third of these drugs had a public-sector patent, and close to 95 percent cited government-funded research.

**Robustness Of Analysis** Above we noted concerns about the possibility of serious underdisclosure of government interests in patents. Because our main indicator of government patent ownership relies on this information, underdisclosure could affect our results. However, previous analyses of academic patents—patents held by a US college, university, medical school,
or funding agency, such as the NIH—show levels and patterns of public-sector influence on drug development similar to those we found.

To test the robustness of our results, we also used academic patents—which would be unaffected by underreporting in government interest statements—as an indicator of public-sector influence on our sample of drugs. We found that 12.7 percent of approved drugs had an academic patent, including 5.8 percent of standard-review drugs and 22.6 percent of priority-review drugs.44 Drugs with academic patents accounted for $3.9 billion of sales reported in MEPS in 2006.25 Here again, the indirect effect was much larger than the direct effect, with 23.7 percent of standard-review drugs, 45.8 percent of priority-review drugs, and 32.7 percent of all new drugs citing an academic patent.

Discussion

**POLICY IMPLICATIONS** Previous research suggests that the public sector plays an important role in pharmaceutical innovation. However, this scholarship—with some exceptions11,15—has not generally drawn much of a distinction between direct versus indirect roles. Using patent and bibliometric data, we found that the indirect influence of the public sector on drug development was much larger than the direct effect. Both effects were much greater for priority-review than for standard-review drugs.

This analysis underscores why it is important to distinguish between the direct and indirect roles of government funding in pharmaceutical innovation. For example, policies such as recoupment and march-in would apply only to drugs in whose development the government had played a direct role.

At least for the drugs in our sample, our estimates suggest that this direct role was relatively small, and the aggregate economic impact of such policies would therefore be limited. To be sure, there could be other arguments for these policies beyond their economic impact. For example, policy makers might want to curb the use of patents to restrict patients’ access to medicines developed through taxpayer rather than private-sector funding no matter how rare that use is. These are, ultimately, ethical issues.

Finally, our analyses suggest the need to be careful in generalizing from one drug class to another. Our data suggest that the class of drugs for HIV/AIDS is an outlier: Both the direct and the indirect roles of the public sector were more pronounced for this class than for others.46 This may reflect the success of advocates for people with HIV/AIDS in lobbying for NIH funding for both basic and clinical research on HIV and AIDS, and also in stimulating FDA approval of drugs for HIV/AIDS.46
**Conclusions**

Our work provides new evidence for policy discussions about the roles of the public and private sectors in pharmaceutical innovation, although our findings are subject to all of the caveats discussed above.

We found that government support—through publicly funded research—had a large indirect impact on pharmaceutical innovation. The direct effect of government support—that is, cases where the government owns the patents outright or has claims on the intellectual property involved in the drugs’ development—is more limited, but still large for the most innovative drugs, those whose applications received priority review by the FDA.

Future research should extend our analyses to broader contexts, such as biotechnology drugs and drugs currently under development; examine other channels of public-sector involvement, including the funding of clinical trials; and complement our quantitative results with small-sample case studies.

This work was supported in part by an unrestricted grant from the Merck Foundation to the Columbia-Stanford Consortium on Medical Innovation. Bhaven Sampat also received financial support from the Robert Wood Johnson Foundation’s Investigator Award Program and from the Ford Foundation. Both authors were paid consultants on a project for the Office of Science Policy of the National Institutes of Health, from which the idea for this paper emerged.

**Notes**


11. Arno PS, Davis MI. Why don’t we enforce existing price controls? The unrecognized and unenforced reasonable pricing requirements imposed upon patents deriving in whole or in part from federally funded research. Tulane Law Rev. 2001;75:631–93.


19. Although less than half of government funding for biomedical research is for clinical research (Note 1), another potential direct impact on the part of the government is via funding of clinical research on drugs, including sponsorship or copossorship of the clinical trials used for FDA approval. The various incentives offered by the Orphan Drug Act of 1983, and tax credits provided for research and development in general, represent other types of direct support that our analyses do not capture.


29 Food and Drug Administration. Antiretroviral drugs used in the treatment of HIV infection [Internet]. Silver Spring (MD): FDA; [cited 2011 Jan 3]. Available from: http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/HIVandAIDSActivities/ucm118915.htm

30 Of the ninety-nine drugs without patents, about one-fourth (twenty-three) were antibiotics of certain types that were not subject to the Orange Book regime until 2008. After these drugs are excluded, drugs without patents accounted for only 5 percent of sales reported in the Medical Expenditure Panel Survey (MEPS) in 2006, half of which came from one drug. The manufacturers of new drugs without patents rely solely on market exclusivity to recoup their investment.


34 To access the Appendix, click on the Appendix link in the box to the right of the article online.


41 Many scholars, such as Carolyn Asbury, believe that public-sector research has traditionally played an especially prominent role in the development of orphan drugs—drugs that target rare diseases. To investigate this question, we looked separately at drugs with and without orphan designations, as indicated at Drugs@FDA. About 16 percent (59 of 379) of the drugs in our sample were orphan drugs. These drugs were more likely to have NIH patents than nonorphans (24 percent versus 6 percent; p ≤ 0.01) and more likely to cite NIH patents or publications (86 percent versus 44 percent; p < 0.01). Asbury CH. Orphan drugs: medical versus market value. Lexington (MA): Lexington Books; 1985.


44 Most of the drugs that we studied (324 of 379) had neither academic patents nor patents citing government funding. A handful (7) had NIH patents but not academic patents. And some (21) had no patents indicating government funding but did have academic patents. When Salomeh Keyhani and colleagues examined data on NIH funding of clinical trials, they found that the NIH role was much stronger with HIV drugs than other classes of drugs. Keyhani S, Dienzer-West M, Powe N. Do drug prices reflect development time and government investment? Med Care. 2005; 43(8):753–62.

Bhaven Sampat and Frank Lichtenberg, both of Columbia University, tackle a key question in this paper: What are the respective contributions of the government and the private sector in research and development of new pharmaceutical drugs?

Drawing on information contained in drug patents, among other sources, they find that direct government funding is important in research and development for the most innovative new drugs, which typically proceed through the Food and Drug Administration’s (FDA) “priority-review” process for approval. Direct government funding is less important for research and development on so-called standard-review drugs that proceed through the FDA’s normal review process.

Their analysis can be helpful in understanding the merits of various policy proposals, the authors say—such as those that would attempt to recapture a share of drug profits and return them to the government.

Sampat is an assistant professor in the Department of Health Policy and Management at the Mailman School of Public Health. His coauthor, Lichtenberg, is the Courtney C. Brown Professor of Business at the Columbia University Graduate School of Business.

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The idea for this paper crystallized after the National Institutes of Health (NIH) Office of Science Policy asked them and other researchers to help think about measuring the effects of the research it funded. This office provided a sounding board, Sampat says, “for our ideas about potential measures and empirical approaches.”

The authors note that although they view their paper as a comprehensive study, they take seriously the caveats offered in the paper that may contribute to an underestimation of the public-sector role. For instance, they ask, does underreporting of government interests lead to an understatement of the public-sector role? The pair say that they plan to continue to collaborate on these issues.

Sampat earned all of his undergraduate and graduate degrees from Columbia University, receiving a doctorate in economics in 2001. He taught at Georgia Tech before returning to Columbia in 2005.

Lichtenberg’s doctorate in economics came from the University of Pennsylvania. He won the 2010 Garfield Economic Impact award from Research!America for research on how new cancer drugs have affected cancer survival in the United States.