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Government Royalties on Sales of Pharmaceutical and Other Biomedical Products Developed with Substantial Public Funding: Illustrated with the Technology Transfer of the Drug-Eluting Coronary Stent

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Abstract

This study develops a detailed description of the successful technology transfer of an invention—the drug-eluting coronary stent—originating in intramural research within the National Institutes of Health. The history of the commercialization of the invention is used to illustrate a new policy, proposed and explained in this study, for the payment to the government of royalties on the sales of biomedical products developed with substantial public funding provided through indirect as well as direct funding avenues. The proposed policy addresses concerns about the high prices that taxpayers as consumers pay for biomedical products that were developed with funding from the taxpayers as investors. The study explains the theoretical circumstances in which the policy would not adversely affect the appropriate level of R&D investment, and then uses the history of the drug-eluting coronary stent as an example where biomedical R&D is consistent with those circumstances.

Keywords: Technology transfer; Federal laboratories; R&D; Pharmaceutical prices; Biomedical research; Government royalties

JEL Codes: O31, O33, O38, H40

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1. Introduction

1.1. A Practical Problem for Publicly-Financed Biomedical Research

Society benefits from the technology transfer of inventions created by the publicly financed and publicly performed research and development (R&D) within the laboratories of U.S. federal agencies.[1] This study describes in detail an important example—the technology transfer of the invention of the drug-eluting coronary stent within the laboratories of the National Institute of Aging (NIA) within the National Institutes of Health (NIH). Society also benefits from the biomedical innovations developed by industry that do not originate with inventions in federal laboratories but nonetheless receive substantial support from public funding for the R&D investment. The example of Remdesivir, developed by the pharmaceutical company Gilead Sciences and used as a treatment for Covid-19, is used to illustrate the case where the invention occurs in industry yet receives substantial public-sector funding to support the R&D that results in the innovation.

The examples of the drug-eluting coronary stent and the Covid-19 treatment were chosen not only because one illustrates the technology transfer of a federal laboratory invention while the other illustrates industrial R&D supported by publicly funded research, but because they both provide good illustrations of the two avenues—one direct and one indirect—through which the public funds biomedical research. In this study, we propose a new policy to address a practical problem, and the policy that we propose is grounded in those two avenues for public funding.

The practical problem that we address remains despite the clear benefits from the technology transfer of inventions from publicly funded and performed research and from public funding that supports industrial R&D. The practical problem is that taxpayers play the role of investors in the R&D that generates the inventions, but then in their role as consumers of the commercialized technologies are sometimes perceived as paying "unreasonable prices" for the very innovations that they in substantial part financed. We propose a new policy of royalties that would address and mitigate the practical problem,

[1] Link and Scott (2019) provide a review of U.S. public policy toward technology transfers from U.S. federal laboratories and describe the social economic benefits—the sum of consumer and producer surplus—generated when private firms commercialize technologies invented in federal laboratories.

and we illustrate the policy using our detailed description for the technology transfer of the drug-eluting stent.

The practical problem is manifest with pharmaceuticals and medical treatments and devices, figuring prominently in public debate and legislative initiatives. The practical problem will not go away by simply explaining that society as a whole has benefited, with the social economic benefit from producer and consumer surplus generated by the commercialization of the invention exceeding the publicly financed R&D costs and the further development costs in the private sector. The distribution of the economic surplus is key to resolving the practical problem. To address the practical problem, various forms of price controls for pharmaceutical and other biomedical innovations have been proposed. The new policy of royalties that we propose in this study could be either an alternative to price controls, or because of the information that would be generated that would be useful in price negotiations, the royalties policy could be a complement to policies aimed at prices.[2]

1.2. Alternative Solutions for the Practical Problem

Since the Medicare Modernization Act of 2003, the U.S. Congress has debated and proposed legislation to authorize the Secretary of the U.S. Department of Health and Human Services (HHS) to negotiate the prices paid for prescription drugs purchased through Medicare Part D. Such negotiation is currently prohibited by the Act. In 2019 alone, legislators proposed to Congress five different pieces of legislation to authorize the negotiation.[3] Complaints about the high prices of pharmaceutical products have been prominent in public debate since as early as the late 1950s.[4] Opponents of any sort of government control of prices express concerns that incentives for R&D would be lessened, resulting in less R&D and consequently less innovation. Thoughtful proposals have

[2] Danziger and Scott (forthcoming) provides a concise presentation of the proposed royalty proposal and refers the reader to this study for the underlying historical details for the story of the invention and successful technology transfer of the drug-eluting coronary stent, and also for the description and analysis of the rivalry among the entrants to the market as competing drug-eluting coronary stents were developed.

[3] Cubanski, et al. (2019) describe the five proposals, the analyses of the Congressional Budget Office about the effectiveness of government price negotiations, and the various sources of leverage that the government would have when negotiating lower pharmaceutical prices.

[4] Scherer (2010, p. 562) observes: "Beginning already in the late 1950s, the drug makers were accused in public fora of profiteering at the expense of consumers. They argued in return that high profits were a reward for superior innovation and a necessary spur to investment in risky R&D."

formulated policies that aim to balance the need for lower prescription drug prices and yet preserve incentives for pharmaceutical innovation.[5] The proposals are necessarily quite complicated, and the concerns about the adverse effects on incentives for innovation remain.

In this study, we propose an alternative, and complementary, approach to address the practical problem—a problem of the distribution of the economic surplus created by innovations—of the high prices taxpayers pay for the pharmaceutical products, and for biomedical products more generally, that their tax dollars supported with publicly financed R&D funds. Seen as an alternative policy, rather than have the government negotiate the prices paid for biomedical products in the post-innovation market and create uncertainty about the resulting price reductions, we propose a new policy to pay, as a narrowly financial return on the taxpayers' investments, royalties from the sales of those products that are developed with substantial public funding. The taxpayers' investments generate broad social economic returns, and the narrowly financial return from the royalties would serve to address the distribution of the economic surplus. In practice, as discussed subsequently, post-innovation oligopolistic rivalry among substitutable products is anticipated. In such circumstances, or even when there was more market power in the post-innovation market, the pass-through of royalties to higher prices would be incomplete and economic surplus would be redistributed to taxpayers. Given the redistribution of economic surplus, the effective prices would be lower. However, the proposed royalties policy could be used as a complement to a policy of government negotiated prices, because the royalties policy would generate information (about the history of public support for a biomedical innovation) useful for price negotiations, and because the price negotiation policy could offset any pass through of royalties to prices.

We identify two distinct avenues through which public funds are provided to support pharmaceutical and other biomedical innovations, and the royalties that we propose are not only for products developed with direct public funding delivered through the first funding avenue, but also for products receiving indirect public funding delivered through the second avenue. To address the concerns about adverse effects on the incentives for biomedical innovation, we examine the economic theory about R&D investment and

[5] See George Mason University (2019) and Frank and Nichols (2019).

identify the circumstances for which our proposal would not have such adverse effects. We make the argument that those circumstances are likely to obtain for most biomedical R&D.

For our primary example, we use the invention of drug-eluting stents in the research laboratories at NIA and the successful transfer of the technology—as commercialized for use in interventional cardiology in the worldwide coronary stent market—to illustrate an important biomedical innovation that was supported with public funds delivered through both of the avenues for public funding for biomedical R&D. We also use the example to illustrate the dual role of the taxpayers as investors in R&D and users of its commercialized results, and to illustrate the circumstances for which the proposed government royalties would not be expected to have an adverse effect on biomedical innovation. Finally, we use the details for the history of the technology transfer of the drug-eluting stent to illustrate the proposed royalties policy.

1.3. An Overview of the Sections

Section 2 describes the two avenues through which biomedical R&D is publicly funded. The two avenues deliver public funding for biomedical research (basic investigation, "academic" research predominantly done outside of industry) and R&D (predominantly done in industry). Although the more basic research investigations are largely done in academic and federal laboratory settings, and the more applied developmental R&D work largely done in industry, there is developmental R&D in the academic and federal laboratory settings, and there is basic investigation in industry. Moreover, there is considerable feedback from more applied to more basic research. We shall refer to the range from more basic research to the more applied research and development simply as R&D.

Section 3 describes the history of the drug-eluting stents. The history is the context for our primary example of the two avenues for public funding of biomedical R&D and the dual role of taxpayers as investors and consumers.

Section 4 addresses the concerns that a policy of new royalty payments to the government would significantly reduce biomedical companies' incentives to invest in R&D and consequently reduce biomedical innovation. We explain the circumstances for which the policy would cause the R&D to be closer to the social optimum despite the fact that the

taxpayers would receive royalties from the sales of the innovations substantially financed with public funds.

In Section 5, we begin by observing that the special circumstances—for which biomedical R&D may reasonably approximate the socially optimal amount even though the R&D-investing firms do not appropriate all of the returns from the investments—align with a prominent view of pharmaceutical R&D that has been published by one of the world's leading scholars of innovation. We then use the example of the NIA/NIH drug-eluting stent (DES) to explain that the necessary circumstances arguably obtained for that case of a product invented and developed with substantial public funding through both of the two avenues for delivering public funding for biomedical R&D. We conclude that the DES case supports the argument that most biomedical innovation would be characterized by the circumstances for which the policy of government royalties would not have an adverse effect on innovation.

Section 6 describes our proposal for government royalties for biomedical products that have received significant public support for their R&D. The proposal is designed to address (1) the concerns about taxpayers who in their role as investors have supported the development of biomedical innovations yet then must pay what are perceived as unreasonable prices for those products, and (2) the concerns about biomedical companies' incentives to perform R&D. The proposal is compared with proposals that have emphasized government control of pharmaceutical prices.

Section 7 concludes by summarizing the main points developed in this study.

2. The Two Avenues for Public Funding of Pharmaceutical and Other Biomedical R&D

2.1. The First Avenue of Public Funding

We identify two distinct avenues through which public funds are provided to support biomedical innovations.

The first avenue delivers funds for research directly. The direct funding is almost entirely publicly funded "academic" research, although some of the direct funding goes for research outside of universities or federal laboratories, including some research performed by biomedical companies. In the case of the drug Remdesivir that has been much in the

news during the COVID-19 pandemic, this first avenue is illustrated by the funding of scientists, such as Dr. Mark R. Denison at Vanderbilt University, who have done research in academia that provided knowledge that underlies Remdesivir's application as a treatment for COVID-19.[6] Dr. Denison received NIH National Institute of Allergy and Infectious Diseases (NIAID) funding totaling $9,480,213 for his studies of coronavirus in a series of 41 projects spanning the years from 1989 through 2014. Five projects over the years 1997 through 2001 studied "Coronavirus 3CL Proteinase Function in Virus Replication,"[7] 26 projects over the years 1989 through 2014 studied "Coronavirus—Analysis of Polymerase Gene Products,"[8] and 10 projects over the years 2003 through 2014 studied "The Cell Biology of Coronavirus Infection."[9]

The research of the academic scientists is directly supported with publicly funded grants administered by NIH or other federal agencies. In addition to their extramural programs, the federal agencies carry out intramural research in their laboratories—within HHS, NIH, Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), and the Department of Veterans Affairs (VA), for prominent examples, but other agencies also sponsor some biomedical research. NIAID sponsored the recent clinical trial of Remdesivir as the FDA moved quickly to approve the drug for emergency use during the pandemic.[10]

Although the research environments and the treatment of intellectual property do differ, when viewed broadly, both the extramural research in universities and the intramural research within federal agencies' laboratories share a nonprofit, academic character. Also, both the NIH programs and those in universities are becoming more entrepreneurial and focused on developing intellectual property (IP).[11] Research in both academia and industry

[6] Kolata (2020).
[7] https://projectreporter.nih.gov/project_info_description.cfm?aid=6372585&icde=50362254&ddparam=&ddvalue=&ddsub=&cr=1&csb=default&cs=ASC&pball=.
[8] https://projectreporter.nih.gov/project_info_history.cfm?aid=3454721&icde=50362254.
[9] https://projectreporter.nih.gov/project_info_description.cfm?aid=8197124&icde=50362254&ddparam=&ddvalue=&ddsub=&cr=37&csb=default&cs=ASC&pball=.
[10] Kolata (2020).
[11] For examples of academia becoming more entrepreneurial, see Stinchcomb (2010) and Mullard (2020).

requires regulation and oversight.[12] Yet, it is difficult to compare such regulatory oversight because transparency is less in the for-profit setting for the R&D in biomedical companies.

Although pharmaceutical R&D and the R&D for biomedical products more generally, such as medical devices like drug-eluting coronary stents, are for the most part financed from gross profits on the sales of the products, biotechnology firms use venture capital and private equity to finance their R&D. Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs support private sector projects that in some cases result in pharmaceutical/medical products, and thus these products receive direct funding by the U.S. federal agencies.[13] Thus, although not the same mechanism for delivering the public funding, the federal agencies' SBIR and STTR programs, especially those of NIH, deliver public funds for biomedical R&D by for-profit companies. Those programs are like the academic, university funding in their direct grants, but they are like the private sector R&D in terms of the for-profit research environment in the case of SBIR, and have the for-profit research environment of the small business joined with the research environment of the sponsoring agency's laboratory in the case of a STTR project.[14]

2.2. The Second Avenue of Public Funding

The pharmaceutical company Gilead Sciences developed and patented the molecule GS-5734, known as Remdesivir. For the second avenue of public funding for pharmaceutical research, there is the indirect funding of for-profit companies' research. Public funding is provided in the sense that a pharmaceutical company's development of a drug like Gilead Science's Remdesivir is indirectly supported with public funds because the government, through Medicare and Medicaid, the VA, and the Affordable Care Act

[12] For clinical trials, both require institutional review board (IRB) approval (https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/institutional-review-boards-irbs-and-protection-human-subjects-clinical-trials).
[13] See https://sbir.nih.gov/about/what-is-sbir-sttr, https://www.sbir.gov/about, and Link and Scott (2018).
[14] In addition to the federal funds supporting their R&D, the small businesses get outside R&D funding from many other sources. For example, for SBIR projects over the years from 1992 through 2001, for a sample of 388 NIH projects, U.S. private venture capital funding averaged 1.34 percent of the total R&D investment funding, with foreign private funding adding on average 0.62 percent of the total funding, and with other private equity funding adding on average 2.31 percent of the total funding. There were many other sources of funding as well, and the information about all of those sources for the NIH sample as well as for the other agencies' SBIR projects is provided in Link and Scott (2010, Table 4, p. 595).

(ACA), purchases drugs. A portion of the pharmaceutical sales revenues from those purchases provides internally generated funds to support the pharmaceutical industry's R&D investment in new drugs.

The GS-5734 story provides a clear example where both avenues for funding are seen with the development of one drug, Remdesivir. The story also provides a clear example of the different circumstances and constraints faced by the participants in each avenue's work. In the two avenues for public funding in support of biomedical research, academic researchers and pharmaceutical/medical industry researchers face very different circumstances and constraints. Unlike directly federally funded research that is largely driven by peer review, the Freedom of Information Act, and publications, biomedical industry R&D is driven primarily by competitive forces, intellectual property, and commercial value. Research funded in the U.S. through NIH and other funding agencies is highly regulated, underwritten only after national peer review via NIH study sessions. In contrast, although the regulatory constraints on commercializing new drugs are well known, the biomedical industry R&D that develops a product to the point of being ready to address the regulatory hurdle for introducing it is not regulated, not subject to the Freedom of Information Act, and directed and designed without external or peer review. Unlike NIH-funded and university-based research, which is publication driven and with investigators who are evaluated by their productivity in papers written, pharmaceutical/medical companies do not have to report their research or findings and frequently do not. Furthermore, the criteria for NIH support and academic research grants are delineated clearly, yet there are no such criteria for the indirect funding of biomedical industry R&D through the purchases of pharmaceutical/medical products. The different circumstances and constraints just described may play a role in why we find a company like Gilead Sciences with a shelf full of unused, but potentially useful molecules like GS-5734, patented well before their usefulness has been established.[15]

In sum, the story of Gilead Science's Remdesivir illustrates the two distinct funding avenues in one drug development. The story illustrates the different treatment and constraints of drug development in the two avenues. It illustrates the resulting for-profit

[15] See Kolata (2020) for discussion of the selection of Remdesivir by Dr. Denison from Gilead Sciences' inventory of unused drugs.

patenting of potentially useful drugs at a very early stage in the development process. In the context of concern about the pricing of Remdesivir when used as a treatment for Covid-19, the story illustrates concerns about asymmetric treatment of the taxpayers as investors in the development of the drug versus the treatment of the drug company's investors. The taxpayers have the unfortunate role of being investors for whom successful innovation brings the reward of paying high prices as consumers of the innovation.

Similarly, there has been a massive effort to develop a vaccine against Covid19; Mullard (2020) provides an excellent description and discussion. In an effort to shorten the normal timeline, which can be years, at least ten different entities, including pharmaceutical companies, universities, institutes, biotech, and consortiums between these, have competed to develop an effective vaccine. In fact, the World Health Organization (WHO) counted over 100 candidates under consideration, although subsequently just a handful remain. Assuming the typical success rate for vaccine development is 6%, it is a very competitive field with few winners anticipated, although the prospects are better for vaccines developed in response to the pandemic.[16] Resources for vaccine development are coming from many sources.[17] Who will bear the cost of the required large clinical trials is yet to be determined, and pricing too is yet to be determined.[18]

The complete stories for Remdesivir and for the COVID-19 vaccine are still evolving. In Section 3, we turn to an example of a biomedical product, the paclitaxel-eluting coronary stent, that received significant public funding through both of the avenues for delivering public funding to support biomedical R&D, and for which we can also observe its commercialization history over the lifetime of its USPTO patents. First, before presenting the history of the paclitaxel-eluting stent, we describe the sizes of the two funding avenues.

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[16] Pronker, et. al. (2013, p. 1) report: "The average vaccine, taken from the preclinical phase, requires a development timeline of 10.71 years and has a market entry probability of 6%. Stratification by disease area reveals pandemic influenza vaccine targets as lucrative. Furthermore, vaccines targeting acute infectious diseases and prophylactic vaccines have shown to have a lower risk profile when compared to vaccines targeting chronic infections and therapeutic applications."

[17] See Mullard (2020).

[18] In June 2020, the 116th U.S. Congress, 2nd Session, was preparing a bill, the Coronavirus Preparedness and Response Supplemental Appropriations Act of 2020, that among several other large appropriations to respond to the coronavirus pandemic would provide $3.1 billion that, among other uses, could be used for development and manufacturing of vaccines and for their purchase (at "fair and reasonable pricing" "affordable in the commercial market") by the government.

2.3. The Sizes of the Two Avenues of Public Funding

To provide a rough estimate of the sizes of the two avenues for delivering public funds to support pharmaceutical and other biomedical R&D, we use two sources. One is the National Health Expenditure Accounts (NHEA), from the Centers for Medicare and Medicaid Services. The NHEA data are the official estimates of total health care spending in the United States.[19] The other source is the BRDIS data. "The Business Research and Development and Innovation Survey (BRDIS) is the primary source of information on domestic and global research and development expenditures and the R&D workforce for companies operating in the 50 U.S. states and the District of Columbia. The survey is conducted annually by the U.S. Census Bureau in accordance with an interagency agreement with the National Center for Science and Engineering Statistics (NCSES) within the National Science Foundation (NSF)."[20]

From the NHEA, we use the *National Health Expenditures by Type of Service and Source of Funds: Calendar Years 1960 to 2018*, and the data therein for 2018. From these data we use two expenditure items.

First, we use the item for health research expenditures (in millions) for 2018. The federal government spent $39,504 million for health research in 2018. The number that we use for our estimate of the size of the direct public funding avenue is then $39.5 billion. That amount is publicly funded direct support for pharmaceutical and medical research from the U.S. federal government; it is the research support provided through the avenue of direct funding.

Second, for the size of the indirect funding avenue, we use a statistic that is just a subset of the federal government's healthcare expenditures that would be included in the indirect avenue for delivering publicly financed R&D funds to the pharmaceutical and medical products industry. The amount we use is for one category of the government's healthcare expenditures, but it includes the majority of those expenditures that would go into the indirect R&D funding avenue. The category is "Total Prescription Drug

[19] https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/NationalHealthAccountsHistorical#:~:text=U.S.%20health%20care%20spending%20grew,spending%20accounted%20for%2017.7%20percent.
[20] https://ncses.nsf.gov/pubs/nsf19318/#&.

Expenditures" in millions of dollars for the year 2018. From that category, we sum the expenditures for Medicare ($107,248 million), Federal Medicaid ($21,339 million), Federal Children's Health Insurance Program, CHIP ($1,883 million), Department of Defense (DoD) ($4,983 million), and the VA ($4,344 million). The sum of these expenditures for 2018 is $139.80 billion. We multiply this sum of expenditures by the R&D to sales ratio for pharmaceutical and medical companies that would be the sellers of the pharmaceutical and medical products purchased by the government. To get the R&D to sales ratio, we turn to the BRDIS data.

Some companies perform R&D and also fund R&D that they contract out to other companies to perform; some companies do not perform R&D but fund R&D that they contract out to other firms, and some companies just perform R&D that they or other companies fund. Among these companies, for some, especially the largest, the R&D to sales ratios exceed 20%. For example, from an annual survey of members of PhRMA, an industry lobbying group, for 2017 the members' R&D spending was 21.4% of the members' total sales.[21] However, the government's purchases of pharmaceuticals will be dispersed over the more diverse set of firms, and so the R&D to sales ratio—that we multiply times the amount of the government purchases to have an estimate of the public's indirect funding of R&D—is the R&D to net sales ratio for all of the U.S. pharmaceutical and medicines firms. For the diverse group of firms, the R&D to net sales ratio (using just the company-financed R&D rather than all R&D, because a portion of company performed R&D is financed by the government) is 14.3 %.[22]

The sum of government's prescription drug expenditures for 2018 is $139.80 billion, and that will be an underestimate of the federal government's expenditures for pharmaceutical and medical products of which prescription drugs are a subset, so our estimate of the indirect funding of R&D will be conservative. We multiply the government's expenditures of $139.80 billion by the R&D to sales ratio of 0.143 for the

[21] See Dunn (2018).

[22] From the BRDIS data, we use the "Detailed Statistical Tables," NSF 19-318, May 13, 2019. We use Table 33, "Domestic R&D paid for by the company and performed by the company and others as a percentage of domestic net sales, by industry and company size: 2016." For the industry "Pharmaceuticals and medicines" NAICS (2012 North American Industry Classification System) code 3254, U.S. domestic R&D as a percent of domestic sales of R&D performers or funders = 14.3%, where the statistics used for both the numerator and denominator in the calculation of the percentage are representative of companies located in the United States that performed or funded R&D.

pharmaceutical and medicines companies, and our conservative estimate for the size of the indirect public funding of pharmaceutical and medical R&D is $20.0 billion.

Thus for the direct public funding of pharmaceutical and medical R&D avenue, we have $39.5 billion in direct support for R&D from the U.S. federal government. For the indirect public funding of the pharmaceutical and medical companies' R&D, we have the conservative underestimate of $20.0 billion. The direct funding avenue is larger, but the two avenues for delivering taxpayers' dollars to support R&D for pharmaceutical and medical products are of the same order of magnitude.

3. The Story of Drug-Eluting Coronary Stents

3.1. The Invention of the Drug-Eluting Coronary Stent

Our detailed example of a biomedical innovation that received significant public funding throughout its history is the story of the drug-eluting coronary stent that was invented in a research laboratory at NIA within NIH and subsequently commercialized for use in interventional cardiology in the worldwide coronary stent market. The technology earned millions of dollars in royalties for the U.S. government. Those royalties repaid many times over the public's investment in the NIA research that created the invention, and more importantly, the technology, when successfully transferred as the commercialized Taxol (paclitaxel—Taxol is the brand name for the drug paclitaxel) coated coronary stents used in interventional cardiology, allowed millions of patients to avoid coronary artery bypass surgery.

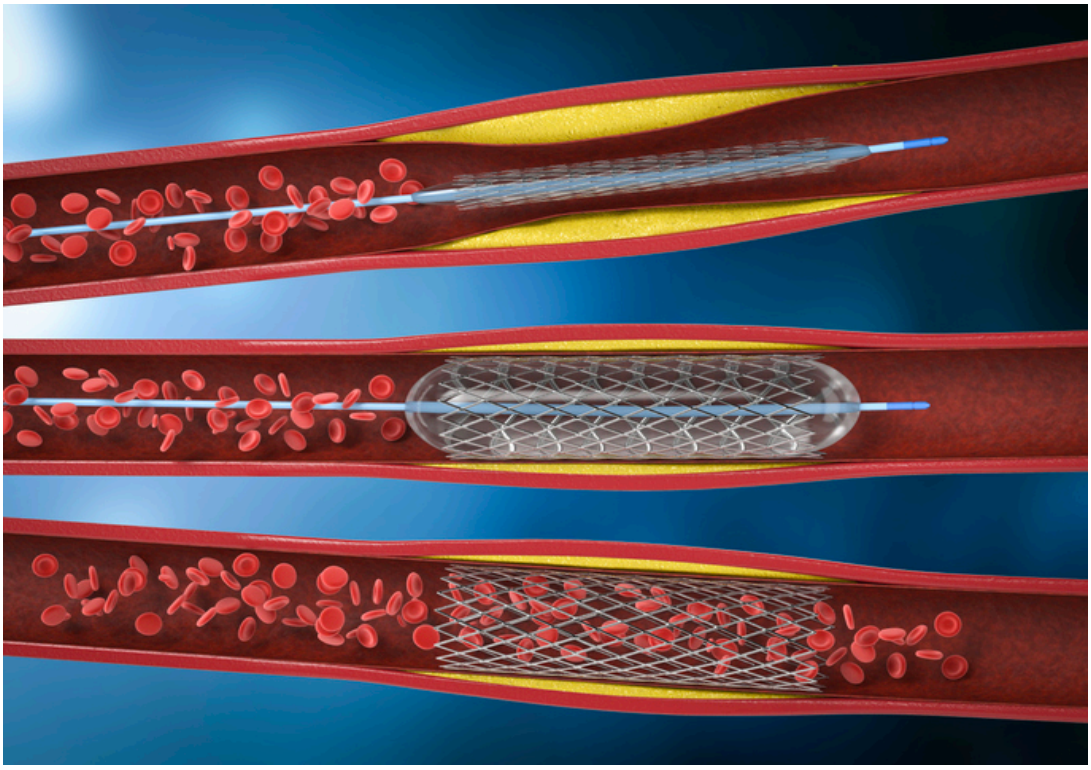
The *NIH Record* observed that 2005 was a banner year for NIH intramural researchers. That year the NIH Office of Technology Transfer collected almost $100 million in royalties from the patented and licensed inventions of the NIH intramural researchers. The *NIH Record* reported: "Even better for medical research are the millions" who would be helped by the commercialization of the inventions. The report touted the invention that was the top royalties earner for 2005. It was the invention of the drug-eluting stent by two NIA scientists, Dr. Steven Sollot and Dr. James Kinsella. They had discovered that implanting coronary stents that were coated with the drug paclitaxel significantly reduced the re-clogging of arteries. The *NIH Record* observed: "The

invention, which went on the U.S. market in 2004, has been a medical marvel for the more than half a million Americans each year who now can avoid heart bypass surgery by having the stent placed instead."[23]

Heart disease is the leading cause of death in America and coronary artery disease or narrowing, secondary to atherosclerosis, that reduces blood flow to the heart is the most common type of heart disease.[24] However, the incidence of coronary artery disease related deaths has declined over the past 40 years.[25] This has in large part been due to "mechanical" ways to treat narrowing of the coronary arteries. The first method used is a form of surgery, known as a coronary artery bypass graft (CABG), in which veins from the legs are used to bypass narrowings in the arteries and thereby increase blood flow to the heart. This requires major surgery and has gradually been replaced in many cases by innovations in interventional cardiology, a field that utilizes the insertion of a catheter (usually through the femoral artery in the leg) into the coronary arteries and, for which, the Nobel Prize in Medicine or Physiology in 1956 was awarded to Werner Forssmann. In 1977, Andreas Gruentzig, a German radiologist, showed that you could reduce the narrowing in a coronary vessel by putting a "balloon" on the end of a catheter and inflating it, i.e., "balloon angioplasty" (Figure 1), thereby initiating the field of percutaneous coronary interventions or percutaneous coronary angioplasty (PCI or PTCA). However, initially these vessels frequently narrowed again, i.e., "re-stenosed." In a major milestone, expandable "bare metal stents" (BMS) were introduced in 1986. These self-expanding stents are placed on the PCI balloon and left in place (Figure 1). However, these arteries were found to frequently re-stenose as well and another innovative approach was clearly needed.

Figure 1. Coronary Artery Stents

[23] Garnett (2006).
[24] https://www.cdc.gov/heartdisease/facts.htm: Heart Disease. Edited by Control CfD2020.
[25] Dalen et al. (2014).



Schematic of steps in stenting a vessel: Top drawing (step 1) depicts an artery with a stenosis (lighter areas along the insides of the artery's wall adjacent the stent) into which an uninflated balloon catheter encircled by an undeployed stent has been inserted. The middle drawing (step 2) depicts inflation of the balloon catheter for deployment of the stent. The lower drawing (step 3) depicts a deployed stent after balloon catheter removal. Drug eluting stents (DES) contain drugs that are released to prevent restenosis. The spheres represent red blood cells.
Source: iStock

It was at this time, that the importance of the endothelium, or inner-most layer of cells in an artery, in preventing the proliferation of underlying vascular smooth muscle cells was realized. The endothelium releases nitric oxide, which diffuses into adjacent vascular smooth muscle cells and, by activating guanylyl cyclase, prevents the smooth muscle cells from proliferating and obstructing arteries. When there is atherosclerosis, the endothelium is damaged and the vascular smooth muscle cells proliferate and narrow the artery. For these discoveries, Robert F. Furchgott, Louis J. Ignarro, and Ferid Murad were awarded the Nobel Prize in Physiology or Medicine in 1998. With the commercialization in 2003-04 of their early-1990s invention, Steven Sollott and James Kinsela, at NIH, translated this knowledge into the treatment of coronary artery disease by coating a metal stent with paclitaxel, an anti-microtubule chemical agent. They reasoned that this would

prevent the vascular smooth muscle cells from proliferating and migrating into the coronary vessel until the endothelium could reform on the stent and prevent restenosis. The efficacy of this strategy in preventing in-stent restenosis was first reported in major randomized controlled clinical trials in 2003 for paclitaxel-eluting stents and followed by several other supporting studies.[26] This was the birth of the drug eluting stent (DES).[27]

Drug-eluting stents now have approximately 95% of the stent market and have evolved through multiple generations and improvements. The first generation of DES began with the Taxol-coated (paclitaxel-coated) stent, introduced by the co-exclusive licensees of NIH's exclusive licensee, Angiotech Pharmaceutical. Thus, the commercialization of the NIH invention of the drug-eluting coronary stent began with its introduction by Angiotech's co-exclusive licensees—first by Cook Inc. in Europe in late 2002 followed by Boston Scientific in Europe in 2003 and then in the U.S. in 2004. During the same period that Angiotech's licensees introduced the paclitaxel-coated stents, Johnson & Johnson's subsidiary Cordis Corporation introduced its sirolimus-coated coronary stent, Cypher, a stent which is coated with rapamycin (also known as sirolimus), an immunosuppressive agent that, like paclitaxel, also inhibits smooth muscle cell proliferation.

The diffusion of the innovation continued when these first-generation drug-eluting stents were followed by a second generation of stents when it was realized that "late" stent thrombosis, i.e., over 30 days after placement, occurred with the original drug-eluting stents.[28] The second generation of DES was defined by the use of different materials for the stent. The stents continued to use a medical grade metal to provide structural support for the artery, but new biocompatible polymers were used to control the release of the eluted drug. The eluted drugs for the second generation of stents included zotarolimus, everolimus, and novolimus. Thus, the metal stent has a thin coating of the drug—for example, everolimus—that is gradually eluted, slowly released into the artery wall around the stent from a thin polymer (a type of plastic) coating. The stent provides mechanical support to the artery while the everolimus is slowly released into the artery wall around the stent from a thin polymer coating that helps control the release of the drug. The release of

[26] Tomberli et al. (2018, Table 1, p. 315).
[27] Stefanini and Holmes (2013).
[28] Camenzind et al. (2007).

the drug is intended to limit the overgrowth of tissue within the coronary stent—i.e. restenosis.[29] These second-generation stents were shown to be associated with fewer heart attacks and in-stent thromboses (clotting). These have now become the most widely used coronary stents in the world.

Thus, the paclitaxel-drug eluting coronary stent from Angiotech licensees Cook and Boston Scientific and the sirolimus-eluting stent from Johnson & Johnson subsidiary Cordis launched the first generation of drug-eluting coronary stents. Over the decade after the launch, drug-eluting stents diffused and evolved rapidly, with a second generation of drug-eluting coronary stents with different metals for the stent platforms, different eluting drugs, and different polymers for the delivery and release of the drug "totally replacing … first-generation DES" (Tomberli, et al., 2018, p. 313). The second generation stents with durable polymers include Boston Scientific's Promus Premiere stent, with major randomized clinical trial (RCT) in 2009; Abbott Vascular's XIENCE family of stents, with major RCTs over the period from 2007-2011, and Medtronic's Endeavor stent, with major RCT in 2009-2010 (Tomberli, et al., Table 1, pp. 315-316, and Table 2, p. 317).

Efforts to improve upon these stents continue, with polymer-free drug eluting, biodegradable, and bioabsorbable stents. However, these stents build upon the concept of incorporating a drug or compound that prevents in-stent restenosis. Currently available stents with biodegradable polymers include, among others, Boston Scientific's SYNERGY stent and Biotronic's Orsiro stent (Tomberli, et al. Table 2, p. 317).

Stent market competition continues to increase through new products and innovation. Industry analysts project the overall global stent market to grow to $11.3 billion in 2027, expanding at compound annual growth rate of 4.7%.[30] However, as the treatment of coronary artery disease has evolved, medical management with drugs, such as statins that treat lipid abnormalities and anti-hypertensive agents, along with diet and lifestyle modifications have also taken on a greater role. Importantly, the results of numerous clinical trials have helped to narrow the clinical indications for stents (versus

[29] For the discussion here, see Boston Scientific, PROMUS® Everolimus-Eluting Coronary Stent System: Patient Information Guide https://www.bostonscientific.com/content/dam/Manuals/us/current-rev-en/EL2077745_Promus_patgde_us_S.pdf; also see Fornell (2019).
[30] https://www.grandviewresearch.com/industry-analysis/coronary-stents-industry.

medical management alone and/or coronary artery bypass surgery). These may cause growth to be in more focused areas.

3.2. NIH Finds an Ideal Exclusive Licensee for the Technology Transfer of the Drug-Eluting Coronary Stent

Table 1 provides an overview of key events in the technology transfer story for the paclitaxel-eluting coronary stents. Accomplishing the successful technology transfer for an invention resulting from the research in a federal agency's laboratory is often a difficult and lengthy process. The successful commercialization of NIA's invention of the drug-eluting coronary stent attests to the length of the process. As seen in Table 1, approval by FDA and the commercial introduction in the United States came over a decade after the initial patent application was filed with the U.S. Patent and Trademark Office (USPTO).

As seen in Table 1, our story about the technology transfer process for the paclitaxel-eluting coronary stent begins with the original USPTO application by the inventors, Dr. Sollott and Dr. Kinsella, and ends with the expiration of the USPTO patents that followed from that original application. The application and the permission to practice for specified uses whatever U.S. and foreign patents ensued from that application formed the basis for NIH granting to Angiotech Pharmaceuticals an exclusive license to use the invention. The family of NIH patent applications and patents worldwide that followed from the initial USPTO application in 1993 is shown in Table 2.

Table 1. Timeline of Events for Commercialization of the NIA/NIH Drug-Eluting Coronary Stent Invention

Date	Event
7/29/93	Patent application Ser. No. 08/099,067 (subsequent applications are continuations of this original application, US9906793A to which the subsequent patents are traced)
4/18/96	Patent application (ultimately granted as US5616608A and published 4/1/97)
11/7/96	*Federal Register*, Vol. 61, No. 217, p. 57694, publishes the pre-license notification of the intent to grant an exclusive license to Angiotech Pharmaceuticals, Inc. to practice the inventions in the patents and patent applications related to U.S. Patent Application Serial No. 08/099,067 filed July 29, 1993; and all continuation applications, divisional applications, continuation-in-part applications, and foreign counterpart applications related to U.S. Patent Application Serial No. 08/099,067.
3/21/97	Patent application (ultimately granted as US6429232B1 and published 8/6/02)
4/1/97	US5616608A published, priority to US9906793A
7/9/97	Angiotech Pharmaceuticals, Inc. grants co-exclusive license to Boston Scientific Corporation

	and Cook Incorporated for the drug-eluting stent technology for which Angiotech will be granted an exclusive license in 11/19/97 agreement with NIH.
11/19/97	NIH grants exclusive license to Angiotech Pharmaceuticals, Inc.
8/17/00	Patent application (ultimately granted as US6403635B1and published 6/11/02)
January, 2002	Cook files for approval to market in the European Community its paclitaxel-eluting coronary stent to combat restenosis, making it the first company to submit for regulatory approval anywhere in the world to market a paclitaxel-eluting coronary stent to combat restenosis.
4/11/02	patent application (ultimately granted as US6500859B2 and published 12/31/02)
6/11/02	US6403635B1 published, priority to US9906793A
8/6/02	US6429232B1 published, priority to US9906793A
September, 2002	Cook receives CE Mark approval for its paclitaxel-eluting ACHIEVE™ coronary stent in the European Community. It will not be launched in Europe until a ruling is reached regarding litigation around the stent.
September, 2002	Cook receives CE Mark approval to market it paclitaxel-eluting V-Flex™ Plus PTX coronary stent in the European Community. Cook will begin selling its new drug-eluting coronary stent to European medical institutions immediately.
12/31/02	US6500859B2 published, priority to US9906793A
January, 2003	Boston Scientific receives CE Mark approval for its TAXUS™ paclitaxel-eluting coronary stent system and plans to launch the product next month in Europe and other international markets; it plans to launch the product in the United States later in the year.
February, 2003	Boston Scientific initiates the launch in Europe and in other international markets of its TAXUS™ paclitaxel-eluting coronary stent system.
September, 2003	Boston Scientific receives approval for sale of its TAXUS™ paclitaxel-eluting coronary stent system in Canada and plans to launch the product immediately in Canada.
March, 2004	Boston Scientific receives U.S. FDA approval to market its TAXUS™ paclitaxel-eluting coronary stent system and plans to launch the product in the U.S. immediately.
September, 2004	Angiotech Pharmaceuticals, Inc. and Cook Incorporated announced changes to their license agreement regarding paclitaxel-eluting stent products and related technologies. The 1997 Angiotech License Agreement has been restructured to accommodate Cook's election to exit the coronary vascular field for business reasons and to focus on the development of paclitaxel-eluting peripheral vascular and gastrointestinal stents.
September, 2004	TAXUS™ was approved for sale in Europe on January 21, 2003 and in the U.S. on March 4, 2004. As of September 30, 2004, U.S. TAXUS™ sales surpassed $1.0 billion (U.S. dollars) and total worldwide sales exceeded $1.6 billion (U.S. dollars), making the launch of TAXUS™ one of the most successful commercial launches in medical history.
November, 2004	Boston Scientific Corporation becomes the exclusive worldwide licensee to Angiotech's coronary drug-eluting stent technology. Under the terms of the 1997 License Agreement between Boston Scientific and Angiotech, Boston Scientific's royalty obligation for sales of licensed coronary vascular products (*e.g.,* TAXUS™) will be increased by one percent. This will have the effect of increasing Angiotech's TAXUS™ royalty revenues by approximately 14% (elevating the royalty tiers to 6%, 8%, and 11%, respectively).
January, 2005	Boston Scientific launched its TAXUS™ Liberte™ paclitaxel-eluting coronary stent system in 18 countries outside of the European Union and the U.S. The TAXUS Liberte stent system features Boston Scientific's next-generation Liberte™ coronary stent.
January, 2005	Boston Scientific announces the implantation of its millionth TAXUS® Express2™ paclitaxel-eluting coronary stent system, marking a major milestone for Boston Scientific and for the treatment of coronary artery disease.
September, 2005	Boston Scientific begins selling the TAXUS Liberté paclitaxel-eluting coronary stent system in Europe
April, 2005	Boston Scientific Corporation receives CE Mark approval for three large vessel sizes (4.0mm, 4.5mm and 5.0mm) of its TAXUS® Express2(TM) paclitaxel-eluting coronary stent system in Europe and other international markets. BSC plans to launch the new sizes immediately and will continue to supply all sizes of its TAXUS stent systems. Previously, the largest drug-eluting stent system size available was 4.0mm, which limited clinicians' options for treating patients with large vessels. The launch of Boston Scientific's three large vessel TAXUS stent

	systems completes its line of sizes available in Europe and international markets, making it the first company to offer a full range of stent sizes.
April, 2007	Boston Scientific receives Japanese approval for the TAXUS® Express2™ stent system.
April, 2008	Boston Scientific receives approval for sale in Canada of the TAXUS® Liberté™ paclitaxel-eluting coronary stent system.
September, 2008	Boston Scientific receives approval from the FDA to market and sell the Taxus Express2 Atom™ Paclitaxel-Eluting Coronary Stent System in the United States. The TAXUS Atom stent systems are the only drug-eluting stents available that are specifically designed to treat lesions with diameters as small as 2.25 millimeters.
October, 2008	Boston Scientific receives approval from FDA to market and sell the second generation TAXUS Liberté® Paclitaxel-Eluting Coronary Stent System in the United States.
May, 2009	Boston Scientific begins sales of the TAXUS Liberté Atom Paclitaxel-Eluting Coronary Stent System in the U.S.
July, 2009	Boston Scientific begins sales in the U.S. of the TAXUS Liberté Long Stent, which at 38 millimeters is the longest available drug-eluting stent.
June, 2010	Boston Scientific began sales of the TAXUS Element paclitaxel-eluting coronary stent in the Europe, its third-generation paclitaxel-eluting coronary stent.
12/29/10	Angiotech entered into an amendment to the November 1997 exclusive license agreement with NIH. Per the amendment, NIH agreed to eliminate (i) approximately $7.2 million of unpaid royalties and interest due on sales of TAXUS by Boston Scientific, and (ii) future royalties payable on licensed products sold by Boston Scientific going forward, in exchange for a 0.25% increase on the existing royalty rates for licensed products sold by Cook and an extension of the term for payment for such royalties of approximately two years.
February, 2012	Boston Scientific receives U.S. FDA approval for the use of the TAXUS Liberte™ and the TAXUS ION™ coronary stent systems in patients experiencing an acute myocardial infarction (heart attack).
7/29/13	US6500859B2 expires
7/29/13	US6429232B1 expires
7/29/13	US6403635B1 expires
7/29/13	US5616608A expires

Source: Authors' compilation based on European Patent Office's worldwide patent database PATSTAT, USPTO data, and U.S. Securities and Exchange Commission filings by Angiotech Pharmaceuticals and Boston Scientific Corporation.

Table 2. The Family of NIH Patents for the Paclitaxel-Eluting Stent: Applications for "Method of treating atherosclerosis or restenosis using microtubule stabilizing agent"

Application*	Filing Date	Published Patent Document**	Publication Date
U.S. Ser. No. 08/099,067	7/29/93	US9906793A	–
EP19940924519	7/29/94	EP0711158B1	12/3/03
AT19940924519T	7/29/94	AT255412T	12/15/03
DK19940924519T	7/29/94	DK0711158T3	3/22/04
PT19940924519T	7/29/94	PT711158E	4/30/04
ES19940924519T	7/29/94	ES2210258T3	7/1/04
DE1994633381T	7/29/94	DE69433381T2	10/7/04
EP20000128626	7/29/94	EP1118325B1	1/4/06
AT20000128626T	7/29/94	AT314845T	2/15/06
DK20000128626T	7/29/94	DK1118325T3	3/20/06
PT20000128626T	7/29/94	PT1118325E	5/31/06
ES20000128626T	7/29/94	ES2255477T3	7/1/06
DE1994634598T	7/29/94	DE69434598T2	10/5/06
JP19950505996	7/29/94	JP4850985B2	1/11/12
WO1994US08578	7/29/94	–	–
DE1994634598	7/29/94	–	–
EP20050027952	7/29/94	–	–
DE1994633381	7/29/94	–	–
AU19940074768	7/29/94	–	–
US19960633185	4/18/96	US5616608A	4/1/97
US19970821906	3/21/97	US6429232B1	8/6/02
US20000641549	8/17/00	US6403635B1	6/11/02
US20020121500	4/11/02	US6500859B2	12/31/02
US20020272496	10/15/02	–	–
US20050304362	12/14/05	–	–
JP20060128856	5/8/06	JP4615478B2	1/19/11
US20060644411	12/21/06	–	–
US20080072067	2/21/08	–	–
US20090618481	11/13/09	–	–
JP20100125458	6/1/10	JP4997318B2	8/8/12
US201113086277	4/13/11	–	–
US201113327548	12/15/11	–	–
US201313904928	5/29/13	–	–

*Subsequent applications are continuations of the original application, patent application Ser. No. 08/099,067 resulting in publication US9906793A, to which the subsequent patents are traced. Country codes: AT = Austria, AU = Australia, DE = Germany, DK = Denmark, EP = European Patent Office, ES = Spain, JP = Japan, PT = Portugal, US = United States, WO = WIPO = World Intellectual Property Organization.
** Publications with the T designations at the end denote translations of the European patent in the cooperating countries. For example, for the publications for Germany (DE), T2 denotes the translation of the corresponding European patent's specification. The T3 designation for Denmark (DK) is Denmark's notation indicating that the corresponding European patent specification is valid in Denmark. The publications for Portugal (PT) with the E designations denote the national translations of the two European patents.
Source: Leech and Scott (2020, Table 2, pp. 164-165), compilation from the European Patent Office's worldwide patent database PATSTAT, and from USPTO data.

In choosing Angiotech Pharmaceuticals as the exclusive licensee for the NIH patented paclitaxel-eluting stent technology, the NIH Office of Technology Transfer had chosen the ideal licensee for developing the technology and realizing its full commercial potential. Angiotech was the ideal licensee because its founder and President and CEO, Dr. William L. Hunter, had developed an Angiotech patent portfolio that was highly complementary to the NIH patent family, shown in Table 2, for the paclitaxel-eluting stent. Dr. Hunter had developed a worldwide family of patents for "Anti-Angiogenic Compositions and Methods of Use."[31] The abstract for the invention at the heart of the family of patents reads:

> The present invention provides compositions comprising an anti-angiogenic factor, and a polymeric carrier. Representative examples of anti-angiogenic factors include Anti-Invasive Factor, Retinoic acids and derivatives thereof, and taxol [paclitaxel]. Also provided are methods for embolizing blood vessels, and eliminating biliary, urethral, esophageal, and tracheal/bronchial obstructions.

Observe from the abstract that paclitaxel is an "anti-angiogenic factor." Also, observe that the paclitaxel has a polymeric carrier. Also, it is worth noting that many of the patents in the Angiotech family that were granted later, after NIH granted the exclusive license to Angiotech, had titles such as "Anti-angiogenic stents and methods of their preparation" as was the case for a patent granted to Angiotech by the European Patent Office in 2006. The Angiotech family of patents included patents from patenting authorities in many countries. The family included patents granted (or recognition of the granted European patent) by the European Patent Office, Australia, Canada, China, Germany, Denmark, Spain, Greece, Japan, Korea (South), Luxembourg, Norway, Portugal, Russia, and the United States. The very first patent granted in the Angiotech family for "Anti-Angiogenic Compositions and Methods of Use" was EP0706376B1, published on June 25, 1997. The patent application to the European Patent Office was filed on July 19, 1994. That application for that patent and all of the others in this Angiotech patent family are continuations of the original application U.S. patent application Ser. No. 08/094,536, filed July 19, 1993, published as US9453693A, to which the subsequent patents are

[31] The following account of the Angiotech family of patents is based on Leech and Scott (2020, Table 3, pp. 172-174) and was compiled by searching the European Patent Office's worldwide database, PATSTAT.

traced.[32] It is the earliest of the two priorities listed for what the European Patent Office would refer to in subsequent litigation upholding it as "the Hunter Patent" EP0706376B1. The European Patent Office lists the priorities for that patent and the others in the family of patents that Dr. Hunter developed for Agiotech as "WO1994CA00373 19940719" and "US19930094536 19930719". The WO (WIPO) application priority is PCT application CA94/00373, filed July 19, 1994, at the same time as the original application to the European Patent Office.[33]

3.3. The Successful Commercialization of the Paclitaxel-Eluting Coronary Stent

The combination of the two highly complementary families of patents provided the necessary intellectual property protection for the development and very successful commercialization of the paclitaxel-eluting coronary stent. Holding the exclusive license to use the technology protected with the family of NIH patents for the paclitaxel-eluting coronary stent, and complementing the NIH patent family with its own strong portfolio of worldwide patents for "Anti-Angiogenic Compositions and Methods of Use," Angiotech then granted co-exclusive licenses, for production and sale of products using the technology, to Cook Incorporated and Boston Scientific Corporation. As the technology transfer process played out, Cook decided to abandon coronary stents and to focus on paclitaxel-eluting peripheral vascular and gastrointestinal stents, and so Boston Scientific was granted an exclusive license for the coronary stents. Boston Scientific continually developed the paclitaxel-eluting coronary stent technology and sold the stent systems worldwide. As seen in Table 3, Boston Scientific's TAXUS paclitaxcel-eluting coronary stents generated billions of dollars in sales and paid millions of dollars in royalties to Angiotech Pharmaceuticals. Angiotech in turn paid millions of dollars in royalties to NIH over the lifetime of the patents.

[32] Thus, the priority for the Angiotech family of patents is dated just 10 days before the priority for the NIH family of patents.

[33] An important benefit of NIH's licensing agreement with Angiotech, rather than entering into a formal dispute over the patents and their claims by each of the entities, is that it expeditiously brought a life saving technology to the people who could benefit from it most. Any related litigation would have protracted the transfer of the technology to clinical practice.

Table 3. Royalties and Sales for Paclitaxel-Eluting Coronary Stents

U.S. nominal $, millions	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Boston Scientific's sales of paclitaxel-eluting coronary stents[a]												
Total			54.9[b]	1426[c]	2400	2200	1600	1200	926	539	363	230
U.S.			0	788[c]	1700	1500	1000	637	411	271	242	149
Rest of world			54.9[b]	638[c]	700	700	600	563	515	268	121	81
Royalties, milestone payments, and other license agreement payments for paclitaxel-eluting coronary stents paid to Angiotech by Boston Scientific[d]	0.0[e]	6.4[f]	4.2[g]	112.3[h]	183.6	159.5	110.5	84.1	57.4	31.0	20.7	15.1
Royalties, milestone payments, and other license fees for paclitaxel-eluting coronary stents paid to NIH by Angiotech[i]	0.0[e]	0.0[f]	1.8[g]	18.1	28.3	26.0	18.7	14.3	10.4	5.89	0.332[j]	0.618[k]

[a]Boston Scientific's net sales, on which royalty payments in a given year to Angiotech Pharmaceuticals are based, are for the period October 1 of the preceding year to September 30 of the given year.

[b]Royalties on sales actually made during the period ending December 31, 2003, were only $2.36 million because Boston Scientific prepaid royalties made on sales in the first quarter of 2004. Angiotech took $1.84 million (U.S.) of the prepayment in 2003, and the rest was taken in 2004. Royalties actually made through December 31, 2003, were approximately 4.3% of eligible drug-eluting stent sales worldwide (there were not yet sales in the U.S. or Japan), so the estimate of worldwide paclitaxel-eluting coronary stent sales is $2.36 million/(0.043) = $54.9 million.

[c]In the years before Angiotech submitted 10K reports, it did not report the sales on which its royalties were based, but it did provide the average ratio of its royalties to date as of the end of 2004 to the eligible net sales worldwide. That ratio of 6.9% was used with the royalties (just royalties, no milestone payments or up-frout licensing fees) of $98.4 million for the year to estimate worldwide sales of the stents. The worldwide sales of $1426 million = U.S. sales + rest-of-world sales. From the SEC reports, Angiotech reported the royalty rate on sales in the U.S. was approximately 8.1%, and on sales in the rest of the world was approximately 5.45%. So, (0.081)x(U.S. sales) + (0.0545)x(rest-of-word sales) = $98.4 million. Solving the two equations, U.S. sales were approximately $788 million, and the sales in the rest of the world were approximately 638 million.

[d]Angiotech Pharmaceutical's royalties and milestone payments received from Boston Scientific for the indicated year ended December 31. Prior to Cook existing the drug-eluting coronary stent business by the agreement with Angiotech in September 2004 and with Boston Scientific becoming the exclusive licensee in November 2004, some of these royalty and milestone payments to Angiotech are from Cook.

[e]For the 12 months ending September 30, 2001.

[f]For the 12 months ending September 30, 2002; includes $4.6 million in milestone payments from Boston Scientific and Cook (royalties on sales were just $0.005 million). The milestone payment from Cook was triggered by Cook filing for regulatory approval to market the paclitaxel-eluting coronary stent in Europe. The milestone payment from Boston Scientific was triggered by its initiation of commercial sales outside the regulated markets of Europe, the U.S., and Japan.

[g]The 2003 amount is for the 15 months ending December 31, 2003.

[h]Includes a $13.9 million payment from Boston Scientific to Angiotech (in conjunction with the November 2004 grant of the exclusive worldwide license for the drug-eluting coronary stents) for the right to sublicense the drug-eluting coronary stent technology to third parties.
[i]For the indicated year ended December 31; includes shared patent costs reimbursed to NIH. The amount will be an overestimate of the payments to NIH for the coronary stents. Although large payments to licensors are noted in the SEC filings and not included in the tabulation of payments to NIH as recorded in this table, the reports to the SEC otherwise describe Angiotech's license and royalty payments to licensors as primarily relating to payments to NIH based on the paclitaxel-eluting coronary stent system royalty revenue that Angiotech received from Boston Scientific. Although any noted payments to other licensors are deducted from the amounts reported here, some smaller amounts may be included. Also, some payments to NIH for Cook's use of the paclitaxel-eluting stent technology for applications other than coronary stents may be included, although such amounts are deducted when identified the SEC reports.
[j]The decline from 2010 to 2011 is due to an amendment to Angiotech's exclusive worldwide license agreement with NIH; the amendment eliminated certain license and royalty fees payable to NIH on the future sales of TAXUS by Boston Scientific Corporation. In particular, on December 29, 2010, Angiotech entered into an amendment to the November 1997 exclusive license agreement with NIH. Per the amendment, NIH agreed to eliminate (i) approximately $7.2 million of unpaid royalties and interest due on sales of TAXUS by Boston Scientific, and (ii) future royalties payable on licensed products sold by Boston Scientific going forward, in exchange for a 0.25% increase on the existing royalty rates for licensed products sold by Cook and an extension of the term for payment for such royalties of approximately two years.
[k]The increase from 2011 to 2012 is primarily due to certain shared patent costs for which NIH was reimbursed in 2012.
Source: Authors' tabulations based on information in Angiotech Pharmaceutical's filings with the U.S. Securities and Exchange Commission.

As observed earlier, the paclitaxcel-eluting stent was NIH's top royalty earner for the banner fiscal year of 2005 when NIH's royalties were almost $100 million. From Table 3, we see that the drug-eluting stents generated about $28 million for NIH in 2005.

To provide some perspective about relative magnitudes of sales and earnings, Table 4 provides rough estimates of Boston Scientific's annual gross profits from the sales of the stents, and then shows the relative sizes of Boston Scientific's profits for the stents and Angiotech Pharmaceutical's and NIH's royalties and milestone payments.[34] As shown in Table 4, Boston Scientific's gross profits on the stents were about ten times its payments to Angiotech for the exclusive license Angiotech had granted to Boston Scientific. From the time that U.S. sales began in 2004 until NIH agreed on December 29, 2010, to eliminate the requirement of Angiotech's payments of royalties, Angiotech's royalties and milestone

[34] Gross profits are net sales minus the cost of the products sold. For the firm as a whole, the gross profits must cover operating expenses (selling, general and administrative expenses), R&D expenses, royalty expenses, and litigation expenses, among other things.

revenues from Boston Scientific's payments for its exclusive license were about six times its payments to NIH for the exclusive license that NIH had granted to Angiotech.

Thus, from Table 4, we see that the narrowly defined financial return to the taxpayers as investors is a very small part of the gross profits on the commercialized paclitaxel-eluting stents. At the same time, as consumers purchasing the stents with public funds through Medicare, Medicaid, VA, and ACA, the taxpayers' funds are supporting a large amount of R&D spending that was used over the years by Boston Scientific for valuable developments of the paclitaxel-eluting stents. Both avenues for delivering public funding to support R&D are well used in the example of NIA's paclitaxel-eluting stents. We emphasize that the relatively small return to the taxpayers as investors is from a decidedly narrowly defined financial point of view. Society as a whole—the taxpayers included—benefited greatly from the commercialization of NIA's invention because of what must be considered by any reckoning to be extraordinarily large benefits for health care. It is important, therefore, that any policy proposal that would improve the return to the taxpayers as investors, or that would lower the price paid by the taxpayers in their role as consumers of the biomedical product, not reduce appropriate incentives to do R&D and generate biomedical innovation. For that reason, before describing our policy proposal, we turn next to a close examination of the incentives issue.

Table 4. Profits and the Relative Sizes of Sales, Profits, and Royalties for Paclitaxel-Eluting Coronary Stent ($ figures are nominal)

	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Boston Scientific's total sales (U.S. $, millions) of paclitaxel-eluting coronary stents[a]	54.9	1426	2400	2200	1600	1200	926	539	363	230
Estimate of Boston Scientific's gross profits (U.S. $, millions) for paclitaxel-eluting coronary stents[b]	39.7	1098	1871	1579	1152	832.0	634.7	359.5	236.4	155.5
Royalties, milestone payments, and other license agreement payments (U.S. $, millions) for paclitaxel-eluting coronary stents paid to Angiotech by Boston Scientific[c]	4.2	112.3	183.6	159.5	110.5	84.1	57.4	31.0	20.7	15.1
Royalties, milestone payments, and other license fees (U.S. $, millions) for paclitaxel-eluting coronary stents paid to NIH by Angiotech[d]	1.8	18.1	28.3	26.0	18.7	14.3	10.4	5.89	0.332	0.618
Boston Scientific's gross profits for the stents / Angiotech's revenues from the	9.5	9.8	10.2	9.9	10.4	9.9	11.1	11.6	11.4	10.3

stent royalties, milestones, etc.										
Angiotech's revenues from the stent royalties, milestones, etc. received from Boston Scientific / NIH revenues from the coronary stent royalties, milestones, etc. received from Angiotech	2.3	6.2	6.5	6.1	5.9	5.9	5.5	5.3	62.3	24.4

[a]From Table 3; see notes there.

[b]Gross profits on the paclitaxel-eluting coronary stents are very roughly estimated as the product of Boston Scientific's net sales of the stents for the year (shown in the first row) and Boston Scientific's ratio for the year of total gross profits to its total net sales as reported in its annual 10K reports to the U.S. Securities and Exchange Commission.

[c]From Table 3; see notes there.

[d]From Table 3; see notes there.

Source: Table 3 and authors' compilations from Boston Scientific's filings with the U.S. Securities and Exchange Commission.

4. The Incentives Issue

4.1. Three Cases for the Effect of Competition on Biomedical R&D

Opponents of any government involvement with the negotiations of prices for biomedical products express the concerns that the negotiated prices would lessen the incentives for biomedical companies to invest in R&D and reduce biomedical innovation. Those concerns may also be expressed about our proposal for government royalties to be introduced subsequently. In this section, we address the incentives issue and explain the circumstances for which appropriate incentives for R&D remain despite our proposed royalties to the government from the sales of biomedical products supported through either of the avenues delivering public funding for the development of the products. Our proposal to return royalties (beyond those generated by the negotiated terms for licenses for federal laboratory patented inventions such as the paclitaxel-eluting stent) would be likely to lower effective prices paid by the taxpayers. Our proposed policy could take the place of negotiated prices, although, as we shall explain, if used as a complementary policy, both it and a negotiated price policy would be more effective.

The royalties that we propose would lower the profits for the successful innovation of a new biomedical product. (1) If a firm had a monopoly of R&D investment to develop the product, the knowledge that the return on the innovative R&D investment would be less

(because of the anticipated royalties) would lower the monopolist's R&D investment. That supports the intuition behind the pharmaceutical industry's position that negotiated prices (or in the case of our proposal, royalties) would lower R&D investment with the result that there would be less innovation. However, (2) if there is rivalry among competitors in R&D who are pursuing the innovation, it is possible that the competitors will together do more R&D investment than the monopolist. Together, they may overshoot the amount of R&D that the monopolist would choose to do, and do so to such an extent that the monopolist's R&D shortfall because of the anticipation of lower profits (whether from negotiated prices or royalties) is completely offset.[35] The reason is that a firm among a group of rivals will invest in R&D as long as it anticipates that its own profits will increase by more than its costs, even though the total profits for the set of rivals increases by less than those costs. Both the reduction in an R&D monopolist's innovative investment when it anticipates appropriating less of the value of its innovation, and the overshooting by competitors of the amount of R&D that would be chosen by the monopolist can be illustrated with formal models of R&D.[36]

In the simplest of the models, that show R&D competitors replacing the shortfall in R&D investment of the monopolist, the rivals are racing to be the winner of the value (diminished by the price negotiations or by our royalty proposal), but that value for which the rivals compete does not diminish with the competition. Each rival's probability of winning the prize does diminish, but not the value to be won by the winner of the R&D race. Or, adding to the simplest model, the rivals may anticipate competing substitutes in the post-innovation market, and anticipate a set of winners who share the value of the new biomedical product. But, again, in the simplest model, that total value (whether received by one sure winner of the R&D race or shared among multiple winners) that the rivals are pursuing with their R&D remains the same. In such models, we find that the competitors may replace the monopolist's shortfall in investment that would be induced by the

[35] These ideas can be traced to a seminal paper by Barzel (1968). Barzel's paper, and other early seminal contributions such as Scherer (1967) and Kamien and Schwartz (1982) to the understanding of how competition affects R&D investment, are reviewed in Baldwin and Scott (1987).

[36] The theory of Loury (1979) as generalized by Lee and Wilde (1980) is one such formal model. An example simulated by using a parameterization of that model, and showing the monopolist's underinvestment in R&D given incomplete appropriation of the investment's value, and also showing a case where in free-entry Nash equilibrium competitors will together overshoot the monopolist's chosen amount of R&D and even get close to the socially optimal amount of R&D investment, is provided in Scott (1993, pp. 93-115).

anticipated price negotiations or by government royalties that reduced the value to the firm or firms introducing the new biomedical product.

More generally, with R&D rivalry and with the expectation that there would be multiple winners who would compete with substitutable biomedical products (for example, multiple types of patented drug-eluting coronary stents) in the post-innovation market, the total value that is anticipated for the innovation for the winners of the R&D race would change as more rivals engage in R&D competition.[37] The anticipated total value would be eroded because greater competition in the post-innovation market would reduce the profitability of each seller. Nonetheless, we could still have case (2) as long as the competition-induced diminishing of value is not too great as competition increases.

However, the erosion of post-innovation profits because of greater competition may be too great for case (2) to obtain. Thus, given the anticipation of negotiated prices or government royalties and a R&D monopolist's consequent reduction in R&D investment, it is possible that R&D competitors pursuing the innovation would together do less R&D than the monopolist would choose to do. The result is that we have two additional cases, and in each of these cases, competition among R&D rivals will not replace the shortfall in the monopolist's R&D that would be caused by government negotiation achieving lower prices or claiming royalties. (3) There may be so many R&D competitors that they anticipate in the post-innovation market many successful competing substitutable innovative solutions to the R&D problem. With the expectation of many substitutable innovations, some developed with imitation using spillovers of ideas from others and whether patented or not, the firms expect that profitability in the post-innovation will be low and less R&D investment is justified. Scherer (1980) called this regime where there is too much competition to justify large R&D investments as one of insufficient "market room."

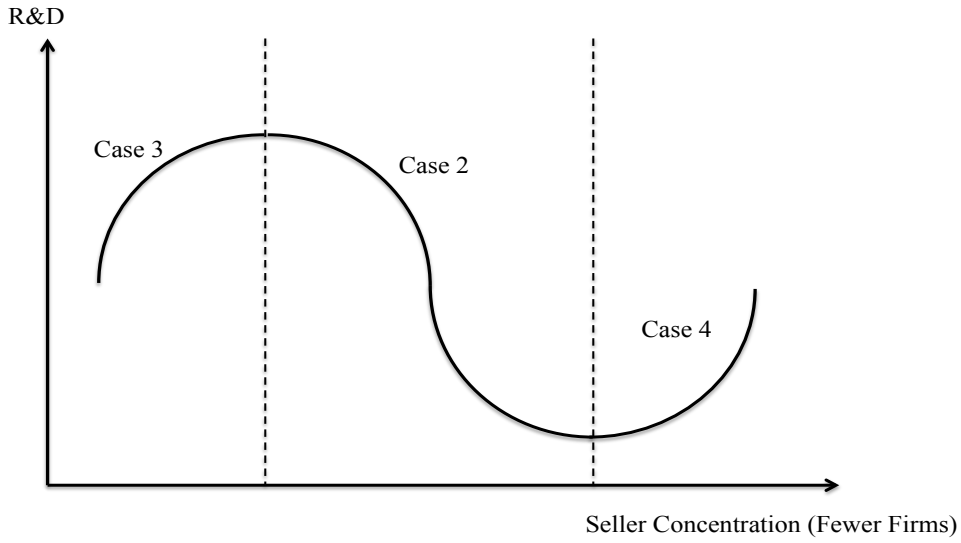
There is another case where R&D competition will not solve the problem of a monopolist's underinvestment in R&D when anticipation of negotiated prices or royalties reduces expected profits from innovation. (4) In this case, there are not many R&D competitors, indeed there are just a few. However, in equilibrium they each hold back on their R&D investment because each anticipates that an increase in R&D would be met by aggressive responses of increased R&D from its rivals. Scott and Scott (2014) refer to this

[37] For analysis of the more general possibilities, see Scott (2009).

regime, where the total R&D for a few competitors falls as the number of competitors increases, as the "Schumpeterian" situation.

Figure 2 illustrates the three cases for the effect of more competition on R&D investment. R&D investment is measured on the vertical axis, and seller concentration, which increases as the number of R&D competitors decreases, is measured on the horizontal axis. Moving from right to left in the diagram, there is more R&D competition. At first, when the numbers of competitors are small and strong strategic responses are expected, we see case (4) where R&D investment falls as the number of competitors increases. Then, in the middle region of the diagram, we see case (2) where R&D investment increases as the number of competitors increases. Then, in the left-most region of the diagram we see case (3) where more competition reduces R&D investment.

Figure 2. Structural Competition and R&D Investment



Source: Authors' adaptation of Scott and Scott (2014), Figure 6, p. 45.

Thus, competition among rivals given the negotiation of biomedical prices or government royalties may or may not offset a monopolist's choice of lower R&D and innovation, depending on whether case (2), case (3), or case (4) characterizes the situation for the development of a particular biomedical innovation.

Developing data to test the hypotheses underlying Figure 2 is challenging. There is in the literature one example that considers together all the relations shown in Figure 2. That example estimates the complex relationship between R&D and the amount of rivalry for U.S. firms' R&D investment to develop innovations to reduce toxic air emissions in manufacturing.[38] Because the firms are highly diversified and each do the particular type of R&D in multiple markets, the seller concentration measure reflects the average situation faced by an industry's sellers across the R&D-performing firms' markets. The empirical test (of the hypothesized relationships in Figure 2) was constructed to take advantage of the unusual fact that the type of R&D observed was performed by very different types of firms that operated in many different industries. Consequently, in Section 5, we will need to develop a very different type of empirical test in order to understand where the competitive circumstances for R&D investments in drug-eluting stents fit within the relationships depicted in Figure 2.

Summarizing, to this point in the discussion, economic theory tells us that if there is a monopolist of the R&D for a new biomedical product, the anticipation of effective government negotiation to lower price or to collect royalties in the post-innovation market will lessen the incentive for the monopolist to do R&D. The monopolist will invest less, and less innovation would be expected. However, if there is rivalry in R&D, with multiple firms (who also anticipate lower profits because of the government involvement with negotiated prices or royalties) competing to develop the pharmaceutical innovation, they may overshoot the monopolist's chosen amount of R&D investment and invest as much as the monopolist would have invested in the absence of anticipated price negotiations or royalties.

Yet it is still the case that the set of rivals would do less R&D than they would do if they did not anticipate the lowering of their profits in the post-innovation market because

[38] The estimation of the set of relationships illustrated in Figure 2 is provided in Scott and Scott (2014), Figure 8, p. 48.

of the government negotiations for lower prices or royalties. What we've shown is that competition can replace the monopolist's shortfall in investment caused by the anticipated government actions. So we've shown that in a special set of circumstances, rivalry does more R&D than monopoly. But both market structures still do less than they would without price controls or royalties. Then, we have found that if the monopolist underinvests (because of unappropriated spillovers, to consumers and to other firms, of its innovation's value) even without government involvement, it will underinvest even more with government negotiations of lower prices or royalties because it anticipates greater spillovers of value—it captures less of the value of its innovation. If there is rivalry in R&D, the rivals may—in case (2)—invest more in R&D than the monopolist would, and in that case, we anticipate that the R&D investment exceeds the monopolist's chosen R&D investment both with and without lower prices or royalties.

4.2. Circumstances for Appropriate Incentives for Biomedical R&D

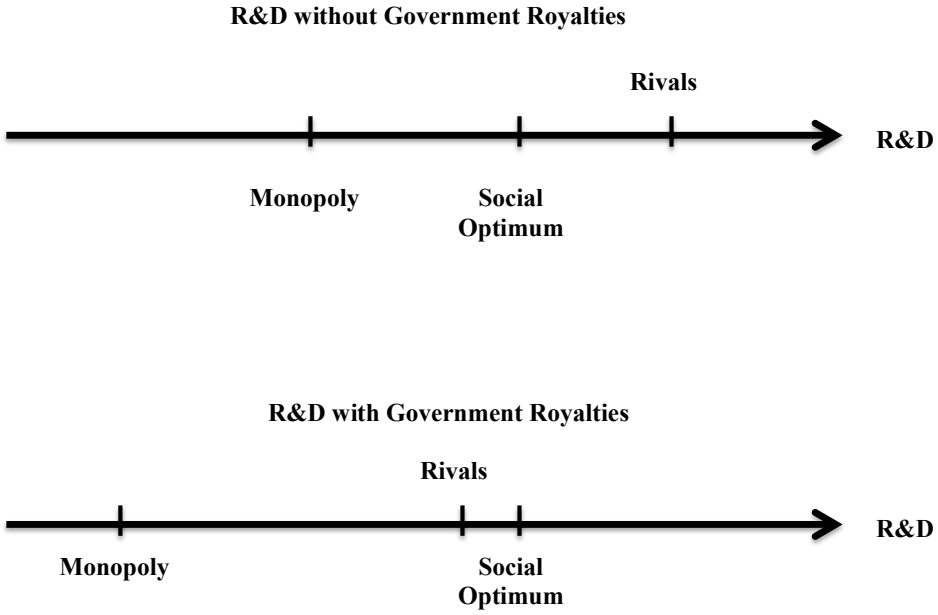
We next add to the discussion the concept of the socially optimal amount of R&D investment. From a society-wide perspective, we would want R&D investment to increase to the point where the additional benefit from more investment equals the cost of the investment.[39] Investing that amount maximizes the net value of the investment; to invest more would lower that net value. Thus, the monopolist's R&D is less than the socially optimal amount because it does not appropriate all of the social benefits. When it chooses to stop investing, its own marginal benefit equals the marginal cost, but the social marginal benefit is still greater. The monopolist's chosen R&D is even further below the socially optimal amount if a government negotiated lower price or royalties are anticipated, because the monopolist's marginal benefit from additional investment is reduced.

[39] The concept of the socially optimal amount of research has two parts. One is that additional research is done as long as the addition to the benefits (a present discounted value of the stream of benefits) exceeds the addition to costs (again a present discounted value, in this case of the stream of costs). The other part of the concept is that by benefits we mean the total economic surplus created, where total economic surplus is the sum of the consumer and the producer surpluses. For illustration of those economic surpluses in the context of the technology transfer of inventions created with research in the U.S. federal laboratories, see Link and Scott (2019). An application of the first part of the concept, i.e., the socially optimal amount of research as compared the amount of research actually performed, is provided by Scott and Scott (2015) for R&D investment in the context of standards – product standards, metrology standards, and regulatory standards to address negative externalities. The concept is one thing; its application in different situations is another.

For case (2), rivalry generates more R&D investment than the monopoly amount, whether or not there are royalties or government negotiations for lower price. So, we conclude that rivalry, if case (2) obtains, may offset the price-negotiation-induced fall in R&D for R&D monopoly, but it suffers its own drop in R&D investment because of the anticipated lower profits for the firms introducing the innovation. In all, the anticipation of royalties or negotiations for lower prices will indeed reduce R&D investment in either market structure—monopoly R&D or rivalrous R&D—but for case (2), the rivals will do more R&D than the monopoly. The rivals' R&D will overshoot the monopolist's R&D and may or may not overshoot the socially optimal amount of R&D.

The top panel of Figure 3 illustrates the case where competition in R&D results in overshooting the socially optimal amount of R&D when the government does not negotiate lower prices or receive royalties. The bottom panel of Figure 3 illustrates the change in a monopolist's R&D and the rivals' R&D if anticipated profits are less because of government royalties that we shall propose in Section 6. For the case shown, the R&D outcome with rivals pursuing the innovation is close to the socially optimal amount. As shown, the outcome is closer to the socially optimal amount of R&D than would be the case if the government did not receive the royalties that we propose in Section 6.

Figure 3. The Case Where Government Royalties Bring R&D Closer to the Optimum



Source: Authors' construction

The top panel of Figure 3 shows the case where R&D rivals overshoot the socially optimal amount of R&D investment, while a monopolist's R&D investment falls short of the socially optimal level. That case has been illustrated with the simulation of a parameterization of the R&D investment model of Loury (1979) and Lee and Wilde (1980).[40] Their model accounts for uncertainty, parallel paths, and Nash noncooperative equilibrium in rivals' R&D investment. Because of unappropriated spillover of the value of the innovation resulting from the R&D, a monopolist invests less than the socially optimal amount, and in the simulation the R&D rivals invest more than the social optimum *despite the fact* that the spillover of the innovation's value is parameterized to be 90% of the innovation's social value. In other words, the successful innovator appropriates only 10% of the innovation's social value. Moreover, accounting for both the social value and the social cost of the R&D investments, compared to the result for monopoly, the free-entry noncooperative equilibrium for the rivals has social profit closer to its maximum that is

[40] The simulation is available in Scott (1993, pp. 93-115).

reached with the socially optimal R&D investment.[41] The royalties proposal to be discussed in Section 6 would not lower an innovator's appropriated returns as dramatically as is the case in the simulation underlying the top panel of Figure 3. The policy of government royalties for innovations developed with substantial public funding might not only result in R&D investment closer to the social optimum as illustrated in the bottom panel of Figure 3, but it might also be the case that the investment would overshoot the socially optimal amount despite the anticipation of the royalties.

The development of biomedical innovations is enhanced by cooperative activities not only among private biomedical companies and researchers in federal laboratories and researchers at universities, but also among the biomedical companies themselves. For that reason, we emphasize that the rivalrous R&D that we have described and that can lead to the fortuitous outcome depicted in Figure 3 does not preclude cooperative activity also being present. Baumol (2002) explains if we think broadly about innovation rivalry in the context of the positive externalities from the spillovers of knowledge and in the context of the actual behavior of firms with licensing and joint ventures and other forms of sharing technology, rivalrous R&D among competitors may—despite the concerns about underinvestment in R&D—perform quite well. In particular, Baumol explains that the R&D rivals have the necessary incentives to share even some of their proprietary technology.[42] It is also important to emphasize that while the good performance of the rivalrous R&D outcome depicted in Figure 3 would not be a perfectly efficient outcome that could be described theoretically, as a practical matter the best solution may well be what Baumol (2002, pp. 19-29) refers to as the "somewhat optimal" performance of R&D rivals.[43]

In the next section, we examine competitive circumstances for the drug-eluting coronary stent and argue that the theoretical situation depicted in Figure 3 actually

[41] Scott (1993, pp. 109-110).
[42] See Baumol's discussions (2002, pp. 73-113) of the voluntary dissemination of proprietary technology and the markets for technology trading even among competitors engaged in rivalrous R&D investments.
[43] Scott (1995) shows that when a monopoly of R&D, or a completely cooperative R&D effort among firms, would result in technical efficiencies, the resulting underinvestment in R&D because of incomplete appropriation of returns can be overcome in theory with a well-designed public policy that simulates the competitive pressures that would increase R&D investment while allowing the technical efficiencies of the monopoly or completely cooperative effort. However, such a well-designed public policy is not practical, and the situation with rivalrous R&D shown in Figure 3 is expected to be the best practical outcome.

describes well the situation for the development of coronary stents as well as biomedical products more generally. Thus, from the many possibilities for the R&D incentive effects from government royalties on the sales of biomedical products developed with taxpayers' investments, the possibility to be expected, we argue, would typically be the good outcome depicted in Figure 3—namely the case where R&D rivalry in the context of government involvement results in an amount of R&D investment close to the socially optimal level.

Thus, to advance that argument, we turn next to looking at the history of R&D competition for the drug-eluting stent example. However, before looking at the example, we observe that two key facts about biomedical R&D competition underlie the argument that government royalties provide a way—without having adverse incentives on biomedical R&D—to avoid the situation where taxpayers pay twice to an unacceptable extent—once to support the development of new biomedical products and then again to purchase them at what are perceived to be unreasonable prices. The two key facts about R&D competition underlying the argument are as follows.

First, no biomedical firm really has a monopoly of R&D. It may be the only firm doing research on its particular product, but typically there are others who are doing R&D on their own product developments that would provide competing substitute products in a post-innovation market. A biomedical firm may create the one winner among all of those pursuing product developments to provide the particular product that all of them are pursuing with their individual R&D investments. But while there may be a monopoly in the post innovation market, there is not a monopoly of R&D. Second, innovation in the biomedical industry often has a "me-too" character because many alternative treatments are developed for the same health condition. A successful innovation is often followed by innovations that offer biomedical products that are competing substitutes; thus, typically there will not be a monopoly in the post-innovation market either.

5. The Circumstances Affecting Incentives for the Development of Drug-Eluting Stents

5.1. Scherer's Virtuous Competitive Rent-Seeking

To illustrate the foregoing ideas and to discuss them in the context of an important biomedical innovation that received substantial public funding from both of the two

avenues that we have discussed in Section 2, we shall consider the details about the R&D competitors in the development of drug-eluting coronary stents, our main example. We want to describe the correspondence between the R&D competition in the biomedical industry, as illustrated with the situation for drug-eluting stents, and the set of circumstances where that competition can make government royalties and appropriate incentives compatible. The essential question to be addressed is whether Figure 3 reasonably describes the situation for biomedical R&D. In fact, Scherer (2010, pp. 564-569) makes the argument that the answer is yes for the development of new pharmaceutical/medical products.

Scherer first observes (2010, p. 562) that the gross margins on sales for the pharmaceutical industry are among the very highest for all industries. Consistent with his observations for the pharmaceutical industry as a whole, looking at our Table 4 in Section 3, we see that our estimate of Boston Scientific's gross margins on the sales for the paclitaxel-eluting coronary stent, a medical device using the drug paclitaxel and the NIA paclitaxel-eluting coronary stent technology licensed from Angiotech Pharmaceuticals, averaged about 70% over the decade from 2003 through 2012. Scherer explains (2010, p. 562) that despite the high gross margins, when R&D expenditures are appropriately capitalized, accounting for the fact that R&D is a long-lived investment, the pharmaceutical industry does not appear to earn a supranormal rate of return given the extreme riskiness of their R&D investments.[44]

Second, Scherer explains (2010, pp. 564-569) the observation of high gross margins, high R&D to sales, and yet returns on investment that (with R&D expenditures capitalized) are only moderately above all-industry norms. He explains the set of observations with a combination of the ideas in Barzel's and his own seminal papers (Barzel, 1968; Scherer, 1967) and empirical evidence. He assumes what in Section 4 we called case 2, and then he creates and explains the theoretical situation where the

[44] Essentially, what appears to be above average profits in a given year (when the R&D in the previous years was just expensed and not treated as a long-lived asset) is really return that is needed to pay a normal return on the investors' investment in the earlier years—a return on their investments in the intangible knowledge capital that R&D spending buys.

relationship between rivalrous R&D and the social optimum is as described in the top panel of Figure 3.

In all, Scherer explains that for the pharmaceutical industry the high gross margins, high R&D, and the absence of supranormal profit may reflect the possibility that rivalrous R&D results in R&D investment close to the social optimum:

> An explanation in … accord with the evidence and consistent with received theory is that pharmaceutical companies engage in competitive rent-seeking behavior … of a virtuous character … . That is, when rents [reflected in the gross margins] are high, the companies compete vigorously to capture them by increasing their R&D (and promotional) outlays, and indeed, the companies compete so vigorously, there is little left over in the end for supranormal profit. (Scherer, 2010, p. 564).

> We conclude that the competitive rent-seeking observed in the pharmaceutical industry can help correct what otherwise might be market failures attributable to uncertainty and the disparity between social and privately appropriable benefits. Whether the "correct" amount of R&D, associated in part with the pursuit of parallel paths, … is a problem on which additional research, both theoretical and factual, is much to be desired. (Scherer, 2010, p. 569)

5.2. R&D Rivalry in the Development of Drug-Eluting Stents

We have seen that Scherer (2010, p. 569) calls for more work to ascertain whether in fact the theoretical possibility of an outcome close to the socially optimal amount of R&D, consistent with the evidence he reviews, obtains for the pharmaceutical industry. To that call, and for the biomedical industry more generally, we respond by developing the history of the R&D rivalry that has driven the evolution of drug-eluting coronary stents. We have emphasized that for the story of Figure 3 to obtain, the relationship between structural competition and R&D investment must be the one for case 2 where a larger number of competitors results in greater R&D investment. Figure 2 shows theoretical possibilities including cases 1 and 3 as well as case 2. The question is: where does the R&D rivalry for the development of drug-eluting coronary stents fit—does it correspond to case 2 and to Scherer's description of virtuous rent-seeking R&D investment by rivals?

To answer the question, we examine the historical record for the FDA premarket approvals for coronary stents and stent systems. The FDA describes premarket approval (PMA) as follows[45]:

> Premarket approval (PMA) is the FDA process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices. Class III devices are those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury. Due to the level of risk associated with Class III devices, FDA has determined that general and special controls alone are insufficient to assure the safety and effectiveness of Class III devices. Therefore, these devices require a premarket approval (PMA) application under section 515 of the FD&C Act in order to obtain marketing approval. …
>
> PMA is the most stringent type of device marketing application required by FDA. The applicant must receive FDA approval of its PMA application prior to marketing the device. PMA approval is based on a determination by FDA that the PMA contains sufficient valid scientific evidence to assure that the device is safe and effective for its intended use(s).
>
> The PMA applicant is usually the person who owns the rights, or otherwise has authorized access, to the data and other information to be submitted in support of FDA approval. This person may be an individual, partnership, corporation, association, scientific or academic establishment, government agency or organizational unit, or other legal entity. The applicant is often the inventor/developer and ultimately the manufacturer.

Coronary stents and stent systems are Class III medical devices and require FDA premarket approval. We can therefore use the time series of FDA premarket approvals to document the intensity of R&D rivalry among the several firms developing coronary stents and stent systems during the time reviewed in Section 3's history for the paclitaxel-eluting coronary stent. As described in Section 3.1, after the launch of the paclitaxel-eluting stent, drug-eluting coronary stents of several firms were being continually introduced, developed and improved. Boston Scientific's paclitaxel-eluting stents were no exception; they continued to evolve as Table 1's history shows.

Several firms were developing coronary stents and stent systems with R&D investments. The results of the R&D competition can be seen in the historical record of the FDA's premarket approvals for the coronary stents and stent systems being developed. We searched the FDA PMA database.[46]

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[45] https://www.fda.gov/medical-devices/premarket-submissions/premarket-approval-pma.

[46] https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm. We searched by year, so for example for 2014, we entered the search dates from 01/01/2014 to 12/31/2014, and for the device we entered coronary stent.

Table 5 shows the yearly premarket approvals and the number of different firms that applied for approvals. The yearly record is shown beginning in 2002, the year before Boston Scientific (the exclusive licensee of Angiotech Pharmaceuticals once Cook Inc. withdrew from the coronary stent market in 2004) began selling the paclitaxel-eluting coronary stent. We end the yearly record in 2012, the last year before the basic USPTO patents for the paclitaxel-eluting stent—that were the basis for the exclusive license to Angiotech and then Angiotech's original co-exclusive licenses to Cook Inc. and Boston Scientific—expired. Because the coronary stents and stent systems were being developed continuously, there are multiple approvals for a firm's stent system as new developments occur and new applications for premarket approvals are made so that the latest development is FDA approved for commercial use. As the development process proceeds, there are changes to the specifications (for example for the size of the stent) or formulations (for example for the eluting drug and details of the delivery of the drug) or target populations or applications (for example those presenting with an acute heart attack). With each change as R&D generates an evolution of a coronary stent system, new applications are filed to ensure that the latest version of the medical device has the FDA's approval.

From Table 5, we see the manifestation of the R&D rivalry between the firms that were developing coronary stents and stent systems. We see the rivalry as it is reflected in the stream of resulting product developments that received FDA premarket approvals. Looking at the premarket approvals over the years, we see just what Scherer's hypothesis of virtuous rent-seeking R&D predicts. Gross margins for coronary stents, just as for biomedical products more generally, were high. The six firms—just five after Cook exited the coronary stent market to focus on using the paclitaxel-eluting stents for peripheral vascular applications—that were developing the new coronary stents and stent systems were competing with R&D to bring improved products to market, products that they continually developed and improved. We see their virtuous rent-seeking behavior in the growing stream of the premarket approvals that the FDA granted to them. Their rivalrous R&D efforts to develop their products and win bigger shares of the coronary stent market are in essence monitored and measured with the record of the PMAs granted by the FDA.

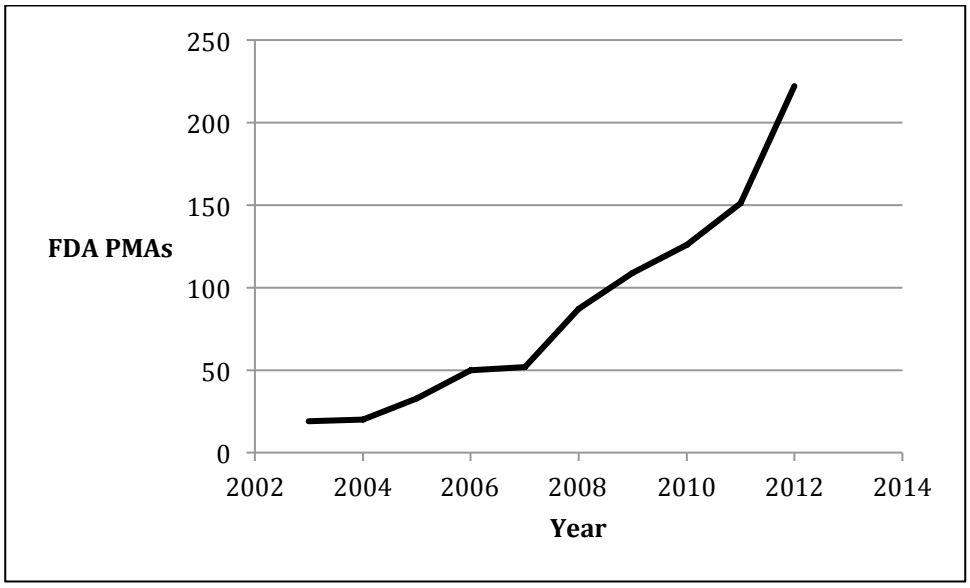
Table 5. U.S. FDA Premarket Approvals (PMAs) for Coronary Stents or Stent Systems

Year	Number of (PMAs)	Number of different firms receiving PMAs	The firms receiving PMAs
2002	28	4	Abbott Vascular, Inc.; Boston Scientific Corp.; Cook, Inc.; Medtronic Ireland
2003	19	4	Abbott Vascular, Inc.; Boston Scientific Corp.; Cordis Corp.; Medtronic Ireland
2004	20	5	Abbott Vascular, Inc.; Boston Scientific Corp.; Cordis Corp.; Medinol Ltd.; Medtronic Ireland
2005	33	5	Abbott Vascular, Inc.; Biotronik GMBH & Co. KG; Boston Scientific Corp.; Cordis Corp.; Medtronic Ireland
2006	50	4	Abbott Vascular, Inc.; Boston Scientific Corp; Cordis Corp.; Medtronic Ireland
2007	52	5	Abbott Vascular, Inc.; Boston Scientific Corp; Cordis Corp.; Medinol Ltd.; Medtronic Ireland
2008	87	5	Abbott Vascular, Inc.; Boston Scientific Corp; Cordis Corp.; Medinol Ltd.; Medtronic Ireland
2009	109	4	Abbott Vascular, Inc.; Boston Scientific Corp; Cordis Corp.; Medtronic Ireland
2010	126	4	Abbott Vascular, Inc.; Boston Scientific Corp; Cordis Corp.; Medtronic Ireland
2011	151	4	Abbott Vascular, Inc.; Boston Scientific Corp; Cordis Corp.; Medtronic Ireland
2012	222	5	Abbott Vascular, Inc.; Boston Scientific Corp; Cordis Corp.; Medinol Ltd.; Medtronic Ireland

Note: Cordis Corp. was a subsidiary of Johnson & Johnson throughout the years covered in Table 5; in 2015, Cardinal Health completed the acquisition of Cordis Corp. from Johnson & Johnson. At times the FDA records use the names of subsidiaries of the parent firms, and we have grouped those and listed the firms by the names of the parent firms. For example, we have just listed Boston Scientific Corp. to represent both the PMAs granted to it and to its subsidiary Boston Scientific Scimed, Inc.
Source: Authors' compilations from https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm.

Figure 4 shows that from the first year of Boston Scientific's sales of the paclitaxel-eluting coronary stents until the last year that the basic USPTO patents for the NIA/NIH technology were in force, the R&D rivals in the market for coronary stents continually developed their products as they fought for larger shares of the gross profits from the worldwide sales of stent systems.

Figure 4. U.S. Federal Drug Administration (FDA) Premarket Approvals (PMAs): 2003-2012



Source: Table 5.

When we compare the historical record for the FDA PMAs with the worldwide sales of coronary stents, we have not only evidence supporting Scherer's conceptualization of the R&D rivalry as virtuous rent-seeking R&D, with the outcome *possibly* the good outcome depicted in Figure 3 where the rivalrous R&D approximates the socially optimal amount. In addition, there is evidence that could support the view that "possibly" could be replaced with "reasonably" in the assessment of the likelihood that Figure 3's theoretical depiction reflects the actual situation. As shown in Table 6 and Figure 5, although FDA PMA's continually climbed throughout the period 2003 through 2012, measuring the continuing and increasing R&D rivalry among the firms competing for market share in the worldwide coronary stent market, in 2006 worldwide sales began a decline. The history behind Table 6 and Figure 5 explains the downturn beginning in 2006. The history also

brings out the story of the virtuous rent-seeking behavior as firms enter new stent systems in the drug-eluting stent market; and consequently, the share of the early market leader, Boston Scientific, declines. As we discuss the history, we will use the nominal values for the sales of coronary stent sales, corresponding to the way those sales were discussed by the participants in the market. We have in Table 6 also provided the sales values in constant dollars of 2012, and then Figure 5 plots the constant dollar sales over time to have the annual sales that are depicted in the figure measured in dollars of constant purchasing power.

Table 6. Worldwide Sales of Coronary Stents for All Companies and for Boston Scientific: Sales ($ millions) for Bare Metal Stents and Drug-Eluting Stents, 2003-2012

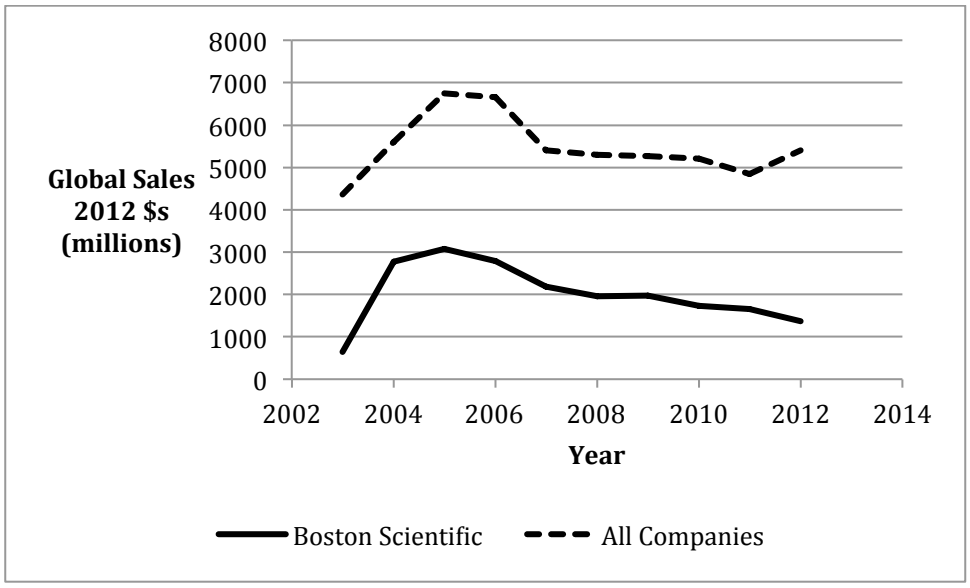
year	Boston Scientific		All Companies	
	Nominal $	Constant 2012 $[a]	Nominal $	Constant 2012 $[a]
2003	528	640	3600	4361
2004	2351	2773	4750	5603
2005	2693	3081	5900	6749
2006	2506	2782	6000	6662
2007	2027	2192	5000	5406
2008	1851	1963	5000	5303
2009	1879	1978	5000	5263
2010	1670	1738	5000	5202
2011	1620	1651	4750	4841
2012	1363	1363	5400	5400

[a]Constant 2012 dollars using the U.S. GDP implicit price deflator; the narrative in the text uses the nominal dollars.

Sources: Boston Scientific's worldwide sales are compiled from its 10K filings with the U.S. Securities and Exchange Commission, https://sec.report/CIK/0000885725/. While the numbers for Boston Scientific's worldwide coronary stent sales are all available in its annual 10K filings with the U.S. SEC, the estimates for the combined worldwide coronary stent sales from all firms were not always provided in the 10K reports. For 2005, 2006, 2007, 2008, 2009, and 2010, Boston Scientific did provide estimates of the worldwide sales across all firms, so the annual 10K filings for those years are the source. For 2011 and 2012, the annual 10K reports had the details about Boston Scientific's worldwide sales in the DES market and in the BMS market. We used those Boston Scientific sales figures along with the information in its annual 10K reports about its shares of the worldwide DES and BMS market, augmented with outside information from GlobalData, Medipoint: Coronary Stents – Global Analysis and Market Forecasts, November 2014, p. 6, https://www.marketresearch.com/product/sample-8538829.pdf, to estimate for 2011 and 2012 the combined worldwide coronary stent sales for all firms. Boston Scientific annual 10K reports for 2003 and 2004 did not provide combined worldwide coronary stent sales for all firms, and there was not in the reports sufficient information to estimate the combined sales. So for 2003, we used for the worldwide combined DES sales the estimate from https://www.massdevice.com/abbott-and-boston-scientific-dominate-46-billion-drug-eluting-stent-market/, and for the BMS estimate we used the estimate provided at https://www.fiercepharma.com/pharma/companies-markets-abbott-laboratories-dominates-global-bare-metal-stents-market, and summed the two figures. The estimate for 2004 is the average of the estimate for 2003 and the estimate for 2005 given in Boston Scientific's 10K annual report for that year. A confirming independent, rough estimate, essentially the same, was found at https://us.sagepub.com/sites/default/files/upm-

assets/14147_book_item_14147.pdf by summing the sales given there for the coronary stent markets for U.S., Europe, Japan, Asian Pacific, and Latin America.

Figure 5. Worldwide Sales (constant 2012 $ millions) of Coronary Stents: Bare Metal Stents and Drug-Eluting Stents, 2003-2012



Source: Table 6.

The first FDA approvals for coronary BMSs were granted in 1993 to Cook, Inc. (for acute closures) followed in 1994 to Johnson & Johnson subsidiary Cordis Corp. (for elective use).[47] Several other companies received approvals for BMSs during the 1990s.[48] In 1998, Boston Scientific-SciMed entered the BMS stent market with the NIR™ stent in the United States after having introduced it in Europe in 1996. Initially, sales were $211 million or 13% of the worldwide coronary stent market.[49] Subsequent models with more advanced features, e.g., self-expanding, bioslide coating, a filter to catch embolic material, and the Liberte™ have been introduced and BMS stents have consistently accounted for

[47] Htay and Liu (2005, p. 264).
[48] Iqbal et al. (2013, p. 196).
[49] https://sec.report/Document/0000950135-99-001755/.

approximately 10-15 % of Boston Scientific's coronary stent revenues and 10-20% on the global stent market.[50]

In 2003 and 2004, Boston Scientific marketed the TAXUS®Express™ stent, first in international markets (primarily Europe) and then in the United States. Despite following Cook's short-lived entry with its paclitaxel-coated stent and Johnson & Johnson's sirolimus-coated Cypher stent, Boston Scientific quickly became the world leader in the drug-eluting stent market.[51] In 2004, coronary stent sales were $2,351 million ($2,143 million DES), which accounted for 38% of Boston Scientific net sales.[52] At the time, the worldwide stent market was estimated to be $4.75 billion.[53] Almost immediately, a second generation of DES, the TAXUS® Liberté ™ coronary stent system, was introduced by Boston Scientific in 18 countries and, in 2005, in the United States.[54] Coronary stent revenue was $2,693 million and represented 43 percent of consolidated net sales for Boston Scientific in 2005. This represented a peak in the sales of DES for Boston Scientific during the time period studied.

In the second half of 2005, Boston Scientific started to experience a decline in US sales of DES revenues compared to the same period the preceding year. This was attributed to both a reduction in market share and pricing pressure.[55] Johnson and Johnson's DES, the Cypher® stent, was a direct competitor.[56]

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[50] See Colombo et al. (2017), and "Coronary Stents – Global Analysis and Market Forecasts," GlobalData, https://www.marketresearch.com/product/sample-8538829.pdf.

[51] Cook was the first to get a drug-eluting coronary stent to market, introducing its paclitaxel-coated V-Flex Plus PTX coronary stent in Europe in September 2002 (see Table 1). But Cook exited the market in 2004 to focus on peripheral vascular applications of the NIH-patented technology (see Table 1). Boston Scientific launched its TAXUS™ coronary stent system in Europe in 2003 before launching it in the U.S. the next year (see Table 1). As Kling (2005) reports in great detail, Boston Scientific had been very deliberative and careful as it used a series of clinical trials to perfect its paclitaxel-eluting stent. By the time it launched the product, Johnson & Johnson (J&J) had already launched its sirolimus-eluting Cypher stent. However, as Kling (2005) details, J&J had heavily marketed its drug-eluting stent, distributing the results of its final, pre-launch clinical trial in advance of the launch and creating great demand. But just before the launch, the FDA informed J&J that it could not sell stents that were more than six months old. Consequently, it had to discard thousands of stents, and for its launch it was left with just 40,000 stents. However there were 100,000 patients in whom cardiologists had expected to implant the stents. Cardiologists were not happy with J&J, and Boston Scientific soon stepped into the breech, and quickly it had 70% of the DES market.

[52] https://sec.report/Document/0000950135-05-001479/. 2004 Boston Scientific 10K SEC Filing.

[53] Ibid.

[54] https://sec.report/Document/0001047469-06-002665/. 2005 Boston Scientific 10K SEC Filing.

[55] Ibid.

[56] ~~https://sec.report/CIK/0000885725/58#documents.~~ 2006 Boston Scientific SEC Filing.

In 2006, there was a further overall decline in Boston Scientific stent sales in spite of the introduction of a second stent system through Guidant's XIENCE™ V everolimus-eluting DES program (which was shared with Abbott). U.S. TAXUS sales declined to $1.561 billion for 2006 as compared to $1.763 billion for 2005 (International sales remained constant). The decline was primarily attributed to a decline in the overall United States market due to concerns of late in-stent thrombosis, a potential complication, and a decline in the overall PTCA market, with lower device utilization. The only DES competitor in the United States marketplace at this time was Johnson and Johnson's Cypher® stent.[57]

The worldwide stent market declined by $1 billion between 2006 and 2007. Even though their product line expanded with the acquisition of Guidant, a competitor in the DES market, and with the marketing of a new privately labeled stent system, PROMUSeverolimus-eluting stents, from Abbott, Boston Scientific's stent business declined.[58] In 2007, TAXUS® stent sales in the United States declined by $555 million or 36%. Still Boston Scientific remained the market leader in the United States with 55% market share.

In 2008, the worldwide stent market remained stable and reduced concern over in-stent thrombosis led to a positive trend in the DES market. However, Boston Scientific's DES stent sales in the United States declined by 17% attributed in part to Abbott's launch of the competing XIENCEV stent system and increased pricing pressure, while the international sales increased by 2%, in part because of increased sales in Japan.[59]

The global market for drug-eluting coronary stents increased in 2009 as concern about in stent restenosis abated, and the DES market share gains were balanced by BMS losses. However, a negative study of the TAXUS® stent by a competitor, adversely affected Boston Scientific's sales (down approximately 30%) of that stent, while sales of Boston Scientific's other DES stent, the PROMUS®, increased and compensated for this decrease. Overall DES sales were up by 9% and overall stent sales remained the same as in 2008.[60]

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[57] Ibid.
[58] https://sec.report/Document/0001072613-08-000584/. 2007 Boston Scientific 10K SEC Filing.
[59] Boston Scientific 2008 10 K filing (https://sec.report/Document/0001072613-09-000419/).
[60] Boston Scientific 2009 10 K filing (https://sec.report/Document/0000950123-10-017254/).

From 2009 through 2012, Boston Scientific's stent sales declined, while the global market exhibited a decline followed by the beginnings of a rebound. However, Boston Scientific maintained its leadership position in the stent market, having a BMS and the two DES stent systems (TAXUS® and PROMUS ®) in their 2nd and 3rd generations and marketed in the U.S., the Europe/Middle East/Africa (EMEA) region and certain Inter-Continental countries, including China beginning in the fourth quarter of 2011. In 2010, net worldwide sales of coronary stents were essentially unchanged compared to 2009, while Boston Scientific's global DES market-share decreased from 41% to 36% with increased competition and pricing pressure. Worldwide stent sales declined in 2011 by 5%, largely due to a decline in the United States market by 7% (international sales increased by 4%). Even though a competitor left the market, there was a significant increase in pricing pressure. Boston Scientific's estimated market share of the U.S. DES market increased by 2% during this period (46% to 48%) with the introduction of a new generation of the PROMUS® Element stent. In 2012, no new stent systems were introduced by Boston Scientific as the global coronary stent market began a rebound, but Boston Scientific's worldwide coronary stent net sales decreased by 16% or $257 million in the face of continued competition and pricing pressures. United States sales of DES by Boston Scientific decreased by 5%.[61]

Even as the gross profits to be won with a larger share of the market declined markedly, the competitors continued to develop their products in the hope of winning a larger share of the declining profits. The behavior strongly supports Scherer's rent-seeking hypothesis and the expectation that the rivalrous R&D would overshoot the socially optimal amount, as in the top panel of Figure 3. The fact that R&D rivalry was so strongly sustained even as the market declined also supports the expectation that a policy of government royalties, which would lower the firms' expected profitability of sales, would not greatly suppress R&D investment. Hence, the bottom panel of Figure 3 may reflect a result to be reasonably expected. We can of course not prove that to be the case, but the evidence supports the result as something reasonable to expect.

[61] Boston Scientific 10K reports for 2009, 2010, 2011, and 2012, respectively at https://sec.report/Document/0000950123-10-017254/, https://sec.report/Document/0000950123-11-015112/, https://sec.report/Document/0000885725-12-000006/, https://sec.report/Document/0000885725-13-000007/.

With a profitable market, even when the anticipated profits are diminished, each of the R&D rivals invests as long as it anticipates the gain in its own profits will exceed its own investment costs, and without regard for the impact of its success on its rivals' profits. It is our case 2 of Section 4 with a vengeance. Such behavior can take the rivals' collective investment well beyond the socially optimal investment as in the top panel of Figure 3. Adding our proposed policy of government royalties to the rivals' expectations may well dampen their enthusiasm for R&D investment just enough to bring their collective investments back closer to the socially optimal amount, as in the bottom panel of Figure 3. We turn next to a description of the proposed policy for government negotiation of royalties on the sales of biomedical products developed with significant public funding.

6. A Proposal for Government Royalties for Biomedical Products Developed with Substantial Public Funding for R&D

6.1. Efficiency Implications of Government Royalties

Kennedy (2019) reviews the literature supporting the perspective that price controls would imply a reduction of pharmaceutical R&D and hence the stream of new pharmaceutical products that bring great benefits to society. As we explained in Section 4, that perspective and the concern it causes, even in the context of contemplated price controls such as those being considered by Congress in 2019, overlooks a scenario—depicted in Figure 3 of Section 4—that can reasonably be expected to characterize R&D for pharmaceutical and other biomedical products. Namely, with R&D rivalry, the private R&D is expected to overshoot the socially optimal amount *despite* the R&D rivals' incomplete appropriation of the returns for R&D investment.

There are exceptions to that expectation, such as for orphan drugs, drugs for rare diseases more generally, or for some vaccines for which anticipated returns fall short of covering costs for development and regulatory approval, and the exceptional cases should be treated differently in any policy proposed to address the issue of consumers having to pay exceptionally high prices for the very products that they financed with their tax

dollars.[62] No less, the exceptional cases must be addressed in the proposal for royalties that we offer in this section. However, the royalties we propose would dampen R&D incentives less than price controls because the controls create uncertainty about the post-innovation price that may be decreased arbitrarily from what would emerge as the market price. In contrast, the schedules and formulas for the proposed royalties would be extant public knowledge.

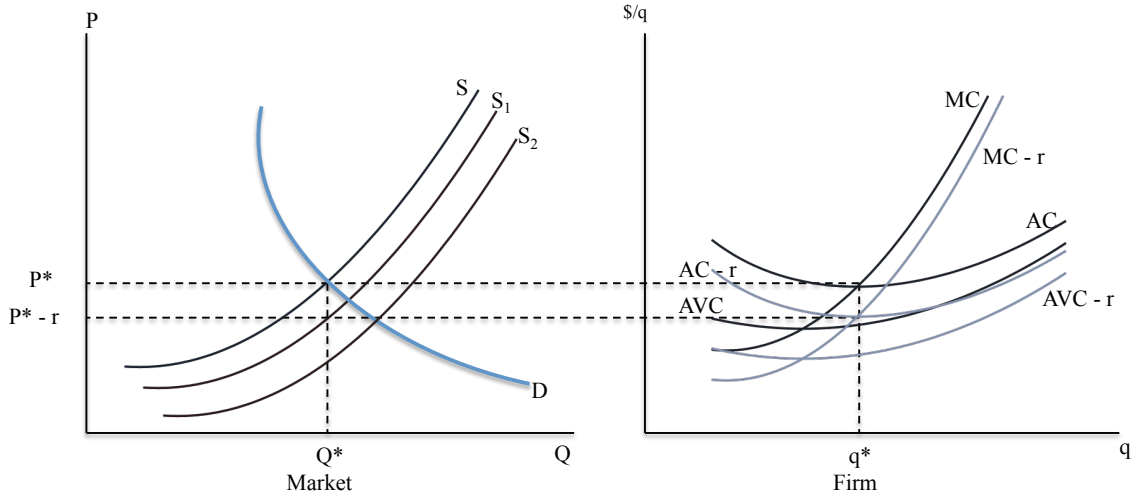
Since we are proposing royalties as an alternative policy, or as a complement to price controls, we begin by discussing the efficiency implications of the royalties. Although royalties are commonly used as a way for investors to recoup a return on their investment, they could be viewed as a tax on the sales of the product that the investment enabled. That the royalties would be viewed as essentially a sales tax would seem especially likely when the investor whose investment is being repaid with the royalties is the government, that is, the taxpayers. Viewed as a sales or excise tax, the royalties would drive the proverbial wedge between the price of the product and its true social cost. However, the royalty payment is not a tax, and instead is intended to cover the opportunity cost of the investors' funds. If the royalty rate were set at a level such that in equilibrium the annual royalty payment equaled the normal annual return on the taxpayers' invested funds, there is no wedge driven between the equilibrium price and the social marginal cost for the good.

To explain the concept, we use a simple case. Figure 6 depicts the case where the annual royalty payment necessary to provide the normal return *H* on the government's investment toward the development of the product is obtained in equilibrium. The case depicted is a very simple case where the government's investment supported an invention of a new product in a laboratory of a federal agency or a university. For the simple case depicted, the federal agency or the university provided nonexclusive licenses to use the

[62] An "orphan drug" is one that has been designated that status by the FDA because the pharmaceutical product is needed by so few patients that pharmaceutical companies could not reasonably anticipate recovering the costs for developing it. The FDA explains: "The Orphan Drug Act (ODA) provides for granting special status to a drug or biological product ("drug") to treat a rare disease or condition upon request of a sponsor. This status is referred to as orphan designation (or sometimes "orphan status"). For a drug to qualify for orphan designation both the drug and the disease or condition must meet certain criteria specified in the ODA and FDA's implementing regulations at 21 CFR Part 316." https://www.fda.gov/industry/developing-products-rare-diseases-conditions/designating-orphan-product-drugs-and-biological-products.

invention, and the licenses were provided to all firms that wanted the licenses. Those firms then used the invention to produce and sell a product in a competitive market. In return for the nonexclusive license, each firm agreed to pay a royalty fee to the agency per unit of the product sold, with that royalty per unit sold denoted by *r*. The right panel of Figure 6 shows the equilibrium output (q^*) and the costs for the individual firm, with its average costs (AC), average variable costs (AVC), and marginal costs (MC). The left panel of Figure 6 depicts the market equilibrium for the industry, with the market demand (D), market supply (S), and equilibrium price (P^*) and equilibrium output (Q^*).

Figure 6. Socially Optimal Production with Royalties



Source: Authors' construction.

In the competitive equilibrium depicted in Figure 6, the annual royalty payment *H* is the amount rQ^*, where Q^* is the competitive equilibrium output for the market, and *H* equals the normal return on the government's investment in the new product. The equilibrium price of the product covers all of its opportunity costs, including the normal return on the government's investment. Observe that if the royalty were eliminated, in the short run the supply curve in the market would shift from S to S_1 with the drop in each firm's costs, and there would be supranormal profits. In the longer run, there would be more capacity in the industry, and the supply curve would shift to S_2 to restore normal economic profits. However, observe that in that equilibrium without the royalty, the

production has gone beyond the amount Q^* for which marginal social value of another unit of output equals its marginal social cost. As a practical matter, it would be impossible to set the royalty rate at the ideal level shown, but the point is that the royalty is to cover an opportunity cost of the product that uses the federal agency's transferred technology.

The situation that would be analogous to our case of the invention of the drug-eluting stent is more involved because the federal agency gave an exclusive license to Angiotech, and it in turn gave a co-exclusive license to Cook and to Boston Scientific, and then ultimately granted Boston Scientific an exclusive license. The ultimate market equilibrium for the sales of coronary stents would be reasonably characterized as a differentiated-product oligopoly equilibrium that would result in the wake of the virtuous rent-seeking R&D for the R&D rivalry as described in Section 5. Whether we have the simplest case as depicted in Figure 6, or instead a more complicated case, the point remains that the royalty payment is not a tax that necessarily drives a wedge between price and true social cost, but instead it is an opportunity cost of a normal return on investment that should be covered by the price of the product. There is, however, an important difference for the more complicated and realistic case with rivalry among oligopolists that offer competing substitutes in the post-innovation market. For the oligopolists, and indeed for other market structures where there is market power, whether a monopolist or a less extreme situation of non-price-taking firms, the royalties would not be passed through completely to price, as they are in the long-run competitive equilibrium depicted in Figure 6 with the royalties paid by price-taking nonexclusive licensees. Appendix A provides a discussion of the incomplete pass through of royalties to price.

As an alternative to using a royalty to provide such a return on the taxpayer's investment, an equity position in the product that the investment makes possible could be used, with the equilibrium price that emerges covering the average fixed cost of the normal return to the investors. However, having the government take an equity position in the firms to which it grants licenses for federal agencies' technologies is probably a nonstarter in the United States.[63] Moreover, the royalties approach is used by investors more generally for practical reasons – they want a return on their investment without the need to be dependent on the legerdemain of companies' determination of the residual from gross

[63] Nonetheless, such policy has been suggested, see for example Mazzacato (2020).

profits that will be available to shareholders. Also, negotiation of royalties has been chosen as the appropriate way to provide some return on the taxpayer's investments in intramural research.

In addition to providing a return to taxpayers to ensure that the opportunity cost of their funds is to some extent covered in the price of a product using an invention that public funds funded to a substantial extent, the royalties can be used to provide an incentive for technology transfer. The Federal Technology Transfer Act of 1986 (Public Law 99-502) mandated the payment of part of a federal agency's licensing revenues from its patented inventions to the inventors, if they were employed by the agency at the time that the invention was made.[64] Thus, providing the incentives that Congress wanted requires negotiating licensing revenues, and royalties and related licensing fees have been used.[65]

There are in fact many ways that the existing negotiated royalties, such as the millions of dollars in royalties earned for NIH by licensing the technology for the paclitaxel-eluting coronary stents, contribute to the technology transfer process and the agency's mission more generally. As GAO observes[66]:

> Under federal law and NIH policy, royalty income from license agreements is shared between the inventors and the institute or center within NIH in which the technology was developed. NIH uses the royalties for multiple purposes that contribute to the technology transfer program and the research of its laboratories. Specifically, the royalty payments can be used to (1) reward employees of the laboratory, (2) further scientific exchange among the laboratories of the agency, (3) educate and train employees of the agency or laboratory, (4) support other activities that increase the potential for transfer of the technology of the laboratories of the agency, (5) pay expenses incidental to the administration and licensing of intellectual property by the agency or laboratory, and (6) support scientific research and development consistent with the research and development missions and objectives of the laboratory.

Thus, there are many reasons for royalties that are already paid to the government for the grant of licenses to use the technologies developed with public funds. Among those reasons, the royalties provide a financial return on the taxpayers' investments for the R&D that generates the technologies. The financial return ideally covers the opportunity cost of the invested funds. The idea that the price in equilibrium will cover the opportunity cost of

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[64] The Federal Technology Transfer Act of 1986 (Public Law 99-502) amends the Stevenson-Wydler Technology Innovation Act of 1980 (P.L. 96-480).

[65] Patenting activity did respond to the incentive, grounded in the market value of the inventions, thereby provided to the agency's inventors. See Link, et al. (2011).

[66] United States General Accounting Office (GAO), (2003, p. 8).

investors' funds may allay any concern that biomedical companies, anticipating the need to pay royalties, would increase initial pricing to compensate for the payment of future royalties. From the perspective of our discussion of the efficiency implications of royalties, the royalties should be reflected in price, because ideally price will cover the opportunity costs, including the normal return to the investors.

However, in the context of market failure that would result in too little R&D investment by the private sector, policy might not recover the opportunity cost of the public funds with a royalty. Even in such cases, it is important to understand that among their many purposes, royalties are returns to investors, public or private, to cover the opportunity costs of their funds. Additionally, here in the circumstances of biomedical R&D, we have good reason to believe that in the absence of the royalties, the rivalrous R&D will overshoot the socially optimal amount of R&D.

Moreover, the evidence, that we now develop, suggests that very modest royalty fees—amounting to only about 1.2% of Boston Scientific's sales of the paclitaxel-eluting coronary stents or about 1.7% of its gross profits on those sales—were more than sufficient to cover the opportunity costs of the public's funds delivered through the direct-funding avenue for Dr. Sollott's and Dr. Kinsella's research at NIA. Even adding royalties to provide financial return on the public's investment through the indirect-funding avenue, the rivalrous R&D among the several firms that developed multiple generations of drug-eluting stents is unlikely to have been much different from what it was.

We turn now to a proposal for royalties to address the concerns about high prices, but to do so in a different way than price controls. The royalties that we propose would take a different form in each of the two avenues for publicly funding biomedical R&D.

6.2. Government Royalties for the Direct Funding Avenue: Intramural Research

For the federal agencies' intramural research in the direct funding avenue, any royalties for inventions based on the intramural research would be negotiated at the time the licenses for using the technology are granted—just as for the drug-eluting stents and with the results as shown in Table 3. The royalties negotiated would be handled just as they are now, and the agencies' offices of technology transfer have procedures for managing the royalties process.

We thus have an example for the royalties from the direct funding avenue's intramural research. The royalties would be as they have been for the inventions, such as the paclitaxel-eluting coronary stents, originating in the intramural research at NIH.[67] For the invention of the drug-eluting coronary stents, we have Table 1 with the history for the licensing agreements, and then Table 3 illustrating the bottom line for the royalties.

In 2003, the first year of Boston Scientific's sales of the paclitaxel-eluting coronary stents, when milestone payments would be expected to be a prominent part of the royalties and related payments, ~~the~~ Angiotech's payments to NIH were 3.3% of sales. After that the payments were consistently about 1.2% of sales through 2010, the last year of payments before NIH and Angiotech negotiated an end to royalty payments based on the sales of the coronary stents. The royalties and related payments as a percentage of Boston Scientific's sales were 1.3% in 2004, 1.2% in 2005, 1.2% in 2006, 1.2% in 2007, 1.2% in 2008, 1.1% in 2009, and 1.1% in 2010.

Table 7 shows the stream of royalty and milestone payments to NIH in nominal dollars and also in constant dollars of 2012, the last year before the expiration of the USPTO patents on NIH's paclitaxel-eluting stent technology. In 1993, the priority date for the original application by NIH for a patent on the invention, when discounted at the 7% that OMB mandated as the opportunity cost for the taxpayer's funds, the present discounted value of the stream of royalties in constant dollars of 2012 is $57 million.[68] Certainly Dr. Sollott and Dr. Kinsella used the accumulated knowledge acquired from many other NIH research projects, but those projects' costs are not a part of the drug-eluting stent research project's cost. Since that cost would have been far less than $57 million, it would appear that the taxpayers earned a return far in excess of the OMB's estimate of the opportunity costs of the public's funds.[69] Stated differently, discounted back at the internal rate of return that would make the present discounted value of the stream of royalties equal to the

[67] See Ferguson and Kaundina (2014).

[68] In millions, from Table 7, $56.6 = 2.18/(1.07)^{10} + 21.35/(1.07)^{11} + 32.37/(1.07)^{12} + 28.87/(1.07)^{13} + 20.22/(1.07)^{14} + 15.17/(1.07)^{15} + 10.95/(1.07)^{16} + 6.13/(1.07)^{17}$. For the 7% discount rate, see U.S. Office of Management and Budget (OMB), 1992.

[69] The project was not a large, costly one, but rather the carrying out of the proof of concept for what turned out to be an extraordinarily important insight. Nijhara, et al. (2005, pp. 3-4) reports that "Taxol, originally discovered in the 1960s, and its equivalents are currently the most successful anticancer drugs on the market. However, nobody thought of using paclitaxel to prevent arterial re-clogging until, over lunch, NIH inventors Steven Sollott, MD, and James Kinsella, MD, brainstormed this very idea. … The experiments were initiated, proof of concept was shown in rat models, and a patent application was filed."

cost of the project as of 1993, that internal rate of return would be greater than the 7% mandated by OMB as the opportunity cost of the invested funds. Further, the benefits to society as a whole from the innovation of the drug-eluting stent were immensely more than the stream of royalty payments to NIH; there are, above and beyond those payments, the economic surpluses generated for the producers and the consumers of the technology.

Table 7. NIH Licensing Revenues from Royalties, Milestones, and Licensing Fees for the Paclitaxel-Eluting Coronary Stent

year	Angiotech's Payments to NIH	
	Nominal $ (millions)	Constant 2012 $ (millions)[a]
2003	1.8	2.180301
2004	18.1	21.34938
2005	28.3	32.37215
2006	26	28.8676
2007	18.7	20.21932
2008	14.3	15.16682
2009	10.4	10.94696
2010	5.89	6.128358

[a]Constant 2012 dollars using the U.S. GDP implicit price deflator.
Source: Authors' construction from Table 3; see notes there.

6.3. Government Royalties for the Direct Funding Avenue: Extramural Research

For direct funding that supports extramural research at universities – such as the research described in Section 2 for Remdesivir that was funded by NIAID, the royalties would be managed by the technology transfer offices of the universities (or other research institutions) receiving such direct support. The universities' (or other organizations') offices of technology transfer already manage the licensing of the inventions that result from the direct public funding support of university research. When the direct funding results in licensing of patented technology, the proposed government royalties would be a part of that process of licensing university-generated technology that was supported with public funds.

However, because of the great uncertainty surrounding the extent to which such technology will ultimately be successfully commercialized, if it is ever commercialized at all, the government's royalties on the taxpayers' contribution of the extramural research funds would only be triggered for transferred technologies that ultimately achieve

sufficiently successful commercialization. The royalties policy for extramural research funding would specify the criterion for sufficiently successful commercialization. For example, it could be as simple as profitability exceeding a stated threshold that could be defined in terms of the actual experience of a specified group of top performers for licensed extramural research inventions. The specified group, just for example, could be the top 25% of those commercialized inventions over the past five years. The royalties would not be tax deductible given their purpose is reimbursement of government funding. The biomedical products paying the royalties would, by design, be among those that are successful. In the unexpected circumstance that a product's successful commercialization ends prior to the expiration of its patent protection (used in the formulation below as the endpoint for the royalties), the royalty payments would cease.

If the royalties were triggered for an invention, the royalties for that direct funding support would be based on the amount of support provided, cumulated to its present value, at the time of the successful commercialization, using the OMB-mandated opportunity cost for the public's funds, with the cumulated value of the support denoted Ω. The R&D support provided would be capitalized as a publicly funded loan that would be paid back over the potential commercial life τ of the licensee's use of the technology where τ equals the number of years remaining for patent protection of the licensed technology at the time that the royalty payments begin. With *k* denoting the public's opportunity cost of funds (discussed in detail subsequently in the exposition of the proposed royalties for the indirect funding avenue), the annual debt repayment due in each of the next τ years is *d* such that $\Omega = d\sum_{t=1}^{\tau} 1/(1+k)^t$.[70] When the publicly funded extramural research that supports a commercialized biomedical product does not itself result in licensed, patented technology, but instead provides R&D support for a private company's patented product as is the case with Gilead's Remdesivir, the royalties for such products that are deemed sufficiently

[70] The university's (or other organization's) technology transfer office would be reimbursed a reasonable management fee for its role in administering the new royalties, and policy would specify that HHS would receive the royalties to be paid to the government for direct support provided to universities and other organizations supported through the first avenue of providing government support for basic research or R&D. The Secretary of HHS could be responsible for distributing reimbursements when appropriate as discussed subsequently in the exposition of the royalties for the indirect funding avenue. A portion of the royalties could be shared with the university inventors to provide incentive for invention and technology transfer.

successful would be paid over the commercial lifetime of the product until the patent for the product expires or when its successful commercial lifetime ends, whichever is sooner.

To ensure the appropriate institutional framework would require some amendments to the Bayh-Dole Act (Public Law 96-517 § 6(a), 94 Stat. 3019), and the Stevenson-Wydler Technology Innovation Act of 1980 (Public Law 96-480, 94 Stat. 2311), and its amendment, the Federal Technology Transfer Act of 1986 (Public Law 99-502, 100 Stat. 1785). The federal agencies already have technology transfer offices that manage the government's intellectual property rights in technologies developed with the agencies' intramural research, and universities and other organizations receiving direct publicly-funded R&D support also have administrative structures for dealing with grants, intellectual property, and licensing. However, while the administrative framework to manage the new royalties policies toward extramural research funding is largely in place, new resources would be required for the additional responsibilities.

Essentially, for the royalties proposed here, in addition to the role played by the technology transfer offices of the universities, the federal agencies' technology transfer offices, with appropriate increases in resources, would oversee and manage on an on-going basis the government and taxpayers' rights in the biomedical products that ultimately emerge from the extramural research that the agencies fund, just as they now do with regard to the biomedical products, like the drug-eluting stents, that emerge from the agencies' intramural projects. Of course, the researchers with extramural support have the mindset that they should profit from their discoveries. The universities and other organizations receiving the agencies' extramural funding could protect the academic inventors' rights, and the agencies could protect the government and taxpayers' rights in whatever deals the universities make with their licensees. The rights of inventors within universities could be protected just as the Federal Technology Transfer Act of 1986 now protects the rights of the inventors in the federal laboratories.[71]

[71]For private sector projects such as the SBIR and STTR projects that receive direct public funding through the extramural programs of the federal agencies, royalties for licensed technologies developed with the SBIR and STTR funding would follow the approach that we have outlined for the licensed inventions emerging from universities that have been funded with the federal agencies' extramural funds. The new royalties would only be triggered when an SBIR or STTR project results in a "sufficiently successful commercialization" as discussed above. With an agency's office of technology transfer and its SBIR program, and STTR program if there is one, the administrative framework, when supplied with additional resources to handle the increased workload, is available to handle the oversight of the new royalties policy. The royalties

6.4. Government Royalties for the Indirect Funding Avenue

For the indirect funding avenue, the royalty fees would be determined by an announced formula that we now develop and illustrate. First, we explain that when the government purchases pharmaceutical and other biomedical products through Medicare, Medicaid, the VA, or the Affordable Care Act, there is a sense in which the taxpayers are providing to the seller a free loan to finance its R&D.

To explain the perspective that government purchases are in essence financing R&D with a free loan—that is, an outright grant of funds for R&D with no reimbursement—we introduce three proportions. The first is the historical ratio, v, of the company's annual R&D expenses to its net sales. In particular, from the overall history for the company, its average annual R&D expense as a proportion of its net sales is an estimate of the proportion, denoted v, of sales used to finance R&D investments.[72]

Boston Scientific's core businesses over the period for our example were all various products with medical uses. By 2012, the core businesses included an endoscopy division developing and manufacturing devices to treat a variety of medical conditions including diseases of the digestive and pulmonary systems; peripheral interventions products including stents, balloon catheters, wires, peripheral embolization devices and other devices used to diagnose and treat peripheral vascular disease; a neuromodulation business with systems used for the management of chronic pain; a urology/women's health division developing and manufacturing devices to treat various urological and gynecological disorders; an electrophysiology business developing less-invasive medical technologies used in the diagnosis and treatment of rate and rhythm disorders of the heart; a cardiac rhythm management division developing and manufacturing and marketing a variety of

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would be triggered only for a small proportion of the population of SBIR projects; only about half of them ever commercialize at all (Link and Scott, 2010). Many of the successful commercialization cases will involve licenses granted by the SBIR firm to other firms to use the publicly supported technology developed from the project. There is a substantial amount of licensing of technologies developed in the NIH SBIR program. Link and Scott (2012, Table 2, p. 379) report that for a random sample of 338 NIH SBIR projects, 28.1% of the firms receiving the NIH funding to develop new technologies reported finalized licensing agreements for the use of the technology developed, and another 22.2% of the firms reported on-going negotiations to establish licensing agreements.

[72] Alternatively, an industry standard for the proportion of sales devoted to R&D could be used. However, using the company's own proportion, will more closely match the royalties to the company's own expericnce.

implantable devices including implantable cardioverter defibrillator (ICD) systems and pacemaker systems that monitor the heart and deliver electricity to treat cardiac abnormalities; and interventional cardiology products with the coronary stent system sales, and in addition to coronary stent systems, balloon catheters, rotational atherectomy systems, guide wires, guide catheters, embolic protection devices, and diagnostic catheters used in percutaneous transluminal coronary angioplasty (PTCA) procedures, as well as intravascular ultrasound (IVUS) imaging systems. Over the decade that we observe Boston Scientific's sales of the paclitaxel-eluting coronary stents, its annual R&D expenses as a percentage of its net sales averaged 12.1%; thus, $v = 0.121$.[73]

For our discussion, we also use a second proportion, *s*, of the company's U.S. sales of the particular biomedical product that is purchased by the government. Table 8 shows Boston Scientific's annual U.S. sales of paclitaxel-eluting coronary stents over the period from when the U.S. sales began in 2004 through 2012, the last year before the NIH U.S. patents for the stent expired. Table 8 also shows the estimated portions of the annual sales that were paid for by the U.S. government with its purchases for programs such as Medicare, Medicaid, the VA, and the Affordable Care Act. To form the estimates, we use assumption that 80% of the stents were used in patients over the age of 65.[74] We also use the information that 94% and 23% of individuals over and under 65 years of age, respectively, are covered by public plans (Berchick, et al., 2019).[75] Thus, the portion, *s*, of Boston Scientific's U.S. sales that were purchased by the government is estimated to be $s = ((0.80 \times 0.94) + (0.20 \times 0.23)) = 0.798$.

The third proportion, denoted *k*, used in our discussion will be the annual rate of return to cover the opportunity cost of the public's funds as determined by the U.S. Office of Management and Budget (OMB). For the period of our example, the OMB determination of the opportunity cost of the public's funds used for investments like the R&D in a federal laboratory was an annual real rate of return 0.07 or 7% (U.S. OMB,

[73] The descriptions of its businesses as well as its annual R&D expenses as a percentage of net sales are from Boston Scientific's annual 10K filings with the U.S. Securities and Exchange Commission. For the ten years from 2003 through 2012, the percentages were respectively 13.0, 10.1, 10.8, 12.9, 13.1, 12.5, 12.6, 12.0, 11.7, and 12.2.

[74] Auerbach, et al. (2012), Figure 1, "Rate of any cardiac stent procedures by sex and age group."

[75] Berchick, et al., 2019, Table 2, "Percentage of People by Type of Health Insurance Coverage by Age: 2017 and 2018," p. 6. Over the years that we examine, these numbers change very little, and so we use the one set of estimates.

1992). The annual rate of return will be approximated as the OMB-mandated real rate of return plus the anticipated rate of inflation. The actual U.S. inflation rate over the period from 2004 through 2012 averaged 0.0216 per year. Thus, with the low rate of inflation, and assuming that the anticipated rate of inflation equaled what actually happened subsequently, the annual rate of return to cover the opportunity costs of the public funds would be well approximated as $k = 0.0916$.

Using the three proportions, we now explain the sense in which the taxpayers, with their purchases of the biomedical products, are providing a free loan to finance the R&D of the company from which the products are purchased. The product's annual U.S. sales multiplied times the proportion *s* of the sales purchased by the government gives the revenues for the company from the government's purchases. Then that amount times the proportion *v* gives the amount of R&D support generated by those sales. That public funding of R&D is essentially a free loan.

Suppose, for example, that the R&D support provided were capitalized as a publicly funded loan that would be paid back over 20 years. Using the proportion *k*, for each $1 of publicly funded R&D in a given year, the annual debt repayment due in each of the next 20 years is *z* such that $1 = z\sum_{1}^{20} 1/(1+k)^t$. With $k = 0.0916$, $z = 0.1108$. In words, a schedule of debt repayment that returns to the taxpayers the real annual rate of 7% (a nominal rate of 9.16%) will return, in each of the next 20 years, $0.1108 or about 11.1 cents for each dollar of R&D support provided in a given year.

The row of Table 8 for "annual debt repayment in each of the next 20 years" shows for each year's R&D supported the amount due in 20 installments to completely repay the "loan" from the taxpayers to support R&D in each year. In the next row of Table 8, for "debt repayment due," we see that because the payments to repay each year's "loan" extend over the next 20 years, as time passes after U.S. sales begin, the yearly debt repayments for each year's loan of R&D funds accumulate. In the next row, labeled "debt repayment as a proportion of U.S. sales," we see that by 2012, the last year before the patents expire, the debt repayments take a large proportion of the U.S. sales. Moreover, at that point, because competition has started to erode the sales, the debt repayments would be particularly onerous. A similar situation would exist for other biomedical products, because patents associated with pharmaceuticals and medical products more generally—that is, those not

originating with inventions in the federal laboratories—would also typically have a much shorter commercialized lifetime than 20 years. The reason is because the process of developing a patented invention to bring it through all the necessary clinical trials and the FDA approval process typically takes several of those 20 years of the patent's life.

Table 8. Boston Scientific Corporation's U.S. Sales of Paclitaxel-Eluting Coronary Stents, the Part of the Sales Paid for with Public Funds, and Hypothetical Debt Repayments versus Royalties Paid to the Government

U.S. nominal $, millions	2004	2005	2006	2007	2008	2009	2010	2011	2012
Boston Scientific's U. S. sales of paclitaxel-eluting coronary stents[a]	788	1700	1500	1000	637	411	271	242	149
Public purchases[b]	629	1357	1197	798	508	328	216	193	119
R&D supported[c]	76.1	164	145	96.6	61.5	39.7	26.2	23.4	14.4
Annual debt repayment in each of the next 20 years for each year's R&D supported	8.43	18.2	16.0	10.7	6.82	4.40	2.90	2.59	1.59
Debt repayment due	0	8.43	26.6	42.6	53.3	60.2	64.6	67.4	70.0
Debt repayment as a proportion of U.S. sales	0	0.0050	0.018	0.043	0.084	0.146	0.238	0.279	0.470
Annual royalty = φkvs x (U.S. sales) with $\varphi = 10$[d]	69.7	150	133	88.4	56.3	36.4	24.0	21.4	13.2
Annual royalty = φkvs x (U.S. sales) with $\varphi = 11.424663$[e]	79.6	172	152	101	64.4	41.5	27.4	24.5	15.1

[a] Boston Scientific's net sales, on which royalty payments in a given year to Angiotech Pharmaceuticals were based, are for the period October 1 of the preceding year to September 30 of the given year.
[b] As explained in the text, public purchases for a year are estimated as annual sales multiplied by the proportion $s = 0.798 = ((0.80 \times 0.94) + (0.20 \times 0.23))$.
[c] R&D supported = (public purchases) x ($v = 0.121$).
[d] $\varphi = 10$, $k = 0.0916$, $v = 0.121$, $s = 0.798$.
[e] $\varphi = 11.424663$, $k = 0.0916$, $v = 0.121$, $s = 0.798$.
Source: Table 3 and authors' calculations.

To avoid the situation of the capitalized debt repayments mounting as the years of sales increase, we propose a different approach of paying royalties. The royalties we propose would serve as a complete fulfillment of the payment of a return to the taxpayers for their support of the company's R&D by means of the government's purchases of the product. The approach matches the payments to the taxpayers with the contemporaneous ability to pay.

For the indirect funding avenue, the royalty fees would be determined by an announced formula. The formula is simply that the annual royalty = φkvs x (U.S. sales), where φ is a multiplier announced as a part of the proposed royalties policy for indirect

funding of R&D through the government's purchases of the biomedical product. The next to the last row of Table 8 illustrates the royalties to the taxpayers that would have been paid by Boston Scientific, using φ = 10, $k = 0.0916$, $v = 0.121$, $s = 0.798$. Those royalties as a proportion of U.S. sales are of course $0.088447 = \varphi kvs$ in each year. There would be no cumulating debt payments due; the royalties in the stated amount are the full amount of the reimbursement to taxpayers for their contribution of R&D support provided indirectly via the government's purchases of the product. Why would the multiplier equal to 10 be sensible?

The choice for the multiplier φ determines the amount of the opportunity costs of the taxpayers' funds that will be covered by the royalties. We can see that the choice of φ = 10 implies that the royalties cover quite a bit of the opportunity costs. To see that result, consider the following.

The government's purchases for a given year are *s* x (U.S. sales). The R&D supported will be *v* x *s* x (U.S. sales), and denote that amount as *R*. For a given year of sales, that amount *R* is provided to the company. That amount for each year is shown in Table 8 in the row for "R&D Supported". Thinking of that amount *R* (that has resulted for a particular year) as an amount loaned to the company at a time 0, the royalties to be received by the taxpayers based on that year's purchases would be computed as the constant amount φkR per unit of time (a year) over one year. Hence, for any particular year, the royalties due would be $\int_0^1 \varphi kR\, dt = \varphi kR$.

If the loan of *R* is repaid with the annual payment of *kR*, to completely repay the loan for a single year's R&D support *R*, the company would have to pay the royalties in perpetuity since $R = \int_0^T \varphi kR\, e^{-kt}\, dt \Rightarrow \varphi = 1/(1 - e^{-kT})$. Hence as *T* goes to infinity, the multiple φ goes to 1. Thus, if the multiple φ = 1, the taxpayers would be receiving just one year of payment from the perpetual stream of such payments that would be required to repay their "loan" to provide R&D support. However, if the multiple φ = 10, then the equation $R = \int_0^T \varphi kR\, e^{-kt}\, dt$ holds when $T = 1.15$ given that $k = 0.0916$. Hence, with the multiple φ = 10, the taxpayers receive one payment that covers almost all of their opportunity costs. Covering them all would require another payment for repayments accrued over the first 55 days of the next year.

The multiple φ that would reduce the number of payment periods T to 1 would be 11.424663. The final row of Table 8 shows the royalty payments using that multiple; with those payments, the taxpayers are fully reimbursed the opportunity costs of their funds that provide R&D support. Thus, the final row in Table 8 computes the annual royalty payments = φkvs x (U.S. sales) for φ = 11.424663, k = 0.0916, v = 0.121, s = 0.798. Those payments as a proportion of U.S. sales are of course 0.10104786. By comparing the row showing the annual R&D supported with the last row showing annual royalties paid with the multiplier = 11.424663, one can see that the result is completely intuitive. In simple mathematics solution, the taxpayers would provide the annual amount of R&D based on the government's purchases, and then a year later would be reimbursed that amount with the interest compounded continuously that has accrued. The reality, analogous to the treatment of Boston Scientific's payment of royalties to Angiotech (see the notes for Table 3), is less precise.[76]

Observe that the proposed royalty payments increase with the amount of research support provided through the indirect funding avenue, and also observe that the support provided increases with the success of the innovation as measured by its sales, and it also increases with the price paid by the taxpayers in their role as consumers of the product. Thus, it is only the very successful innovations that would be paying a lot in royalties, and for such innovations the company could afford to pay the taxpayers' opportunity cost for the R&D support provided to the company. Observe also, that the R&D supported with the indirect public funding would be generating new developments and subsequent sales and gross profits that may not be observed in the time series for the particular product for which government purchases provided the R&D support. Finally, observe also that the royalties can, given they are not completely passed through to revenues, allow the government to in effect pay much lower prices for the innovations that the taxpayers have supported with research funds derived from their purchases as consumers of the products; and moreover,

[76] Recall that Angiotech received royalties as of December 31st of the current year for the Boston Scientific paclitaxel-eluting stent sales from October 1st of the preceding year through September 30th of the current year.

any escalation in the prices of the products would result in an escalation in the royalties returned to the taxpayers.[77]

We have chosen the value for the multiplier φ that resulted in the full reimbursement of the taxpayers' opportunity cost; however, that need not be the choice preferred by policy. Legislated policy would determine with public debate and formal legislation a fair and equitable choice for φ. The policy would not choose φ directly, but rather indirectly. The policy would stipulate that taxpayers would receive only the one royalty payment φ*kR* for each year's amount of R&D generated by the government's purchases for that year. That amount of R&D depends on the U.S. sales, the proportion s, and the proportion v. Then the one royalty payment for the year's amount of R&D provided would be φ*kR* = φ*kvs* x (U.S. sales). The legislated policy would determine how many years of that royalty payment would be required to completely repay the taxpayers the opportunity cost for their funds to support that year's R&D expenditures. They will get only one payment, and that one payment will repay their opportunity cost completely if the multiple φ that would reduce the number of payment periods *T* to 1 is used.

We have chosen the multiple that reduces *T* to 1 to determine the royalty payments in the last row of Table 8, but it need not be the choice. Presently, with no such royalties policy, the implicit choice is for a multiplier of 0, and hence no royalty payment at all. If the choice were for the taxpayers to receive one payment of the perpetual stream that would be required to repay their opportunity cost, the multiplier would be 1, and at the other extreme, if the choice were that they be fully repaid with the one royalty payment, then, given $k = 0.0916$, the choice would imply that $\varphi = 11.424663$.

The legislated choice for the number of periods of the single royalty payment that would be required if the taxpayers were to be fully repaid for their R&D support (a choice that will implicitly determine the multiplier φ given *k*) should be adjusted based on the type of biomedical product. For example, special allowance—that is, lower royalty rates—to foster research would be made for orphan drugs and biomedical products for rare diseases

[77] The policy could specify that the royalties would be paid to HHS. For purchases paid by the government through Medicare or other government insurance programs, policy need not specify a procedure for transferring the royalties to the consumers. The taxpayers paid the high prices via the government's purchases, and the government received some reimbursement via the royalty payments, in effect reducing the prices paid. If the policy is designed to address high prices paid by consumers whose purchases were not paid by the government, the Secretary of HHS could be responsible for distributing reimbursements proportionately to those consumers.

more generally, for some vaccines where the context of their use would not allow sufficient revenues to cover the costs of developing, producing, and marketing, and for other exceptional cases as appropriate.

Why would royalties be better than price controls? With price controls, biomedical companies would anticipate an arbitrary and uncertain revenue reduction to be imposed after a product succeeds. In contrast, the royalties to be imposed are known, as a percentage of whatever sales result, before the development of the product. Further, as a proportion of the sales, the absolute amount increases, in a way known prior to the development, with the success of the commercialization and the ability to pay the royalties. Just as for private investors, the taxpayers in their role as the public investors obtain a return that is increasing in the success of the project.[78] A result is that when the market price of the product turns out to be high, the royalties paid to the government are higher and hence the funds to offset the high prices are greater.

It is important to note that the royalties that we propose do not constitute an equity position for the government. The government is not a residual claimant to the profits of the biomedical firms that will pay the royalties—just as NIH had no equity position in Angiotech, but instead received a royalty based on sales as specified in the licensing agreement of November 19, 1997.

We have set out the broad outline of a policy of royalties as a financial return on the taxpayers' investments in biomedical products that are developed with substantial amounts of public funding. The proposed royalties provide funds that the government could use directly to offset high prices paid for pharmaceuticals and other biomedical products. However, such a royalties policy would not preclude the possibility that additionally, as contemplated by Congress in the legislative proposals in 2019, the Secretary of HHS would be granted through new legislation the right to negotiate the drug prices to be paid by Medicare and Medicaid. If the legislation supporting negotiations for lower prices were enacted, our broad royalties proposal would provide information that could be helpful for the price negotiations, and negotiations could offset any pass through of royalties to higher prices.

[78] Also, successful projects' increased volume will typically be accompanied by decreased average total cost, and profits may be especially high even as royalties increase.

With the information available from the royalties policy, any legislated bargaining right granted would be supported by the information about the amount of R&D funding directly or indirectly provided for the drugs being purchased. Any price negotiations could be grounded in clear, publicized knowledge of the amount of funding for the drug, or biomedical product more generally, that the government had provided, because such information would be readily available as it was gathered for the purpose of determining royalties on the government's investments through each of the two avenues for delivering biomedical funding.

7. Conclusion

In the macroeconomic literature about the relationship between R&D investment and economic growth as it is observed across different countries, there is thoughtful commentary about how intellectual property regimes that are too strict can inhibit the ability of R&D investment to drive economic growth.[79] In the history of the technology transfer of the invention of the drug-eluting coronary stent, we have an example where the set of international patents protecting the intellectual property of the invention allowed successful commercialization of the product.[80] The patent protection however did not prevent the entry of new firms with their competing patented versions of the drug-eluting coronary stent. The rivalrous R&D investment of pharmaceutical and medical device companies competing in worldwide markets was vigorous, and a new generation of drug-eluting coronary stents was developed. Rivalrous R&D generated improvements to the technology that benefited the millions of patients treated with interventional cardiology. Effective patents, within IP regimes that avoid overly restrictive patents, are desirable.

There is also much thoughtful commentary in the policy literature about how price controls for pharmaceutical or other biomedical products would inhibit R&D investment.[81] However, the evidence that we have developed for the technology transfer of the drug-eluting coronary stent is consistent with Scherer's (2010) description of pharmaceutical

[79] See, for example, van Stel, et al. (2019).
[80] Leech and Scott (2020) provide a history of the foreign patent litigation for the paclitaxel-eluting coronary stent, and they also provide general econometric evidence, over time and across U.S. federal agencies, about the importance of foreign patent protection for successful transfer of technologies invented in the laboratories of U.S. federal agencies.
[81] See, for example, Kennedy (2019).

R&D as virtuous rent-seeking R&D that can actually overshoot the socially optimal amount of R&D. Moreover, because we observe the rivalrous pharmaceutical and medical device companies developing their own versions of pioneering products, just as happened with the drug-eluting coronary stent with FDA PMAs growing even during a period when the overall market was contracting, it is possible, and perhaps likely, that imposition of price controls might result in R&D investment closer to the social optimum. Nonetheless, expectation of price controls might well introduce sufficient uncertainty, about the amount of the expected reduction in appropriated returns, to reduce R&D investment below desirable levels. As an alternative policy, the royalties policy proposed would create less uncertainty and yet provide a way to mitigate the problem of taxpayers paying what are perceived to be unreasonable prices for the very products that their tax dollars supported with funds for R&D.

The pricing for Remdesivir was announced on June 29, 2020, in an open letter from Gilead Sciences. For VA and DoD, the price will be $2,340 per patient for a typical five-day treatment course. Medicare and Medicaid will not get that discounted price, but instead the price for a five-day treatment will be $3,120 per patient.[82] Considerable effort is put into thoughtful analysis of biomedical prices and their reasonableness.[83] With the policy we propose, whether one finds the prices reasonable or not, the taxpayers would be reimbursed some of the opportunity costs of the R&D investment funds that they provided through direct funding for academic research that supported the commercialization, and also that they would be providing indirectly to Gilead with the purchases of the drug.

Finkelstein and Temin (2008, p. 113) explain that the price of drugs needs to cover the cost of failed efforts to develop other drugs.[84] The gross profits for a biomedical company must cover many costs, R&D among them, and the point is that the R&D costs to be covered are considerably more than just those for the successful biomedical product. That is another reason why a royalties policy is preferable to price controls. With the royalties, as formulated in our proposal, price is left to find its level as determined in the

[82] Howard and Thomas (2020).
[83] See, for example, Whittington and Campbell (2020).
[84] Finkelstein and Temin (2008, chapter 7, "How to Lower Drug Prices") propose divorcement of pharmaceutical companies' drug development operations from their marketing and distribution operations, and propose an independent, public, nonprofit organization that would license FDA-approved drugs developed by the drug developers, and then auction the distribution rights to the firms that would sell the drugs.

(very complex) market, and part of that level has to do with prices needing to cover the costs of failed development efforts. But, whatever the price and extent it reflects royalties, the taxpayers are getting a piece of it with the royalties policy that we have proposed, and the policy is designed so that royalty payments coincide with the company's ability to pay them. With post-innovation oligopolistic rivalry among substitutable products, as well as with other market structures (other than the simple case of nonexclusive licenses and pure competition depicted in Figure 6), pass-through is incomplete, and surplus is redistributed to taxpayers.

The policy for royalties that we have proposed would certainly require new legislation, just as would the many proposals for price controls that have recently been considered by the U.S. Congress. We have suggested the royalties as an alternative or complement to price controls; the royalties could mitigate high prices, while they would create less uncertainty, and therefore would be less likely to cause an undesirable reduction in R&D investment. However, the process of determining the royalties would generate information that could be used as the basis for price negotiations, and for that reason the policy of royalties could be a complement to the new policies that are being proposed for negotiation of pharmaceutical prices. There is also the possibility, however faint it may be in the fractious policy environment of the day, that the policies of royalties and negotiated prices could be accomplished with voluntary cooperative agreements among the parties involved—especially in the light of the information that would be developed, for the royalties policy, about the amounts of public funding devoted to support R&D for biomedical products.

Appendix A. Incomplete Pass Through of the Royalty to Price Given Market Power

As observed in Section 6.1 of the study, a royalty is not expected to be completely passed through to price when the producer has market power. This appendix discusses that expectation.

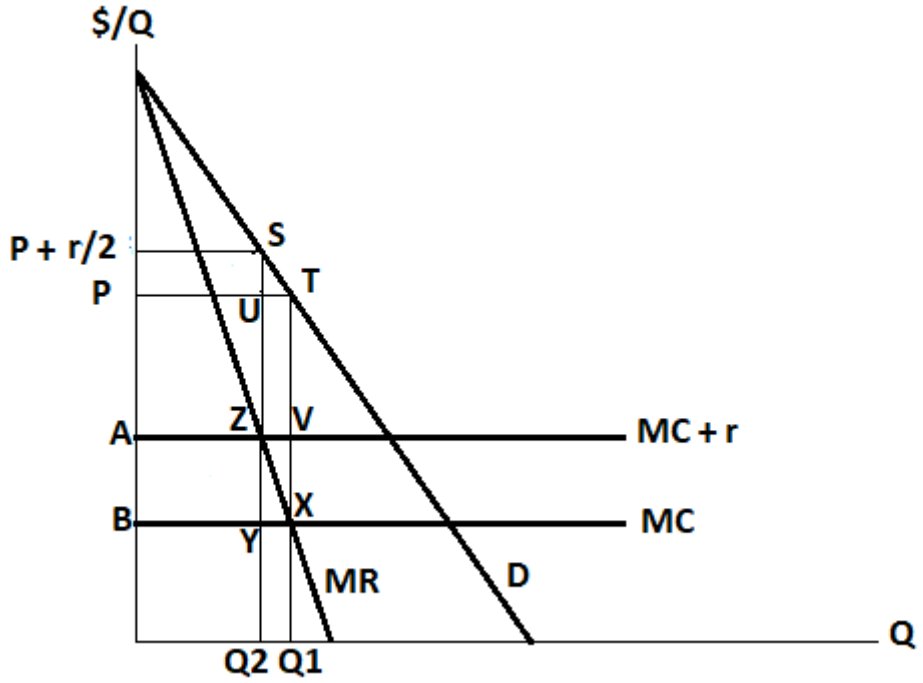
To describe the incomplete pass through to price of the royalty per unit sold, consider the following general observations. A simple monopolist, and more generally a firm with market power, faces a downward sloping demand curve from which to choose a profit-maximizing price where marginal revenue (*MR*) equals marginal cost (*MC*). If the royalty is imposed, *MC* increases and a new equilibrium is found where *MR* = *MC*. First, the increase in *MC* from the initial equilibrium of *MR* = *MC* without royalties to the new equilibrium is less than the royalty per unit because *MR* has a negative slope and *MC* has a positive slope; or if *MC* is constant, the increase in *MC* in the new equilibrium equals the royalty per unit. Second, the increase in price from the initial equilibrium where *MR* = *MC* to the new equilibrium is less than the increase in *MC* from the first to the second equilibrium, because the *MR* curve is steeper than the demand curve (i.e., its negative slope has a larger absolute value than the negative slope of the demand curve).

Figure A.1 illustrates the incomplete pass through of the royalty to price for a monopolist in the case of a straight-line demand curve (D) and constant unit costs. The monopolist faces a linear downward-sloping demand for its product. The marginal cost (*MC*) is constant. If a royalty of r per unit is imposed, the price set by the monopolist will rise by $r/2$ because the *MR* curve is twice as steep as the demand curve and therefore the amount measured by line segment $\overline{SU}$ equals one-half of the amount measured by line segment $\overline{ZY}$.

Algebraically, let the inverse demand curve be $P = d - eQ$, where P denotes price, and Q denotes output. Total revenue is $PQ = dQ - eQ^2$, and $MR = d - 2eQ$. Initially, *MR* = *MC* implies $Q = (d - MC)/2e$, and then $P = d - e(d - MC)/2e = (d + MC)/2$. If the royalty is imposed, at the new profit-maximizing equilibrium,

$MR = d - 2eQ = MC + r$, and $Q = (d - (MC + r))/2e$. The new price is $(d + MC + r)/2$ and exceeds the original price by $r/2$.

Figure A.1. Incomplete pass through with monopoly with straight-line demand and constant unit cost



Source: Authors' construction.

Consumers, with the government as their agent, collect the area *AZYB* in royalties, a transfer out of what was producer surplus without the royalties. As explained in Section 6.1, the payment can be thought of as contributing to the consumers' opportunity cost for their funds provided for R&D in their role as investors. For the quantity that they buy in the new equilibrium, the consumers pay more, by the amount given by the rectangle with vertices $P + r/2$, *S*, *U*, and *P*, than was the case without the royalty. But the royalties received are greater (the area *AZYB* is twice as large as the area from $P + r/2$ to *S* to *U* to *P*, and there is a net gain for consumers that exceeds the area of the small triangle *STU* of lost consumer surplus because of the reduction in output. In addition to the monopolist's net loss in producer surplus because it loses the rectangle *AZYB* (transferred to consumers) and

gains back only half that amount with the rectangle from $P + r/2$ to S to U to P, the producer loses producer surplus in the amount of the area of the two rectangles *UTVZ* and *ZVXY*, but the lower of those two rectangles is a portion of the opportunity cost of consumers' invested funds that, without the royalties policy, is transferred to the producer.

As discussed in the body of the study, a policy of price control can be used as a complement to a policy of royalties. If the royalties policy is combined with a policy of negotiated prices, the transfer of surplus from the producer to the consumers can be effected without any loss of total surplus. A negotiated price of P, the original price without the royalty, changes the demand curve to a horizontal line from P to the original demand curve, and then from that point follows the original demand curve. The producer's *MR* is then the horizontal line from P to the demand curve and then at that point drops discontinuously to the original *MR* curve. With the negotiated price and the royalty, the equilibrium price and output would then be the same as without the royalty, but consumers would collect royalties equal to the sum of *AZYB* and *ZVXY* to cover a portion of the opportunity cost of their invested funds. The royalties are transferred to the consumers from what would otherwise have been producer surplus. Observe that the price control could theoretically be set at an epsilon above $MC + r$ and eliminate essentially all of the deadweight loss in the post-innovation market for the innovative product. However, such a price along with the royalties would eliminate essentially all earnings above the post-innovation costs, and those earnings are a necessary incentive to get the innovation in the first place.

Observe that with upward sloping marginal cost, the pass through of the royalty to price is even less than is depicted in Figure A.1. Also, observe that the reality of the post-innovation market is likely to be a few firms that offer somewhat substitutable products. Those firms in the post-innovation market sell differentiated products, and each firm has market power—i.e., it faces a downward sloping demand curve. Thus, the situation for each firm could be considered to be more or less the same as what is depicted in Figure A.1, with each firm facing a downward sloping demand curve, for the part of the market it serves given the presence of the other firms and their choices, and choosing its price independently of the others.

The situation in the post-innovation market is expected to be evolving and typically quite dynamic, and so a simple Nash noncooperative equilibrium is probably unlikely to obtain. Yet, if it did, we can also see the incomplete pass through of the royalty to price. To illustrate, consider the simplest case where instead of differentiated products, the firms sell a homogenous product and have the same constant unit cost as depicted in Figure A.1. By exploring the Nash equilibrium in this simple context, we can learn about the pass through of the royalty in Nash equilibrium, while having just a single price to keep track of, instead of having a different price for each of the competitors, as would in general be the case with competitors with differentiated goods.

To develop the example, we begin with the same inverse demand curve for the market: $P = d - eQ$. For the example, there are *n* symmetric quantity-setting firms in Nash equilibrium. Given the market demand, and given the output of its rivals, the i^{th} firm's inverse demand curve, with q_j denoting the output of the j^{th} rival, is $P = d - e(\sum_{j \neq i} q_j + q_i) = (d - e\sum_{j \neq i} q_j) - eq_i$.

In Nash equilibrium, maximizing its profits given the output of its rivals, the i^{th} firm chooses to produce such that its marginal revenue equals its marginal cost:

$$MR_i = (d - e\sum_{j \neq i} q_j) - 2eq_i = MC .$$

With symmetry (i.e., the firms sell homogeneous products and have the same costs), in the Nash equilibrium, each firm produces the same amount $q_i = q_j = q^*$. The quantity for each firm that solves the *n* identical equations (one for each firm choosing its output where its marginal revenue equals its marginal cost) will be the same for all of the firms in the equilibrium. Thus, in the Nash equilibrium without the royalty, with each firm making its best response to the others, for each firm:

$$MR_i = (d - (n-1)eq^*) - 2eq^* = MC \Rightarrow q^* = (1/(n+1))((d - MC)/e) .$$

The market output is: $nq^* = (n/(n+1))((d - MC)/e)$.

Price is: $P = d - e(n/(n+1))((d - MC)/e) = (d + nMC)/(n+1)$.

With the royalty, the Nash equilibrium price is:

$P_r = d - e(n/(n+1))((d-(MC+r))/e) = (d+n(MC+r))/(n+1)$.

Thus, with the royalty, the price exceeds the original price by $(n/(n+1))r$. Observe that when n = 1, we have the same result as for monopoly—half of the royalty is passed through to price. With two firms in symmetric Nash equilibrium, two-thirds of the royalty is passed through to price. With three firms in symmetric Nash equilibrium, three-fourths of the royalty is passed through to price, and so on. With a large number of firms competing with the same product in the post-innovation market, the output and price approach the competitive output and price where, as we saw in Section 6.1, the royalty is completely passed through to price.

However, a large number of competing, substitutable, innovative products is not expected in the post-innovation market. Moreover, even with the smaller number of firms for which Nash equilibrium can be a sensible expectation, remember that the results here are for the simple straight-line demand and constant cost case. For any *n*, pass through is less with rising marginal costs. Also remember that the expectation for the post-innovation market is not only for a few firms with differentiated products, but those few firms are expected to be choosing their outputs and prices in a dynamic, rapidly evolving market where the static Nash equilibrium is not expected to obtain. Thus, the simple story for a firm with market power that is depicted in Figure A.1 is what is expected. The most likely situation in the dynamic context would then be analogous to the so-called "monopolistic competition" model but with just a few firms selling differentiated products, and with the market evolving rapidly and precluding entry of sufficient competitors to establish the textbook zero profit equilibrium for the market.

Importantly, as explained in the discussion of Figure A.1, a policy of price negotiations complements the policy of royalties, because the transfer of producer surplus to the consumers to repay the opportunity cost of their invested funds can be accomplished without the loss of any of the total surplus.

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