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The Role of Intellectual Property and Licensing in Promoting Research in International Health: Perspectives from a Public Sector Biomedical Research Agency

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I. Introduction

In the past fifty years, the intensity of research and the pace of discovery in the biomedical and health fields have accelerated quite dramatically -- within both the public (government and academia) and private sectors. The result is an unprecedented increase in the number of proven safe and effective drugs, vaccines, and medical devices for a broad range of illnesses and conditions. Most of these new drugs, diagnostics and devices (hereafter considered together as "medical technologies") target diseases that are prominent in the wealthier nations conducting the research and where the resulting products are commercialized.

This paper is concerned with the public good aspect of U.S. federal research investments viewed in a global context, and considers how it may be possible to enhance the benefit of such investments on behalf of the poor in societies beyond the borders of the United States. Historically, biomedical R&D as a national public good in the U.S. has had clear objectives and has been backed by a large public constituency. In contrast, until very recently, R&D investment for global public goods has received far less attention. Sparked by media attention to the AIDS epidemic sweeping Africa and escalating in Asia and Latin America and the Caribbean, as well as the appearance of "exotic" contagious diseases within the U.S.,[1] the American public is evidencing greater concern and awareness for the public health problems of the developing world. In recognition of the sheer magnitude of these problems and being in the public limelight, companies and universities are also seeking ways to demonstrate their concern.

Public research agencies, such as the U.S. National Institutes of Health (NIH), have a clear commitment to provide global benefits from its research. For the NIH this is because it is part of the Agency's mission, and because NIH leadership has realized the direct connection between global health improvement and the health and well-being of U.S. citizens. NIH has exercised this commitment both through allocations of its own budget resources toward research and research training related to specific developing country health needs (e.g. HIV/AIDS, tuberculosis, malaria, and others), as well as through technology transfer negotiations that it enters into with private entities.

It is only in the past decade that global attention has focused on the health needs of poor and marginalized populations in developing countries and some transitional economies, e.g. in Eastern Europe and the former Soviet Union. This new attention has perforce opened to public view the system of protections for intellectual property and trade, embodied in national rules and in the global TRIPS (Trade-related intellectual property) agreements. Recent debates over access to drugs for low-income populations in developing countries have highlighted the controversies embodied in the often arcane details of the patent system and intellectual property laws.[2] The debates have often been portrayed in the media as a struggle between rich and poor countries, big drug companies

[1] Washington Post, "West Nile Virus Extends its Reach," October 12, 2001.
[2] See extensive media coverage in 2001of the South Africa AIDS drug controversy, Brazil's decision to issue compulsory licenses for AIDS drugs, and the Nader et al letter to Secretary Thompson, DHHS.

against sick people, and insensitive bureaucracies against caring relief organizations. Such portrayals may be effective in gaining public and policy-makers' attention to a problem, but they are at best simplistic and often obscure the true nature of the problems, creating barriers to reaching solutions.

Like the proverbial elephant being examined by the blind, the "problem" will be described by various beholders in different ways, viewed from their own vantage point and biases. For some, it is the high prices of life-saving or life-prolonging drugs that prevent the poor from gaining access to them. For others, it is the failure of developing countries to implement and enforce laws protecting intellectual property (IP). For still others, it is the uncertain, risky and costly nature of the drug development process itself. Regardless of how it is described, the current attention to the issue from so many stakeholders and the often strident debate suggests that here is a problem in great need of solving.

This paper will assess these issues as they are playing out in the United States from the perspective of a public biomedical research funding agency, the National Institutes of Health. It does so by first discussing the role of the public sector to deliver public goods by investing in biomedical research (Section II.). It describes the reasons for a government role and examines the difficulty of defining an appropriate return to the public sector from this investment. In Section III., the key U.S. laws governing technology transfer from federally-funded research are briefly described along with a synopsis of the legislative and media discussions surrounding passage of the laws to provide the context in which they were enacted. This section also looks at the impact of those laws and new issues that have arisen since they were implemented 20 years ago. Section IV presents an array of potential options for the public sector and universities to work within existing law to extend the benefits of biomedical research to poor countries or global beneficiaries. Upstream options that are closely related to the federal research mission as well as direct provisions for creating global public goods are described for the purpose of stimulating further discussion. The paper concludes (Section V.) with a summary of the major legal, economic and policy barriers that continue to inhibit delivery of global public goods for health.

II. Public Sector Investment in Health Research

It is generally acknowledged that publicly supported basic research makes an invaluable contribution to the development of new medical technologies. This is obvious in the United States where the immensely productive basic ("upstream") biomedical research community is supported to a great extent by federal funding, primarily from the NIH. The heavy reliance on public funding applies to scientists conducting biomedical and behavioral research in universities and academic hospitals across the country (the "extramural" scientific community) as well as to scientists working in government laboratories at the NIH and to a lesser extent at certain other U.S. government agencies (the "intramural" scientific community).

Out of an estimated $70 billion in health R&D expenditures globally, $30 billion is estimated to come from public sources.[3] In the United States, most public funding of biomedical and behavioral research comes through the NIH, whose spending on research, both extramural and intramural, was approximately $16 billion in 2000 and $18 billion in 2001. Private sector expenditure on biomedical R&D is estimated to be considerably more than public sector investment. Total foundation spending on biomedical research adds another $8-$10 billion.[4] On a smaller but still substantial scale, many states support medical research in the form of research programs in their public universities and hospitals.

About 90 percent of the NIH research budget is directed to the extramural program consisting of grants, cooperative agreements or contracts to researchers in universities and other research institutions, while just over 10 percent of the funds are allocated to the intramural (on-campus) research program. Two-thirds to three-fourths of extramural research support is for investigator-initiated research, while the remainder is targeted by the NIH for research in need of, and ripe for, new funding. Thus, the full spectrum of NIH's research involves a combination of investigator-initiated projects and directed basic and applied research, all of which has been deemed to be of scientific significance through the rigorous peer review system of research pioneered by NIH.

Rationale for Public Sector Investment in Biomedical Research

What has been the rationale to justify the government's role in funding research? Several arguments have been put forth. First, funding basic research illustrates a classic role of government to provide public goods. Because the market alone typically under-invests in knowledge creation and utilization, government support of basic biomedical and health research is an efficient use of society's resources. It is expected that the fruits of publicly funded research – whether in genomics, developmental biology, aging, molecular virology, cancer or other fields of science –will benefit the public in many ways. These benefits are delivered in the form of new medical technologies, as well as in unspecified and unforeseen ways. An example is the NIH's investment in retrovirology that paved the way for an earlier understanding of HIV when the epidemic began two decades ago.

Second, publicly-supported research can fill knowledge gaps not addressed by private industry. Because the public sector operates with a different set of incentives from the ultimate profit motive of the private sector, the government research enterprise can set priorities based on society's needs, scientific promise, and other factors that are not of paramount concern in the private sector. One consequence of this is the ability of publicly funded research to address fundamental questions without undo concern for the immediacy of the applications of the research. How public sector funding priorities are themselves established will be explored briefly in the next section.

Third, public funding of research ensures the availability of data at the earliest possible time to the scientific community at large. Academic research careers are dependent on research productivity, often expressed as the "publish or perish" dictum. Discovery in

[3] Global Forum for Health Research, 2001
[4] Moses et al, 2001

federal labs and universities is often placed immediately in the public domain through presentations, publication and professional networks. Privately-funded researchers are under no obligation to make their findings available to other researchers or to the public. In recent years, however, some of these distinctions between public and private funded research have blurred. As one reviewer of this paper noted, "companies publish and universities patent".

However, this does not belie the reality that, while both the public and private sectors invest substantial sums in biomedical research, there are significant differences in the kinds of research and the extent and speed of dissemination of research supported by public funds versus private investment. This is obvious in the difference in philosophy between the publicly funded human genome project and the private sector funded sequencing research. The former placed the data in the public realm in real time via the internet, whereas the private sector efforts did not but could still benefit from the publicly funded program's findings. Public agencies are also more likely to emphasize basic research for which there is no necessary immediate or obvious commercial application. When patents are derived from federally-supported science they are generally for early stage technology – often processes and materials to be used by other researchers.[5] Rarely does discovery occur in federal labs that does not require years of additional funding to be advanced into the market. Herein lays the mutual dependence of public and private investment in biomedical research: public sector invention is usually brought to market by private sector product development. 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 gets rationed according to the priorities of the private sector.

For most purposes, this synergistic relationship between the public and private sectors is highly efficient and productive; however, the potential of this arrangement to create public goods from the investment of the public sector is uncertain. In principle, the case can be made that beyond the support for the research itself public agencies have a role to insure that the benefits of basic research get delivered to the public. How it can best carry out this role is, however, not necessarily 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 costly and, in addition, are not aligned with the public sector's comparative advantage.

Setting Priorities for Public Investment in Biomedical Research

Priorities for public funding are identified by a public process involving interested groups of scientists within government and the academic community, scientific professional organizations, consumers, patient advocacy groups, and to some extent lawmakers and budget managers. Setting priorities often raises conflicts over disease burden and scientific opportunity, and the proper balance between these and other elements in decision-making. The process is arduous and complex and, along the way, requires that a

[5] Seventy-five percent of licensed inventions from universities are "proof of concept," Jensen and Thursby, 1998. 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.

case be made that research undertaken with public funds will complement what is being done by private industry, rather than compete with it.

Complementing private sector investment in health is easier said than done. It requires investment from the public sector in two different directions: 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 great care is taken to insure that the balance between them is maintained.

No single approach will suffice to provide an adequate answer to the question: how much public investment in health research is needed? Because of the inherent inaccuracies of measuring inputs and outputs of the research enterprise, as well as the difficulties in measuring the health care outcomes that are the eventual target of the R&D process, it is impossible to know what the "right" amount of research is. Further, the benefits and the costs of public research depend on how the investment is allocated among the many research needs. Nevertheless, various efforts have been made to provide guidelines and principles for how much and what kind of research should be funded.

Disease burden approach A principle often invoked is that investment should be targeted toward the health problems that impose the greatest toll on society. The ranking of these health problems can be made by the public through organized interest groups or through an objective scientific process, but both methods are inherently imperfect.

Society's appreciation of investments in health research is based in large part on the value society places on health improvements of various types and for different diseases. One way in which these values are expressed in the U.S. is through funding priorities within the Congress, directed in part by public risk perceptions and lobbying efforts. This carries the risk that groups that are more organized and have more public presence may have more influence on resource allocations than their case merits on balance, considering disease burden, feasibility and scientific opportunity, and the need for investments in rare diseases and new scientific frontiers.

Scientific efforts to measure the burden of specific diseases and conditions or, equivalently, the benefits of specific health improvements, have expanded considerably in recent years. Among the methods used are willingness-to-pay surveys of targeted populations, market-based evidence about the value of life and injuries, and health-based metrics such as DALYs (disability-adjusted life years).[6] These measures suggest ways to set priorities according to the health burden of a particular disease. They also are founded on experts' judgments of inter-personal well-being. None are currently exclusively used by government to determine where public health investment should be made, but are being seriously explored by some governments as the basis for spending allocations for

[6] The DALY attempts to compile a burden of premature death and years lived with disease-related disability into a single estimate of society's disease burden.

health. A renewed effort to identify global disease control priorities is underway, in part through valuation and cost-effectiveness analyses.[7]

Rate of return on investment approach Periodic suggestions are made to allocate public expenditures on health research in order to maximize expected return on investment, measured by patents, royalties, licensing fees, or other performance measures. The greatest technical obstacle to using a formula-driven approach to allocate public funds for R&D in health, such as highest expected rate of return, is the uncertainty about the benefits of research. By its very nature, research rarely has a pre-determined outcome or time-frame and almost always follows a winding path, often with long periods of apparently limited advance or a seemingly continuous run of negative, albeit still useful, information. An additional factor limiting the potential use of rate of return for public sector expenditures is the moral aversion to tying health care to economic principles.

Like research activity in the private sector, the research enterprise supported by public investment produces both winners and losers. Universities, university laboratories, and researchers have shared in the sometimes substantial royalty payments earned through patents issued to the university and the subsequent licensing agreements related to inventions derived from federally-funded research. However, "winners" in the public sector include those inventions that contribute a public benefit, not only those that will be financially profitable. There is some risk that current laws and practices have narrowed the way in which the benefits of publicly-funded research are measured to more closely resemble a private sector yardstick. Furthermore, in a more globalized world – where risk of disease and benefits from research can come from any corner of the globe – it is important to insure that the society that benefits from the public sector health investment is the global one.

Most in the scientific community believe that considerations other than measures of disease burden and rate of return alone must remain prominent in the priority-setting exercise, including scientific opportunity and feasibility and attention to rare diseases otherwise overlooked by disease burden estimates. Furthermore, much of basic research is not disease-specific. None the less, research on general principles of biology often proves to be invaluable in understanding etiology, mechanisms and regulation of specific disease conditions. At the NIH, this research may be primarily supported by one of the disease categorical institutes, but its relevance may be broad or, indeed, even greatest for the diseases supported by the other institutes.

The conundrum for public research agencies is that, however large their public funding may appear, their resources are still limited relative to scientific opportunity. The result is that they are often unable to carry a technology far enough to determine how much public benefit might be derived from the full and vigorous exploration of the real potential. It should also be recognized that the incentive for academic researchers is, generally, the thrill of discovery; the more applied needs of product development are of lesser concern. These latter steps in the development process are usually performed by the private sector.

[7] Originally published by Jamison, D. and W. Mosely, Disease Control Priorities for the Developing World, Oxford University Press, 1993; also ongoing efforts by WHO.

The cost is great, and the attrition rate – explorations that end without a product or a profit – is very high. There remains the concern, however, that some explorations end prematurely, because the estimated market at the end of the road is insufficient to justify the needed investment up front. This may be particularly true of research for products that target the diseases of the poor or developing nations, for example, tropical parasitic diseases.

In an effort to increase what is known about the results of early-stage research, the NIH is working to develop improved outcomes measures for its research investments that will track inventions that support the research enterprise, and separately identify those that result in outputs for use by others, such as vaccines.[8] Nonetheless, the ultimate measure of the benefits of research output will remain an *a posteriori* exercise.

III. Intellectual Property Laws Governing Public Research Investment

The successful research endeavor creates intellectual property; it is the ownership and use of this to enhance the public good that is currently being so closely scrutinized. The status and ownership of intellectual property 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 governing the use of knowledge obtained through publicly-supported R&D were put in place two decades ago, and have been amended and enhanced in minor ways in the intervening years. These are the Stevenson-Wydler Technology Innovation Act (P.L. 96-480) pertaining to intramural research, and the Bayh-Dole Act (officially Amendments to the Patent and Trademark Act, P.L. 96-517), pertaining to extramural research.[9] Both Acts were passed in 1980 to stimulate greater use of technologies developed through government support. The legislative history is instructive in putting into context the public benefit the laws were designed to create.

Legislative History of Bayh-Dole and Stevenson-Wydler Acts

Congressional concern about the use of patents as a means to encourage the development and use of federally-funded R&D arose in the mid-1970s. At the time, only 5 percent of the 28,000 patents retained by the U.S. government were actually in use, whereas 25-30 percent of patents licensed to industry were being applied.[10] These circumstances prompted Congressional inquiries into the ways in which federal research was transformed into usable technology. The conclusion was 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. No discussion occurred at the time regarding public sector involvement in downstream activities.

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[8] Roumel, 2001

[9] 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 U.S. GAO, ibid, for further details about federal patent law.

[10] U.S. General Accounting Office, 1998, p. 3

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 also complained that even the attempt to obtain non-exclusive licensing was an excruciatingly slow process. Agencies imposed many paperwork requirements and other burdens on its licensees in an apparent effort to protect the public 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.[11]

The Bayh-Dole and Stevenson-Wydler Acts (and subsequent amendments) were intended to rectify this situation. They did this by creating a uniform licensing system for all federal agencies, reducing 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.[12] The Stevenson-Wydler Act effectively allowed federal labs conducting intramural research to exercise the same privileges. The effect was to transfer the ownership of intellectual property and benefits derived therefrom by allowing companies to license and develop products based on discoveries of federally funded university and federal scientists with full legal protection from competition.

The legislative intent was to expand the use of new technology by making it more financially attractive for private companies to develop products from it. It was believed that only increased benefit to industry would lead to greater dissemination and utilization of the discoveries emanating from this research. Ultimately, it was expected that greater investment in technology would be an engine of economic development across the country where research was conducted. 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."[13]

It is interesting that 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.[14] While the legislative history demonstrates that there was a widespread acceptance of the principle

[11] Ibid.
[12] A 1983 presidential directive extended licensing rights to large businesses.
[13] CRS, 2000a, p. 11
[14] NIH, 2001, p. 10

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.[15]

None-the-less, 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 intellectual property specialists and anxiety from the private sector about when and with what justification they would be invoked by the government. The legislation expressed Congress' view that use of the 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…."[16] The means to achieve that goal were codified in the following provisions that reserve certain rights for the Government:

- The right to a non-exclusive, nontransferable, irrevocable, paid-up license to practice for or on behalf of the U.S. throughout the world[17];

- "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[18];

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 there is continuing concern among private pharmaceutical companies that changes in the interpretation could expand in such a way as to threaten their economic interests.[19] 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* (emphasis added)," some have suggested that there appears

[15] Prompted by persistent Congressional concerns regarding the return 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 NIH, 2001 for discussion.

[16] 35 U.S.C. ss.202

[17] 35 U.S.C. ss.202c.(4). Exclusivity grants the licensee the sole right to use the intellectual property which serves essentially as a monopoly. Non-exclusive rights allow the grantee to use the intellectual property, but does not provide the right to be the only user.

[18] 35 U.S.C. ss. 203(1)

[19] McGarey, 2001.

to be a limited scope for NIH action in this regard.[20] However, the Department of Health and Human Services with its public health mission might have a clearer justification to invoke the "government use" clause in pursuit of its mission.[21]

The second clause, the so-called "march-in" right of government, has attracted greater attention and has been more extensively litigated. 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.[22] This test case provided the opportunity for both the government and affected parties (primarily third-party recipients of government research funds or prospective licensees) to indicate their views on how restrictive the "march-in" rights should be.[23] The debate centered around 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 "march-in" would undermine licensing rights under Bayh-Dole.[24] 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.

Public Debate Surrounding Bayh-Dole and Stevenson-Wydler Passage

As much as the Congressional debate itself, the media coverage amplifies the arguments and their context motivating passage of the Stevenson-Wydler and Bayh-Dole Acts. The issues of utmost concern to the public and to Congress at the time were notably different from those of today. In 1980, both the public and Congress feared that America was losing its innovative edge that underlay technological superiority and economic success in international markets. At the time, R&D expenditures as a percentage of economic output were dropping in the U.S. and rising elsewhere. Books and many news articles expressed concern that other industrialized nations such as West Germany and Japan, which were putting increasing amounts of money into R&D, might threaten America's command of new technology development.[25]

In addition to blame for shrinking budgets, government "red tape" and a de-emphasis on basic research, the discussion in the media focused on government economic and regulatory policies and their role as causes of the "innovation problem." Patent laws in

[20] McGarey and Levey, 1999, p. 1114

[21] This provision is not the same under which the U.S. government might have compelled the owner of the antibiotic ciproflotoxin to allow manufacture by another company in order to meet public health needs in response to the November, 2001 anthrax threat in the U.S. Such action would have followed the guidance of the WTO TRIPS agreement which is further discussed below.

[22] CellPro Petition to DHHS, March 3, 1997, cited and discussed in McGarey and Levey (1999). 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.

[23] Both the timeliness clause and the public health and safety clause were tested in the CellPro case.

[24] McGarey, op cit.

[25] "Building a Better Mousetrap – Is Government Getting in the Way? National Journal, September 1, 1979

particular were blamed for drying up ingenuity. Three major issues were repeatedly cited:

1. The government could not, by itself, transfer the technologies for which it had assumed ownership. Though the government had sponsored the research that led to the discoveries, it lacked the resources and links with industry needed to develop and market inventions. Between 1970 and 1975, federal funds supported the development of 53,000 inventions. The government acquired some form of ownership in 80% of these; however only 10% were licensed to private producers, and only 5% were used commercially.[26]

2. Exacerbating its technology transfer problems, the government was generally unwilling to grant exclusive licenses to the private sector, since the prevailing belief was that taxpayers, not private corporations, should benefit from the inventions produced through federally sponsored research.[27] In turn, most corporations were unwilling to develop products without exclusive rights to the technology, because they would not invest heavily in development of a product only to find it reproduced by another company.

3. The few federal agencies that could grant patent rights to universities had conflicting licensing and patent policies. In addition, the process was extremely time-consuming for universities and their faculties. Specific cases were cited in the media, in which bureaucratic problems led to the failure of federally-supported researchers to pursue projects that might have become successful new technologies.[28]

The media placed the blame for "losing the innovative edge" squarely on the government's inability to transfer technology, its unwillingness to grant exclusivity to the private sector, and conflicting policies. The conclusion was inevitable that, not only was America's economic standing damaged by these policies, but taxpayers were being deprived of useful products that could have been manufactured and sold as a result of the research their taxes supported. Business people, university researchers, and patent attorneys supported the Bayh-Dole proposal, hoping that a move to grant exclusive licensing would foster the development of products beneficial to the public.[29]

But the legislation was not without opponents. Consumer advocates argued that what the government pays for belongs to the people, and that no one producer should be granted a monopoly.[30] Even Members of Congress decried the emphasis on commercialization of government funded research for profit.[31] Further concerns were expressed that the act might impede the development and dissemination of technology, promote greater

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[26] Ibid
[27] An exclusive license allows monopoly use of the technology.
[28] Ibid
[29] "Patent Bill Seeks Shift to Bolster Innovation" Washington Post, April 8, 1979.
[30] Op cit.
[31] Congressman Jack Brooks, Minority Report, Committee on the Judiciary, Report to accompany H.R. 6933, 1980.

concentration of economic power in the hands of large corporations, and make it possible for industry to reap unfair profits at the public expense.

20 Years After Passage of Bayh-Dole and Stevenson-Wydler

Since the 1970s, the driving force behind Congressional attention to intellectual property arising from the federal R&D effort has been the belief that economic prosperity increases with improved technology transfer to the private sector. This belief is completely consistent with the role of government in subsidizing biomedical R&D; creation and dissemination of knowledge as a public good. Insufficient government support would yield a sub-optimal quantity of research as a public good, reduced innovation and technological improvement, and lower societal output of goods and services.

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 on their ability to meet their original legislative intent. Recent assessments of the impacts of the Bayh-Dole Act and related legislation have suggested that the laws performed as Congress intended.[32] Most independent analyses have concluded that the Acts greatly increased technology transfer from researchers to private industry, improved the governmental patenting and licensing process, and made available to the public products that improve their health and well-being.[33] Royalties received by universities engaged in technology transfer have grown by 20-30 percent annually, implying that sales of medical products and processes generated by the patents are in the tens of billions of dollars.[34]

Thus, the goal of greater private sector utilization of the research output by federally-funded scientists seems to have been achieved. The question remains whether or not the social returns to public investment in research have likewise increased. There is no simple answer.

The difficulty of measuring the public benefit from federal research investment was discussed earlier. Reduced burden of disease and economic rate of return on investment were found to be flawed measures of social return for reasons already mentioned. Even if one attempts to use those measures as proxies for the social benefit from federal health sector research, the results are ambiguous. Longevity has increased marginally in the U.S. in 20 years, during which time expenditures on health care have soared, while disease incidence has risen in some cases and not in others. Studies have shown consistently high social rates of return to investments in health research, but are often based on inexact measures of benefits.

Much has changed in the 20 years since the Bayh-Dole and Stevenson-Wydler Acts were passed – not the least of which is the increasing concern for global health and the realization of the connection between health of poor country populations and the U.S.

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[32] National Academy of Sciences, 2001, Donald Kennedy, Science, June 2001

[33] CRS, 2000b, p. 11

[34] Despite these benefits, most university technology transfer offices have licensed few or no commercialized products and often operate at a loss (NIH, 2001).

populations, as well as between the health and economic and social prospects of poor country populations. 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. This has forced many countries into a quandary over how to deliver health technology to poor and technologically marginalized populations. In the process, questions are raised about the balance of interests between the use of new technology to reduce threats to health and the ownership rights to that technology.

The Bayh-Dole debate revolved around the perception that full use was not being made of the government investment in research and technology development, and that corrections to patent laws could stimulate productivity and economic growth overall. It should be noted that the expectations of technology development as an economic growth engine were focused less on health technologies – although that was a big portion of the government research investment – than on technologies used in other sectors, such as jet aircraft, plastics, computers and electronics. The legislation was passed amidst a general mood of needing to "catch up" to the international competition in many of these sectors. To say the global economic balance is different today would be an understatement. Twenty years after Bayh-Dole, the understanding of the mechanisms of international economic competition, as well as the awareness of global social inter-connections, is far beyond what it was. Further, it seems safe to say that a debate focused on health technology development would carry with it different considerations than a general debate about government intellectual property ownership.

Current Debates

These new developments give rise to debates never envisioned in the 1970s. While it would be surprising to find a reference to the Bayh-Dole Act in the press today, the provisions of that Act, together with other laws governing the use and availability of intellectual property, are all lurking just below the surface of the media's gaze. Hardly a day passes without mention in the major media about some aspect of medical research or health care issues in the U.S. or globally.

The rights of and obligations to a larger, more global public emerge as critical questions demanding resolution – just who is the public and what return on the investment is due the public? Debate continues on how to insure the availability of effective treatments to all in need while assuring that public-private partnerships with industry that is supportive of new technology discovery and development 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 the 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 there economic, legal and policy issues involved, but complex ethical and social considerations posed by decisions on the application of intellectual property laws.

The prominence of these issues in the public arena is indicated by the discussions in the 106th Congress concerning IP for biomedical research discoveries[35]:

- Disputes over competing claims to intellectual property developed under government-industry ventures;

- Delays in negotiating Cooperative Research and Development [CRADA] agreements 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;

- Problems obtaining technologies for research developed in the private sector for use in federal laboratories because of competitive concerns from industry;

- Parallel imports of drugs from Canada because of lower prices;

And more recently, other issues have emerged or remain on the horizon as well that could easily command Congressional attention, including:

- Considerations by the U.S. government to follow the initial decision by Canada in October, 2001 to provide a compulsory license to generic manufacturers to produce the antibiotic Ciprofloxacin to address the anthrax threat (Canada's decision was later modified in negotiations with the patent-holding manufacturers).

- How to handle requests from consumer groups for the exercise of "march-in" rights on the basis of public health and safety. This will require a thoughtful discussion of who is the "public" and how much does its health and safety need to be threatened before action is taken;

- What are the respective roles of IP protection, the market price of products and technologies, and the lack of infrastructure in preventing developing country populations from access to needed medical technology[36];

- How can the government claim a rightful return for its investment in biomedical research[37];

- What are the opportunities to reduce costs of medical technology development and manufacturing and how would they affect access;

[35] CRS, 2000b, op cit.
[36] Discussed as a major issue at the Doha, Qatar WTO meeting in November 2001.
[37] A question raised in legislation proposed by Senator Ron Wyden in the 107th Congress

- Would greater provision of non-exclusive licensing for limited distribution to poor populations increase the global supply and use of needed products;

- What would be the impact of granting exclusive rights for limited distribution.

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 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. These include directing the new research enterprise and expanding access to the existing fruits of federally-funded health research.

IV. Options for the Public Sector to Promote Research for GPGs

A. Focus on Upstream Actions

The government has a long-established and logical role in guiding biomedical research in directions that will benefit the public through upstream actions (primarily involving support for basic and applied research.)

Public-Private Partnerships

The nature of science and its conduct has 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 in the new scientific milieu. For legal, economic, and scientific reasons, public-private partnerships (PPPs) are being increasingly looked to as the mode of operation for future biomedical research leading to the rapid development of products. Nowadays, the complementary human capital and financial resources of the public sector (including the charitable foundations), academia and industry are all needed to bring scientific inquiry to the fruition a deliverable product represents.

The situation becomes more complex when resource poor markets are involved. Absent even the potential prospect of blockbuster products, the private, for-profit sector has shown little interest in development of products serving a small or insecure market. While this is consistent with the fiduciary responsibility of private industry, even government has been reluctant to undertake the role of product development, as that has properly been allocated to the private sector with its knowledge of both process and market needs. This leaves a large and vulnerable population whose needs will most probably not be addressed unless a yet broader set of players that includes government, foundations, and civil society organizations takes the decision to do so.

Recent trends are positive, however. Increasing numbers of PPPs involving foundations and international agencies in consortia of one sort or another have been created to address

health problems of poor countries.[38] An unusual but successful model for a "global public good for health partnership" is the Franco-American Aids Foundation (FAAF). Begun in 1989, the FAAF, is the beneficiary of royalties to the U.S. NIH and the French Institut Pasteur for patents on the HIV serological test. A portion of the proceeds derived from royalties paid to the FAAF are transferred to the World AIDS Foundation (WAF), which was created by the FAAF and is funded with approximately $2 million per year to support projects for AIDS community-based research and education in AIDS impacted developing nations.

The aspect that distinguishes the FAAF from a typical invention-patent-license-royalty process is that – by agreement among the parties sharing the intellectual property rights – a portion of the royalties is diverted to create a global public benefit (WAF) closely related to the purpose of the invention. Both organizations, NIH and Institut Pasteur, invest these funds through an objective application-based process that is judged by a peer review mechanism that operates to insure appropriate scientific review of all projects submitted to the WAF and maintains an accountable mechanism to set funding priorities. Thus, not only was there a global public good in the usual sense in the form of the product of the invention, an HIV test that could be used everywhere, the creation of the WAF was an additional mechanism to reinvest the profits from the invention into another form of global public good, WAF grants, projects and training conducted in developing countries.

Future efforts to create global public goods from the proceeds of successful research can be informed by an understanding of the conditions that created the WAF. Which among the elements present was crucial to its creation? Was it the availability of the royalty stream produced by the blockbuster technology of the first HIV diagnostic test, the competitive ambience created by the litigation surrounding the discovery of HIV and the diagnostic test that drove a settlement, or simply that the inventers and others involved had the mindset to consider the broader public benefit? Undoubtedly it a combination of all of these --simultaneously a need, a vision and the means to achieve it – that created the WAF. It is unlikely that such an entity and agreement could have been born without a large expected revenue stream. It is, after all, far easier to carve up a large or growing pie than a small or shrinking one.

Thus, it is inescapable to conclude that financial considerations will continue to drive the choices made about development and use of technology, and how it is delivered to the public. In the context of global public goods, particular attention is necessary to ensure that academic-industry, public-industry, or public-academic-industry alliances make some choices that ultimately lead to improved access to medical technology for developing countries. The Global Forum on Health Research, based in Geneva, is currently conducting a compilation and assessment of PPPs in an attempt to provide new insights into the means and mechanisms for doing so.

[38] For instance, Global Fund for Children's Vaccines, International Aids Vaccine Initiative, Medicines for Malaria, and the Global Alliance for TB Drug Development, among others.

Academic-industry partnerships The relative importance of private sector funding has also increased, both within and apart from the university research environment. Private companies are estimated to spend three times as much on biomedical research as NIH does, most of it within their own research laboratories.[39] Authentic and accurate information is, however, hard to obtain. For example, while one source indicates that a small portion of private R&D (about 12 percent) is conducted within U.S. academic institutions[40], another source reports that one-fifth to one-half of industry expenditure on biomedical R&D supports university-based research. These funding arrangements have blurred the distinction between the objectives of universities and private industry. For example, Columbia University petitioned Congress in 2000 to extend its patent on a drug making process. Success would have earned the university an additional $70 million in royalties and cost consumers an equivalent amount.[41]

University officials generally state that money is not the motivator behind good research while simultaneously and correctly noting that money is necessary to turn research into usable products and that licensing to industry is the only way to serve the goal of product development. One prominent university technology transfer official has listed the reasons for universities to hold intellectual property rights as: income generation, regional economic development, and research fund raising, in that order.[42] Another has said that a university faculty's primary job is to create knowledge, and their secondary job is to earn licensing income.[43]

If research partnerships are to help promote research that leads to global public goods, it seems axiomatic that there should be agreement about and commitment to that goal at the outset. This will necessitate creative financing and intellectual property sharing arrangements. It will also require that scientists put a priority on delivering global public goods and that university officials fully embrace the larger role of universities in society and in the global community.

An example is the recent step by MIT to place its curriculum in the public domain via the Internet with the financial support of private foundations.[44] "Our hope," said Paul Brest, president of the Hewlett Foundation, "is that this project will inspire similar efforts at other institutions and will reinforce the concept that ideas are best viewed as the common property of all of us, not as proprietary products intended to generate profits."

Strengthen capacity for research in developing world

One of the results of the current system of allocating funds for biomedical research is that diseases and health problems of the poor receive less attention than those of the well-off. The gap between disease burden and research allocations has been captured by the Global Forum for Health Research as the 10/90 disparity, the proposition that 90 percent of

[39] Goldberg, 2001. This includes product development expenditures.
[40] Blumenthal, 1995
[41] Ibid.
[42] Mowery at NAS, 2001.
[43] Michael Crow, ColumbiaUniversity, in the New York Times.
[44] Mellon, Hewlitt Foundations grant $11 million to launch free MIT course materials on web, June 18, 2001, http://mit.edu/newsoffice/nr/2001/ocwfund.html

global research dollars are spent on diseases afflicting 10 percent of the world's population.[45] Thus, one approach to analyzing the social return to public sector investment in health research is to ask what the proper target is in terms of population disease burdens.

Under current arrangements, funding to develop early stage technology into products for the market comes largely from the private sector which invests heavily in the research necessary to transform discovery into products. Globally private sector investment in biomedical research is variously estimated at $40 billion to $55-60 billion in 2000 -- a considerable portion of which is for applied and clinical research oriented to licensing and marketing medical technologies.[46] The vast majority of this research is done by developed country industry and aimed at developed country consumer markets.

Research conducted in the developing world, especially by developing-world scientists, is potentially more likely to address the needs of the developing world than research done by researchers from the developing countries, unless the developing world diseases are targeted by a funding agency such as the NIH. Such funding also results in partnerships between developed and developing country scientists, creating more sustainable research environments and the opportunity for human capacity building and research infrastructure development. It is also apparent that public sector funded research is more likely than private sector funded research to address the health problems of the poor. There is some evidence for both of these assertions in the agricultural sector,[47] for example the science underlying the green revolution, where research support has created major public goods. Increasing the support for research in developing countries is, if sustainable, one of the most direct ways to create a global public good, and ultimately increase access of the world's poor to the results of scientific research.

An obvious, but oft-ignored principle is that investments in human research capacity and physical and administrative infrastructure should precede major investments in medical R&D in developing nations. Because the traditional role of universities is to educate the next generation and generate new knowledge, the universities are also the most likely institutions to take the lead and commit themselves to capacity building for developing nation scientists and their scientific enterprise. Many U.S. universities are already doing this, even investing university funds to educate and train developing country students. The sources of support for these efforts, however, can be as varied as the provision of federally supported training grants for non-U.S. students on the one hand to the set aside of university scholarship funds to be used for global diversity, another traditional goal of the university. In the future consideration could be given to the use of a small portion of royalty and licensing fees from discoveries supported by public funds for this type of global public good.

In analogous manner, a portion of the royalties from the NIH intramural program is returned to the lab that discovers and invents new technology. This additional source of

[45] Global Forum on Health Research, 10/90 Report
[46] Global Forum on Health Research, 2001 and Moses, 2001.
[47] United Nations FAO, 2001.

funding to successful federal researchers obviously serves to enhance the capacity of their laboratories and programs to conduct research, a traditional incentive for the public sector research community. A portion of these revenues could also be specifically directed to enhance particular public health benefits in the developing world, for example to support collaborative research with, or training of, developing country scientists in these highly successful laboratories.

B. Delivery of Benefits through Technology Transfer

It is universally agreed that intellectual property protection plays a substantial role in R&D and is, in fact, critical to the scientific enterprise. The question for public funding agencies is how to facilitate delivery of the benefits of publicly-funded research in the current setting of ownership rights conferred by intellectual property laws. These rights translate into economic value through the mechanisms of patents, licenses and material transfer agreements (MTAs). Along with direct placement of knowledge into the public domain, these mechanisms of technology transfer constitute a continuum of ways to move research output into the public arena. There are, however, problems in relying on technology transfer to achieve the goal of delivering global public benefits.

Some observers have judged that the government has not sufficiently used its IP rights to either transfer technology where it is needed or to benefit from its investment in research. They argue for immediate placement of government-supported technology into the public domain. Some consumer interest groups have proposed that the U.S. Department of Health and Human Services license technology owned by NIH to the World Health Organization (WHO) or other international agencies, such as UNICEF.[48] In the case of newly-developed technologies, this could mean granting only non-exclusive licenses to develop products. For existing technologies already licensed to private developers, these groups suggest that the march-in provision of the Bayh-Dole Act should be invoked to grant use rights for public health and safety reasons.[49]

The NIH has rejected such proposals to date, arguing in 1999 that: 1) the "government use" right allowed in legislation would not necessarily result in greater drug accessibility while at the same time it would put at risk existing arrangements; 2) the U.S. government should not intervene in the public health of foreign populations without direct requests from foreign governments; and 3) affordable and accessible drugs are not sufficient by themselves to solve public health problems without adequate medical infrastructure. [50]

In contrast, advocates of government march-in do not accept, or perhaps do not understand or find it relevant, that the international organizations targeted may not have the expertise nor the capacity to carry out the task proposed for them. The early-stage characteristics of most of the technology developed and owned by government labs and university research enterprises funded in whole or in part by NIH is not suited for direct

[48] Nader, Love, Weissman, March 2001
[49] Ibid
[50] Harold Varmus, October 1999

transfer to a user. [51] The 1999 NIH response states, "It is well documented that technologies with potential as therapeutics are rarely developed into products without some form of exclusivity, given the large development costs associated with bringing the product to market." [52] The letter goes on to restate the narrow interpretation discussed above of the "government use" right to patents developed with federal funding.

Any consideration of "march-in" on government-owned patents must contend with the reality of the government role. Most ready-to-use medical technology today is produced after years of product development and testing. As noted above, there is often a "cat's cradle" tangle of patents and licenses that apply to the processes, materials and components that form a final product ready for consumer distribution. Any effort to use a final technology – even with a non-exclusive license from the federal government – could infringe upon multiple patents and would likely be the catalyst to initiate time consuming and costly legal actions. In the pharmaceutical sector, efforts to invent around the existing patents are estimated to add 40 percent to the cost of developing a new product.[53] Although the development of a competitive product may ultimately lead to reduced prices for the user, it cannot be assumed that the balance between redundant development costs and competitive pricing is in favor of the consumer. Without prior agreements from all parties, multiple stacking patents constitute a large barrier to any government attempt to provide non-exclusive licensing to third parties or international agencies wishing to distribute therapeutics in developing countries.

In the two decades since passage of the Bayh-Dole Act, the major research universities have developed highly proficient offices of technology transfer, staffed by professionals who deal with patents and licensing. Through this infrastructure, they have come to expect financial rewards from their research effort 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.

It has also made university administrations the target of challenges to deliver biomedical products to the needy public. Under protest by its students, Yale University reassessed the exclusive licenses it granted to Bristol-Myers-Squibb to manufacture d4T, a frequent component of antiretroviral drug cocktails for the treatment of AIDS. The Wall St. Journal reports that the Yale students "succeeded in gaining 600 signatures from faculty, researchers and students 'demanding' that the university pressure Bristol-Myers Squibb Company to give up patent rights for an AIDS drug in South Africa. Six days later, Bristol-Meyers Squibb became the first drug manufacturer to relinquish patent rights for

[51] According to Maskus (2000), the costs of research are estimated to be only 25 percent of the total cost of turning invention into technologies for use (a higher figure pertains to pharmaceutical or medical technology.)

[52] Varmus letter and Ted Roumel, op cit.

[53] Mansfield et al, 1981

an AIDS drug in South Africa, although a company spokesperson denied that the Yale students 'played [any] role' in the company's actions."[54]

It is understandable that university presidents and scientists would tenaciously guard the prerogatives granted by Bayh-Dole to retain ownership of the innovation emerging from their science labs for the benefit of the university. Millions of dollars a year in unrestricted extra income to a university can pay for many projects, additional faculty, and new program developments (not necessarily related to biomedical research) that are otherwise hard to get off the ground.

Yet there is no guarantee of financial returns from research and most universities have long operated without this extra income, and still do. The intent of Bayh-Dole was not to produce supplemental revenue streams to universities. Rather it was to engender innovation and increased use of technology for economic development. The occasional blockbuster technology has produced large royalties for a few universities holding patent rights while some others generate a few million dollars annually. However, most universities are still barely in the technology development business. Table 1 shows the 15 U.S. universities earning more than $10 million in royalties and licensing fees in 1999.[55]

Table 1: Royalty Earnings from Patents and Licenses, 1999

Institution	Gross Income (Millions of $)
1) Columbia University	89
2) University of California System	74
3) Florida State University	57
4) Yale University	41
5) University of Washington / Wash. Res. Fndtn.	28
6) Stanford University	28
7) Michigan State University	24
8) University of Florida	22
9) W.A.R.F. / University of Wisconsin – Madison	18
10) M.I.T.	16
11) Emory University	15

[54] Wall St. Journal, April 12, 2001

[55] AUTM, 2001. Note that figures include royalties and fees from all patents and licenses. In comparison, NIH royalties from intramural licensing were $52 million in fiscal year 2000.

12) SUNY Research Foundation	14
13) Baylor College of Medicine	12
14) New York University	11
15) Johns Hopkins University	10

Source: AUTM Licensing Survey

These amounts are just a fraction of the funding needed for a real global effort, estimated by the economist Jeffrey Sachs to be $10-12 billion per year for AIDS alone. If the ultimate global public good is the delivery of medical technology to those unable to pay the costs, then royalty and licensing fees are not the means to achieve it.

There is some evidence that twenty years after Bayh-Dole universities are still struggling to put their entrepreneurial activities in their proper place vis-à-vis the institutions' paramount role as centers of intellectual and social leadership. The link that has been established between discovery in the academic setting and economic return is now in direct conflict with the historical role of the university to create and disseminate knowledge through its research and teaching as the ultimate global public good. Universities do accept their responsibilities to contribute to public goods, but these are generally focused on state and national health issues. To enlarge the concerns of the university beyond the needs of the local academic and public communities they serve requires a genuine appreciation of both global needs and the responsibility of the university to create such global public goods.

The evolution of technology transfer practice since Bayh-Dole places NIH and research universities in a difficult position. The delicate balancing of their scientific interests, responsibilities to the public, and need to maintain a competitive position vis a vis the private sector for retention of expertise has been jarred repeatedly in the past few years. For NIH, there is also the responsibility to attend to global public health, with the understanding that it is one of the few providers in the world of health research as a global public good.

The following outline presents some possible ways that NIH and universities can more effectively use technology transfer to create global public goods for health. We have included a range of possible approaches, however practical or feasible to implement. It is essential to understand that any consideration to change current operating principles will require the engagement and involvement of all the stakeholders – change will not be accomplished by fiat.

1. A direct way to deliver social dividends from the research conducted is to use public benefit provisions in licensing agreements to direct this transfer. On an ad hoc basis, NIH has incorporated voluntary provisions for public benefits (sometimes referred to as "White Knight" provisos) into license agreements with private industry. Since 1986, about 80 percent of licenses granted by NIH have included a public benefit of

some sort.[56] The types of public benefits called for in these purely voluntary arrangements include educational websites, or product donations and drug delivery to needy communities. The initiative has been palatable, as no specific level of benefit or outcomes is requested in the license provisions.

There are several ways in which the public benefit provisions could be expanded, with the aim to specifically benefit poor countries. NIH could forge an agreement to tailor the public benefits to include their delivery to poor countries, either directly through drug donations or indirectly through a non-profit organization that would deliver the benefits where they are most needed. For instance, a page could be taken from the WAF book such that a reasonable proportion (however difficult it is to determine the meaning of "reasonable") of the royalties from the license would be diverted to a foundation established to support global public goods in health.

2. Another method open to NIH is to bundle technologies so that companies are obliged to accept a less profitable technology for development as a condition of obtaining a license for more lucrative technologies. This is consistent with the paramount aim of NIH licensing to get the technology used. While this may seem to be a simple and obvious way to deliver the results of government R&D investment to developing populations, there have so far been few takers for this type of arrangement and its impact will likely be small.[57] Many available technologies do not interest the private sector because of their perceived lack of profitability. This perception seriously retards the NIH's ability to deliver the benefits of its in-house research to developing countries.

   It is none the less possible that this perception is mistaken, or perhaps ways can be devised to improve the profitability of licensing for developing country delivery of medical technology. For example, if the NIH could serve as the intermediary between a private company wishing to receive a license for an NIH technology and a guaranteed buyer (such as WHO, UNICEF, a large foundation such as the Gates Foundation or another agency or organization whose mission is to deliver public goods), the profit outlook could change. With a large buyer to take the initial output, perhaps a profitability threshold would be reached (if the price from the bulk purchaser met minimum average cost of production at the appropriate scale), and a private company could anticipate potential profits by establishing itself in developing countries.[58] For example, Merck provided the technology to produce recombinant hepatitis B antigens in China and 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.

[56] Ted Roumel, personal communication, June 2001.
[57] Ibid
[58] It is important to note that many existing bulk purchase arrangements through WHO and non-profits are on off-patent medicine and technology. Thus, the recent bulk purchase through a competitive bidding process by WHO for TB drugs allowed a 30 percent lower unit price through the purchase of generic drugs from manufacturers based in The Netherlands and India (NYT, June 22, 2001).

Developing country markets can also be segmented so that the technology could be provided at low or no-cost to the poorest countries, a fair price in middle-income developing countries, and a higher price as the market develops. Such an arrangement would be consistent with economic theory in which price discrimination can increase efficiency and equity in a market.[59] This approach bears some resemblance to the pricing methods currently used by pharmaceutical companies in developed country markets. It requires, however, measures to insure there is no parallel importation or smuggling from the low price to the higher price nations.

A variant of this approach would be for NIH to increase efforts to work with non-profit organizations to deliver technology, rather than seeking commercial avenues for technology adoption. NIH currently uses CRADAS to work with WHO and NGOs (e.g. PATH) to move malaria drugs and other less profitable technologies into use. The overriding concern of NIH officials involved in the development of a CRADA is whether there is capacity within these organizations to carry out the necessary R&D to develop a product. It is estimated that the private sector spends on average $700 million and 9 years to create the manufacturing capacity for many of the existing technologies[60], and non-profit organizations just do not have the capacity to sustain such an investment. However, as already noted, it is extremely difficult to make such estimates, because the necessary information is not in the public domain and it is possible that the goals are achievable at lower cost. Medecins sans Frontieres (MSF) is exploring the viability of implementing such a mechanism, a public not-for-profit pharmaceutical company, to develop medical technologies for the poor.

3. NIH has recently increased efforts to license vaccine technology to meet the public sector demand in selected developing countries. Companies requesting to license NIH technology are asked to produce a plan to market the technology within 2 years of regulatory agency approval. They can either opt to deliver the product themselves, or initiate a joint venture with another company that would do so. The goal is to use the potential profits from sales in developed countries to encourage companies to manufacture as well for the developing world. The product could be sold in developing countries at lower prices achievable through economies of scale and lower overseas manufacturing costs.[61] So far, the tie-in has not successfully been negotiated with any NIH licensees. It is recognized that ultimately somebody in the developed world bears the costs if drugs are provided at reduced cost to the developing world.

4. There may exist some limited opportunity for NIH to deliver technologies for developing country use by identifying and licensing basic technology for specific fields of use (for instance, a cancer vaccine) and requiring the same company to do parallel development of the same technology for another field of use (for instance, an

[59] 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.
[60] Roumel, op cit.
[61] The domestic manufacturing requirement in the law can be waived and applies only to U.S. sales.

HIV vaccine). This would require a renegotiation of licensing agreements and would certainly be strongly resisted by licensees. Looking forward, however, with the AIDS drug wars of 2001 over, greater public awareness of the issues involved, and the plight of the developing world worsening, there may be room for change.

5. A more radical approach would be to exercise the Government's march-in rights on already-licensed technology to meet special health or safety needs that are not being met. This may entail authorizing compulsory licensing for overseas manufacturing of needed drugs and other products solely for distribution in developing countries. In addition to violating the spirit of already-negotiated exclusive licenses, there would be no guarantee that granting such licenses would result in a significant decline in the price of needed drugs in developing countries.

6. A final option for NIH to use current powers to extend access is to include in license agreements a clause allowing the U.S. government use of technologies for foreign treaty purposes. Under this clause, foreign governments can be granted non-exclusive rights to technology licensed by U.S. government agencies. This use must be agreed upon as part of licensing negotiations, thus it would not be retroactively applicable to any existing licensed technology. Further, international treaties would need to include such requests and be approved through the usual U.S. Senate ratification process. For blockbuster technology or therapeutics with expensive development paths ahead, some would consider the loss of monopoly even in a foreign country to be the death knell of licensing negotiations. However, treaty requests may be a way to achieve some buy-in from developing country governments about their priorities, as well as a commitment to health as a national public good.

7. Alternatively, any of the activities from early stage development to manufacture and distribution could be performed by a government agency itself, or a contractor. For instance, NIH could move its 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 non-profit entity. Although this is clearly not the priority for a research agency such as NIH, in a few instances programs already exist to develop medications at NIH, rather than wait for the private sector to show an interest in producing them.[62] These examples may provide insight into the process needed to address clearly prioritized global public goods needs. It is estimated that less than 5 percent of promising technologies submitted by NIH researchers are picked up and developed.[63] However, the issues of capacity and expertise would need to be fully explored before commitment of the substantial resources needed could be seriously considered. There are significant costs associated with such a step, and these would represent a diversion from the usual research priorities of the agency.

It must not be overlooked that approximately 90% of NIH research funds go to support extramural research in universities and that control of technology from that research was transferred to universities by the Bayh-Dole Act. By far the greater impact of any of the

[62] McGarey, op cit.
[63] Benson, op cit

innovations in intellectual property will come from decisions made by university Presidents and their technology transfer officials, who control the use of intellectual property derived from publicly-supported research. Most of the public benefit or licensure arrangements discussed above for NIH could be adopted by universities for their own technologies. For instance, they could include public benefit clauses in their licenses, or divert part of their royalty stream to a foundation, or license technologies to non-profits or others who would develop and manufacture for poor countries, and they could bundle technologies so as to encourage development of those aimed at diseases of the poor.

We repeat for emphasis that the adoption of any of these options by universities would require a consultative process among interested parties, including public research agencies, developing country representatives, potential funding partners, and industry. It would be necessary for universities and their faculties to embrace the moral and social imperative of enhanced delivery mechanisms and to be full partners in the means selected to achieve them.

V. Conclusions

Challenges and Barriers

The set of economic, legal, and policy arrangements currently in use for transferring technology from research to consumers presents significant access barriers to the poor. The main economic barrier is the high cost of developing a product from a basic discovery. The main legal barrier is the complex ownership system in place to protect the interest of those who invest in research and development, and to maintain incentives to continue such investment. The policy barrier is represented by need to clearly choose or balance the elements among competing interests – scientific community, consumers, and industrial development – that vie for advantage in this increasingly lucrative world of health products. This section briefly explores these barriers with an eye toward seeking ways to reduce them.

Economic Challenges: Pharmaceutical companies have pointed to the large investment they make in bringing products to market, and the need to retain incentives to do so in a risky scientific and economic environment as the justification for protection of its intellectual property. The argument is legitimate and not new – it is codified in Article I of the U.S. Constitution. However, perhaps there are ways to maintain incentives for research and development while reducing the eventual product price. There are several components to the costs of developing a new health care product and it is useful to briefly examine specific ones to evaluate the potential to reduce overall costs.

Costs of working with government

One reason that technologies developed in government laboratories are not readily licensed, *ceteris paribus*, is that companies are wary of bureaucratic slowdowns, restrictions, and requirements of openness. There can be great reluctance on the part of private industry to get entangled with the federal government for patent rights. Some companies (Eli Lilly, Merck until recently) refused to even approach the federal

government for licenses. There is quiet but palpable concern among companies about government exercising march-in rights – even though it has never happened.[64] At stake is their ability to make business decisions when hundreds of millions of dollars in product development and marketing may be lost. Thus, one part of the economic challenge is how to lower the costs to industry of working with government.

One barrier to greater licensing of NIH technology may be the impasse over NIH's new effort to require that a license application include a plan for product development right at the outset, including benchmarks for delivering a product to market and termination rights if those targets are not met. Government officials want some assurances that their technology will be delivered for public use as rapidly as possible, while companies state that the licensing stage is too soon for them to know the timeline for delivery. Hence, companies will not agree to legal commitments they might not be able to meet. So far, these fears born of mutual distrust have not been resolved. Greater flexibility in the development plans – not relinquishing any of the public interest goals but creating steps along the way to review the reasonableness of them – might allay the private sector concerns and bring more of them to the table.

Costs of delivering a product to market

Pharmaceutical companies generally tout $400-$500 million[65] and twelve years as the investment they must make to bring a new drug to market. The figure is based on a 1991 study of 12 companies and 93 drugs in development.[66] The original figure of $231 million in 1987 dollars was adjusted to reflect inflation and then augmented again to reflect increased costs of performing clinical trials. It also includes the opportunity cost of the invested funds and the cost of failed attempts –which together may account for as much as 75 percent of the $400-$500 million.[67] More recent estimates are even higher ($802 million per approved new drug in 2000 dollars[68]) although some dispute even the earlier figures as being far too high

To the extent that new regulatory or scientific procedures can reduce the time required or reduce the failure rate of new drug development, the willingness of industry to take on non-blockbuster ventures may increase.[69] One estimate is that new technologies using

[64] The recent anthrax scare may have altered the perceived threat of march-in, as Canada decided (and then modified its request) to issue a compulsory license for generic production of Cipro, owned by Bayer A.G., and the U.S. government was under serious pressure to do so (New York Times, October 21, 2001.) It is interesting to note the conditions that constitute a reason for compulsory licensing in North America are several deaths and fears of possible exposure. This can be compared to the extreme conditions of mortality and morbidity that have prevailed for years in some developing countries that have still not been deemed to constitute a sufficient health and safety threat for compulsory licensing to take place.

[65] This estimate has recently risen as high as $1 billion, "What's a fair price for drugs?" Business Week, April 30, 2001.

[66] DiMasi, J. 1991. Tufts Center for the Study of Drug Development Economic Analysis

[67] It is worth noting that many companies and universities are also now spending large sums to protect their patents (Bethesda Gazette. June 20, 2001, Mowery at NAS, 2001)

[68] DiMasi, J. 2001. Tufts Center for the Study of Drug Development Economic Analysis

[69] The rapidity with which new compounds can be tested is increasing dramatically with biotechnology and the genomic revolution. Experts believe the costs of identifying successful products will increase

genomics may reduce by $300 million and two years the costs of bringing a new drug to market.[70] This may be wishful thinking, however, as the new science will identify new targets for drug development but will not inherently change the process (or the cost) of bringing products to market. Human clinical trials are the most costly phase of product development and this is the stage where most experimental technologies fail.[71] Increasing public investment in carrying out human clinical trials can therefore complement the activities of industry, and may provide leverage in the creation of global public goods when the product is proven and ready for clinical introduction.

Another possibility for reducing costs of delivering a product to market is to transfer the responsibility to develop a product to a not-for-profit entity with both the social purpose and the capacity to develop the technology. Such an enterprise would face a whole different set of economic realities starting with the absence of the need to produce a market rate of return. To this might be added special licensing and regulatory arrangements in return for commitments to deliver products to the underserved public, the caveat being that quality is at the same level as industry products. Considerable discussion in the U.S. has centered on marketing costs for drugs which have been estimated to constitute 30 percent of the market price of the average drug. High profits are reflected in the pharmaceutical industry stock index that substantially outperformed stock market averages in recent years, although the outlook for the future may not be as bright. In addition, the opportunity costs that face private industry would not be a real cost for the public sector because it is not necessarily looking for a financial return on its investments.

Legal Challenges The legal barriers to delivering products to the poor are the intellectual property protections deemed necessary to protect industry's interests in their R&D investment such as the monopoly rights to manufacture and sell products through patents and licenses. The provisions that have been commonplace in many developed countries for years were extended to developing countries in the Uruguay Round of trade agreements through the TRIPS mechanism. Developing countries are required to comply with TRIPS by 2005. These IP mechanisms prevent the poor in developing countries from acquiring drugs and other medical technology in two ways: higher prices caused by exclusive licensing and the weak or absent protective mechanisms within many developing countries that limit the interest of companies to seek licenses for the sale of their products in these countries.

Currently, few products are produced just for developing country markets because of the low profit potential in the poor countries. Products developed and priced for advanced market economies are simply unaffordable to most developing country citizens. In addition, products sold in the developed countries are often not registered in developing

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dramatically in the short-run, but likely fall in the longer-term (Lehman Brothers, cited in Boston Globe, June 20, 2001).

[70] Boston Globe, June 20, 2001.

[71] 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

countries because the underdeveloped intellectual property systems in these countries are unlikely to provide adequate protection against manufacture of counterfeit products.

A solution to the first issue may be tiered pricing arrangements, perhaps accompanied by foreign manufacture to reduce to the lowest possible level the marginal costs of production of the product necessary to meet demand, assuming again that quality of the product is not sacrificed. Both steps would require either revision of or reinterpretation of laws governing global intellectual property arrangements. Ways in which the underlying costs of developing and distributing needed drugs could be reduced were mentioned above. The implications of tiered or differential pricing for drugs sold in countries at different levels of economic development have been extensively discussed elsewhere.[72]

The second issue, that of developing country systems of intellectual property protection, has been less discussed. There is clearly a need to improve capacity of developing countries to comply with TRIPS, as well as a need for TRIPS to accommodate special public health circumstances in those countries. While some institutional mechanisms exist at the WTO (World Trade Organization) to support developing country compliance, there is a widespread concern that these are not adequate and that developing countries will become further marginalized from global trading relationships. The outcome of the new trade round kicked off in November 2001 in Doha, Qatar demonstrates an understanding of these issues and the initiation of positive steps to address them. Both global and local efforts to study tropical disease would likely increase with stronger IP protections in the developing countries.[73]

Policy Challenges The public's interests in biomedical research are many and decisions about how to balance those interests are difficult. Since October 15, 2001 the world's health focus has turned to protection from biological threats used in warfare and terrorism, and the day-to-day disease scourges of the developing world are fading from the headlines. Perhaps more than ever, however, economic development, drugs for the poor, breakthrough technologies for the world's most common diseases, and investing in scientific advances for tropical diseases are all legitimate social goals for all nations. Indeed, all have a role to play in improving the political stability, social welfare, and economic wherewithal that are needed to combat terrorism and civil strife. All are addressed in part by the government investment in the public good of R&D, although experience has shown that the inputs into research do not always translate into the outputs desired by the public.

The policy challenge is to work toward an agreement among relevant parties about the proper social return to public investment in health research, and how best to achieve it. It may well be that the major barrier is not any adversity to such social goals but a lack of focus or awareness that the fundamental purpose of the research investments is to create knowledge, technology, and products for the benefit of the public. For economic, legal, and policy reasons, the creation and delivery of global public goods are enormously more difficult than the creation and delivery of national public goods. Yet this must be done.

[72] See Danzon, 2001 and Lanjouw, 2001
[73] Maskus, 2000

To change the current reality will require a coalition of university officials, government, industry, and NGOs to identify priorities and opportunities and then to carry them out collectively.

Whereas IP has clearly spurred development of new health technologies that promote the public good of the wealthier nations, the impact of IP in promoting global public goods for health is, at best, mixed. The fundamental premises of IP protection as a spur to innovation and a reward for risk-taking are not different in pharmaceuticals than any other industry. However, there are characteristics of the health care industry that set the industry apart from other fields where intellectual property is important. Quite simply, in health care, the outcomes of technology development and its availability are life and death matters - this does not pertain to durable goods, or television sets, etc. It requires a broader view of the means to achieve the desired end goals.

Reflecting on such issues the London *Economist* recently said, "Given the conflicting needs of different industries, different companies and different peoples around the world – the patenting authorities need to find a greater variety of tools for protecting intellectual property than they have at present."[74] Without diminishing the importance of IP in the development of new medical technologies, this lesson may also be true for governments supporting public health research, for the universities that conduct essential research using public funds, and for industry in its critical role of completing the research and development leading to the commercialization and availability of these essential life saving and quality of life improving products.

[74] The Economist, June 23, 2001, p. 42

References

Association of University Technology Managers, Inc. AUTM Licensing Survey, FY 1999: A Survey Summary of Technology Licensing (and Related) Performance for U.S. and Canadian Academic and Nonprofit Institutions, and Patent Management Firms, © 2000.

Benson, Robert, (2001), Supervisor of Infectious Disease Technology, OTT, NIH/OD, Personal communication.

Blumenthal, M.D., M.P.P., 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.

_____, M. Gluck, K. Lewis, and D. Wise, (1986), "Industrial support of university research in biotechnology," Science 231: 242-246.

Congressional Research Service, (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.

_____, (2000b), R&D Partnerships and Intellectual Property: Implications for U.S. Policy, 98-862 STM, Updated December 6.

Danzon, Patricia, (2000), "The Economics of R&D: IP and Prices," presentation to CMH Working Group 2, Hinxton Hall, England.

DiMasi, J.A., R.W. Hansen, H.G. Grabowski, and L. Lasagna, (1991), "Cost of innovation in the pharmaceutical industry," Journal of Health Economics 10, 107-142.

_____, (2001) Cited by Robert Pear, New York Times, December 1, 2001, Section C, Page.

Global Forum for Health Research, (2001), "10/90 Report on Health Research," Global Forum for Health Research, WHO, Geneva; http://www.globalforumhealth.org.

Goldberg, Robert, (2001), "In changing times, NIH, NSF look outdated," Trendspotter, May.

Jamison, Dean and W. Mosely, (1993), Disease Control Priorities in Developing Countries, Oxford Press.

Jensen, Richard and Marie Thursby, (1998), "Proofs and Prototypes for Sale: The Tale of University Licensing," National Bureau of Economic Research, Cambridge, MA.

Kennedy, Donald, "Drug Prices: Real problem, Wrong Solution," Science, 8 June, 2001, p. 1797.

Lanjouw, Jean, (2001), "A Patent Policy Proposal for Global Diseases," draft manuscript presented to CMH Working Group 2, June.

Mansfield, Edwin, Mark Schwartz, and Samuel Wagner, (1981), "Imitation costs and patents: an empirical study," The Economic Journal, December.

Maskus, Keith, (2000) "Regulatory Standards in the WTO: Comparing intellectual property rights with competition policy, environmental protection and labor standards," Institute for International Economics Working Paper, Washington, DC, January.

McGarey, Barbara, (2001), General Counsel, NIH Foundation, former deputy director, OTT, NIH/OD, personal communication, May.

_____ and Annette Levey,(1999), "Patents, Products and Public Health: An Analysis of the CellPro March-In Petition," Berkeley Technology Law Journal, v.14 n.3, Fall.

Médecins Sans Frontières, 2001, "Fatal Imbalance, The Crisis in Research and Development for Drugs for Neglected Diseases," Access to Essential Medicines Campaign, Geneva.

Moses, Hamilton III and Joseph Martin, (2001), "Academic relationships with industry, a new model for biomedical research," Commentary, JAMA, v. 285, n.7, February 21.

Nader, Ralph, James Love, Robert Weissman, (2001), Letter to Secretary Thompson, March 28.

National Academies 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, see URL: http://www.nas.gov

National Journal, "Building a Better Mousetrap – Is Government Getting in the Way?

National Institutes of Health, (2001), "NIH Response to the Conference Report Request for a Plan to Ensure Taxpayers' Interests are Protected," at http://www.nih.gov/news/070101wyden.htm

_____, (1994), "Reports of the NIH Panels of Cooperative Research and Development Agreements: Perspectives, Outlook, and Policy Development." Washington, DC.

Roumel, Ted, (2001), Assistant Director, OTT, NIH/OD, personal communication, June.

U.N. Food and Agriculture Organization, (2001) The State of Food and Agriculture 2001, Rome, Italy.

U.N. WHO, (2001), "More equitable pricing for essential drugs: What do we mean and what are the issues,?" Background paper for the WHO-WTO secretariat workshop on differential pricing and financing of essential drugs, Norway, April 8-11, 2001.

_____, (1995), 10/90 Report on Biomedical Research

U.S. Congress, Conference Committee Report on DHHS Appropriation for FY 2001, p. 142.

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

Varmus, Harold, Letter to Robert Weissman, October 19, 1999.

Viscusi, Kip, "Valuing the health consequences of biomedical research," Presented to NIH Panel on Valuing Biomedical Health Research, Washington, DC, October, 1995.