HEALTH & MEDICINE

Are We 'Paying Twice' for Pharmaceuticals?

The use of prizes could resolve concerns that drugmakers receive improper rents for their discoveries.

BY DAVID A. HYMAN AND CHARLES SILVER

Pharmaceutical companies charge high prices for branded products, but in most instances the research that results in these drugs is supported financially by the National Institutes of Health (NIH) or other public sources. This leads many patient advocates to contend that Americans "pay twice" for drugs: once when tax dollars support research and development, and the second time when patients buy the drugs for personal use.

The paying-twice critique is a common lament. It appears in statements by politicians, opinion journalists, historians, and progressive economists. The policy implications of this critique are straightforward: we should stop paying twice.

Is paying twice really a problem, and if it is, what should we do about it? To answer those questions, one must work through complicated factual, legal, and philosophical puzzles. In this article, we lay out some basic facts and highlight the difficulties.

THE PAYING-TWICE CRITIQUE

In the pharmaceutical context, the paying-twice critique surfaced during debates over the 1980 Bayh–Dole Act. Bayh–Dole was a response to the perception that government-funded research was being commercialized too slowly, if at all. The act authorized nonprofit institutions (including colleges and universities) to retain ownership of inventions that resulted from government-funded research. Specifically, government kept a nonexclusive license for its own use and "march-in" rights to grant licenses to other parties under four specified circumstances. One of those circumstances involves the failure to take "effective steps to achieve practical application of the subject invention," with "practical application" defined, in part, as requiring that the "benefits are, to the extent permitted by law or Government regulations, available to the public on reasonable terms."

Bayh–Dole effectively privatized the rewards of research done by universities at public expense. That strategy was controversial; Sen. Russell Long (D–LA) gave voice to the paying-twice critique on the Senate floor when the legislation was being debated:

> There is ... absolutely no reason why the taxpayer should be forced to subsidize a private monopoly and have to pay twice: First for the research and development and then through monopoly prices.... This proposed legislation is one of the more radical, far-reaching giveaways that I have seen in many years.

This criticism has resurfaced repeatedly. Indeed, the paying-twice critique prompted the Department of Health and Human Services to require "reasonable" pricing of products that relied on a subset of government-funded basic research from 1989 through 1995. HHS abandoned that policy after concluding it was more trouble than it was worth, despite the now-familiar criticism from Sen. Ron Wyden (D–OR) that taxpayers would be "forced to pay twice for their medicines—through their taxes and again at the pharmacy."

GOVERNMENT INVOLVEMENT IN DRUG R&D

The government can contribute in a variety of ways to drug R&D. It can conduct the research itself, and it can (but need not) patent the resulting inventions. It can help fund basic or applied research in an area, and any resulting invention might (but need not) be patented by a private entity. It can invest a little or a lot in any given disease, molecule, or drug regimen. And the government's investments can be tightly linked or be quite remote to a given treatment.

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In a more extended version of this article recently published in the *Yale Journal on Regulation*, we present detailed case studies of two high-profile medications whose histories illustrate the complex interaction of public and private institutions and funding during the drug-development process. In this piece, we briefly review the literature on government involvement in drug R&D. Both approaches highlight the difficulty of disentangling public and private contributions to pharmaceutical development.

The conventional wisdom is that the government funds basic research while pharmaceutical companies fund clinical trials. The conventional wisdom supports the policy of allowing pharmaceutical companies to secure the exclusive right to sell new medicines because it implies that private companies shoulder the substantial costs of conducting "translational research." In reality, financial responsibility for basic research and translational research is divided less neatly than the conventional wisdom posits. Businesses have long sponsored a good deal of basic research, and in recent decades their share of the burden has increased. Drug-company investment in basic research soared from $3 billion in 2008 to $8.1 billion in 2014, according to the most recent National Science Foundation data by business sector. The second component of the conventional wisdom—that the private sector bears most of the cost of translational research—appears to be sounder. In 2015, the pharmaceutical and biotech industry spent $102 billion on R&D, according to Research!America, an Arlington, VA–based advocacy group.

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Researchers have also used patents to study the contributions made by public funding to the creation of new drugs and found a trend toward increasing public-sector involvement in translational research. The researchers wrote that this is consistent with "large manufacturers investing proportionally less in internal basic and translational research" as their business models shifted toward "purchasing drugs developed in start-up companies, many spun out of public sector research institutions."

A recent study focused on 248 novel drugs that received Food and Drug Administration approval from 2008 to 2017. In addition to scouring patents for signs that public-sector institutions were involved in late-stage research, they compiled their own drug-discovery histories and identified spin-off companies whose origins included publicly supported research. Their efforts revealed that 62 (25%) of the novel drugs had documented late-stage research contributions from a publicly supported research institution or spinoff company. Forty-eight products (19% of all new drug approvals) had evidence of direct publicly supported research. For all but one, the contributions were related to the drug's initial discovery, synthesis, or other key intellectual property leading to a patentable invention. For 30 of these drugs, publicly supported research institutions directly held one or more of the key patents. Another seven drugs had direct publicly supported research origins, although the patents were held by a spinoff company.

The same study found that public support was concentrated on drugs with special therapeutic importance. Drugs created with help from publicly supported research "were substantially more likely to receive FDA approval

through one or more expedited development or review pathways ... and to be first in class." They attributed the "flow of publicly funded research knowledge into the private sector for commercialization" to an increase in public funding for biomedical research and to Bayh–Dole.

A different group of researchers assessed the importance of public support by studying the contribution that NIH funding made to published research associated with 210 new molecular entities that received FDA approval from 2010 to 2016. They located more than 2 million publications relating to these drugs, found that 600,000 "were associated with NIH-funded projects," and further determined that the relevant projects received more than $100 billion in public funding. Their efforts showed that NIH funding contributed to the discovery of every new molecular entity, including the 84 that were first-in-class treatments.

Another study focused on the various models of public–private collaboration for 113 molecular and biologic drugs approved by the FDA between 2006 and 2016. They also examined the same information for 39 failed drugs that the same companies pursued during the same time period. Approved drugs had an average of 60 original research papers. Failed drugs averaged only 13. The authors inferred that "approved drugs are often associated with a more robust data set provided by a large number of institutions." When they examined the affiliations of the researchers who produced the publications, they found that academics contributed significantly to 79% of the publications associated with newly launched biologics and to 76% of those associated with new molecular entities (NMEs).

This major contribution by academics held true for all companies and across all therapeutic areas. Conversely, top pharmaceutical companies published only 10% of the papers for biologics approvals and 13% for NME approvals, while all other institute types contributed 5% or less of the publications for biologics and NMEs. For failed drugs, academics contributed 72% of the pre-termination publications on biologics and 60% on NMEs. By focusing on drugs rather than drug targets, the authors showed that academic researchers contribute significantly to translational research and are especially likely to focus on new drugs that are eventually approved.

These studies make it clear that both public and private organizations make important contributions to the discovery of new medications. Although businesses appear to spend more dollars on research overall, the public's contribution is sizeable and the research it supports is disproportionately important.

Given this factual background, how should we think about the merits of the paying-twice critique? What, if anything, needs to be done about this situation? We now turn to that issue.

A FRAMEWORK FOR THINKING ABOUT THE PAYING-TWICE CRITIQUE

The paying-twice critique has considerable intuitive appeal, which helps explain why it has been a policy perennial. Yet, that appeal does not necessarily translate into well-founded policy because there are additional considerations that the critique obscures or ignores. To clarify those issues, we begin with a short parable. We then discuss the inherent difficulty of quantifying the importance of contributions from multiple sources in the absence of a market where ex ante bargaining can occur. Finally, we consider various solutions to the paying-twice problem, including a prize system that would incentivize drug development and avoid the deadweight losses that monopolies create.

Public and private sources both make important contributions to drug research. Businesses appear to spend more dollars overall, but the public's contribution is sizeable and disproportionately important.

Parable of the ACC / The Austin Convention Center (ACC) is a handsome building that was constructed from 1990 to 1992 and subsequently renovated from 1999 to 2002 using only public funds. In May 2019, the Austin City Council unanimously approved spending $1.2 billion to expand the ACC yet again.

Like all convention centers, the Austin facility is surrounded by hotels and restaurants, including some very expensive offerings. The ACC's presence obviously increases the demand for those hotels and restaurants. Pre-COVID, a large number of people converged on Austin to attend events held at the convention center, each looking for places to stay and eat. In economic terms, by building the ACC, the city of Austin created some positive externalities (increased demand for hotel rooms and restaurants) as well as some negative externalities (increased traffic and congestion). Alternatively, to the extent that the convention center is nonrival and nonexcludable, the city of Austin was simply investing in a public good.

What should we make of the fact that Austin taxpayers paid for the ACC? More specifically, do these circumstances provide a valid basis for capping the amounts that hotels and restaurants near the ACC can charge for their wares? For requiring those hotels and restaurants to offer a lower price to residents of Austin? For taxing people who stay in hotels and eat at restaurants near the convention center? For taxing people who stay in hotels and eat in restaurants in Austin more generally or in Travis County, where Austin is located? Or should the city of Austin view a convention center as an infrastructure investment that should be funded solely by the taxpayers?

As it happens, Austin partially funds the ACC by imposing a dedicated tax on all hotel stays, whether near the convention center or not. By contrast, Austin does not impose a dedicated tax on restaurants to fund the ACC. More importantly, Austin does not impose a price cap on the amounts that hotels and restaurants can charge or attempt to ensure that these hotels and restaurants are charging only reasonable amounts, even when the customers are only in town because of an event being held at the convention center.

We begin our analysis with the parable of the ACC to make three key points:

- For pure public goods (i.e., goods that are nonrival and nonexcludable), the public should not expect users to materially contribute to funding. Stated differently, for such goods there is likely to be one principal payer: the taxpayers.
- For products and services that have elements of a public good but are to varying degrees rivalrous and excludable (like the ACC), there are likely to be multiple payers, with the precise details of their contributions varying depending on institutional dynamics and politics.
- If we want to ensure that the public receives a fair return on whatever funds it has invested in nonpublic goods (and we should), it is implausible that the optimal strategy for doing so is to require reasonable pricing of the products and services that benefit directly or indirectly from those investments. Imposing and enforcing a reasonable pricing constraint requires taxpayers to fund a complex administrative system to monitor and adjust prices. The history of government price-setting is not one that inspires confidence, even if one does not factor technological change and the public-choice dynamics into the equation. It is not an accident that we do not observe government-imposed price constraints on either hotels or restaurants, even in the area immediately surrounding the ACC.

Our parable also points to a plausible set of regulatory responses to the circumstances we confront when the government contributes to the development of a valuable product or service. One approach (exemplified by Austin's tax on hotels) is to allow the market to set prices for the desired goods and services and then tax the producers to secure a reasonable return on the government's investment. An alternative approach (exemplified by Austin's non-taxation of restaurants) is to treat the convention center as a public good that must be funded by the government if it is to exist at all, and the benefits to the restaurants as a positive externality that need not be recouped.

Of course, we should not be naive about the larger context in which these cost-allocation decisions are being made. Austin opts for one approach (taxing hotel stays) when dealing with people who are likely to be from out of town and another (not taxing meals bought at restaurants) when dealing with people who are more likely to be residents that vote in local elections. A similar dynamic applies to car rentals at the airport vs. car rentals in the community. Regardless, these two approaches are far easier to administer and adjust to changing circumstances than the reasonable-pricing model envisioned by proponents of the paying-twice critique.

Of course, the ACC is not a drug. But even for goods and services that are necessities of life, the same basic analysis applies. Believing otherwise will not work out well for anyone involved, least of all those who want to obtain the next generation of life-saving drugs.

Our theoretical framework / There are endless examples of multiple parties joining forces to contribute to the creation of a valuable asset. Some of these assets are trivial while others are vital contributors to human health and wealth. Sometimes all the involved parties are private entities, but there also are public–private partnerships and partnerships between different governmental entities.

How should we go about sorting out the relative contributions of each of these parties, thereby ensuring that they receive what they are due? Contracts provide the most obvious solution, at least when the parties can negotiate ex ante. Individuals who are starting a business together can choose their corporate form (e.g., corporation, partnership, joint venture, or limited liability corporation, for-profit or nonprofit) and allocate ownership interests based on their ex ante agreement of the relative value of the assets contributed by each party. For some transactions and circumstances, sweat equity or political connections will be highly valued, while for others it is cash or hard assets that are more important to the success of the enterprise. Some individuals will want equity while others will prefer debt. Some employees will want stock options while others will prefer salary. Salary may be tied to success, hours worked, or both. And so on.

If the parties have not negotiated a binding agreement, or if the agreement they negotiated is silent on the issue in question, the law has developed various default rules for sorting out such matters. For example, the Uniform Commercial Code provides gap-fillers in the event the parties did not explicitly contract as to any element other than quantity. More broadly, the law of restitution is designed to prevent unjust enrichment of one party at the expense of the other.

Once again, as with our parable of the Austin Convention Center, the takeaway is simple: When parties can negotiate with one another in advance, they reach terms that reflect the relative value of their anticipated contributions to the joint enterprise. In the absence of an ex ante contract that speaks to the issue, the legal system has developed various default rules, again seeking to capture the terms the parties would have negotiated if transaction costs were low and they had thought about the issue.

In the context of the drug-pricing issue, it is simply implausible that the government could insist on reasonable pricing for all drugs where the government had any involvement whatsoever in

the underlying R&D process. It is not an accident that the NIH's attempts to insist on a reasonable-pricing term from 1989 to 1995 prompted so much push-back that NIH dropped this term from its contracts, observing that its inclusion was detracting from the goals set by Bayh–Dole.

If the government wants a better deal than the royalty-free structure created by Bayh–Dole, the obvious solution (as long as we are maintaining the current patent-based system) is for the government to demand a royalty reflecting the risk-adjusted value of its contribution to the ultimate product. Those funds can be used to defray the cost of future publicly funded research (reducing the paying-twice problem going forward) or to subsidize the treatment costs of everyone who needs the drug in question. Alternatively, the government can take the royalty in the form of a price reduction for beneficiaries of government-funded programs. Finally, the money could be deposited into the general fund and be used for whatever purpose Congress desires. These royalty-based strategies are far more achievable and administrable than the reasonable-pricing model proposed by the paying-twice crowd.

Alternatively, we can side-step these difficulties by moving to a prize system to reward pharmaceutical innovation. The competition spurred by a prize regime would also make it much harder for drug companies to set inflated prices. Under a prize regime, drug companies could only charge the marginal cost of production and payers could even run an auction to determine which manufacturer would have the right to supply any given drug to their beneficiaries.

Substituting prizes for patents would also make it possible to rationalize the financial incentives for developing new drugs. Currently, expected prices and sales volumes determine the strength of these incentives. This arrangement encourages pharmaceutical companies to create new cancer treatments that retail for hundreds of thousands or even millions of dollars despite extending patients' lives only briefly. By contrast, it gives the drug makers little reason to develop new antibiotics with the potential to save lives because doctors will use the new antibiotics only when all previously existing medications fail. By linking financial rewards to delivered benefits, prizes will focus researchers on drugs that are needed.

A prize system will also eliminate the need for programs that use the prospect of earning monopoly rents and tax breaks to encourage researchers to develop treatments for uncommon diseases and establish the efficacy and safety of drugs that were on the market before testing requirements were imposed. Pharmaceutical companies have gamed these programs before and will do so again, but a prize system would render such stratagems useless.

A prize system has the potential to revolutionize the way public and private funds are used across the board, for all types of inventions. Because universities would no longer be able to patent discoveries made with public funds, as they have since the enactment of Bayh–Dole Act, grants funded with tax dollars could require open access to all results, thereby eliminating trade-secret protections as well. Expensive acquisitions of spinoffs would disappear, along with the resulting whopping private returns on research undertaken with public funds. The change would also facilitate cooperation among scientists because there would be little to gain by keeping secrets from others.

With all publicly funded basic research in the public domain, private entrepreneurs would be free to take advantage of new discoveries when trying to develop the treatments for which prizes are on offer. Presumably, prizes would offer lucrative compensation to talented researchers who reach the goal before others. But researchers would have only their talents to sell and private entities would bear the costs and risks associated with the process of turning basic research into marketable drugs. Consumers would continue to fund research, but they would buy the resulting drugs far more cheaply.

CONCLUSION

The paying-twice critique is simultaneously far more complex and far less compelling than its proponents have acknowledged. Some publicly funded research is basic research that qualifies as a true public good. Other publicly funded research does not involve public goods, but even here the relative contribution of all parties (including the risks that each one bears) must be considered. Given these dynamics and past unhappy experiences with regulatory price setting, it is wholly implausible that the efficient solution to this complex problem is to require reasonable pricing for all comers.

That is not to say that all is well with the pharmaceutical market, for reasons that go well beyond the paying-twice problem. However, if we want to address the paying-twice problem, the obvious solution is to require the payment of a royalty reflecting the contribution of publicly funded research to the drug in question, with the precise details varying depending on the nature of those contributions and the risks borne by each of the parties. *R*

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