# Global Health: Lessons from Bayh-Dole

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## ABSTRACT

Public sector institutions help deliver public health goods. By extension, universities that receive public research funds must deliver a benefit to the public that goes beyond licensing a discovery to the private sector for development. In the United States, 25 years of experience with the Bayh-Dole Act, which governs the use of intellectual property (IP) derived from public research, offers both lessons and warnings for developing countries currently establishing their own IP systems. Bayh-Dole successfully created a large body of IP from publicly funded research. Absent a strong profit motive for the private sector, however, the Act has been much less successful at producing public goods for health. Current practice undervalues the "public benefit" aspect of the mandate, especially for the poor. Possible ways to address this mandate would be for public sector entities (and their academic partners in the biomedical sciences) to invest some of their earnings from licensing publicly funded discoveries into programs for neglected diseases of the poor. IP rights from public funded research could also be leveraged in negotiating licensing agreements with the private sector to address these neglected diseases. IP laws and institutions should be designed to encourage such sharing. The public and academic research sectors should also seek a new compact with the private sector aimed at reducing the burden of disease affecting the poor.

## 1. INTRODUCTION

In the past 50 years, the intensity of research and the pace of discovery in the biomedical and health fields have accelerated dramatically in the United States, in both the public and private sectors. As a result, the number of safe and effective drugs, vaccines, and medical devices for a broad range of illnesses and conditions has skyrocketed. But current laws and practices may mismeasure the benefits of publicly funded health research by relying too closely on a private sector yardstick. Furthermore, in an increasingly global world—where the risk of disease and the benefits of research can come from any corner—the society that benefits from public sector health investment should be the global society. The "public benefit" aspect of U.S. federal research investments should thus include the poor in societies inside as well as outside of the United States, and IP laws and practices should be changed to enhance the benefit of our investments.

Out of an estimated US$106 billion in health R&D expenditures globally, about 50% is estimated to come from public sources.[1] In the United States, most public funding of biomedical and behavioral research is through the National Institutes of Health (NIH), whose spending on research is approximately US$28 billion in 2006. Those numbers dwarf the amount of public research funding in developing countries, but developing country R&D investment will continue to grow, along with IP derived from it. As IP systems evolve in developing countries, they should avoid or reduce barriers to the development of health and medical products for the poor.

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Only in the past decade has global attention focused on the health needs of poor and marginalized populations in developing countries.[2] This new attention has opened to public view the system of protections for IP and trade embodied in national rules and in the global Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement. Moreover, recent debates over access to drugs for low-income populations in developing countries have highlighted the controversies found in the often arcane details of the patent system and IP laws.[3] The media often portray these debates as a struggle between rich and poor countries, big drug companies and sick people, or insensitive bureaucracies and caring relief organizations. While such portrayals may gain the attention of the public and of policy-makers, they at best oversimplify and at worst obscure the true nature of the problems, and thus create further barriers to finding solutions.

The economic, legal, and policy arrangements that move innovation from research labs to consumers are the same ones that erect barriers between those same labs and the poor. The main economic barrier is the high cost of developing a product from a basic discovery. The main legal barrier is a complex ownership system, one that goes too far in protecting the interests of those who invest in research and development. Finally, there is a policy barrier: the inability to balance the competing interests of the scientific community, consumers, and industrial development, all of which vie for advantage in the increasingly lucrative world of health care products. As IP systems evolve in developing countries, they should avoid repeating mistakes and act to reduce barriers to development of health and medical products for the poor.

This chapter outlines several ways that public and university decision makers can reorient their IP strategies to remove these barriers. It first considers the rationale for government investment in biomedical research, and then explains what kind of public benefits should be expected from that investment. The chapter then examines the key U.S. laws governing technology transfer from federally funded research and provides a synopsis of the legislative context of their passage. Some creative options for extending the benefits of biomedical research to poor countries or global beneficiaries are then proposed for the public sector and universities. A few of these options could also be adopted by developing-country research funders and universities.

Indeed, there are several ways for public institutions to increase the resources and tools devoted to public health needs in the developing world. At the upstream end, public institutions could direct funds toward research in developing countries and their diseases; they could also partner with private and nonprofit entities wishing to do the same. At the downstream end public institutions could directly render assistance to developing country institutions in building research capacity, provide products to users in poor countries, reduce barriers to the transfer of technology, or partner with industry and academia to expedite the development of products from research. Most of these steps also apply to fields outside of health and medicine.

## 2. PUBLIC SECTOR INVESTMENT IN HEALTH RESEARCH

It is generally acknowledged that publicly supported basic research invaluably contributes to the development of new medical technologies. Creating such benefits is part of the mission of the U.S. National Institutes of Health (NIH). Moreover, the U.S. Congress and the NIH leadership recognize the direct connection between global health improvement and the health and well being of U.S. citizens. Public research agencies, such as the NIH, have a clear commitment from Congress to provide global benefits from their research. NIH has therefore allocated some of its resources for research and research training related to specific developing country health needs (for example, HIV/AIDS, tuberculosis, malaria, tobacco-related illness, cognitive development, and others). It has also advanced such efforts through technology transfer negotiations with private companies developing the discoveries of NIH laboratories.

It is worth emphasizing that about 90% of NIH research funds support extramural research,

the vast majority in universities. Control of technology from that research was placed in the hands of universities by the Bayh-Dole Act of 1980. Therefore, by far the greatest impact of any innovation in intellectual property (IP) management comes from decisions made by university presidents and their technology transfer officials. They determine how IP derived from publicly supported research is used. Most of the following suggestions are meant for their special consideration. Similar arrangements, of course, could be adapted in developing countries.

### 2.1 *Rationale for public sector investment in biomedical research*

Several arguments have been put forth to justify the government's role in funding research. Although this discussion mostly focuses on biomedical research, the same arguments apply to other sectors. First, funding basic research is a classic example of the role of the government to provide public goods, as applications for health are built on the foundation of fundamental knowledge. Because the market typically underinvests in fundamental knowledge creation and utilization, government support of basic biomedical and health research is an efficient use of society's resources. Furthermore, it is important that the public sector continues to invest lest the increasing expenditures of the private sector unduly control access to basic knowledge. The fruits of publicly funded research—whether in genomics, developmental biology, aging, emerging infectious diseases, molecular virology, cancer, or other fields of science—benefit the public in many ways. These benefits are delivered, not only in the form of new medical technologies, but also in ways unspecified and unforeseen. An example of the latter is the NIH's investment in basic retrovirology, which paved the way for an early understanding of the nature of HIV.

Second, public funding of research ensures that data is available to scientists at the earliest possible time. Academic research careers depend on research productivity, often expressed as the "publish or perish" dictum. Publicly funded research discoveries are often placed immediately in the public domain through presentations, publication, and professional networks. Privately funded researchers, however, are under no obligation to make their findings available to other researchers or to the public and indeed may in some instances be prevented from doing so by company policies.[4] This difference is illustrated in the approaches of the publicly funded human genome project and the privately funded sequencing research. The former placed the data in the public realm in real time via the Internet, whereas the latter did not—though the private sector could still benefit from the publicly funded program's findings.

Third, publicly supported research can fill knowledge gaps not addressed by private industry. Because the public sector is based on incentives other than the profit motive, government research can set priorities based on society's needs, scientific promise, and other factors that—when no market for a product exists—are not of paramount concern to the private sector. Therefore, the choice of whether to develop new ideas into products is largely left up to the private sector. The implication of this is that technology development from public research by and large gets rationed according to the priorities of the private sector, typically from a "return on investment" perspective. Admittedly, there are tensions across these public and private sector interests. However, in the United States these divergent paradigms are sorted out through a multi-agent lobbying and vetting process that occasionally produces disagreement but is generally accessible and transparent.

One important consequence of this third point is that publicly funded research can address fundamental questions without undo concern for the immediacy of its application. When patents are derived from federally supported science they are in fact generally for early-stage technology—often processes and materials to be used by other researchers.[5] Rarely does a discovery occur in federal labs that does not require years of additional funding to enter into the market. This is why public and private investments in biomedical research are mutually dependent: a public sector invention is usually brought to market by private sector product development. Still, inherent in this relationship is the reservation of the choice of

whether to develop new ideas into products being largely left up to the private sector. The implication of this is that technology development from public research gets rationed according to the priorities of the private sector.

### 2.2 *Balancing public and private research investment*

The synergistic relationship between the public and private sectors is generally highly efficient and productive; however, the potential of this arrangement to create public goods from the investment of the public sector is by no means certain. In principle, the case can be made that beyond the support for the research itself, public agencies have a role to ensure that the benefits of basic research get delivered to the public. How it can best carry out this role, however, is not obvious. Under current arrangements, the public sector has limited capacity and experience in the downstream steps of developing and delivering products to consumer markets. These steps are not only costly but are also not aligned with the public sector's comparative advantage.

The public sector, therefore, requires two kinds of investment: one enhances private sector investment by supporting basic research that will eventually lead to private sector product development; the other augments the private sector by investing in those areas that are unattractive for private sector investment. Both avenues are essential for the public sector to pursue, and shifting public health needs require the frequent rebalancing of priorities.

The conundrum for public research agencies is that however large their public funding may appear, their resources are still limited relative to scientific opportunity. They must prioritize research investments and are often unable to take a technology far enough to determine how much public benefit might be derived from the full, vigorous exploration of its potential. The cost of fully developing a new technology is great, and the rate of attrition—explorations that end without a product or a profit—is very high.[6]

This underlies the crucial concern that some explorations end prematurely because the estimated market is too small to justify the needed up-front investments. In the health sciences, this may be particularly true of research for products that target diseases of the poor or of developing nations (for example, tropical and parasitic diseases) or that are more appropriate for delivery and application in developing country health systems. One hopeful note in the past five years has been the substantial expansion in R&D investment in neglected diseases of the poor via public/private partnerships (PPPs): between 2000 and 2004, R&D expenditures from public/industry nonprofit partnerships grew from US$23 million to US$44 million per year.[7]

To help balance the above interests, the NIH has created guidelines for sharing research tools.[8] It is also tracking inventions produced from NIH investments that result in therapeutic drugs or vaccines. FDA-approved therapeutic drugs and vaccines developed with technologies from the intramural research programs at NIH are reported on the NIH Web site.[9] Eventually this system will document the public health outcomes of any commercial technology developed with NIH support. These steps may be worth emulating as developing countries establish their own systems for tracking the results of their research investments. But while this system will produce valuable information about the benefits of research investments, it is still an a posteriori exercise.

## 3. IP LAWS AND PUBLIC RESEARCH INVESTMENT

A successful research endeavor creates IP, but when does this ownership enhance the public good? The status and ownership of IP derived from government-funded research in the United States is framed by a series of public laws that establish the current principles and procedures used by the U.S. government and its private partners. For purposes of this discussion, the most important laws date from a quarter-century ago, although the laws have been amended and enhanced in minor ways since then. These are the Stevenson-Wydler Technology Innovation Act (P.L. 96-480) pertaining to intramural research in government laboratories, and the Bayh-Dole Act (officially Amendments to the Patent and Trademark Act,

P.L. 96-517), pertaining to extramural research outside of government laboratories.[10] Both Acts were passed in 1980 to stimulate greater use of technologies developed through government support. Their legislative history is instructive for understanding the public benefit the laws were designed to create.

### 3.1 *History of Bayh-Dole and Stevenson-Wydler acts*

In the mid-1970s, Congress became concerned about the failure to use federally owned patents to encourage product development stemming from federally funded R&D. At the time, only 5% of the 28,000 patents retained by the U.S. government had been licensed for use, whereas 25%–30% of industry patents were being applied.[11] These circumstances prompted Congress to inquire into how federal research was transformed into usable technology. Congress concluded that the barriers were too great and the incentives too small for academia or the private sector to develop technology from the patents produced with government research support. At the time, there was no discussion about public sector involvement in downstream activities.

The main barrier to the use of federally patented technology was believed to rest with the unwillingness of the responsible agencies to grant exclusive licenses for companies to use the patented technology and invest in product development. An exclusive license would allow one company to have a monopoly in the invention produced with government funds as an incentive to develop and test the product. Companies complained also that even the attempt to obtain nonexclusive licensing was an excruciatingly slow process. Federal agencies imposed many paperwork requirements and other burdens on their licensees in an apparent effort to protect the public's interest in the invention. It became clear to Congress that private companies would not accept the risk and expense of developing technology for the marketplace without some exclusive rights and without a more streamlined way to obtain patent rights across agencies.[12]

The Bayh-Dole and Stevenson-Wydler acts were intended to rectify this situation. They did this by creating a uniform licensing system for all federal agencies, reducing the steps needed to grant licenses, and providing incentives for industry to invest risk capital in product commercialization from federal patents. Most importantly, Bayh-Dole allowed universities and small-business government contractors to receive title to inventions derived from government support, rather than the prior arrangement in which government was the sole holder of the patent. It also allowed the grantees and contractors to license the technology developed under these patents for use by small business and private industry.[13] The Stevenson-Wydler Act effectively allowed federal labs conducting intramural research to exercise the same privileges.

The effect of these new statutes was to transfer the ownership of IP and the benefits derived from it. They allowed companies to license and develop products based on the discoveries of federally funded university research with full legal protection from competition. According to the Congressional Research Service, "*Proponents of this approach contend that these benefits are more important than the initial cost of the technology to the government or any potential unfair advantage one company may have over another in their dealings with the federal departments and agencies.*"[14]

Interestingly, the Bayh-Dole legislation initially proposed a formula for repayment to the taxpayers of the government investment when a patent yielded commercialized technology. This provision was dropped in the final stages of passage because of disagreements over technical aspects of the repayment mechanisms.[15] While the legislative history demonstrates that there was widespread acceptance of the principle of a rightful return to the public from private sector use of publicly funded technology, it was the details of implementation that ultimately defeated its inclusion in the bill.[16]

Nonetheless, the legislation was passed with several clauses intended to ensure that the monopoly powers granted to patent holders and licensees would not be abused. These clauses have been the subject of much debate among IP specialists and are a cause of anxiety for the private sector, which is concerned about when and with

what justification they would be invoked by the government. The legislation expressed Congress's view that the use of discoveries from federal research to improve health was clearly in the public interest, even if it must be carried out by government action.

The Bayh-Dole law states the intention "*to ensure that the Government obtains sufficient rights in federally-supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions…*"[17] The means to achieve that goal were codified in the following provisions that reserve certain rights for the government:

- The right to a nonexclusive, nontransferable, irrevocable, paid-up license to practice for or on behalf of the United States throughout the world.[18]
- "March-in" rights that enable the government to require the licensee or patent holder to grant use rights to another user with due compensation under special circumstances. The special circumstances envisioned in this clause refer to lack of use within an agreed-upon time frame or special health or safety needs that are not being met by the licensee or patent holder.[19]

The first clause, allowing government use of the technology, has been narrowly interpreted to refer only to a true government purpose. This interpretation has not been fully litigated and therefore it is likely that private pharmaceutical companies remain concerned that changes in its interpretation could expand to threaten their economic interests. This provision could theoretically allow the government to practice the technology—or contract with a third party to have the technology practiced—for authorized government purposes. Because the mission of the NIH is "*to secure, develop and maintain, distribute and support the development and maintenance of resources needed for research,*" some have suggested that there appears to be a limited scope for NIH action in this regard.[20] However, the Department of Health and Human Services might, due to its public health mission, have a clearer justification to invoke the government-use clause in pursuit of its mission.

The second clause, the so-called march-in right of government, has attracted greater attention and has been more extensively explored. It has been formally tested just once, in a case in which the NIH declined to initiate march-in proceedings, thereby disallowing the petitioner use of the technology.[21] This test case provided the opportunity for both the government and affected parties (who were primarily third-party recipients of government research funds or prospective licensees) to indicate their views on how restrictive the march-in rights should be.[22] The debate centered on questions of what constituted timely delivery and how critical the public health or safety need had to be to in order to warrant government action. The voluminous record produced for this petition demonstrated that universities and industry were extremely concerned that the march-in provision would undermine licensing rights under Bayh-Dole. It also demonstrated that petitions for march in would prompt a full-blown legal procedure, imposing both time and financial costs on any potential petitioner.

### 3.2 *Twenty-five years after Bayh-Dole and Stevenson-Wydler*

The laws that govern the disposition and use of technology derived from U.S. government investment in health R&D must be judged first and foremost by how well they have met their original legislative intent. Assessments of the impacts of the Bayh-Dole Act and related legislation suggest that the laws performed as Congress intended.[23] Most independent analyses have concluded that the acts greatly increased technology transfer from researchers to private industry in the biomedical sciences, improved the governmental patenting and licensing process, and made available to the public products that improve their health and well being.[24] Thus, the goal of greater private sector utilization of the research output by federally funded scientists seems to have been achieved.[25]

Simultaneously, research universities experienced significant upheavals as agendas and researcher time focused more and more on revenue

opportunities. In the two and a half decades since passage of the Bayh-Dole Act, the major U.S. research universities have developed highly proficient offices of technology transfer, staffed by professionals who deal with patents and licensing. Through this infrastructure, these universities have come to expect financial rewards from their research efforts in the form of royalties and fees from patents and licenses. In the eyes of some university officials, this income flow is justified as partial compensation for the costs incurred during the conduct of federally supported research—an enterprise most universities believe costs them more than the infrastructure support provided with federal grants.

Yet there is no guarantee of financial returns from research, and most universities have long operated without this extra income. They still do, albeit there are consequences on investments in expansions of faculty and facilities. The intent of Bayh-Dole was not to produce supplemental revenue streams to universities. Rather, it was to engender innovation and increase the use of technology for economic development. Universities do accept their responsibilities to contribute to the public good, but these have generally focused first on university, state, and national health issues, in that order. Most universities have either not addressed or achieved a balance between entrepreneurship and the generation, use, and dissemination of knowledge for the public good.

Recent analysis concludes that, although more university technology transfer operations have become profitable over time, many universities do not earn profits from licensing the results of research.[26] The occasional blockbuster technology has produced large royalties for a few universities holding patent rights, and some others generate a few million dollars annually. Most universities, however, are still barely in the technology development business. Out of almost 1,500 licenses executed during 2004, only 1.5% (67) generated more than US$1 million in revenues. In 2004, US$1.4 billion in earnings from licenses and US$1.2 billion in royalties was reported by the 196 U.S. institutions that responded to an annual survey of university research technology offices. The survey respondents reported about US$41 billion in research expenditures for the same year, and over 10,000 new patent applications filed.[27]

Much has changed in the 25 years since the Bayh-Dole and Stevenson-Wydler acts were passed. Not the least of these changes is an increasing concern for global health, a concern arising from a recognition that the health issues of poor country populations and the U.S. population are connected, as are the health of poor country populations and their economic and social prospects. For example, the devastating impact of HIV/AIDS and the limited use in impoverished developing countries of technological advances for diagnosis and management of this infection and its complications is very much in the news today. As a consequence, many countries are trying to figure out how to deliver health technology to poor and technologically marginalized populations. In the process, questions are being raised about the balance of interests between the use of new technology to reduce threats to health and the ownership rights to that technology.

### 3.3 *Current debates*

The obligations to a larger, more global public—and the rights of this public—are raising critical questions: just who is the public and what return on the investment is due the public? Debate continues about how to ensure the availability of effective treatments to all in need while ensuring that research partnerships with industry remain viable and productive. Public research and research funding agencies such as NIH, the academic community, and industry will be challenged to consider how to interpret and apply IP laws and regulations in the context of how a patent or a license, granted or denied, will affect the public good. Not only are economic, legal, and policy issues involved, but there are also complex ethical and social considerations created by decisions to apply IP laws.

The controversial nature of IP for biomedical research is illustrated in public debate and in proposals in recent sessions of the U.S. Congress:[28]

- disputes over competing claims to IP developed under government/industry ventures

- delays in negotiating Cooperative Research and Development Agreements [CRADAs] because of issues related to dispensation of IP
- controversies over the rights of drug companies to set prices on drugs developed in part with federal funding
- uncertainties due to the increasing mix of funding sources among government, foundations and the private sector, and the portion of IP that represents the public good return
- problems obtaining technologies for research developed in the private sector for use in federal laboratories (A more general problem of access to research tools has not been considered by Congress.)

This list of issues is not exhaustive and raises more questions than answers. Moreover, each could be—and indeed most have been—the subject of a rousing debate and the occasion for a flurry of letters, testimony, articles, op-ed pieces, and books. One place to start searching for ways to increase the return to the public—both global and U.S.—of the public investment in research is to review the arrangements currently or potentially in use to deliver these benefits.

## 4. THE PUBLIC SECTOR AND GLOBAL HEALTH RESEARCH

There are several ways that government research funders can increase the resources and tools devoted to the public health needs of the developing world. At the upstream end they can direct funds toward research on specific diseases; they can also partner with private and nonprofit entities wishing to do the same. At the downstream end they can directly provide products to users in poor countries, reduce barriers to the transfer of technology, or partner with industry and academia to expedite the development of products from research. Some of these steps could be adopted by academic recipients of public funds, especially those that actively develop IP ownership derived from public research funds.

The following specific actions could be taken by public funders and their academic and private sector partners to increase global public goods for health. Many of these actions could also be adapted, by implementing IP rules and procedures, for use in developing countries.

### 4.1 *Action within the research enterprise*

**Strengthen capacity for research in developing world**. Increasing funding for research in developing countries is, if sustained, one of the most direct ways to create a global benefit and ultimately increase access to the results of scientific research for the world's poor. Such funding can also lead to collaborations between developed and developing country scientists, creating more sustainable research environments and the opportunity for human capacity building and research infrastructure development.

Government research awards can contain provisions requiring researchers to train developing country scientists in these highly successful laboratories. In the health sciences, for example, a portion of the royalties from the NIH intramural program is returned to the lab that discovers and invents new technology—this also applies to university labs that produce patentable inventions. These funds could be devoted to training new scientists. In addition, the same opportunities could be provided in developing countries.

**Academic/industry partnerships**. Both within and apart from the university research environment, the relative importance of private sector funding has increased. Private companies are now estimated to spend three times as much on biomedical research as the NIH, most of it within their own research laboratories.[29] However, industry-funded university research is also growing. It is unclear how involved industry is in academic biomedical research at present, although one source indicates that a small portion of private R&D (about 12%) is conducted within U.S. academic institutions.[30] Whatever the magnitude of industry's involvement, it is large enough to possibly blur the distinction between the objectives of universities and private industry, and it has caused some to question university motives for carrying out research.[31]

The nature of science and its conduct has also changed since Bayh-Dole was instituted.

Few academic or public research organizations have the particular combination of scientific know-how, application tools, and commercialization potential that it takes to turn ideas into real deliverable products. Public/private partnerships are increasingly looked to as the mode of operation for future biomedical research that rapidly develops products. Nowadays, the complementary human capital and financial resources of the public sector, academia, and industry are all needed to bring scientific inquiry to fruition. The power of the Gates Foundation to influence this process is a major new force shaping this landscape.

In recent years, new approaches have been devised to sweeten the pot and bring new players into the development of health technologies for the poor. These include public/private partnerships such as MIHR (Centre for the Management of Intellectual Property in Health R & D,) established in 2002 precisely to address public sector needs in IP management. It provides a forum for multiple public and private entities to improve the management of health IP for the benefit of developing countries through information exchange, training, defining best practices in licensing, and help in developing norms for IP management.[32] MIHR is working with developing countries to help them bridge the gaps between what the public and private sectors can provide in addressing global health needs.[33]

Many universities prominent in health research are also seeking to balance their financial objectives, their charge to advance scientific discovery, and their dissemination of the benefits of those discoveries to the public. Universities in both developed and developing countries could explore how to create research partnerships with one another and with the private sector that achieve a public benefit goal, while still meeting the profit motive of private companies.

### 4.2 *Technology transfer options*

The evolution of technology transfer practices since Bayh-Dole has placed public sector institutions and research universities in a difficult position. The delicate balancing of their scientific interests, their responsibilities to the public, and their need to maintain a competitive position vis-a-vis the private sector to retain expertise has been jarred repeatedly in the past few years. Developing country institutions are particularly challenged by the lure of greater research opportunities and higher salaries and benefits for their top and young scientists in the U.S.

The following list suggests how public investment can use technology transfer more effectively to create global public-health goods. The list also makes the important point that all possibilities should be open to discussion among committed and interested parties—including policy-makers and research leaders in the developing world. Many of the suggestions are derived from NIH experiences, but they could be applied far more widely. Most importantly, the engagement and involvement of all stakeholders is essential, without this it will be impossible to change current operating principles. Change will not be accomplished by fiat.

1. A straightforward way to deliver social dividends from research is to write provisions into licensing agreements. On an ad hoc basis, NIH has incorporated voluntary provisions for public benefits into license agreements with private industry. As a result, many licenses granted by NIH include a public benefit of some sort.[34] The types of public benefits called for in these purely voluntary arrangements include educational Web sites, product donations, and drug delivery to needy communities. The initiative has been palatable because no specific level of benefit or outcomes is requested in the license provisions. It appears, however, that the public benefit delivered through this approach has been, at best, modest.

   Public-benefit provisions in licensing agreements could state a specific aim to benefit poor countries. Both publicly funded research agencies and university technology transfer offices could increase the use of such provisions. If employed in developing country licensing agreements, the provisions could ensure the delivery of drugs or technologies to the poor by whatever direct mechanism the

commercial partner prefers (for example, drug donations or reduced prices), or even indirectly through a nonprofit organization. For instance, a reasonable proportion (however difficult it is to determine the meaning of *reasonable*) of the royalties to a university from the license would be placed within a foundation established to support global public-health goods. It is necessary to recognize that the funds available for diversion are meager, if they exist at all, at most universities.

2. The private sector lacks interest in many available technologies because of its perceived lack of profitability. Therefore, ways to increase profitability need to be explored. One method open to the public sector and academic institutions is to bundle technologies developed in their laboratories. This would require companies to license another, less profitable technology for development in order to obtain a license for more lucrative technologies. This is consistent with the paramount aim of the Bayh-Dole Act to get technologies used.

   So far in the United States, there have been few takers for this type of arrangement, and its impact will likely be small. The argument is that bundling may help license less-attractive technologies, although it will not make them more profitable for companies to develop. However, in a developing country setting, the economics of bundling may be different. For instance, if the public institution can help identify a large buyer to take the initial output, a profitability threshold might be reached if the price from the bulk purchaser met minimum average cost of production at the appropriate scale. A private company wishing to expand its capacity in a developing country could anticipate potential profits.[35] Merck reached such a level when it chose to produce recombinant hepatitis B antigens in China for that market. It even built a state-of-the-art plant to produce vaccine. This led to widespread use of the vaccine in China and a foothold for the company in the country—a win-win situation.

   The economics of bringing products to market in developing countries differs from those in developed countries.[36] Human clinical trials are the most costly phase of product development; this phase is also when most experimental technologies fail. Developing countries have the opportunity to streamline procedures for carrying out clinical trials, including establishing more rational and less time-consuming institutional review board (IRB) processes. Other components of the R&D process that generally cost less in developing countries are legal, marketing, and regulatory fees. Also, the medical research companies in developing countries may be more willing to take risks than are those companies in the United States. Moreover, both companies and their government regulators may be more strongly motivated by the clear, urgent need for improved diagnostics and therapeutics.

   Developing country markets can also be segmented: the technology could be provided at low or no cost to the poorest countries through a subsidy mechanism (market *pull*), at a sustained rather than reduced price in middle-income developing countries, and at a higher price as the market develops. Such an arrangement would be consistent with economic theory, in which price discrimination can increase market efficiency and equity.[37] It actually resembles the pricing methods that pharmaceutical companies currently use in developed country markets and could make some technologies suddenly more financially attractive. For this approach to work, measures must be taken to ensure that there is no parallel importation or smuggling from the low price to the higher price nations. This is a difficult goal, but one that might be expedited through TRIPS to allow trade in generics among developing countries.

   A variant of this approach would be for technology transfer offices (TTOs) to

work more with nonprofit organizations to deliver technology, instead of seeking commercial avenues. NIH currently uses CRADAs to work with the World Health Organization (WHO) and nongovernmental organizations (NGOs) (for example, PATH) to move malaria drugs and other less-profitable technologies into use. The overriding concern for a CRADA is whether the organization can carry out the necessary R&D to develop a product. The current fully capitalized cost (including post-approval R&D costs) to the private sector to develop one drug is estimated to be nearly US$900 million. And with more than eight years required for the clinical and approval phases of development alone, nonprofit organizations just do not have the capacity to sustain such an investment.[38] However, as already noted, it is extremely difficult to make such estimates because the necessary information is not in the public domain; it is likely that goals can be achieved at much lower cost in developing countries , and this can be put to the test.

3. In an effort to increase the licensing of vaccine technology in selected developing countries, the NIH is now requiring companies seeking to license NIH technology to produce a plan to market the technology in developing countries within two years of regulatory agency approval. They can either opt to deliver the product themselves or initiate a joint venture with another company. The goal is to use the potential profits from sales in developed countries to encourage companies to manufacture for the developing world at or near cost, although the expense of adding manufacturing capacity or the opportunity cost of shifting existing production to this product should be factored in. Another way to achieve access and affordability for the poor is by manufacturing in developing countries at lower cost than in the United States.[39] This sort of a tie-in is difficult to accomplish from the United States, but a developing country government could arrange it much more easily.
4. Delivering technologies for developing country use through multiple-use licensing is too rarely used. This approach identifies and licenses basic technology for specific fields of use (for example, a cancer vaccine) and requires the same (or another) company to do parallel development of the same technology for another field of use (for instance, an HIV vaccine). In the existing regulatory framework, an expansion of this approach would require renegotiating existing licensing agreements and would certainly be strongly resisted by licensees. However, in an open playing field such as exists in some developing countries, it could become common.
5. A radical approach open to the U.S. government but not to universities is to exert march-in rights on already-licensed NIH-derived technology to meet special health or safety needs that are not being satisfied. This option, referred to as compulsory licensing, should be retained by developing country governments in case of public health emergency—and it should be used when necessary, and never frivolously.
6. Finally, all activities—from early-stage development to manufacture and distribution—could theoretically be performed by a government agency, university, or contractor. For instance, government research institutions could move their own involvement further down the development pipeline to include whatever steps would be needed to get the product ready for uptake by a private or nonprofit entity. Although this is clearly not a priority for a research agency such as NIH, there are already some programs to develop medications at NIH instead of relying on the private sector. It is worth emphasizing that, within the context of the Bayh-Dole Act in the United States, by far the greatest impact from IP innovations will come from decisions made by university presidents and their technology transfer officials. They control how IP

derived from publicly supported research is used.

If universities decide to adopt any of these options, the decision, in our view, should come from a consultative process among all interested parties, including public research agencies, developing country representatives, potential funding partners, and industry. Universities and their faculties would have to embrace the moral and social imperative of enhanced delivery mechanisms and become full partners in the means selected to achieve them. Because most of the relevant technology is developed by a small subset of research-intensive universities, it would not be necessary to bring all universities on board; instead, a focus on the leaders would establish standards that others could follow. The process would be strengthened if developing countries joined and were led, for example, by a multinational organization such as the Inter-Academy Medical Panel.

## 5. CONCLUSION

### 5.1 *Considerations for senior policy-makers*

Economic development, drugs for the poor, breakthrough technologies for the world's most common diseases, and scientific advances for treating tropical diseases are legitimate social goals for all nations. But these goals vie for limited financial and expert resources and are not always compatible with each other. Policy-makers must ensure that the public's investment in research is rewarded. A system should spur economic development and creative innovation, as was the intent of the Bayh-Dole Act. Just as importantly, the IP system should clearly articulate and codify an overarching social goal.

It is understood that subsidies to research universities in the form of indirect costs in grants funded by the government may not cover the actual cost of supporting research infrastructure, and that industry risks capital in R&D for products that fail somewhere along the path, and that this has implications in terms of fiduciary responsibility to stockholders due a return on investment for success in product development. None-the-less, policy-makers should insist that, as a condition of receiving the protections of patents and licensing, companies and universities must pay some "dividend" back to the public. This dividend could be indirect and used to support further research to address needs the market alone does not satisfy. Further, policy-makers should retain the government's right to exercise a technology license on behalf of the public, as well as full march-in rights. The government should be prepared to exercise these rights in the event of a real public-health emergency or in the event that the private sector licensee fails to develop or bring to market a product that has potential public benefit. The government must accept its responsibility to ensure that the public's investment pays returns to the public. As it turns out, the option for government action itself will likely provide companies with a strong incentive to make products available in the market. Government should also embrace principles of segmented markets and tiered pricing for vulnerable populations in the U.S. and abroad—the poor, the elderly and the vulnerable in particular. In this way, the government accepts its responsibility to ensure that the public investment pays returns.

### 5.2 *For presidents of universities*

In their approach to IP laws, the academic community is faced with complex ethical and social issues. If partnerships are to promote research that leads to global benefits, there should be agreements that explicitly commit all of the partners to this goal at the outset. Creative financing and IP sharing arrangements will have to be developed. And scientists will need to prioritize the delivery of global benefits. Similarly, university officials will have to fully embrace the larger role of universities in society and in the global community. Leadership must come from the very top of the institution, for example valuing applied research and including the creation of global public goods among the criteria for academic advancement.

Many universities prominent in health research are seeking to balance their financial objectives, their commitment to scientific discovery, and the dissemination of benefits to the public. PIIPA (Public Interest Intellectual Property Advisors) is one example of how U.S. universities can use their stock-in-trade to serve the global public need by offering expertise and training.[40] PIIPA is a newly formed consortium of universities and companies that provides pro bono legal and professional assistance about IP issues to entities in developing countries, including governments and universities.

There are many ways that universities can help meet global public health needs. They can include including public benefit clauses in their licenses to the private sector, investing part of their royalty stream in a foundation, ensuring that returns to the university itself are used in part to support capacity building and applied research of global relevance, establishing an "ethical" investment fund,[41] licensing technologies to nonprofits or others who would develop and manufacture for poor countries, or bundling technologies to encourage the development of medicines aimed at diseases of the poor. Research universities or public funding agencies could unilaterally adopt any or all of these options, but a multilateral approach would have far greater public awareness and public health impacts. Ideally, this approach would be an international, multi-institutional effort.

### 5.3 *For the technology transfer officer*

The job of the TTO is to create the incentives needed to move discovery into the product development arena, motivating academic researchers not by the sole promise of high profits—which rarely appear—but by applying royalty toward the support of research in the inventor's laboratory, and by balancing some financial reward to the inventor with the satisfaction of seeing his or her work used for public benefit. Although not the responsibility of the technology transfer officer, the latter can become so. This will require creating opportunities for various forms of licensing (including exclusive licensing where appropriate, but a nonexclusive license should be insisted upon if that is likely to move a promising technology to market sooner), maintaining a very low paperwork and expense burden for private (including nonprofit) companies wishing to license government-funded technology and insisting on explicit public-benefit clauses. Technology transfer officers should report such efforts and their potential impact to the President him/herself.

### 5.4 *For a university scientist*

Individual researchers in the United States have established product development companies in large numbers, and developing country research scientists and their institutions will feel pressure to do the same. When considering a research collaboration with a scientist from the United States, developing country scientists should be certain that they receive equitable treatment in whatever IP ownership arrangements are made. While IP protection is often necessary to convince industry to move discovery into product development, something neither academia nor government, for that matter, do with distinction, not every discovery should or need be protected. Scientists should be capable of participating in these discussions. Developing country scientists should also resist the excessive protections that are sometimes placed on research output in the United States—protections that delay and sometimes prevent discoveries from being published and shared in the scientific community. It is very important for developing country researchers to get the professional exposure and opportunities that scientific publication can offer. Narrow-minded efforts to establish property rights can inhibit those benefits.

### 5.5 *A global vision*

Creating and delivering global public health goods is much more difficult than creating and delivering national public health goods. Yet we are committed, in the words of Tennyson, "*to strive, to seek, to find, and not to yield*." To change the current reality will require a coalition of university officials, government, industry, foundations, and NGOs to identify priorities and opportunities and then collectively carry them out.

Although IP has clearly spurred the development of technologies that promote the public health of wealthier nations, the impact of IP in promoting global public health goods is mixed at best. Although the fundamental premise of IP protection—that it acts as a spur to innovation and a reward for risk-taking—applies equally to all industries, some characteristics of the health care industry set it apart from other fields where IP is important. Quite simply, in health care, the outcomes of technology development and its availability are matters of life and death.

In 2002, *The Economist* observed "*Rich countries should accept that considerations of how IP rights affect poor countries are not just a concern of overseas aid agencies but play a part in broader trade and economic relations too*."[42] This chapter builds upon the truth of that insight. Indeed, if Bayh-Dole were being debated today, then surely the economic development objectives at the core of the legislation would take on a much broader meaning. ■

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1 Global Forum for Health Research. 2006; Monitoring Financial Flows for Health Research 2005. Global Forum for Health Research: Geneva. www.GlobalForumHealth.org.

2 This attention has been prompted significantly by the World Bank's publication of *Investing in Health*, which was the World Development Report of 1993 (World Bank. 1993. *Investing in Health*. World Development Report 1993. The World Bank: Washington, DC). The concern has been reinforced by the expanded activities of the Bill and Melinda Gates Foundation for global public health, as well as the development of many other partnerships for public health.

3 See extensive media coverage in 2001 of the South Africa AIDS drug controversy, Brazil's decision to issue compulsory licenses for AIDS drugs, and the stalemate subsequent to the November 2001 WTO meeting in Doha, Qatar, over drug access in public health emergencies.

4 Thursby and Thursby report that 27% of university research licensed by industry allows for prepublication deletion of information from research papers; 44% of them allow for publication delays of about 4 months, on average (see Thursby J and M Thursby. 2003. Intellectual Property, University Licensing and the Bayh-Dole Act. *Science* 301: 1052).

5 Seventy-five percent of licensed inventions from universities are "proof of concept" (see Jensen R and M Thursby. 1998. *Proofs and Prototypes for Sale: The Tale of University Licensing*. National Bureau of Economic Research: Cambridge, MA). This means that most university inventions are at an early stage of development at time of license and require further involvement from the inventor to reach the commercial stage.

6 One rule of thumb is that one of 5,000 drug candidates discovered in labs will be commercialized, *Business Week*, July 9, 2001. p. 96.

7 Moran M and J Guzman. 2005. *Drug R&D for Neglected Diseases: Are Public Funds Appropriately Distributed?* chap. 2. Global Forum For Health Research: Geneva.

8 Nass S and B Stillman (eds). 2003. *Large-Scale Biomedical Science: Exploring Strategies for Future Research*. National Academies of Science, Washington, DC. p. 168.

9 ott.od.nih.gov/about_nih/fda_approved_products.html.

10 Stevenson-Wydler established technology transfer as a federal agency mission, creating rules by which federal agencies could license discoveries for commercial use and receive royalties and fees. Bayh-Dole extended these powers to other organizations performing federally sponsored research, including universities. See Congressional Research Service (various) and *supra* note 11 for further details about federal patent law.

11 U.S. General Accounting Office. 1998. Technology Transfer, Administration of the Bayh-Dole Act by Research Universities. *RCED* 98-126, Washington, DC. p. 3.

12 Ibid.

13 A 1983 presidential directive extended licensing rights to large businesses.

14 CRS. 2000a. Patent Ownership and Federal Research and Development (R&D): A Discussion on the Bayh-Dole Act and the Stevenson-Wydler Act. RL30320, December 11. Congressional Research Service: Washington, DC. p. 11.

15 National Institutes of Health. 2001. NIH Response to the Conference Report Request for a Plan to Ensure Taxpayers' Interests Are Protected. NIH, Washington, DC. p. 10. www.nih.gov/news/070101wyden.htm.

16 Prompted by persistent Congressional concerns about returns to taxpayers from federal research, NIH later attempted to impose a policy of "reasonable pricing" on the technology developed from certain types of federal research. The private sector refused to comply with this arrangement and it was eventually dropped. Reference is made to NIH Cooperative Research and Development Agreements (CRADAs); see *supra* note 15 for discussion.

17 35 U.S.C. § 202.

18 35 U.S.C. § 202(c)(4). Exclusivity grants the licensee the sole right to use the IP, which serves essentially as a monopoly. Nonexclusive rights allow the grantee to use the IP, but they do not provide the right to be the only user.

19 35 U.S.C. §.203(1).

20 McGarey B and A Levey. 1999. Patents, Products and Public Health: An Analysis of the CellPro March-In Petition. *Berkeley Technology Law Journal* 14(3): 1114.

21 CellPro Petition to DHHS, March 3, 1997, cited and discussed in McGarey and Levey (see *supra* note 20). CellPro petitioned for a license to practice a stem-cell separation technique developed by a researcher at Johns Hopkins University. CellPro had not been able to negotiate a license agreement with Johns Hopkins or the existing licensee but had used the technology. It was found guilty of willful infringement on the Johns Hopkins patent. CellPro argued in its petition for government march in that Johns Hopkins and the licensee had failed to commercialize the technology in a timely fashion and that public health and safety needs were not being met. The NIH rejected both grounds of the petition. More recently, NIH was petitioned in 2004 to march in due to steep price increases imposed by Abbott Labs on ritonavir, an HIV/AIDS drug developed in part from public funds. NIH declined the petitioner's request. www.aamc.org/advocacy/library/washhigh/2004/060404/_4.htm.

22 Both the timeliness clause and the public health and safety clause were tested in the CellPro case.

23 National Academy of Science. 2001. Board on Science, Technology, and Economic Policy; Committee on Intellectual Property Rights in the Knowledge-Based Economy, Workshop and Related Papers. April. NAS: Washington, DC www7.nationalacademies.org/step/STEP_Projects_Intellectual_Property_Rights.html.

24 CRS. 2000b. R&D Partnerships and Intellectual Property: Implications for U.S. Policy. 98-862 STM, Updated December 6. Congressional Research Service: Washington DC. p. 11.

25 See *supra* note 4.

26 See *supra* note 4.

27 AUTM 2005. AUTM Licensing Survey™: FY 2004. Association of University Technology Managers: Northbrook, IL. www.autm.net. Note that figures include royalties and fees from all patents and licenses. In comparison, NIH royalties from intramural licensing were US$52 million in fiscal year 2000.

28 See *supra* note 24.

29 Goldberg R. 2001. In Changing Times, NIH, NSF Look Outdated. *Trendspotter* (May). www.genomeweb.com. This includes product development expenditures.

30 Blumenthal MD and M David. 1995. Capitalizing on Public Sector Research Investments: The Case of Academic-Industry Relationships in the Biomedical Sciences. Presented at NIH Economics Roundtable on Biomedical Research: Bethesda, October 19.

31 See for example: Bok D. 2002. *The Commercialization of Higher Education*. Princeton University Press: Princeton, NJ; Kennedy D. 2005. Bayh-Dole: Almost 25. *Science* 307: 1375; Krimsky S. 2003. *Science in the Private Interest*. Rowman & Littlefield: Lanham, MD.

32 Mission statement and partners in MIHR can be viewed at www.mihr.org.

33 See also Widdus R and K White. 2004. Combating Diseases Associated with Poverty: Financing Strategies Associated with Public Health and the Potential Role of Public/Private Partnerships. The Initiative on Public/Private Partnerships for Health, Global Forum for Health Research: Geneva.

34 Ted Roumel, former deputy director of OTT/NIH. Personal communication, June 2001.

35 It is important to note that many existing purchase arrangements through WHO and nonprofits are on off-patent medicine and technology. Thus, the bulk purchase through a competitive bidding process by WHO for TB drugs allowed a 30% lower unit price through the purchase of generic drugs from manufacturers based in The Netherlands and India (*The New York Times*, June 22, 2001).

36 Light D. 2005. Basic Research Funds to Discover Important New Drugs: Who Contributes How Much? chap. 3 in Global Forum for Health Research: Geneva.

37 Efficiency is maximized with an arrangement of perfect price discrimination (in which each buyer pays his maximum price), but can also be improved by using block pricing according to the willingness to pay of different market segments. This pricing scheme is referred to as Ramsey pricing.

38 Tufts Center for the Study of Drug Development. *Outlook 2004*. csdd.tufts.edu/InfoServices.

39 The domestic manufacturing requirement in the law can be waived and applies only to U.S. sales.

40 For information about PIIPA, see www.piipa.org and Gollin M. 2003. Answering the Call: Public Interest Intellectual Property Advisers. Paper presented at the Biodiversity and Biotechnology Conference, Washington University School of Law, St. Louis, MO, April 4–6, 2003.

41 Ethical investment funds or other financial tools are recommended among the "Top 10 Biotechnology" approaches for improving global health by a commission of the Joint Center for Bioethics at the University of Toronto (see Daar AS, H Thorsteinsdottir, DK Martin, AC Smith and PA Singer. 2002. Top Ten Biotechnologies for Improving Health in Developing Countries. *Nature Genetics* 32: 229–32).

42 *The Economist*. 2002. September 14. p. 14.