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TO: J. ALLEN
FROM: N.T. LUTHER
2 Pages

From Steam Engine to Search Engine

By Harold Evans

The latest crop of headlines about insurance malfeasance brings yet more odium to the image of the American businessman, already spattered with mud from Enron and Tyco. Wrongdoers who prey on public credulity deserve a taste of the truncheon and the obloquy that goes with it, but in the process the stunning achievements of American business are being forgotten. There is actually so much more to celebrate than prosecute since the U.S. has been—and remains—the source of most of the innovations that created our modern world, and many of them have sprung from a desire to serve rather than steal.

I challenge anyone to get through a day without reliance on an innovation that was developed by an American. Rutgers University, which keeps the notebooks of Thomas Edison, has just published a volume of his papers on the occasion of the 125th anniversary of his invention (on Oct. 22, 1879) of the high-resistance incandescent light bulb (after 3,000 failed experiments).

The bulb was only the beginning. The innovator has to bring the brainwave to market, and that, more than invention, is the distinctive characteristic of America. In less than three years, Edison had, by September 1882, built a central power station in a dilapidated warehouse he found at 255-257 Pearl Street and illuminated 85 premises in lower Manhattan. That means he'd installed the labor and machinery to produce vacuum bulbs in quantity; designed and manufactured his own dynamos economically to convert steam power to electrical energy; ensured an even flow of current; connected a 14-mile network of underground wiring; insulated the wiring against moisture and electrical shocks; designed commercially efficient motors to use electricity in daylight hours for elevators, printing presses, lathes, fans and the like; designed and installed meters to measure individual consumption; and invented and manufactured switches, sockets, fuses, distributing boxes and lamp holders. For all this, he had to win the approval of Tammany Hall, whose aldermen were less turned on by illumination than the champagne banquet he threw for them. He put up most of the capital himself and marketed electricity against opposition from aggressive gas companies. What enterprise! What courage!

Edison lit the world, expensively at first. But it was his assistant, Samuel Insull, a naturalized American and business genius in his own right, who some years later in Chicago found the way

Invention—and innovation—is in America's DNA.

to make electricity prices fall over six decades, an incalculable boon to life and work.

So much might be obvious, as obvious as the American innovations of the airplane and the PC, jeans and the cellphone, bio-tech and the sewing machine, TV (and 24-hour news) and the search engine, but we forget the invisible innovations. A day without rubber would be a day where nothing works. No shower, light, clean clothes; nothing unspoiled in the fridge; no shoes, cars, trains, planes; no TV, no radio, no computer, no phones; yet we owe this material not to a research lab, still less government, but to a Yankee tinkerer who hadn't the faintest idea of the organic chemistry he was meddling with to convert useless raw rubber to practical use.

Charles Goodyear was the very opposite of the left's stereotype of the grasping American capitalist. A Dickensian hero going nobly into a world of cynics and thieves, he was typical of many innovators in America's advance. More of them were (and are) fired by an ambition to be remembered for achieving something worthwhile than for making money. The Google IPO with its overtones of moral superiority was seen as the latest oddity out of California, but the Google boys were in a long tradition. Amadeo P. Giannini, innovator of popular banking and progenitor of the Bank of America, went to great lengths to avoid leaving money. "No man owns a fortune," he said, "It owns him." The notebooks of Elisha Otis are an elevation in themselves for the moral epigrams he jotted down among sketches of machines and elevator platforms. "Machines," he wrote, "are the tools of liberty."

It is a truth not universally acknowledged. Here is a curious fact of American culture, supposedly so obsessed with business. The Founding Fathers promised life, liberty and the pursuit of happiness, and there have been thousands of presidential biographies and histories tracing the political struggles to honor those ideals. But none of the promises could have been honored without the business innovators who have had nothing like the same attention. You cannot much pursue happiness if you are starving, or unable to move your family to a better place, or protect it along the way, or communicate.

Politicians could make promises, but while government could provide the framework of freedom it could not aspire to deliver these necessities. We owe them to men like Cyrus McCormick (the reaper), Robert Fulton (steamboat), Theodore Judah (transcontinental railway), Lewis Tappan (credit rating), Sam Colt (six-gun), and Samuel Morse (telegraph). McCormick's invention, and then his revolutionary buy-on-credit marketing, enabled thousands of farmers to harvest the Great Plains and feed the world. He also freed labor for the industrial revolution and the preservation of the Union. And so has our progress continued down to this day with the founding of the biotech industry by Herbert Boyer and Robert Swanson, and the software industry made possible by the operating system for PCs from the unsung Gary Kildall.

Innovation will continue in America. It is in the nation's DNA. But if the scope of it is not to ebb in the face of global competition—in large part the consequence of Malcom Maclean's innovation of container shipping—we must honor more the risk-takers who really get things done.

Sir Harold is the author of "They Made America," just published by Little Brown.

WSJ 11/3/2004

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WSJ 11/3/2004

TO: J. ALLEN
FROM: N.J. LATKER
2 Pages

WASH. POST 11/7/04

Milton Stewart Dies; Small-Business Expert

By Patricia Sullivan
Washington Post Staff Writer

Milton D. Stewart, 82, a well-known advocate for small businesses in Washington who was known as "Mr. Small Business," died of pneumonia Nov. 5 at St. Luke's Hospital in Phoenix.

Mr. Stewart was appointed in 1978 by President Jimmy Carter as the government's first chief advocate for small business. He organized three White House conferences on small business, in 1980, 1986 and 1995. His career took him from Wall Street to the editorship of Inc. magazine, to academic posts and into the White House and the halls of Congress.

As the Small Business Association's chief counsel for advocacy, he championed small solar firms, independent gas stations and patent-seeking inventors and argued against government regulation.

In 1980, when a study found that time-consuming, duplicative but legally required government forms cost the nation's 10 million small businesses $12.7 billion a year, Mr. Stewart appeared at a Senate hearing to urge congressional action.

"Much of the sense of being overwhelmed by paperwork that small business feels comes from the seeming unpredictability, aimlessness and lack of apparent control of the paperwork flood," he said. "This is where the psychological crunch on the entrepreneurial manager is greatest—the sense that he does not know what will hit him from the government in the next mail."

He held the government job until 1981, when he formed the Small Business High Technology Institute, a nonprofit agency that promoted innovation in small businesses and fostered relationships between those firms and universities, large companies and the government.

Born in Brooklyn, N.Y., Mr. Stewart received a bachelor's degree from New York University and a master's degree in journalism from Columbia University in 1945. He received a law degree from George Washington University in 1952.

During World War II, he worked in the Office of War Information in Washington, then served as research director for the U.S. Commission on Civil Rights, which produced a 1948 report titled "To Secure These Rights." The report defined the nation's civil rights agenda for the next generation and proposed anti-lynching and anti-poll-tax laws, as well as strengthening the civil rights division of the Department of Justice.

Mr. Stewart then served as an administrative assistant to U.S. Rep. Franklin D. Roosevelt Jr. (D-N.Y.), an analyst in the Bureau of the Budget, a special counsel to New York Gov. Averill Harriman and general counsel to the New York State Thruway Authority. He also worked in the private banking division of a New York investment banking firm in the mid-1950s.

He was a partner in a Wall Street law firm from 1961 to 1965, when he became president of two venture capital companies that later would play a part in his nomination for the SBA job.

He served a year each as president of the National Association of Small Business Investment Companies and the National Small Business Association. In addition to editing Inc. magazine in the early 1980s, he was a radio commentator on business. He served on Columbia University's Graduate Faculty of Public Law and was an assistant professor at the New School for Social Research.



Milton D. Stewart became known as "Mr. Small Business" for his longstanding advocacy efforts.

Mr. Stewart's nomination to the SBA job ran into criticism after it was shown that in 1974 he signed a consent decree with the Securities and Exchange Commission and was suspended from investment activities for 60 days for violating SEC rules. The incident involved whether he adequately advised shareholders of the risks involved in an affiliated firm's building lease. His nomination, however, was supported by 125 organizations and individuals, including all the former heads of the SBA.

He moved from Washington to Phoenix in 1981.

His marriage to Dorothy Stewart ended in divorce.

Survivors include his wife of 24 years, Joan Graves Stewart of Phoenix; two daughters from the first marriage, Ricky Perkins of Lancaster, Calif., and Abigail Stewart of Ann Arbor, Mich.; a son from his first marriage, David Stewart of Garrett Park; eight grandchildren; and four great-grandchildren.

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Review

Technology Transfer

A Review for Biomedical Researchers

Robert Kneller[1]

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ABSTRACT

Why is technology transfer important for cancer and other biomedical researchers? What do biomedical researchers need to know about technology transfer? This report will address these questions in the context of the United States technology transfer system, which is now ~20 years old. To accomplish this goal, this report first summarizes the importance of technology transfer and the role of intellectual property rights. Then it describes the sequential steps in technology transfer from universities to industry. Next, it describes technology transfer from the NIH intramural laboratories and other federal laboratories to industry. Finally, it describes unique aspects of technology transfer involving clinical trials. URL citations to the latest federal guidelines and regulations governing technology transfer are provided. Where appropriate, comparisons will be made with technology transfer systems in other countries. I hope that this step-by-step description of the

technology transfer process will enable
thus increase the likelihood that their discoveries will be successfully commercialized. I also hope that this report will assist such researchers to understand the policy and institutional considerations that underlie current debates concerning technology transfer.

Introduction

Technology transfer is the mechanism by which societies try to ensure that publicly funded research discoveries are transferred to companies so that they can be developed and commercialized as products that benefit the public. Approximately one-third of all R&D[2] and one-third of all biomedical R&D in the United States and most Western European countries is funded by government (1, 2, 3). In the case of medical research in United States academic institutions, ~60% is funded by government (1). Thus society, academic institutions, and publicly supported biomedical researchers all ought to have an interest in the effective development of publicly supported discoveries. However, most governments that support scientific research cannot commercialize research discoveries. The private sector can. But there must be an effective system to transfer information to industry, and there must be incentives for industry to develop and commercialize discoveries originating in academic laboratories.

For most pharmaceutical and many diagnostic-related academic discoveries, patent protection is essential to encourage their development by companies. From discovery to marketability, much costly development work is needed. Only 1 in every 250 drugs that enter preclinical testing is approved by the FDA, and the cost of developing each new drug is $350-$500 million after factoring in the cost of failures (2).[3] However, once marketing approval is obtained, it is often easy to copy and manufacture the chemical entity at the core of most pharmaceutical and many diagnostic inventions. IP rights, primarily patents, confer the legal right to prevent or stop such copying or to require fair compensation. This right is crucial to most academic-based bioventure companies. Most such companies have no sales income. The only resources they have to attract development funding are their researchers and IP. Without strong IP protection, most bioventures could not obtain funding. Therefore, one of the main focuses of this report will be the role of IP rights in technology transfer.

Of course, technology transfer can occur by publication of information, transfers of personnel, and other avenues. However, technology transfer of biomedical technologies to companies with the expectation that the recipients will actively exploit or develop the technology and share benefits with the academic inventors usually occurs under one of the following three types of arrangements: (*a*) licenses or assignments of preexisting technologies; (*b*) collaborative or sponsored research agreements to develop new information or technologies; and (*c*) formation of start-up companies, usually financed largely by private venture capital. Taken together, these methods constitute the technology transfer "system" between publicly supported research institutions and industry.

Technology transfer under any of these three types of arrangements usually involves the transfer of IP rights, although sometimes corporate sponsors of research ask only for information. Transfers of IP rights involve either licenses or assignment (*i.e.*, complete sale or transfer) of IP rights. Therefore understanding how IP rights are acquired and transferred is key to understanding any technology transfer system.

The United States Technology Transfer System: Part 1. Universities

Scope of Technology Transfer Past and Present.

In the United States prior to 1980, there was no uniform policy regarding IP rights to university discoveries made with United States Government support. Procedures differed according to the laws or policies of each

funding agency waived its rights (4) . Agencies tended to license discoveries on a nonexclusive basis. In 1980, fewer than 250 patents were issued to universities per year (5) , only a fraction of which were for inventions made with Government support.

However, between 1969 and 1974, universities did manage to hold or obtain title to 329 inventions generated under research support from the DHEW. During this period, the universities negotiated 78 exclusive licenses and 44 nonexclusive licenses for these inventions. The patent counsel for DHEW noted that there was increasing pressure from the pharmaceutical industry to license university inventions made with DHEW support, and several United States universities were working out Institutional Patent Agreements with the DHEW under which the DHEW would more or less automatically grant the universities ownership over these inventions so that they could be licensed to private companies (4 , 6) .

Today, the situation is dramatically different. In 1998, the 158 United States universities, research institutes, and research hospitals responding to the annual survey of the Association of University Technology Managers received 10,520 invention disclosures, filed 4,596 new United States patent applications, received 3,088 United States patents, issued 3,394 licenses or license options for a total of 6,834 income earning licenses, received $726 million in license income, received over $2.18 billion from industry for sponsored research and formed 305 start-up companies for a total of ~2,400 start-ups formed since 1980, ~70% of which remain operational (7) . Probably the majority of this activity is biomedical related.[4]

The respondents to the Association of University Technology Managers survey identified 385 products based on their inventions that were first made commercially available in 1998. Just a few examples of such products commercialized in previous years include hepatitis B vaccine and a method of using yeast to produce IFN from the University of Washington, phycobiliproteins developed at Stanford to detect tumors, cisplatin developed at Michigan State University, a nicotine patch developed at UCLA, a method developed by a Florida State chemist to synthesize paclitaxel and thus conserve Pacific Yew trees, and Panretin from the Salk Institute to treat Kaposi's sarcoma and Targretin to treat lymphoma (7 , 10) .

This tremendous growth in technology transfer activities by United States universities and academic medical centers has been attributed to two factors: (*a*) the growth of new biomedical technologies, which increased incentives for companies to cooperate with universities where the new fundamental discoveries were being made, and thereby impelled universities to work out mechanisms to ensure development of these discoveries; and (*b*) reforms of United States technology transfer laws that reduced administrative barriers and increased incentives for universities to take an active role to manage their technologies and ensure their effective commercialization (9) .

Legal Basis of the Present System.

The legal basis of university-industry technology transfer is set forth in 1980 amendments to United States Patent Law (Public Law 96-517 codified as 35 USC sections 200–212) and regulations issued in 1987 implementing these amendments (37 CFR section 401). The Patent Law amendments are known as the "Bayh-Dole Act" after the sponsors of the Senate bill, and the regulations are known as the Bayh-Dole Regulations. The Bayh-Dole Act and Regulations allow universities to claim worldwide patent rights on inventions made under United States Government grants and contracts. The Regulations also require universities to establish procedures to ensure that university employees inform their universities of such inventions soon after they are made and of any public disclosures or sales of such inventions. Furthermore, they require universities to report such information to the Government funding agencies and to inform the agencies whether the universities will elect title to such inventions (*i.e.*, apply for United States and foreign patents in a timely manner). If a university chooses not to file for patents, it must so inform the funding agency, which then has 60 days to request in writing that the university transfer title to the funding agency.

Grantees are encouraged to use the system, named "Edison," and >120 institutions are authorized users. Approximately 3–4% of NIH grants result in invention reports, and >75 new inventions are reported to the system per week. As of December 1997, the institutions with the highest number of invention reports using Edison were Scripps Research Institute (n = 1221), University of California (n = 635), University of Wisconsin Madison (n = 433), Stanford (n = 409), and Harvard (n = 365) (communication from the NIH Office of Extramural Research).[5]

The Bayh-Dole Act and Regulations do not require inventors to assign their inventions to their universities. However, beginning in the 1930s and following the example of Massachusetts Institute of Technology and private industry, many universities began to require such assignment (13) . By the year 2000, the incentives that the Bayh-Dole laws gave universities to manage their inventions and the strict Bayh-Dole reporting requirements had lead almost all major United States universities to require assignment of employee inventions, at least when the inventions arise in part under Government funding. (The University of Wisconsin requires assignment only of inventions made with Government funds. Case Western does not require assignment from graduate students who are not federally supported.)

Some universities require employees and graduate students to assign to the university prospectively and in writing any inventions related to their university work. Others (for example, Texas A&M) simply state that faculty must report all inventions to the university and, upon request, execute a formal assignment document.

The Bayh-Dole Act permits funding agencies to grant inventors' requests to retain title, provided the universities have waived election of title. However, if universities believe an invention is valuable, they will usually elect title, apply for patents, and then license rights exclusively back to the inventors. This is the procedure usually followed in the case of inventors who obtain venture capital to form venture companies to develop their discoveries. However, a number of universities, among them Stanford and the University of California, have been supportive of employees who wish to retain title to their inventions, provided they have realistic plans to ensure development.

Most universities also assert ownership over nonpatentable materials created by their employees and recorded information generated by their employees. Whether universities can assert ownership over copyrightable works (particularly software) or tacit knowledge are issues of current debate but beyond the scope of this report (14) .

Although the Bayh-Dole Act applies only to inventions made with United States Government funding, such inventions account for a significant proportion of all university inventions.[6] Therefore, the procedures set forth in the Bayh-Dole Regulations have influenced the way universities manage technology, regardless of the source of funding. The Regulations have become the "operating manual" for technology transfer officials in United States universities. They have encouraged universities to assert control over all their technologies and to ensure that discoveries are transferred to companies that will effectively develop and commercialize them. They have prompted the creation of technology development offices or TLOs, which have become the focal point of university technology transfer activities.

Deciding Whether and How to Commercialize.
Technology transfer begins with individual researchers, with their discoveries and their reporting of such discoveries to their universities' TLOs. Universities typically require the reporting of any discoveries that researchers think might be patentable or might have commercial applications. Once TLOs receive invention reports, they must determine whether a discovery has commercial potential and, if so, how best to ensure its development. This usually requires consideration of the following factors:

noncommercial research or as an observation that should simply be published? Discoveries that have only noncommercial research use are usually transferred using MTAs.[7]

(*b*) If a discovery has commercial potential, is significant additional investment (research, development, obtaining regulatory approval, marketing, and other considerations) needed to commercialize it? If so, patent protection and an exclusive license of these patent rights are likely necessary to attract such investment, at least in the case of most pharmaceutical and many medical diagnostic discoveries.

However, TLOs may patent inventions that do not need significant additional investment and then license such inventions nonexclusively to (i) provide a royalty stream to the university; (ii) ensure recognition of the university's contribution; (iii) monitor use of the invention; and (iv) try to ensure that the university shares in rights to derivative inventions or at least is kept appraised of improvements made to the original invention.

(*c*) What is the anticipated commercial value of the discovery? Stanford's Office of Technology Licensing generally will not patent or license inventions that will not be able to generate at least $100,000 per year in royalties at some point.[8]

(*d*) Is there a company that is already interested in the invention and capable of developing it? Advice from the inventors can be very helpful in this regard. In the case of inventions arising under sponsored research agreements, the sponsoring company will usually become the licensee if the invention has commercial value.

(*e*) Are patent rights obtainable? The basic requirements for obtaining a patent under most national patent systems are that the invention be novel, useful (or have "industrial utility"), and non-obvious (or "embody an inventive step"). In addition, United States patent law requires that the description of the invention in the patent application be sufficient to "enable any person skilled in the art to make and use the invention" (35 USC 101–103, 112). A detailed analysis of these requirements is beyond the scope of this article. However, several points are germane to academic biomedical inventors.

First, publication of research results prior to filing a patent application, whether by presentation at a conference open to the public or outside persons, publication in a journal, posting on the internet, and so forth, destroys the novelty requirement for an invention based upon the disclosed information. Even submission in a grant application of information that allows a person skilled in the art to duplicate the invention can constitute publication, if the grant application is obtainable under the Freedom of Information Act (16) . The United States has a 12-month grace period within which inventors can file for patents that have been published as described above. Japan has a 6-month grace period. But European countries have no grace period; therefore, any publication destroys the ability to obtain patent protection in a European country. Thus, inventors should report their inventions so that their TLOs have enough lead time to determine whether to file a patent application and to prepare an application. Once a patent application is filed in any country that is a party to the 1967 Paris Convention for Protection of Industrial Property (this includes all major industrial countries), publication no longer risks undermining the novelty requirement, so long as patents are pursued in other countries in a timely manner [see (*h*) below].

Second, the requirements for patentability for a drug-related invention are often satisfied many years before the regulatory requirements of safety and efficacy are met and a product can be marketed. In the case of pharmaceuticals, the precise type of experimental data necessary to satisfy the utility and enablement requirements varies according to the mode of action of the new compound and the type of disease it treats. In general, however, the USPTO has moved away from requiring *in vivo* data. Therefore, patent protection is the principal mechanism that permits early publication while preserving incentives to invest in the risky development of early-stage discoveries.

Third, there is considerable doubt in the United States "enablement," particularly in the context of partial genetic sequences that are submitted to support a patent claim to the corresponding complete genes or to proteins coded for by the genes, or when the function of a gene can only be inferred from similarity with other genes (sometimes from nonhuman organisms), the functions of which are known. In December 1999, the USPTO issued guidelines imposing stricter standards to meet the utility and enablement requirements, but uncertainty remains concerning patentability in the above contexts (see Federal Register: 21 Dec. 1999).[9]

(*f*) How long will it take to obtain patent protection? Currently, United States patents issue 2–3 years after filing, on average. In cases where technology is changing rapidly and there is immediate demand for new discoveries, for example software or biological probes and reagents (often classified as "research tools"), it may be better from a scientific and financial perspective simply to license such inventions without applying for patent protection. Even without patent protection, such research tools often are valuable, because they save other laboratories the time and expense of making them themselves. NIH has developed streamlined procedures to allow TLOs to license nonpatented inventions made with NIH funds.[10] NIH's policy behind these procedures is to ensure that the nonprofit research community will have access to such tools. Thus, NIH usually requires that TLOs agree either to license nonpatented research tools nonexclusively or to license them exclusively to a company that will then undertake to make them widely available at reasonable cost.

(*g*) How much time does a TLO have before it must make a patenting decision? Usually this depends upon when disclosures will occur that might jeopardize patentability. If disclosures are not imminent, patenting may be deferred until the technology can be developed more or a prospective licensee can be found. As a general principle, freedom to publish is paramount, and if a choice must be made between publication and securing patent protection, the inventor makes the choice (5) .

(*h*) How much will patent protection cost and what are the TLO's resources? A United States TLO spends on average $10,000 to obtain a United States patent. Approximately 90% of this cost is attorneys' fees. Costs in Japan and Europe for domestic inventors are similar. Unless the invention arose under a sponsored research agreement or a licensee is waiting in the wings, TLOs with lower revenues must often make patenting decisions based upon uncertain estimates of future commercial value. Relatively few universities have TLOs whose license income substantially exceeds expenditures (17) . Many universities, *e.g.*, Case Western, Texas A&M, and the University of Maryland, defray some of the patenting or personnel expenses of their TLOs. Some of these have become profitable after 5 or 10 years of operation, suggesting that strategic long-term investments in patent protection and marketing can pay off. Conversations with representatives of several TLOs suggest that if 25–50% of inventions for which patents are applied ultimately are licensed, this is consistent with an appropriate level of patenting of invention disclosures.

A "provisional" application can be filed simply by submitting to the USPTO the names of the invention and the inventors, the $75 provisional application fee for not-for-profit institutions, and the manuscript or other document on which the invention is based. No claims are necessary (37 CFR 1.51). (A normal patent application consists principally of the "specifications," which describe the invention, and one or more claims that state concisely and precisely the type and scope of the patent protection that is sought.) Unless a provisional application is converted into a normal United States or PCT application within 1 year, it is considered abandoned. A provisional application is not examined. Its purpose is to provide an inexpensive, simple, fast way of establishing a filing priority date. In other words, if the inventor or another researcher publishes in print or at a conference the findings that are described in the provisional application, the inventor can still go on to make a full application for non-United States as well as United States patents. Also, if a competitor makes a similar invention after the filing date of the provisional application, the inventor will have

application before the inventor does. Thus, provisional applications are useful for universities with meager patenting budgets as a way of buying time to further develop an invention and to find a licensee. However, the value of a patent depends greatly upon the breadth and clarity of its claims and the extent to which the body of the patent (*i.e.*, the specifications) supports such claims. Otherwise, the scope of patent protection may be unclear or narrow, allowing competitors to design around the patent. Therefore, simply submitting a manuscript with no claims or hastily drafted claims as a provisional application leaves open the door for competitors to submit well-drafted complete applications that claim many of the potential commercial uses that the provisional application did not clearly spell out. This is particularly likely if the first inventor discloses his discoveries soon after filing the provisional, so that rivals have an opportunity to submit well-drafted applications that design around the disclosed information or that claim inventions that the first inventor could have anticipated but did not claim in the provisional application.

Obtaining foreign patent protection increases costs substantially. Fortunately, the decision of whether to obtain foreign patent protection can be made in stages. The first stage in obtaining such protection is the filing of a PCT application in one of three designated "receiving offices," the USPTO, the European Patent Office, or the Japanese Patent Office. This must occur within 1 year of the initial patent application. Eighteen months after the initial patent application, the PCT receiving office publishes the PCT application. (Note that if a United States patent applicant has no intention to file a foreign patent application, the United States patent application is not published until the United States patent is issued, thus keeping a veil of secrecy over the invention that is unique in the world.) Approximately 28 months after the initial application, the PCT receiving office issues a nonbinding opinion on the patentability of the invention. However, the real value of the PCT process is that it delays until 30 months after the initial application the time at which applications must be made in the individual patent offices of foreign countries. This final "national stage" is expensive because of translation costs, foreign patent attorneys' fees, and the application fees of individual patent offices. A United States applicant needs about $50,000 to obtain a Japanese patent and a similar amount to obtain patents in the major European countries. Japanese and European applicants face similarly high costs to obtain foreign patent protection. Even Stanford's TLO, which has one of the highest revenues of any TLO, seldom seeks foreign patent protection.

Thus, decisions on whether and how to develop inventions submitted to TLOs often involve complex considerations. TLOs must assess the technical merits of an invention and whether it is patentable, and they must try to find a licensee. Close communication with the inventors is vital to success. The staff of a TLO in a major research university typically has expertise in marketing, licensing, and various areas of science and engineering. In the case of a decision to apply for a patent, the patent prosecution work is usually contracted to private patent law firms. The Stanford TLO has no attorneys on its entire staff of 27 persons, whereas Massachusetts Institute of Technology has only 1 among its entire staff of 28.[11]

The experiences of technology transfer organizations that are remote from inventors, such as Research Corporation Technologies, BTG (formerly British Technology Group), the technology transfer office for the various Max Planck institutes, and the Japan Science and Technology Corporation (JST) suggest that TLOs that are based in individual universities are better able to work with inventors to find ways to develop high risk but nevertheless promising technologies. However, an in-depth analysis of these experiences is beyond the scope of this report.

Marketing and Licensing.

Although TLOs often list available technologies on the internet and mail information about new technologies to possibly interested companies, one study suggests that targeting a few potential licensees and building upon long-standing personal contacts are the most effective ways to interest companies in university

technologies. Examples of successful [illegible]
discuss new technologies, visits to university laboratories by company officials, or visits to company laboratories by university scientists (18) . Often the inventors themselves are the best source of information about potential licensees.

TLOs almost always license, rather than assign, their rights in inventions. Under the Bayh-Dole Regulations, universities must obtain permission from the funding agency before they assign any invention made under United States Government funding. In addition, sometimes the best way to develop an invention is to license separate fields of use to different companies. For example, in the case of a method to detect precancerous lesions by distinctive mRNA or protein markers, one company may be best suited to develop the discovery for lung cancer, whereas another company might be best suited to develop the technology for bladder or colon cancer. Finally, universities often want to retain some control over their discoveries to ensure their development. For example, even under an exclusive license for the lifetime of a patent, a university usually exercises its residual ownership rights through "due diligence" or "benchmark" clauses in the license. Such clauses enable the TLO to revoke the license if the licensee does not develop the invention. In the case of biomedical technologies, such clauses often involve both annual (often graduated) license renewal fees and development milestones.

Examples of such milestone clauses are: "licensee must develop two water soluble analogues within one year of executing the license agreement"; "licensee must complete initial preclinical pharmacology and toxicology studies within two years of executing the license"; and "licensee must obtain FDA approval to begin human clinical trials within three years of executing the license." Such benchmark commitments are best derived from business plans that all applicants for exclusive licensees should be required to submit during the license negotiation process. In other words, the benchmark clauses merely reflect what the licensee's own business plan says the licensee will do and the revenues it expects to earn. Most TLOs will renegotiate benchmark clauses in the event the licensee is making a good faith attempt to develop an invention but unforeseen circumstances have prevented it from meeting the benchmarks. However, such clauses are an important means to pull an invention back from a licensee that has lost interest in developing the invention.[12]

The provisions discussed above are incompatible with assignment agreements but are easily accomplished using licenses. Therefore, license agreements have become the common means of technology transfer in the United States. As a general principle, nonexclusive licenses are preferred because this allows university discoveries to be widely used and avoids one company obtaining control over an important new discovery (17) . However, as noted in (*b*) above, exclusive licenses are often necessary to provide incentives for companies to develop biomedical inventions. Rationales for nonexclusive licensing, rather than simply open publication or distribution, were discussed in (*b*) and (*f*) above.

Even if an invention has commercial value and could be licensed exclusively, if its main value is as a "research tool," TLOs should try to ensure that researchers in other non-for-profit laboratories can easily use it.[7] NIH is particularly concerned about the following three scenarios: (*a*) in the case of a research tool developed by a university researcher with NIH funds, the university's TLO grants an exclusive license to the research tool. Subsequently, the TLO's licensee restricts access to the tool by researchers in other universities, either by charging high prices or by requiring that other universities agree to transfer to the licensee any discoveries their researchers make using the tool or a portion of any royalties the university earns from commercializing such discoveries. (These requirements are known as "reach through" provisions.); (*b*) the same scenario as (*a*), except that the licensee is a company that co-funded the development of the research tool along with the NIH; and (*c*) in the case of an NIH-supported scientist who needs a proprietary research tool from another organization, the provider requires the TLO to agree to "reach

through "provisions, giving the provider the right to share in any royalties from such commercialization.

In December 1999, the NIH issued "Principles and Guidelines on Obtaining and Disseminating Biomedical Research Resources" to address these situations.[13]

To avoid scenario (*a*), the Guidelines state that exclusive licenses for research tools that require no further development should generally be avoided, except in cases where the licensee undertakes to make the tool widely available through unrestricted sale, or the TLO retains rights to make the tool widely available. When an exclusive license is necessary to promote development of the tool, the TLO should ordinarily limit the license to the commercial field of use, while retaining for itself the right to use the discovery and distribute it to not-for-profit institutions.

To avoid scenario (*b*), the Guidelines recommend that universities include in sponsored research agreements terms that either (i) allow the university to distribute research tools freely to not-for-profit organizations or (ii) that obligate the sponsoring company to make the research tools available to the academic research community on reasonable terms. The underlying rationale for this recommendation, as well as that related to scenario (*a*), is that universities' Bayh Dole rights to patent and license NIH-sponsored inventions are accompanied by corresponding obligations to promote the utilization, commercialization, and public availability of these inventions. The statement of principles preceding the Guidelines states, "Restrictive licensing of such an invention, such as to a for-profit sponsor for exclusive internal use, is antithetical to the goals of the Bayh Dole Act." To avoid scenario (*c*) when obtaining research tools from a not-for-profit institution, the Guidelines state "It is expected that agreements to acquire NIH-funded materials...for use in NIH-funded research will not include commercialization option rights [*e.g.*, exclusive license options], royalty reach-through, or product reach-through rights back to the provider." To mitigate scenario (*c*) when negotiating for research tools from a for-profit entity, the Guidelines state, "Agreements to acquire materials...for use in NIH-funded research may... provide an option for an exclusive...commercialization license to new inventions arising directly from the use of the material. [Such agreements] should be limited to circumstances where the material sought... is unique...and not reasonably available from any other source....In determining the scope of the license or option rights..., Recipient should balance the relative value of the provider's contribution against the value of the rights granted, cost of the research and importance of the research results....Recipients should reserve the right to negotiate license terms that will ensure: (1) continuing availability to the research community if the invention is a unique research resource; (2) that the provider has the technical and financial capability and commitment to bring all potential applications to the marketplace in a timely manner; and (3) that if an exclusive license is granted, the provider will provide a commercial development plan and agree to benchmarks and milestones for any fields of use granted." In other words, universities should try to assure that other academic researchers will have access to any inventions they make with research tools obtained from private companies, and that the companies that provide such tools will have exclusive rights to commercialize these inventions only to the extent that they remain able and committed to such commercialization.

Successful implementation of these guidelines will depend upon researchers, TLOs, and companies developing consensus concerning what constitutes "research tools,[7] " and on appropriate limits to companies demanding exclusive rights to university inventions and on the universities' freedom to license their inventions exclusively.

The licensing of diagnostic inventions raises similar concerns. Athena Diagnostics obtained exclusive licenses from Baylor for genetics tests for Charcot-Marie-Tooth disease type 1A, from Duke for use of the *apolipoprotein E* gene to detect predisposition to Alzheimer's disease, and from the University of Minnesota

Athena Diagnostics will permit clinical laboratories to perform these tests under reasonable sublicense terms.

Many TLOs may favor exclusive licenses of research tools and diagnostic technologies, because they find it burdensome to negotiate, collect, and audit a large number of nonexclusive licenses. However, Stanford and the University of California licensed the patent rights to the Cohen and Boyer's recombinant DNA (gene splicing process) technology nonexclusively, and this invention has generated more license revenue ($250 million from 1981 to 1997) than any other university invention. Also, Columbia University's single most profitable invention has been the Axel patents for a new process to insert genes into mammalian cells to make proteins (9) . These examples suggest that nonexclusive licensing of research tools and diagnostics can generate great financial returns to TLOs and university inventors.

Important factors in most royalty negotiations are the type of technology, the perceived risk associated with the technology, its stage of development, the projected cost of bringing a product to market, the size of the potential market, the anticipated profit margin, the strength of the patent claims, whether patents have actually issued, the prospects for pending patent applications, the estimated cost of the research that lead to the invention, the scope of the license (exclusive or nonexclusive, field of use, geographic scope, among others), and royalty rates for comparable inventions. Initial fees for exclusive licenses often are under $100,000, because technologies usually are in early stages, have uncertain commercial potential, and require considerable investment to be developed into marketable products. The majority of running royalty rates based on net sales are probably in the range of 1–8% (5, 1997 personal communication from the NIH Office of Technology Transfer, in 1997). However, royalties can also be very high. In 1995, Amgen paid Rockefeller University $20 million in up-front royalties for exclusive rights to the mouse *leptin* obesity gene and pledged to pay considerably more if it chose to continue the license (4) .

The Bayh-Dole Regulations impose specific obligations on licenses of inventions made with Government support:

(*a*) University inventors must receive a share of royalty income with the remainder to be used for research, education, and expenses associated with technology management. Usually, TLOs will use initial royalty income to pay inventors a minimum level of royalties and to cover TLO operations and patent expenses. Then they will divide any remaining income between the inventors, their departments, and the university as a whole, according to formulas that vary from university to university.

(*b*) Universities must make efforts that are "reasonable under the circumstances" to attract small business licensees and give licensing preference to a small business if the TLO determines that the small business is equally as likely as a large company to "bring the invention to practical application."[14] The decision of whether to give such a preference in any particular case is at the discretion of the university, although the Department of Commerce has authority to review the licensing programs of individual universities to determine whether they need to implement this provision more effectively. I know of no cases of such a review. The GAO report on university administration of the Bayh-Dole Act (10) found that major research universities license the majority of their inventions to small businesses, despite the absence of specific university policies to implement this provision of the Bayh-Dole Act and despite NIH and other government funding agencies not collecting data to monitor compliance with this provision. In other words, TLOs appear to be complying with the small business licensing preference largely on their own accord. Therefore, they will probably continue to preserve their discretion on how to implement this provision.

(*c*) If a university grants an exclusive license to use or sell in the United States an invention made with Government funds, the licensee must agree to manufacture substantially in the United States products made

using the invention. This requirement [illegible]
The funding agency may waive this requirement if the university shows it has made reasonable but unsuccessful efforts to find a company that would manufacture in the United States.15 According to NIH guidelines for handling requests for waivers of this requirement, NIH may take into account benefits other than domestic manufacturing such as: (i) the rapid availability of a product that will benefit public health; (ii) investment by the potential licensee in United States facilities, equipment, or research; (iii) the creation of new or higher quality United States jobs; and (iv) the enhancement of job skills among United States workers.

(*d*) Universities must report annually to funding agencies on the utilization of inventions, including development status, date of first sale, and royalties received. The agencies must keep this information confidential. NIH encourages TLOs to use the Edison electronic reporting system for such reports.

(*e*) The Government must receive a nonexclusive, nontransferable, irrevocable royalty-free license to practice the invention throughout the world or to have the invention practiced on its behalf. This ensures that the Government can continue to use for its purposes the inventions it has funded. It functions primarily as a research use license for the Government. Commercialization of inventions or assisting competitors of licensees to commercialize inventions is not regarded as a legitimate government purpose. I know of no examples where companies have disputed the Government's use of this license.

(*f*) The Government can require third-party licensing if the university or its licensee is not taking effective steps to develop the invention or such action is necessary to meet health or safety needs. The Government has never fully exercised these "march-in rights." To do so would be difficult and would require many procedural steps designed to protect the interests of universities and their licensees.

(*g*) In United States patent applications, universities must acknowledge Government support that lead to the invention and the Government's residual rights mentioned in (*e*) and (*f*) above. They must also inform licensees of these rights and the other requirements set forth in (*a*)–(*f*) above.

Sponsored Research Agreements and Academic Bioventures.
Although licensing is at the heart of technology transfer, technology transfer involves more than licensing. As noted above,[4] income from sponsored research agreements with industry is three times greater than license income. Often a simple license agreement or MTA leads to a sponsored research agreement offering long-term benefits in the form of interesting and practical research opportunities for faculty and students, employment opportunities, interchanges with industry scientists, development of university discoveries, as well as increased research funding (17) . In 1998, the leading academic users of industry-sponsored research funds were the University of California ($162 million), Massachusetts Institute of Technology ($74 million), Penn State ($66 million), Duke ($65 million), and Georgia Tech ($57 million). For comparison, the leading 1998 recipients of adjusted gross license income were University of California ($73 million), Columbia ($62 million), Stanford ($43 million), Florida State ($47 million), and Sloan Kettering ($38 million; Ref. 7).

However, increased collaboration with industry raises concerns related to academic freedom, inappropriate shift in research emphasis away from fundamental research, conflict of interest, and misappropriation of publicly funded research. Discussion of these issues is beyond the scope of this report, except to note the following:

(*a*) About 20% of academic life scientists responding to a survey said that companies had delayed publication of their research results by >6 months, and 9% reported refusing to share research results with academic colleagues on at least one occasion. Refusal to share research results was more common among researchers collaborating with industry, genome researchers, and more productive faculty members (20, 21,

22]).

(*b*) A time series analysis of patenting and licensing at the University of California and Columbia and Stanford detected little evidence that the Bayh-Dole reforms were associated with a shift toward applied research topics (9) . Analysis of publication data also does not indicate that increasing cooperation with industry is skewing university research toward more applied topics or lower quality research. In fact, scientific papers that are co-authored by university and industry researchers are somewhat more likely to be highly cited papers than those written by university researchers alone (23) .

(*c*) Conflict of interest policies (regarding whether faculty may have a financial interest or management position in a company that might be affected by their research, what extent of disclosure is required, and so forth) vary between universities (24) (see also 42 CFR 50.603–605). In 1998, the FDA issued regulations requiring companies submitting drug approval applications to the FDA to disclose compensation to investigators or any financial interests the investigators may have had in the outcome of their research (21 CFR 54).

(*d*) The grant of future exclusive license options to corporate research sponsors should be specific to the scope of the sponsored research, and TLOs should not grant to corporate research sponsors rights to all Government-supported inventions from major units of the university, such as departments, centers, and laboratories (5) . NIH guidelines state that in considering whether universities should grant sponsors the right to license future NIH-supported inventions, universities should: (*a*) take into consideration if the sponsor has the capability and commitment to develop the inventions; and (*b*) require development commitments before a sponsor can exclusively license a particular technology. Also, sponsors should have only 6 months to exercise their option to license inventions.16 These guidelines were developed in the wake of criticisms that a 10-year $300 million sponsored research agreement between Sandoz and the Scripps Research Institute (which received $123 million in NIH support in 199917) could restrict academic freedom and could give Sandoz too much control over Scripps's research projects and results (25) . NIH concluded this agreement was unique among sponsored research agreements, and Scripps and Sandoz subsequently modified the agreement (26) . The fact that NIH continues to support the vast majority of university biomedical R&D[4] should ensure that the NIH guidelines carry considerable influence.

One aspect of government- and corporate-sponsored research funding that is not common in Europe or Asia is that United States faculty, nontenured researchers, and technicians often depend on such "soft money" for a significant proportion of their salaries. The percentage of salaries that are guaranteed for tenured faculty varies between universities, but most researchers know their economic as well as professional survival depends on being able to receive government and industry grants. Such soft money supports a much larger manpower pool in universities than would be possible if salaries were guaranteed. This large soft money-based manpower pool, coupled with levels of government support for biomedical research unparalleled and the competitive peer-review mechanism to allocate such support, has made United States academic institutions important generators of new biomedical technologies, whereas European and Japanese academic institutions have lagged in this regard (1 , 27, 28, 29) .

Another unique feature of technology transfer in the United States is the important roll start-up or bioventure companies play in developing university discoveries to the point where larger companies become interested in commercializing them. The only European country where bioventures have played an important role in the technology development process is the United Kingdom (27) . Recently, the number of bioventures has increased in Germany, but German companies face significant labor mobility constraints not faced by United States companies and tend to focus on niche areas of process technologies rather than on pharmaceutical and diagnostic development (30) . In Japan, the current number of independent bioventures is probably <50, and those based upon university technologies or that have significant links with university researchers are even

fewer in number.

Formation of a bioventure can be an effective means to mobilize committed researchers, private capital, and management expertise to push forward the development of promising biomedical discoveries that are not immediately attractive to large companies or that do not fit within the competencies of established companies (27, 31).[18] In effect, venture companies can take over from TLOs the task of championing promising university technologies and shepherding them through the intermediate development process between university research and end-stage commercialization. In 1998, the universities that spun off the most new companies were Massachusetts Institute of Technology (19), University of California (19), Cal Tech (11), Georgia Tech (9), and Stanford [(9) (Ref. 7)]. Some universities, such as Massachusetts Institute of Technology, play an active role in the formation of their start-up companies (raising capital, recruiting management, developing a business plan, and other activities). Others, such as Stanford, expect entrepreneurial faculty to rely on their own or locally available resources.

Many universities are willing to support venture start-ups by their faculty by exclusively licensing to them key inventions (often the faculty members' own inventions) in return for equity in the new companies rather than cash royalties. In 1998, the universities executing the largest number of licenses with equity were Johns Hopkins (19), University of North Carolina Chapel Hill (16), University of Tennessee Research Corp. (12), Cal Tech (10), and Massachusetts Institute of Technology [(10) (Ref. 7)]. Only recently has Stanford begun to take equity from its start-ups in lieu of up-front royalties. Some universities have created their own venture funds to support their start-up companies. Atkinson provides a history of the early experience of the funds established by Harvard, Johns Hopkins, and University of Texas Southwestern to develop biomedical discoveries (32). Lerner (33) examined the experience of ARCH Venture Partners (Argonne National Laboratory/University of Chicago) and the management challenges faced by university venture funds.

The conflict of interest issues discussed above are especially pertinent in the case of faculty who also have a financial, management, or scientific interest in venture companies. Researchers who are contemplating forming a company, especially those who are considering assuming a management position or having their graduate students work in the new company, should consult with their universities' administrators and review their universities' policies on these issues.

The United States Technology Transfer System: Part 2. NIH and Other Government Laboratories

In 1993, federal government laboratories performed ~10% of all health R&D in the United States, compared with 43% by higher education and other nonprofit institutions and 45% by industry. Of the federal laboratory share, 60% was performed in the intramural laboratories of the NIH (3).

Prior to 1980, the DHEW owned work-related inventions made by NIH intramural scientists. In 1976, the IP portfolio of DHEW consisted of ~400 patents and patent applications, most for inventions made by employees of DHEW laboratories, particularly the NIH. A small proportion of these patents were licensed. Between 1969 and 1976, the DHEW had issued 19 exclusive licenses and 90 nonexclusive licenses (6).

The authority of the DHEW to issue such licenses had not been clarified in laws or regulations. This clarification came under section 207 of the Bayh-Dole Act, which specifically granted the Department of Health and Human Services and other federal agencies authority to patent and license inventions arising within their respective laboratories. Section 209 of the Bayh-Dole Act imposed many of the same conditions that it imposed on licenses from universities: specifically, the United States manufacturing preference, march-in rights, and submission of a development and commercialization plan (conditions imposed on all licenses), as well as the small business preference in the case of exclusive licenses. In addition, it stipulated

university licenses.

However, the Bayh-Dole Act did not give individual laboratories, such as the NIH, IP ownership or management rights. The first step in this direction came the same year under the Stevenson-Wydler Technology Innovation Act of 1980 (Public Law 96-480) authorizing individual federal laboratories to establish "Research and Technology Applications Offices" to promote technology transfer to industry and local governments.

However, the key legislation authorizing federal laboratories to manage their own discoveries was the FTTA of 1986 (Public Law 99-502). The FTTA explicitly gave individual laboratories authority to patent and license inventions by their employees. It also specified that the inventors should receive at least 15% of annual royalty payments and that the laboratory should receive at least half of the remaining royalties. (Agencies have the option to distribute the remaining royalties among their other laboratories, but it appears that most agencies let the inventing laboratory manage 100% of royalties.) Under separate legislation, the Government must obtain rights to all work-related inventions by its employees (37 CFR 501 and 45 CFR 7). Thus, the FTTA gave individual federal laboratories incentives to manage their employees' inventions that are similar to those that the Bayh-Dole Act gave to universities.

In terms of number of licenses and royalties, the NIH is far ahead of any other federal laboratory. In fiscal year 1999, NIH employees made 294 invention disclosures, and the NIH filed 169 patent applications, received 163 patents, executed 204 licenses, and received $45 million in license royalties, which would rank the NIH in first to fourth place in comparison with United States universities (7) . From fiscal years 1996–1998, the NIH granted 87 exclusive licenses and 514 nonexclusive licenses and received $102 million in license royalties (95% of total royalties received by the NIH, Department of Energy, National Aeronautics and Space Administration, Army, Navy, and Air Force combined). Fifty-seven % of the NIH's licenses were to small businesses, and 86% to domestic entities (34) .[19] It should be noted that the NIH's largest source of royalties, the HIV/AIDS diagnostic kit co-invented with French researchers at the Institut Pasteur, has been licensed nonexclusively, again showing that nonexclusive licensing can result in wide, reasonably priced access and high royalty income.

The FTTA also authorized federal laboratories to enter into CRADAs, the federal laboratory equivalent of sponsored research agreements. CRADAs are the only mechanism under which a company or other non-government organization can support research in federal laboratories and, in exchange for research support, receive the right to license resulting inventions or other rights to future inventions.

The basic exchange that occurs under CRADAs is: (*a*) research support (personnel, equipment, laboratory space, know-how, and/or money) contributed by the CRADA partner in return for (*b*) (i) research support (personnel, equipment, laboratory space, and/or know-how, but not money) contributed by the Government laboratory and (ii) IP rights to inventions that may arise under the CRADA research. The NIH grants CRADA partners "an exclusive option to elect an exclusive or nonexclusive commercialization license" to any inventions by Government employees made under the scope of the CRADA research plan. However, the CRADA partner must still negotiate fair licensing terms with the NIH, including due diligence clauses.

Certain restrictions apply to CRADAs that do not apply to university-industry sponsored research agreements. The NIH is reluctant to use CRADA funds to pay part of the salaries of permanent professionals, although CRADA funds are often used to hire postdoctoral-level researchers and technicians. CRADA opportunities must be advertised in the Federal Register prior to execution, unless the laboratory can demonstrate that only one company could be a suitable CRADA partner. Also, the FTTA requires that the Government retain a nonexclusive, irrevocable, paid-up license to any CRADA inventions, including

additional 30 days upon written request) to review proposed publications of CRADA data to prepare patent applications or to make sure that confidential information is not being divulged. However, CRADA partners have the exclusive right to use CRADA data for drug approval applications to the FDA or for other regulatory applications.[20]

A special short form "Materials Transfer" CRADA has been in use since 1997 to enable NIH researchers to obtain research materials from companies that would not release the materials absent an option to license inventions made using the materials. In effect, this Materials Transfer CRADA represents a pragmatic response to the same situation described as "scenario c" in "Marketing and Licensing" above; to obtain proprietary research materials, scientists and their institutions sometimes have no choice but to promise the providers rights to inventions made using these materials. The issue for negotiation becomes the nature and breadth of such rights.

In fiscal year 1999, the NIH executed 48 standard CRADAs and 78 Material Transfer CRADAs. Under a CRADA signed in the mid-1990s, Bristol-Myers Squibb and the National Cancer Institute collaborated on clinical trials to develop paclitaxel (Taxol) as a first-line treatment for breast and ovarian cancer. Paclitaxel is one of the most important cancer drugs introduced in the past 15 years. A unique feature of the paclitaxel CRADA was that Bristol-Myers did not receive license rights to the basic compound, because the compound was not patentable, its structure having been published many years previously. However, it did receive exclusive access to clinical data from NIH-supported researchers, which it needed to obtain regulatory approval from the FDA.

Some Government-owned contractor-operated laboratories, for example Los Alamos, Lawrence Livermore, and most of the Department of Energy's other university-operated laboratories, have agreements with Department of Energy that collaborative research with companies will be conducted under CRADAs. In such cases, the Government-owned contract-operated laboratory functions almost as if it were a Government-owned laboratory, and the only way a collaborating company can obtain future IP rights to discoveries made in the laboratory is through a CRADA.

Clinical Trials and Regulatory Approval in the United States

Background.
Clinical trials involve the testing of new drugs, diagnostics, and medical devices in humans to demonstrate safety and efficacy and to determine suitable doses. The goal of most clinical trials is to obtain regulatory approval for marketing. Marketing in the United States requires approval from the FDA.[21] Approval requires three trial phases. Phase I determines safe doses and pharmacology with an eye to therapeutic effects. Usually 15–80 patients are involved. In the case of oncology drugs, these are patients who have already failed conventional therapy. In the case of noncancer drugs, healthy volunteers are sometimes used. Phase II estimates the response rate and also identifies risks of side effects in a defined patient population, usually consisting of 30–300 subjects. Phase III involves hundreds to thousands of patients to determine whether the new drug offers significant advantages over standard therapies and to monitor adverse reactions. In almost all Phase III trials, matched or randomized controls are required (2 , 35) . In the case of new cancer drugs, the number of patients in each phase is usually in the lower ranges cited above.

The approval process for oncology drugs is expensive but less so than for most other new prescription drugs. The NCI of the NIH spends on average $2500 to $3000 per patient enrolled in NCI-sponsored clinical trials just to cover study management, data collection, and data monitoring costs. Costs of the drug, physicians' and nurses' time, additional tests, other hospital charges, and data analysis are all additional. My review of

all new oncology drugs approved by the FDA from 1990 through 1999 indicates that over half the new drugs received initial approval without Phase III trials. Often approval was granted on the basis of results from 2 to 5 Phase II trials that were preceded by less than 10 Phase I trials. For a new oncology drug, typically 100–500 trial participants are need for approval. The average approval time for an initial indication for a new oncology drug (from filing of the Investigational New Drug application to the New Drug Approval) was between 12 and 24 months. In contrast, for new drugs as a whole, FDA approval requires on average 4200 patients participating in 68 clinical trials over a 6–7-year period for each new drug (2) . The pharmaceutical industry spends ~$6 billion annually for clinical trials in the United States, its largest single category of R&D expenditures (36%; Ref. 2).

NIH-supported Clinical Trials.

Unlike other governments, the United States Government provides substantial financial as well as scientific support for such trials. Most of this support is from the NIH, which spent $1.2 billion to support clinical trials in 1995, ~13% of its R&D budget (36) .[23] The NIH justifies its support for clinical trials on the basis that such support is necessary (*a*) to bring drugs for some rare diseases closer to commercialization; and (*b*) to test existing drugs or combinations of drugs for diseases or populations that otherwise would not be the subject of clinical trials. In addition, the NIH has active drug discovery and preclinical development programs, and often it is willing to support clinical trials to accelerate the commercialization of drugs emerging from these programs.

Although the NIH has its own 250-bed hospital, most NIH-supported clinical trials are conducted in extramural academic medical centers. NIH awards grants to individual researchers who submit well-qualified clinical trial proposals. It also supports clinical trial centers or units in a number of teaching hospitals. For example, the NCI funds about 17 centers for Phase I trials and an equal number for Phase II trials. The NCI pays the costs of study management, data collection, and data analysis plus overhead. However, non-experimental costs must be covered by the patients' normal health insurance, the providing hospital, or some other source.

Often NIH-supported clinical trials involve collaboration with industry, particularly the company that owns the investigational drug. Such cooperation usually occurs under either a Clinical Trial Agreement or a CRADA between the company and the NIH. In either case, NIH scientists, the university principal investigators, and the company jointly develop the protocol.

Under a typical NIH Clinical Trial Agreement, the company will supply the NIH-supported university researcher with enough of its drug to complete the trial. In return, the company will receive the trial data that it needs to obtain FDA approval.

Under a typical clinical trial CRADA, an NIH-sponsored university researcher will receive sufficient drug from the company. The NIH will receive some money to offset its costs. The company will receive (*a*) exclusive access to the data it needs to obtain FDA approval and (*b*) the right to obtain an exclusive license to inventions that arise under the CRADA research, including inventions consisting of methods of medical treatment.

Industry Support for Clinical Trials.

As noted above, ~80% of support for United States clinical trials comes from industry. Companies contract either directly with medical centers or with Contract Research Organizations that will manage the trials for the companies. In general, corporate funds can be used to pay salaries of physicians, nurses, and other personnel. Some physicians and nurses working in clinical research units of major university hospitals rely on soft money from corporate contracts, or grants from the NIH or other non-profit outside institutions, for

There is concern that corporate support may influence researchers' conduct of trials or their interpretation of trial data. Conflict of interest concerns also arise when investigators are shareholders or managers in companies formed to commercialize their discoveries. Since 1998, companies submitting drug approval applications to the FDA must disclose compensation to investigators and any financial interests investigators may have in the outcome of the research (21 CFR Part 54). However, when investigators themselves discuss or publish their findings, their understanding varies concerning when and to what extent they should disclose financial interests in the outcome of their research (37) .

IP Rights and Regulatory Exclusivity.
Rights to inventions arising in the course of clinical trials are determined in the same way as other inventions; extramural institutions receiving NIH funds can patent and license such inventions, NIH can patent and license intramural NIH inventions, and medical centers and industry can decide among themselves how to patent and license inventions arising under industry-funded trials. Inventions arising under clinical trials are usually method-of-use inventions, *e.g.*, a new combination of drugs, a new route of administration, or a new duration of administration. Although not as valuable as inventions claiming a new chemical compound, such inventions may be valuable to companies, particularly if it is not possible to obtain a patent on the basic chemical compound, as in the case of paclitaxel. Therefore, corporate sponsors of clinical trials sometimes will bargain hard to ensure they have the right to patent or exclusively license such inventions.

If a new drug is either a new chemical entity or an orphan drug, a company seeking FDA approval also receives a period of regulatory exclusivity, regardless of whether it obtains patent protection. Under the 1984 Drug Price Competition and Patent Term Restoration Act (also known as the Hatch-Waxman Act, Public Law 98-417), once the FDA approves a drug that does not contain a previously approved active moiety, no other person may submit an application for a drug based upon the same (or substantially the same) active moiety for 5 years (21 USC 355). Under the Orphan Drug Act (Public Law 97-414), the FDA may designate as "orphan drugs" drugs for diseases affecting <200,000 persons in the United States per year. If the FDA approves an orphan drug, it will not approve the same drug submitted by another company for the same indication for a period of 7 years (21 CFR 316).

In the case of paclitaxel, Bristol-Myers Squibb used data from NCI-sponsored clinical trials to obtain FDA marketing approval as a new chemical entity, which it subsequently marketed as Taxol. Because patent protection on paclitaxel was not obtainable, Bristol-Myers had only the 5 years of regulatory exclusivity to market Taxol before generic manufacturers of paclitaxel began marketing competing versions of the same drug.

Concluding Observations from an International Perspective

I hope this report has given biomedical scientists an understanding of the United States technology transfer system that enables them to deal effectively with TLO officials and industry representatives to increase the chance that their discoveries will be developed into commercially successful or widely used products. I also hope it helps scientists understand current trends and policy concerns regarding technology transfer, and that it helps persons outside the United States to understand better a system that is being imitated in Europe, Canada, China, and other countries.

The system described above, characterized by ownership and management of IP by the research institutions, is not the only model of technology transfer. Alternative models include: (*a*) leaving ownership and management of publicly financed discoveries in the hands of the inventors; (*b*) ownership and management

by central government agencies; (c) [illegible]
with decreased emphasis on patenting and, in particular, exclusive licensing; and (*d*) voluntary assignment of ownership rights to for-profit corporations that will assume responsibility for technology management.

A systematic comparative analysis of these models is the subject of future reports. Suffice to note that Japanese, German, and Scandinavian universities have followed system (*a*). However, Denmark has recently switched to university ownership and management of IP, and Germany is seriously considering the same change, leaving Japan as the only major industrialized country that for the foreseeable future will leave ownership and management of most university inventions in the hands of faculty-inventors. Also, it should be noted that a combination of (*b*) and (*c*) characterized the pre-Bayh-Dole United States system and the United Kingdom system when the British Technology Group (BTG) was still a public corporation responsible for managing university technologies. It still characterizes a small percentage of inventions made in Japanese universities (so-called "national inventions"), as well as the majority of inventions made in Japanese government research institutions (28 , 38 , 39) . Examples of (*d*) include today's privatized BTG; traditional United States technology management corporations (*e.g.*, Research Corporation Technologies), the numbers of which have dwindled in recent years; and a host of relatively small, new technology brokers.

Criticism of the United States system, with its emphasis on financial rewards to motivate individual research institutions to perform effective technology transfer, often centers around perceived tendencies for these institutions to charge high royalties and unnecessarily grant exclusive licenses (see the discussions of research tools and diagnostics in "Marketing and Licensing"), thereby imposing multiple "rents" or "highway tolls" on the technology transfer process (4 , 9 , 19 , 40) . These criticisms emphasize the benefits of (*c*) and advocate the issuing of exclusive licenses only when necessary to mobilize private sector investment in technologies that need further development. An analysis of these criticisms is beyond the scope of this report. However, it seems likely that the following factors have driven the development of the United States system and accounted for many of its indices of "success" (*e.g.*, increases in licenses and royalties, increases in sponsored research, and imitation in other countries):

(*a*) Strong IP protection is often essential to encourage development of early-stage biomedical discoveries, particularly those that may be the basis for future drugs. Therefore, the demand for exclusive licenses in this field will remain high.

(*b*) Most university inventions are early-stage technologies, the ultimate feasibility and marketability of which is uncertain, although this is often not the case for clinical research inventions. Most early-stage inventions need a champion (more likely, a series of champions) if they are to have a chance for successful development. Such champions or innovation agents need to push forward the development of their discoveries from both scientific and business perspectives. They must recruit and motivate researchers, acquire capital, develop business plans, seek development partners, and obtain customers. An important part of this championship process involves TLOs making far-sighted, sometimes risky patenting decisions, selecting committed licensees, and negotiating license terms that require development commitments from the licensees. However, much more is needed. Scientists must believe that they stand a reasonable chance of reaping significant rewards (not only monetary) if they invest energy and time to develop promising but risky discoveries. The same is true for companies that provide venture capital, pharmaceutical and biotechnology companies that invest in such discoveries, and administrators who attempt to build successful technology-business incubator facilities.

Financial incentives are necessary to motivate the many actors involved in this complex process. Whether the present incentives are necessary for the system to work or whether they encourage excessive patenting, exclusive licensing, and royalty collection by publicly supported institutions is at the heart of the present debate.

My 5 years in Japan studying [illegible]
the Japanese technology transfer system is that neither inventors, university officials, nor companies have significant incentives to develop inventions made in university or government research institutes. Public sector inventors, if they bother at all with technology transfer, usually pass inventions informally to companies with whom they have long-standing relationships. The terms of transfer impose few if any obligations on companies to develop the inventions or to pay royalties. Because these companies receive publicly financed discoveries essentially for free, they lack incentives to invest in development, except in the case of clearly spectacular inventions. Japanese TLOs manage only inventions that inventors voluntarily pass to them, and thus universities are still largely left out of the technology transfer process. Available evidence suggests that they vast majority of university discoveries are undeveloped, and this may have profound negative implications for several high technology Japanese industries, including biomedicine and software (28, 38, 39). Although this observation does not validate aggressive patenting and licensing by United States universities and government laboratories, it does reinforce the importance of IP rights in creating financial incentives for public research institutions and the private sector to champion risky, early-stage discoveries.

However, scientists, universities and other public research institutions should keep in mind that the essential purpose of technology transfer from not-for-profit institutions is the development of publicly financed discoveries for the public good. Generating money for inventors, universities, and private investors is not the goal. However, it is an important incentive to make the system work.

Fortunately, the present United States system of technology transfer and the model outlined in (*c*) above are not necessarily incompatible. For example, a policy of issuing exclusive licenses only when necessary to provide incentives to commercialize university inventions may result in an attractive revenue stream for many TLOs while *minimizing* situations where exclusive licenses can impede other researchers and companies from carrying forward further development.

FOOTNOTES

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

[1] To whom requests for reprints should be addressed, at Department of Intellectual Property, Research Center for Advanced Science and Technology, University of Tokyo, 4-6-1 Komaba, Meguro-ku, Tokyo 153-8904, Japan. E-mail: kneller@ip.rcast.u-tokyo.ac.jp.

[2] The abbreviations used are: R&D, research and development; FDA, Food and Drug Administration; IP, intellectual property; DHEW, Department of Health, Education, and Welfare; USC, United States Code; CFR, Code of Federal Regulations; TLO, technology licensing office; MTA, Materials Transfer Agreement; USPTO, United States Patent and Trademark Office; PCT, Patent Cooperation Treaty; FTTA, Federal Technology Transfer Act; CRADA, Cooperative Research and Development Agreement; NCI, National Cancer Institute.

[3] Available at: http://www.phrma.org/publications.

[4] In 1996, ~86% of licensing revenue was for life science inventions (8). An analysis of technology transfer activity at Stanford and Columbia Universities and the University of California showed that biomedical inventions accounted for the majority of invention reports at the latter two universities throughout the 1980s,

(9) . The overwhelming importance of biomedical discoveries was confirmed in a study of technology transfer activities in 10 major United States universities after passage of the Bayh-Dole Act (10) . In 1994, life science companies supported over $1.5 billion of research in United States academic institutions, ~12% of all R&D funding in United States academic institutions (11) . Equivalent NIH support was $6.2 billion (1) . United States university faculty participated in founding 24 Fortune 500 companies and over 600 smaller life science companies (12) . By the mid-1990s, over a thousand small businesses were developing life science technologies (11) .

[5] Detailed information on Edison is available at http://era.info.nih.gov/Edison.

[6] Thirty-five leading universities reported that in 1989 and 1990, they received 4380 invention disclosures from employees, of which they attributed 1072 to NIH or National Science Foundation funding. During the same period, licensing revenues reported by these universities amounted to $113 million, of which $82 million was attributable to inventions supported by NIH or the National Science Foundation (15) .

[7] The 1999 NIH "Principles and Guidelines on Obtaining and Disseminating Biomedical Research Resources" state that "research tools" can include cell lines, monoclonal antibodies, reagents, animal models, growth factors, combinatorial chemistry and DNA libraries, clones and cloning tools, laboratory methods, and software. In considering whether the Guidelines should apply to a particular resource, the following considerations are applicable: (*a*) Is the resource's primary usefulness as a discovery tool rather than an FDA-approved product or component thereof? (*b*) Is the resource a broad enabling invention that will be useful to many scientists or companies rather than a project-specific resource? (*c*) Is the resource readily usable, or is private sector involvement necessary to develop or distribute it? (See footnote [13] for internet address.) Nevertheless, what may be an important research tool for many university scientists may also be a company's core business; and sometimes the development or improvement of research tools depends on a company having incentives to invest in such development or improvement. For example, Ligand Pharmaceuticals licensed technology from the Salk Institute, which enabled Ligand to isolate and duplicate intracellular receptors. Ligand then developed these as research tools for drug discovery and drug targets. Several large companies had half-heartedly experimented with the Salk discovery before the license to Ligand. Once Ligand had an exclusive license to the technology, it focused its efforts on this technology and was able to attract the necessary private capital to develop and market these research tools. Another example, although not one originating in universities, is the original PCR technology developed by Cetus Corporation. This was not suited to large-scale automation, but subsequent improvements by Hoffman-La Roche, Johnson & Johnson, and other companies that acquired IP rights to the original invention have made PCR the important widely applicable technology that it is today. But a counter example showing that exclusive rights are not always necessary for the development of important research technologies is the recombinant DNA (gene splicing) technology invented by Cohen and Boyer, for which the University of California and Stanford jointly applied for a patent in 1974. These universities decided to license this technology nonexclusively for only a $10,000 one-time payment per licensee. The technology became widely used, and the two universities became the leading earners of royalty income. For transfers of research tools between not-for-profit laboratories, NIH recommends using the Uniform Biological Materials Transfer Agreement, the basic provisions of which are as follows: (*a*) ownership remains with the Provider, but the Provider is not liable for damages arising from the Recipient's use of the material; (*b*) no reimbursement except for Provider's preparation and distribution costs; (*c*) no use in humans; (*d*) no commercial research use, such as for drug screening; (*e*) no distribution to third parties; and (*f*) the Recipient must acknowledge the Provider as the source.

[8] Internet address: http://www.stanford.edu/group/OTL.

[9] See http://www/uspto.gov and http://www.nih.gov/od/ott for related comments.

[10] Internet address: http://www.edison.gov/biological-materials.html.

[11] Internet addresses: http://www.stanford.edu/group/OTL/ and http://web.mit.edu/tlo/.

[12] Benchmark clauses are less important in licenses to venture companies, partly because the development path for such technologies is less certain but also because the private capital investors and the managers whom they appoint can usually be relied upon to push forward the development of the technology.

[13] Internet address: http://www.nih.gov/od/ott/RTguide_final.html/.

[14] The following are criteria to qualify for "small business" status: independent ownership and operation (*i.e.*, not affiliated with a larger organization); total employees (including those of any affiliates) do not exceed 500; not dominant in its field of operation; principal place of business located in the United States; at least 51% owned (or in the case of a company whose stocks are publicly traded, at least 51% of its voting stock is owned) by United States citizens or permanent resident aliens (13 CFR 121.4).

[15] Internet address: http://era.info.nih.gov/Edison/604new.html.

[16] Internet address: http://era.info.nih.gov/Edison/sponsored.html/.

[17] Internet address: http://grants.nih.gov/grants/award/award.htm.

[18] Available at: http://www.nber.org/papers/w6846.

[19] Available at: http://www.nih.gov/od/ott/.

[20] See the NIH model CRADA at http://www.nih.gov/od/ott.

[21] Although marketing in other countries requires approval of respective national regulatory agencies, substantial progress has been made to harmonize regulatory approval procedures in the United States, Japan, and the European Union. The goal of this effort is to have similar approval criteria and data collection procedures (satisfying good clinical practice guidelines) so that if one regulatory authority approves a drug, the other authorities will also approve, requiring at most one or two relatively small "bridging" trials. More information on harmonization is available at http://www.fda.gov/cder/guidance/index.htm.

[22] Available at: http://www.fda.gov/cder/.

[23] Available at: http://www.nih.gov/news/crp/97report.htm.

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REFERENCES

Foundation 1998.
2. Pharmaceutical Research and Manufacturers Association (PhRMA). Industry Profile 2000 Washington, DC PhRMA 2000.
3. NIH Data Book 1994 (NIH Pub. No. 95-1261). Bethesda, MD: NIH, 1995.
4. Eisenberg R. S. Public research and private development: patents and technology transfer in government-sponsored research. Virginia Law Rev., *83:* 1663-1727, 1996.
5. Council on Governmental Relations (COGR). University Technology Transfer. Questions and Answers Washington, DC COGR 1993.
6. Latker, N. (Patent Counsel, U. S. Department of Health Education and Welfare). Statement before the Subcommittee on Science, Research, and Technology of the U.S. House of Representatives, May 26, 1977.
7. Association of University Technology Managers, Inc. (AUTM). AUTM Licensing Survey FY 1998 Norwalk, CT AUTM 1999.
8. Association of University Technology Managers, Inc. (AUTM). AUTM Licensing Survey FY 1996 Norwalk, CT AUTM 1997.
9. Mowery D. C., Nelson R. R., Sampat B. N., Ziedonis A. A. The effects of the Bayh-Dole Act on U. S. research and technology Branscomb L. Kodama F. Florida R. eds. . Industrializing Knowledge: University-Industry Linkages in Japan and the United States, *:* 269-306, MIT Press Cambridge, MA 1999.
10. General Accounting Office (GAO). Technology Transfer: Administration of the Bayh-Dole Act by Research Universities (GAO/RCED 98-126). Washington, DC: GAO, 1998.
11. Blumenthal D., Causino N., Campbell E., Louis K. S. Relationships between academic institutions and industry in the life sciences. N. Engl. J. Med., *334:* 368-373, 1996.[Abstract/Free Full Text]
12. Blumenthal, D. Capitalizing on public sector research investments: the case of academic-industry relationships in the biomedical sciences. Unpublished paper presented at the NIH Economics Roundtable on Biomedical Research, National Institutes of Health, Bethesda, MD, October 19, 1995.
13. Etzkowitz H. Knowledge as property: The Massachusetts Institute of Technology and the debate over academic patent policy. Minerva, *32:* 383-421, 1994.
14. Reichman J. H. Overlapping proprietary rights in university-generated research products: the case of computer programs. Columbia-VLA J. Law Arts, *17:* 51-125, 1992.
15. General Accounting Office (GAO). Report on University Research (GAO/RCED 92–104). Washington, DC: GAO, 1992.
16. Association of University Technology Managers, Inc. (AUTM). . AUTM Technology Transfer Practice Manual, *Vol. III:* Norwalk, CT AUTM 1994.
17. Nelsen L. The rise of intellectual property protection in the American university. Science (Washington DC), *279:* 1460-1461, 1998.[Free Full Text]
18. Hsu D. H., Bernstein T. Managing the university technology licensing process. Findings and case studies. J. Assoc. Univ. Technol. Managers, *9:* 1-34, 1997.
19. Merz J. Disease gene patents: overcoming unethical constraints on clinical laboratory medicine. Clin. Chem., *45:* 324-330, 1999.[Abstract/Free Full Text]
20. Blumenthal D., Campbell E. G., Causino N., Louis K. S. Participation of life science faculty in research relationships with industry. N. Engl. J. Med., *335:* 1734-1739, 1996.[Abstract/Free Full Text]
21. Blumenthal D., Causino N., Campbell E. G. Academic-industry relationships in genetics: a field apart. Nat. Genet., *16:* 104-108, 1997.[Medline]
22. Blumenthal D., Campbell E. G., Anderson M. S., Causino N., Louis K. S. Withholding research results in academic life science. Evidence from a national survey of faculty. J. Am. Med. Assoc., *277:* 1224-1228, 1997.[Abstract]
23. Hicks D., Hamilton K. Does university-industry collaboration adversely affect university research?.

24. Association of University Technology Managers, Inc. (AUTM). . AUTM Technology Transfer Practice Manual, *Vol. I:* Norwalk, CT AUTM 1996.
25. Hilts, P. Health chief assails a research deal, pp. A12. *New York Times*, March 12, 1993.
26. NIH. Panel Report of the Forum on Sponsored Research Agreements: Perspectives, Outlook, and Policy Development Bethesda, MD NIH 1994.
27. Henderson R., Orsenigo L., Pisano G. P. The pharmaceutical industry and the revolution in molecular biology: interactions among scientific and institutional and organizational change Mowery D.C. Nelson R.R. eds. . Sources of Industrial Leadership, *:* 267-311, Cambridge University Press Cambridge, United Kingdom 1999.
28. Kneller R. University-industry cooperation in biomedical R&D in Japan and the United States: implications for biomedical industries Branscomb L. Kodama F. Florida R. eds. . Industrializing Knowledge: University-Industry Linkages in Japan and the United States, *:* 410-438, MIT Press Cambridge, MA 1999.
29. Coleman S. eds. . Japanese Science: From the Inside, *:* London Routledge 1999.
30. Casper S. Institutional Adaptiveness, Technology Policy, and the Diffusion of New Business Models. The Case of German Biotechnology. Organization Studies, *21:* 887-914, 2001.
31. Kortum S, Lerner J. Does Venture Capital Spur Innovation? Working Paper No., 6846 Cambridge, MA National Bureau of Economic Research 1998.
32. Atkinson S. H. University-Affiliated Venture Capital Funds. Health Affairs, *13:* (Summer)159-175, 1994.[Abstract/Free Full Text]
33. Lerner J. Venture capital and the commercialization of academic technology: symbiosis and paradox Branscomb L. Kodama F. Florida R. eds. . Industrializing Knowledge: University-industry Linkages in Japan and the United States, *:* 385-409, MIT Press Cambridge, MA 1999.
34. General Accounting Office (GAO). Technology Transfer: Number and Characteristics of Inventions Licensed by Six Federal Agencies (GAO/RCED 99-173). Washington, DC: GAO, 1999.
35. National Cancer institute (NCI). Investigator's Handbook. A Manual for Participants in Clinical Trial of Investigational Agents Sponsored by the Division of Cancer Treatment, NCI Bethesda, MD NIH 1997.
36. NIH. The NIH Director's Panel on Clinical Research Report to the Advisory Committee to the NIH Director. December, 1997. Bethesda, MD: NIH, 1997.
37. Stolberg, S. G. Financial ties in biomedicine get close look. *New York Times*, February, 20, 2000.
38. Kneller R. Intellectual property rights and university-industry technology transfer in Japan Branscomb L. Kodama F. Florida R. eds. . Industrializing Knowledge: University-Industry Linkages in Japan and the United States, *:* 307-347, MIT Press Cambridge, MA 1999.
39. Kneller R. Intellectual property rights and university-industry technology transfer in Japan. Science Public Policy, *26:* 113-124, 1999.
40. Heller M. A., Eisenberg R. S. Can patents deter innovation? The anticommons in biomedical research. Science (Washington DC), *280:* 698-701, 1998.[Abstract/Free Full Text]

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reserves in the government the authority to challenge the prices of any marketed product licensed or owned under a patent resulting from government funded research covered under the Act, and if thereafter not satisfied, the authority to terminate the license. Amazingly, the authors further maintain that these authorities carry with them the burden of providing company "...data showing that it charged a reasonable price" (page 653, lines 3-6).

There are absolutely no such expressed authorities in the Act, and to presume these authorities are implicit in the Act flies in the face of common sense. Clearly no commercial concern would knowingly invest in the commercial development of any invention (whether or not funded in part by the government) knowing that their sales price could be challenged by the government after marketing. Clearly, such authority would put in doubt not only the possibility of profit, but recoupment of their development costs, which include failed initiatives.

It is further clear that such authorities would frustrate the stated policy and objective of the Act to create incentives for commercial development by assuring, when necessary, an exclusive patent position (see 35 U.S.C. 200). Indeed, if the article's thesis were implemented, the only inventions that would be effected would be those near or already in the marketplace. As such, involved developers could

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justifiably complain that the government had involved itself in a "bait and switch" scam.

If implemented, no sensible concern could justify the costly development of life science inventions touched by government funding. The clock would be turned back over twenty years, and not only would little be achieved in lower prices, much of the government's research funding would be wasted as it could not produce the tangible results produced by the incentive of clear patent exclusivity.

The primary basis for the author's thesis is the Act's requirement that an invention owned or licensed under the Act be "available to the public on reasonable terms" followed by the article's conclusion that "reasonable terms" includes or is equivalent to "reasonable prices". This concept is put forward in face of the article's understanding that there may be no "...clear legislative history of the term" in the Act (see page 649, line 12). This acknowledgement appears to have triggered the authors need to fabricate the legislative history found on pages 656-667 discussed above.

At this point, we submit that an objective analysis of the Act would have stopped, as the Act and its legislative history as defined above makes clear that one of the primary incentives to industry involvement can be an exclusive position granted to a developer which includes the right to establish

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prices without any authorities in the government to challenge the developer's decision. If an authority to challenge pricing was intended, its importance would have most certainly resulted in its explicit identification and discussion, especially regarding the requirement to provide proprietary pricing data.

Instead, as noted from 35 U.S.C. 200, the general description of the authorities reserved to the government are limited "...to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against non-use or unreasonable use of the invention..." (underlining added). This general reservation of rights in the Government is specifically implemented in the march-in provision of 35 U.S.C. §203, which we submit cannot be read to be any broader than intended in the general reservation of 35 U.S.C. §200, which would be necessary to grant the requested march-in request.

In addition to the fact that there is no expressed authority in the Act permitting the government to challenge a developer's pricing determination or require delivery of proprietary data establishing such pricing, practice over twenty years clearly supports the fact that these authorities were not provided by the Act.

Notwithstanding the author's failure to support their thesis through a credible legislative history or by established

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practice, they further maintain that the ordinary meaning of "reasonable terms" is unambiguous and includes price, and that its definition requires no further judicial inquiry except in rare and exceptional circumstances (page 650, lines 1-4).

This they maintain is supported by the Scalia rule:

> [First], find the ordinary meaning of the language in its textual context; and second, using established canons of construction, ask whether there is any clear indication that some permissible meaning other than the ordinary applies. If not - and especially if a good reason for the ordinary meaning appears plain - we apply the ordinary meaning.

The authors support their position by citing a number of court decisions that the authors maintain defines "reasonable terms" as including price. However, even if this was considered to be correct, the inclusion of price within "reasonable terms" in these cases is in a "textual context" completely different from the context of the Bayh-Dole Act. As such, these cases provide no insight whatever of the definition of "reasonable terms" in the "textual context" of the Bayh-Dole Act, and should be dismissed as irrelevant.

Further, we submit that the authors have completely misapplied the Scalia rule, as it is clear that "reasonable terms" is unambiguous within the "textual context" of the Act, and even if it was not (which is not the case), a permissible meaning other

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than the ordinary must apply to permit the Act to achieve its intended objectives. In short, it is clear that to define "reasonable terms" in the manner suggested by the authors would preclude reaching the objectives of the Act, which is clearly in conflict with the intend of the Scalia rule which requires defining terms in a manner consistent with the objectives of the statute from which they are derived.

Our views are also clearly consistent even with the authors own comment that,

> U.S. law always has held that absent a clearly explicit statutory intent to the contrary, ordinary words ... must be interpreted with their ordinary meaning (page 649, lines 14 on through line 1 on page 650).

A clear explicit statutory intent is present in the Act which requires "reasonable terms" to be read consistent with that intent, and not in a manner that defeats such intent and the proper application of the Scalia rule.

Accordingly, we feel strongly that Mr. Love's request should be denied, as there is nothing whatever within the Act and its legislative history that supports his view that the Act reserves in the government the authority to challenge the price of drugs licensed under a patent resulting from Department funded research,

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especially since to do otherwise is contrary to the stated policy and objective of the Act. It is even clearer that the Department has no authority to require data from the developer supporting that prices charged are reasonable.

We further note for the Department's consideration that the article maintains that its thesis is also applicable to the Federal Technology Transfer Act of 1986 (page 648, lines 1-5). This is incorrect on its face, as there is no expressed authority whatever in the FTTA to challenge the pricing of inventions made in the performance of CRADA's. However, the grant of Mr. Love's request would most likely act as incentive to make similar requests involving inventions made in performance of CRADA's.

SUMMARY OF THE TESTIMONY OF ANDREW NEIGHBOUR

Over the past twenty years or so, the NIH and research universities throughout the United States who receive their funding support from extramural NIH grant programs have developed a collaborative and effective alliance that yields enormous benefit for our society and for mankind.

In this testimony, I will describe some of these benefits as well as some of the challenges and controversies that have the potential to impede this success.

The passage of the Bayh-Dole Act in 1980 was a bold and inspired move that shifted from the government to universities the responsibility for protecting and commercializing inventions made with federal funds. NIH has played a lead role in its implementation and in building a strong alliance with research universities.

Universities have built effective programs for managing the intellectual property generated from federal grants and contracts. They are committed to disseminating the results of their research through publication and technology transfer to the public and industry so that innovative products can improve the quality of life for our society.

Technology transfer is a complex and resource intensive activity. The University of California spends approximately $20 million per year to manage a portfolio of more than 5,000 inventions, and 1,000 active licenses. 1,000 new inventions are disclosed each year.

Major discoveries that resulted from NIH-funded research at the University of California have included new technologies for improving radiographic imaging, improved methods to develop and deliver therapeutic drugs, and novel diagnostics for people and animals. In addition, NIH funding has formed a major platform of research that has fostered additional federal and private funding spawning a plethora of high value products.

Success has resulted in some criticism which, I believe, is founded mostly on three misunderstandings that are discussed in this testimony in greater detail:

- Technology transfer is not a linear process;
- Money is an incomplete measure of technology transfer performance; and
- Universities do not do technology transfer to make money.

The reality is that fundamental advances in life sciences and biomedicine have arisen from NIH funding, and the technology transfer laws and practices have aided their development into useful and valuable knowledge and products from which the public derive enormous benefit.

Disturbing this activity would impede the advantages and benefits that accrue from the alliance between the NIH, universities and industry that has emerged from passage of the Bayh-Dole Act.

Prepared Witness Testimony

House of Representatives, Committee on Energy and Commerce
Subcommittee on Health
Michael Bilirakis, Chairman

National Institutes of Health: Moving Research from the Bench to the Bedside
Subcommittee on Health
July 10, 2003
10:00 AM
2123 Rayburn House Office Building

Andrew Neighbour, Ph.D.
Associate Vice Chancellor for Research
The University of California, Los Angeles

Chairman Bilirakis, Ranking Member Brown, Representative Waxman and Members of the Subcommittee:

On behalf of the University of California, I welcome this opportunity to testify before this subcommittee on the topic of "NIH: Moving Research from the Bench to the Bedside." As the Executive Director for the Office of Research Administration at UCLA, I am responsible for the management of both publicly and privately sponsored research for the campus, and for the transfer of its innovative technologies to the marketplace. I have enjoyed more than twenty years working in the realm of technology transfer in both academic and corporate sectors. I also serve as a Board Member of the Council on Governmental Relations (COGR), an association of more than 150 leading US research universities, and am the incoming chair of COGR's Committee of Contracts and Intellectual Property.

BACKGROUND

Over the past twenty years or so, the NIH and research universities throughout the United States who receive their funding support from extramural NIH grant programs have developed a

collaborative and effective alliance that yields enormous benefit for our society and for mankind. In my remarks today, while I will describe some of these benefits, I will also discuss the challenges and controversies that have the potential to impede this success.

The passage of the Bayh-Dole Act in 1980 was a bold and inspired move that shifted from the government to universities the responsibility for protecting and commercializing inventions made with federal funds. The Act applies to research funded by any federal agency. However, because most life sciences and biomedical research is supported through the NIH, and this segment tends to generate the most intellectual property, it is the NIH that plays perhaps the most visible role in Bayh-Dole implementation. Over the past twenty years or so, the guidance, oversight and coordination provided by NIH has served to build a collaborative alliance between academe and the government leading to more and more effective technology transfer.

In the University of California alone, more than 6,500 individual scientists have reported new inventions since the enactment of Bayh-Dole representing the creation of a vast research enterprise that has brought immeasurable and invaluable benefits to society.

Perhaps the prototypical example of the benefit of federal/university collaboration is the 1973 discovery by Cohen and Boyer of recombinant DNA technology, otherwise known as "gene splicing." In research funded by the American Cancer Society, National Science Foundation and NIH, these two scientists at Stanford and the University of California discovered the means to insert genetic material artificially into native DNA. This technique launched an entire new industry called "biotechnology." As you will note, this invention predated Bayh-Dole. However, because of a special "patent agreement" with NIH, Stanford and the University of California were allowed to elect title to the patent and, in so doing, assumed the responsibility for licensing

the invention. During the life of the patent, Stanford's technology transfer office executed and managed more than 300 non-exclusive licenses with this growing biotechnology industry.

With this experience in view, many individuals and organizations believed that the task was well beyond the means and capabilities of the government. Consequently, they encouraged the Congress to consider moving the responsibility for commercializing federally funded inventions from the government agencies to the University receiving the federal grants. Passage of Bayh-Dole conferred not only the right to take title to inventions arising from government-funded research, but also an obligation to commercialize these inventions diligently for the benefit of the public. With this mandate, Universities began the difficult task of developing technology transfer programs equipped to steward their newly acquired intellectual property assets.

TECHNOLOGY TRANSFER AT THE UNIVERSITY OF CALIFORNIA

With the largest academic research enterprise in the US and perhaps the world, the University of California system has built a technology transfer program that many consider to be among the most effective yet developed. Initially, the program was centered in the Office of the President as a central Office of Technology Transfer. As experience grew, the University realized the merits of moving some of the activities to the local campuses, particularly those with large research programs. Presently, the larger campuses (and the federal laboratories managed by the University) perform most of the technology activities at the local campus. The system OTT provides coordination, oversight, policy review, legal support and some licensing support. The individual campuses that have their own technology transfer offices manage the licensing of their portfolios locally. The system as a whole expends approximately $10-12 million per year in operating expenses and the same amount in "out-of-pocket" patenting costs to manage almost 1,000 new inventions received each year. The University has accumulated a total portfolio of more than 5,000 active inventions in its system wide portfolio and monitors

almost 1,000 patent licenses with industry. In FY02, the University executed 125 new patent licenses and 55 plant licenses. In summary, the process involves the evaluation of inventions, protection of the intellectual property through patent or copyright, marketing to industry, negotiating and executing licenses, and monitoring the licensees' diligence in commercializing inventions.

Since the Cohen-Boyer invention, major discoveries that resulted from NIH-funded research at the University of California have included new technologies for improving radiographic imaging, improved methods to develop and deliver therapeutic drugs, and novel diagnostics for people and animals. In addition, NIH funding has formed a major platform of research that has fostered additional federal and private funding spawning a plethora of high value products. UCLA alone has brought to the public many valuable advances in healthcare including devices to correct brain aneurisms, the nicotine patch to control tobacco addiction, positron emission tomography (PET scanning), and new diagnostics for breast and prostate cancer. All of these examples were either directly or indirectly supported by NIH and the technology transfer process.

Unfortunately, however, these very successes have turned a spotlight onto the process which, in turn, has caused some to ask just how successful are we? Are we getting too rich from tax-payer supported research? Or perhaps we are wasting this resource and not realizing adequate return on investment.

While oversight and monitoring of federally supported programs is clearly appropriate and desirable, some of the criticisms appear to be founded on misunderstandings of the process and the drivers that motivate its participants.

In my view, there are three myths that underlie most of the criticism of the technology transfer process. They can be briefly summarized as:

(i) Technology transfer is a simple linear activity from "bench to bedside;"

(ii) Money is a sound measure of performance and value; and

(iii) Universities commercialize their inventions to create wealth for themselves.

I will now amplify each of these myths.

MYTH #1: TECHNOLOGY TRANSFER IS A LINEAR ACTIVITY

Previous speakers have provided definitions of the term "technology transfer." Many people who are not familiar with technology transfer conjure in their minds a somewhat linear activity, whereby federally funded research in the university results in a new discovery. Then driven by the Bayh-Dole Act, the university technology transfer office: reviews the invention for commercial viability; elects title; files a patent; markets it to industry; negotiates a license; and the product, perhaps a new therapy for a major disease, goes to market. In other words, an academic researcher discovers a new drug and soon afterwards it shows up in the pharmacy.

Like many other things, this process is not as simple as that. In observing that gravity could bend light waves, Einstein showed nearly a century ago that the shortest distance between two points is not a straight line but a curve. Thus, we too should imagine a technology transfer process that is not linear, but rather one whose beginnings and endings merge to form a circle. For example, while public funding supports discovery, the early stage inventions made in the basic science laboratory of a university frequently attract support from the private sector. Collaborations with industry that follow may then lead to the building of new products on the knowledge and platform technologies made by the university scientist. Industry turns these

through lengthy development cycles over many years into products. Most product candidates wither along the way; few make it through development and testing to the market. Product sales generate profits and wealth, some of which is returned through taxation to restore the federal coffers. In addition, through sponsored research and philanthropy, industry reinvests some of this wealth into new research. Sometimes new discoveries become the platform for the creation of new companies that bring new jobs to our communities and sustain economic development through taxes. Royalties paid to the university are shared with the inventor and the university portion is used to sustain the technology transfer process, build new research infrastructure, and support new discovery programs.

In fiscal year 2002, 973 new inventions were reported to University of California technology transfer offices adding to a total invention portfolio of more than 5,000 active cases. On receipt of a new invention disclosure, the first task for the technology transfer office (TTO) is to determine what funding sources were used to support the research yielding the new discovery. This is done to establish whether prior rights may be attached to the invention based on commitments to the funding source. If supported with any NIH grants or contracts (or any other federal agency), the invention will fall under the conditions of the Bayh-Dole Act requiring that we report the invention and decide whether or not to elect title and file for intellectual property protection through the US Patent and Trademark Office. To arrive at this decision, the TTO must exercise professional judgment based on a scientific, technical and business assessment to determine the commercial viability of the invention. Is it a profound scientific breakthrough with no commercial utility? Is it perhaps, simply a better mousetrap for which there is no market need? Or perhaps it is so new, that there are no comparable products in the market. The point being that technology transfer is not a straightforward process in which research by NIH always generates inventions with an obvious value in the marketplace. A certain medical school dean once asked me why we didn't only patent "the good ones." Because many University inventions

are so unrefined and untested, it is difficult to determine with certainty the future path for the majority of the inventions that faculty researchers disclose. Illustrative of the process is the oft used axiom of the princess kissing frogs in search of a prince.

Once the patent application is filed, the TTO sets about marketing the invention to appropriate industry partners in the hope of finding one willing to develop the invention into a product under a suitable contract or license. Frequently, the inventions themselves are valuable not as an actual saleable product, but as a technology that will assist the corporate partner in developing their own products. A common example arising from NIH-funded research might be the discovery of a new cellular component that is responsible for triggering cancer growth. It may be possible to gain a patent on the discovery of this protein and on its use as a target for drugs that might inhibit its function and stop cancer cells from spreading. The drug, in this example, would be developed exclusively by the company. However, they might need a license to the original invention and access to the knowledge and skill of the university inventor in order to develop their commercial product effectively.

Having found a company interested in licensing the invention, the TTO negotiates a license that establishes the obligations of the licensee to develop the invention diligently at its expense and to pay fees and royalties against future product sales in return for the license to make, use and/or sell the invention.

The "frog-prince analogy" is a good one as there is an enormous winnowing effect with very few discoveries getting through this process and reaching the marketplace. On average, the University of Califomia files new patent applications on 45-50% of the new inventions disclosed each year. Approximately 30% of these will issue as US patents, and less than half of those will

ever be licensed. To recap, of the 973 new discoveries received in 2002, only 5% will be licensed. Many of these will fail to reach the market.

To close the loop on this circular process, however, it should be stressed that the discovery is often the beginning of a new process. Exposure to the researcher and his or her invention by the company frequently generates a new interest that results in the company becoming a private sponsor of a new research program in the inventor's laboratory. In addition, under those rare circumstances where a highly commercial invention does yield a successful product in the marketplace, income earned from royalties by the University is reinvested into research, and the companies tax obligations result in sources of revenue to fund future agency research appropriations, thereby completing the circle.

From this discussion, the Subcommittee will I hope appreciate the complexity of technology transfer and the relative difficulty of moving inventions from bench to bedside.

MYTH #2: MONEY IS A SOUND MEASURE OF PERFORMANCE AND VALUE

For the external observer, it is tempting and easy to measure technology transfer by the amount of money it yields. For any given University, this would mean examining the annual gross revenues derived from licensing its inventions. The technology transfer circle is like a catherine wheel, a firework (popular in Great Britain) consisting of a disk with rockets equally spaced around its perimeter. When lit, it spins at high speed and showers energy and light in a broad circumference. Indeed, some licenses generate income, but the research enterprise yields so much more. In reality technology transfer includes the training and graduation of students who move into the world as trained scientists and professionals. Knowledge is created and shared through publication and presentation. Faculty scientists serve as consultants and advisors to

the public and private sectors. While some inventions must be patented to ensure commercial interest and value, not all discoveries benefit society through licensing and commercialization. Counting dollars to quantify technology transfer ignores these other sometimes more valuable benefits that accrue from federally supported research activities in the University.

A letter from Carl Feldbaum, President of the Biotechnology Industry Organization, dated June 11, 2001 to Dr. Maria Friere, then Director of Technology Transfer at NIH, succinctly and thoroughly lists the varied and significant returns on investment that accrue to the public from NIH-sponsored research. These include basic science knowledge and understanding; the development of new therapeutics and diagnostics; scientific training that provides employees for a rapidly growing new biotechnology industry; research tools to advance scientific research; and the licensing of new inventions from both intramural and extramurally-funded research.

Furthermore, a quantitative performance assessment is predicated on the assumption that more money means greater societal value. Is a University that makes many millions of dollars from an improvement in cell phone technology necessarily more successful at technology transfer than one that develops a cure for a rare disease that may yield less than one hundred thousand dollars?

Critics of academic technology transfer who focus on the revenue streams derived from licensing often erroneously contend that universities should not get rich from exploiting tax payer's funds. Simply put, universities do not "get rich" from their technology transfer activities. The University of California, widely held to be one of the most successful university systems in the field of technology transfer averages an annual gross income from licensing of approximately $80 million. After payment of legal expenses, the cost of providing technology transfer services, and the inventor's share, $20-25 million is returned to the system to support

ongoing research. This amount represents less than one percent of the total research expenditures of the UC system. The annual survey published by the Association of University Technology Managers (AUTM) shows that fewer than ten universities generated more than $20 million in gross revenues in FY2002. In virtually all cases, this was because each had a single invention that yielded the majority of the income. At the University of California, 25 inventions from its total active portfolio of 5,000 produced 68% of its annual income.

Similarly, few individual inventors receive significant funds from their inventions. Since most inventions yield less than $10,000 in gross royalties per year, few faculty inventors realize any significant gains from the 35% revenue share that must be split with their co-inventors.

It has also been argued by some that royalty bearing licenses of federally funded discoveries contribute to unreasonable pricing of "blockbuster" drugs. While it has been clearly documented that few if any of these drugs arose directly from federally funded research, it has been unequivocally demonstrated that drug pricing is determined by the high cost of development and testing required before a drug can be sold, and that royalty obligations have negligible effect on market price of these treatments.

Paradoxically, NIH was recently criticized for not charging a high enough royalty for technology it developed that was part of a major drug now marketed by Bristol-Myers Squibb.

Therefore, measuring technology transfer accomplishments by the amount of money an invention generates for the university or the inventors fails to capture the broader benefits to the public that accrue from NIH-funded research and the larger research enterprise.

MYTH #3: UNIVERSITIES COMMERCIALIZE THEIR INVENTIONS TO CREATE WEALTH FOR THEMSELVES

Focusing on the income derived from licensing for one moment, an experienced businessman would conclude that based upon return on investment ratios, University technology transfer is largely unsuccessful. A quick search of the Patent Office database shows that the Regents of the University of California have been awarded 4,313 US patents since 1975. That's more than Pfizer, Inc., (2,774) and less than Merck (6,346). While the University may thus be in the same league as certain Fortune 100 companies, there are fundamental difference in its commercialization strategies. For profit companies focus their research in market segments in which they do business. Typically, they support internal research and development for the purpose of expanding their targeted strategic business interests. Universities not only attempt to broaden their research enterprise across all disciplines, they do not direct the research objectives of their faculty. Another particularly critical point is that the university relies on their own faculty to decide whether or not to publish their findings or to seek a proprietary position on their discoveries before they are more broadly disseminated. Protecting the right of its faculty to select topics on which they conduct their research and to publish whatever and whenever they see fit are among the basic tenets of academic freedom. Consequently, university inventions that may have great potential value do sometimes find their way in to the public domain for all to use without the exclusionary protection of a patent. If universities were to run technology transfer as a business, we would behave very differently.

The mission of the research university is education, the pursuit of knowledge, and public service. Basic academic studies of bacteria in hot springs in far away places may seem eclectic to some. But imagine how a drug for cancer would have been discovered by a major multinational pharmaceutical company had it not been for laboratory processes that use

enzymes isolated from these very bacteria to manipulate genes to produce the drugs that now treat patients.

The primary purpose of technology transfer in a research university is to provide a supportive and sustained environment for the researcher to flourish. Licensing generates corporate collaborations building partnerships with industry. Companies have resources that Universities cannot afford that academic scientists need access to for their research. Some inventions will stall without corporate involvement. Many potential life science-based discoveries need the formulation, manufacturing, testing and marketing skills of corporations to turn them from an academic discovery to one that can be dispensed from the pharmacy. As indicated above, revenues from technology licensing represent less than one percent of our total research budget and a fraction of a percentage point of total operations. Given the cost of technology transfer and the relatively low cash returns, this is an ineffective source of operating capital and the University does not view its purpose to be one of budget supplementation.

Universities measure their success by their contribution to the spinning catherine wheel. Not only how many inventions has it yielded, and how many have made it into the market to provide benefit to the public, but also how many graduates has it prepared for the world. State universities support and contribute to local economic development. Growth of its research enterprise creates jobs in the university itself. Sometimes it generates new ventures that grow in to new companies. The leading biotech companies like Amgen and Genentech all grew from academic origins. At the University of California alone, more than 200 new companies have been spun out based on new technologies invented by its faculty in recent years.

CONCLUSION

In supporting the Bayh-Dole Act and our role in technology transfer, universities are faced with a conundrum. On one-hand, some believe that we are getting rich using tax payers' support through federal grants from NIH and other agencies. Conversely, some argue that we should derive a greater financial return on investment and criticize us for being incompetent and wasting federal or public funds.

The reality, however, is revealed when one measures the broader value and benefits that emanate from the university academic enterprise – namely the fundamental advances in knowledge and technology arising directly and indirectly from the creative efforts of hundreds of thousands of expert academic scientists and their students. The enablement of new products that have changed our world, especially in the form of improved understanding of disease, of accurate diagnostics, and effective therapeutics that allow the dying to live and improve the quality of life of so many.

What would the world be like today without our knowledge of the human genetic code; recombinant DNA tools to splice and correct genes; ways to map and fingerprint DNA to convict the guilty and let the innocent free? All of these technologies together with vaccines and new drugs began in universities that were financed in whole or in part with federal funds through the NIH. Imagine a world where our collective expertise that has been built over the past 20 years to bring these and other innovations forward is eroded and impeded by changing the law because a minority feel it's not working – a feeling founded on a lack of knowledge and understanding of the complexity of the task.

The alliance with NIH is working. Guidelines developed and promulgated by the agency encourage the broad dissemination of research tools developed in universities that can facilitate

new research discoveries. Giving Universities the opportunity and the right to manage their inventions assures that they will be transferred diligently and effectively in a manner beyond the capabilities and resources of the agency if it were to carry this responsibility alone.

Mr. Chairman, Subcommittee Members, it is my fervent belief that this alliance between the NIH, the universities and the industrial sector is working well. We must preserve it, but we must also continue to strive to enhance its effectiveness, and to ensure that arbitrary impediments are removed for the sake of the public and this Nation. With a greater knowledge and understanding of the technology transfer process and the accomplishments of NIH and their academic partners, you will play a key role in protecting these beneficial outcomes.

Thank you very much for the opportunity to testify before you today.

Volume 78 Number 8 25 April 2000

EDITORIAL

Drug research: A growing gap

The costs of developing a new drug keep escalating as the research behind the discovery of every new candidate molecule becomes ever more sophisticated and the regulatory process becomes more stringent and long drawn out. An estimate made some years ago suggested that it costs as much as 500 million dollars (Rs 2000 crores) to develop a single successful product. There are lower estimates, but these would only scale down the cost by a factor of two, at best. The costs, of course, include the expenses of following many false trails. In order to keep ahead of the competition multinational pharmaceutical companies need to make huge investments in research and development; an imperative that has catalyzed many mergers in the drug industry. The marriage of Glaxo Wellcome and Smith Kline Beecham has created a behemoth, with an estimated revenue last year of $23.6 billion and an annual R&D expenditure of about $3.7 billion. But, if these figures look large, the Pfizer–Warner Lambert alliance seems to have created a competitor for the position of champion R&D spender; with the research budget of $4 billion from a total revenue of $29.1 billion. (To help readers, who like this writer find conversions difficult, 1 billion dollars translates to approximately Rs 4000 crores.) In analysing the spate of mergers a recent article sums up succinctly: 'being the biggest kid on the block has become the hottest game in town' (B. Agnew, *Science*, 2000, **287**, 1952).

But why is research aimed at new drug development becoming so expensive. After all Alexander Fleming discovered the antibacterial properties of mold secretions serendipitously; although it did take a few years and the skills of Ernest Chain and Howard Florey, spurred on by the exigencies of wartime, to produce penicillin in the 1940s. Did not Edward Jenner produce the almost magical smallpox vaccine based solely on his keen observation of the resistance of milkmaids exposed to cowpox? Was not Pasteur's rabies vaccine discovered with little investment? Is it not a fact that aspirin, so widely used today, has had many of its beneficial effects discovered accidentally over the course of a century of use? Unfortunately in modern times the process of drug discovery has become more complex, the criterion that must be met before human use has become extremely strict and the range of diseases for which therapeutics are sought has widened dramatically. The thalidomide tragedies of the 1960s provided a lesson that will not be forgotten. Today any new and promising molecule must pass through several phases of testing to detect toxic effects before approval for human use. These procedures cost both time and money.

An obvious corollary of the high cost of drug research is that companies will invest only in R&D activities, that ensure the highest returns if a successful product emerges. Research in the areas of diabetes, hypertension and cardiovascular disease, central nervous system disorders and the ailments of old age and cancer among others, may have the highest chances of a pay off, with large, anticipated markets in the developed world. In contrast, many 'Third World diseases' like malaria, filariasis, leishmaniasis ('kala azar') and a host of others may be poor targets for attack. Even if a successful therapeutic is developed, the possibilities of recovering the costs of R&D and turning a tidy profit are poor. Focusing on diseases which afflict a large population steeped in poverty can hardly be considered as a viable strategy for a pharmaceutical company driven by the imperatives of the market place. The recent resurgence of tuberculosis research in the West may be traced directly to the reemergence of the disease in the developed world, in the wake of immune suppression in AIDS victims. The emergence of drug-resistant strains adds a new dimension of urgency. The fight against the orphan diseases of the Third World has sometimes benefitted from the munificence of rich governments subsidizing the costs of private R&D and from a few acts of philanthropy by large companies; African river blindness and trypanosomiasis ('sleeping sickness') are two examples, where successful therapeutics have emerged from multinational R&D laboratories. But, it is unlikely that future struggles against the diseases specific to the Third World can rely exclusively on well-intentioned charity.

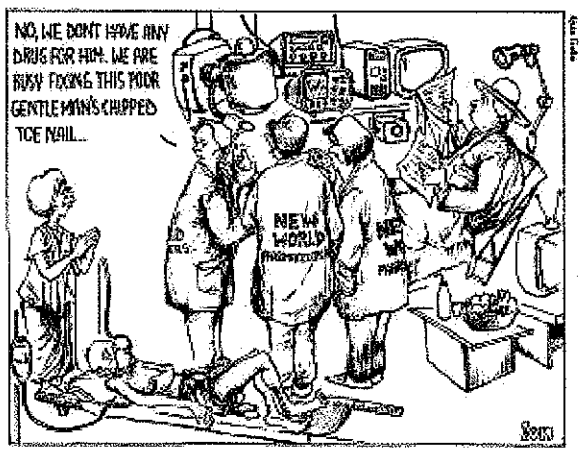
What is the situation in drug research in India? The pharmaceutical industry in this country has grown on two strengths; synthetic chemistry and chemical engineering. Clever process development has permitted the economical production of well-known drugs, under the umbrella of patent laws which do not allow protection of molecules; the process patent and not the product patent has allowed cheap, legal production of bulk pharmaceuticals. Understandably, multinational companies which invest hundreds

of millions of dollars on R&D have always felt cheated; but most often these companies have engineered abnormally high prices in their own native markets, pleading high costs of production. But the rules of the game are set to change soon, as the implementation of the TRIPS agreement will result in the protection of product patents in India. This sceptre has seen Indian pharmaceutical companies enhance their R&D spending; but no single company in India has the financial muscle power to even imagine competing with the multinationals. The pragmatic strategy appears to be the hope that R&D efforts can result in some leads, which can then be licensed to major international companies, which in turn will then underwrite the costs of future development. The Third World's basket of diseases are unlikely to attract much support in this scenario.

As in most other spheres, thus far the Government has been the major supporter of research in the area of drug development. Several national laboratories and academic institutions have ongoing programs in this broad area; the Central Drug Research Institute, Lucknow serving as the flagship of this enterprise. But, as in other areas, the sheer pace of advance in biomedical research has left Indian institutions completely in the lurch. From a field which relied predominantly on chemistry, pharmacology and clinical sciences, contemporary drug research requires major inputs from fast moving fields like genomics, structural, molecular and cellular biology, which constitute the fundamental core of modern biotechnology. The rapidly developing methodologies of combinatorial chemistry and high throughput screening, which are at the heart of the new paradigm of 'irrational drug discovery' are still largely unknown and unpractised in India. The level of technological accomplishment in the laboratories is primitive, handicapped as we are by a lack of resources and more importantly, manpower of the right kind. The cutting edge of drug discovery research is a confluence of several disciplines, which bud off from the major streams of chemistry, biology, physics and computer science. This interdisciplinarity poses many problems, in an environment where boundaries between departments are drawn in immovable stone. Modern drug research also requires an organized effort; an orchestrated team game in which individual interests may prove subservient to a larger goal. Paul Ehrlich knew what he was talking about when he said: 'Laboratory work is child's play in comparison; either a thing will go or it will not, and that is the end of it. But if you have to depend on hundreds of collaborators, and each of them believes that he can do better than any other, life really can be made rather difficult and bitter'.

Our successes in other 'mission mode' projects in the strategic R&D arena are sometimes held as models for the conduct of organized research, directed from the top. But it must be remembered that the committment of resources and organizations to these programs have been substantial and the technical goals clearly defined. The construction of an atomic bomb or even the vastly more useful communications satellite require the implementation of tested designs and procedures. The true 'intellectual property' is already available. In the area of drug research the identification of targets and the methodology for attacking the enemy are much less well defined. There are also no visible institutions and personalities to champion major initiatives in this area. But the fact remains that we need to effectively combat the many threats to human health, particularly infectious disease caused by microbial pathogens in our surroundings. Some years ago Daniel Koshland, then editor of *Science*, highlighted the problem by emphasizing the fact that 'because of the capacity of microbes to adapt to new circumstances there will probably be a continuing battle for many years, a subterranean war in which complacency and lack of determination can result in pain and death' (*Science*, 1992, **257**, 1021). There are many wars to be fought in the quest for the new therapeutics of the future. It is time that our agencies and institutions recognize the magnitude of the problem and the all-too-obvious limitations of our laboratories.

P. Balaram



Plenary Thurs.

The Enactment of Bayh–Dole

Ashley J. Stevens

ABSTRACT. The Bayh–Dole Act of 1980 reversed 35 years of public policy and gave universities and small businesses the unfettered right to own inventions that resulted from federally funded research. The Act was opposed by the Carter administration, which had a different view of how to utilize the results of federally funded research to drive economic development. It is not widely appreciated that the bill had died in the regular sessions of the 96th Congress and was only passed into law in a lame duck session necessitated to pass the budget. Only a magnanimous gesture of respect for Senator Birch Bayh, who had been defeated in the 1980 election, on the part of Senator Russell Long allowed the bill to receive the unanimous consent needed to pass a bill in lame duck session. This article lays out the roles of the key congressional staffers who forged this historic compromise and the last minute maneuvers needed to obtain President Carter's signature.

JEL Classification: O, O3, O31, O32

A recent article in the *Economist* (2002) said:

> Possibly the most inspired piece of legislation to be enacted in America over the past half-century was the Bayh–Dole act of 1980.

It is unlikely that anyone in the technology transfer community would dispute this statement, and foreign countries are now adopting the Bayh–Dole model, most recently Germany and, in the United Kingdom, Cambridge University, because they want to replicate the high technology-led economic development that Bayh–Dole is generally credited with having helped create. In the United States, however, a small number within academia and on Capitol Hill have expressed concerns about some of the consequences of Bayh–Dole, discounted its impact and advocated reforms of some of its provisions (Nelson et al., 2001).

Given Bayh–Dole's success, it is surprising that there is not more general awareness of how fragile the coalition was that passed Bayh–Dole and indeed that it almost didn't get passed at all. Bayh–Dole was passed in a lame duck session of Congress thanks to an incredible example of Senatorial courtesy and barely survived a pocket veto by Jimmy Carter, who signed it into law on the last day possible.

Joseph Allen, currently the President of the National Technology Transfer Center in Wheeling, West Virginia was at the center of the drama. In 1974, Joe was 24 years old and got his first job on Capitol Hill on the staff of Senator John Tunney (D., CA). Tunney was defeated in the 1976 election and Senator Birch Bayh (D., IN) took over Tunney's Subcommittee of the Senate Judiciary Committee. Allen joined Bayh's Subcommittee staff.

Coming out of World War II, the United States was unchallenged in its political and economic leadership of the free world. However, by the end of the 1970s it was clear that U.S. industry had lost its international competitiveness to Europe and, particularly, to Japan. This process had started with the success of the U.S. programs to rebuild its Allies and former enemies and was completed by the impact of the oil shocks of the 1960s and 1970s on an economy dependent on cheap domestic energy. Examples of the loss of competitiveness abounded, from the loss of U.S. leadership in both mature industries, such as automobiles and televisions, and emerging industries, such as memory chips, and the creation of new industries dominated by Japanese companies but based on American and European innovations, such as VCR's and compact discs.

Stock market indices vividly quantify the swings in relative economic power. On August 6, 1957,

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Introducing the Bill to the Senate on September 13, 1978, Birch Bayh said:

> A wealth of scientific talent at American colleges and universities—talent responsible for the development of numerous innovative scientific breakthroughs each year—is going to waste as a result of bureaucratic red tape and illogical government regulations...
>
> The problem, very simply, is the present policy followed by most government agencies of retaining patent rights to inventions.
>
> Government sponsored research is often basic rather than applied research. Therefore, many of the resulting inventions are at a very embryonic stage of development and require substantial expenditures before they actually become a product or applied system of benefit to the public.
>
> It is not government's responsibility—or indeed, the right of government—to assume the commercialization function. Unless private industry has the protection of some exclusive use under patent or license agreements, they cannot afford the risk of commercialization expenditures. As a result, many new developments resulting from government research are left idle.

The bill was circulated for support and comments so that it could be rapidly re-introduced when Congress re-convened in 1979 for the 96th Congress.

Bayh and Dole reintroduced the bill in 1979 as S. 414, the Bayh–Dole Bill, titled "The University and Small Business Patent Procedures Act". A significant change from the earlier Dole–Bayh Bill was the addition of provisions for licensing Government-owned patents.

On April 8, 1979, the *Washington Post* published an article on the bill, highlighting the shameful treatment of Norman Latker, who had been fired by Joseph Califano, Secretary of HEW, for his work on establishing Institutional Patent Agreements which the Carter administration vigorously opposed. Several of the universities that had benefited from Institutional Patent Agreements—in particular Wisconsin and Purdue—rallied to Latker's defense. They met with Allen and asked him to get Bayh and Dole to intervene on Latker's behalf, which the Senators did, publicly. Latker was reinstated.

Two days of hearings on the bill were held on May 16 and June 6, 1979, before the Senate Judiciary Committee, pitting two heavyweight witnesses on opposite sides of the argument. Arguing the case for Bayh–Dole was Elmer Staats, Comptroller of the United States. He testified to the failure of non-exclusive licensing to stimulate investment in early stage inventions. Howard Bremer talked about WARF's experiences. He said:

> Prior to the effective date of the IPA, December 1, 1968, no invention made at the University of Wisconsin with funds from DHEW (Department of Health, Education and Welfare) had been licensed to industry—one invention not falling under the IPA was licensed after that date. Since December 1, 1968, the Wisconsin Alumni Research Foundation has received a total of 69 invention disclosures under the Institutional Patent Agreements, has filed 79 applications on 55 of these disclosures and has had 55 U.S. patents issued.
>
> A total of 20 licenses were issued under one or more of these patents and patent applications, of which 14 are still extant.

Arguing the case against Bayh–Dole was Admiral Hyman B. Rickover, famous as the "Father of the Nuclear Navy" and a close ally of Senator Russell Long, who had long been a vocal critic of private use of government patent rights. Rickover argued that he had been able to develop nuclear power systems for the navy without having had to give up property rights to the contractors. He said:

> In my opinion, government contractors—including small businesses and universities— should not be given title to inventions developed at government expense. That is the gist of my testimony. These inventions are paid for by the public and therefore should be available for any citizen to use or not as he sees fit.

It should be noted that in fact the Department of Defense routinely gave waivers to its contractors, which were invariably large companies, to allow them to retain title to patents. The bill's handlers tried to balance Rickover's views by having small businesses testify, pointing out that when they get government research contracts, the

> What sense does it make to spend billions of dollars each year on government-supported research and then prevent new developments from benefiting the American people because of dumb bureaucratic red tape?

However, trouble was brewing on the other side of the Capitol. The Carter Administration's bill, the Kastenmeier Bill (Robert Kastenmeier, D., WI) was passed out of the House Judiciary Committee as HR-6933. On September 24, 1980, Russell Long wrote to Bayh expressing his concerns about the big business aspects of HR-6933. On September 26 Bayh wrote back to Long promising to amend HR-6933 when it came to the Senate. However, time ran out and Congress adjourned for the 1980 elections with Bayh–Dole having no corresponding House counterpart that could lead, after a House-Senate conference, to a bill that the President could sign.

The 1980 elections produced one of the major changes in the course of American history. Ronald Reagan defeated Jimmy Carter and the Republicans won control of the Senate for the first time since the Truman Administration. Birch Bayh was defeated by Dan Quayle. Adlai Stevenson retired. Robert Kastenmeier barely won reelection. Legions of staffers would be out of work come January 15, 1981. Washington was turned upside down and all bets were off.

However, Congress had adjourned without passing the budget and had to return for a lame duck session, so there was one last opportunity to pass Bayh–Dole before one of its two named sponsors departed Capitol Hill forever. First Allen tried to add Bayh–Dole to several "must pass" House bills with the help of the Small Business Committee staff, but no suitable vehicle could be found. Then Bruce Lehman, who was on Kastenmeier's staff and who would one day become Commissioner of the U.S. Patent and Trademark Office, called Allen with a deal. The House Judiciary Committee, which Kastenmeier chaired, had passed out an Omnibus Patent Bill. Kastenmeier would add the provisions of Bayh–Dole to his bill in the House if Bayh would agree to accept the other parts of the House bill affecting the operations of the Patent and Trademark Office. Bayh had competing bills in the Senate on these provisions but Allen accepted the deal. The House then passed HR-6933 with Bayh–Dole inserted. However, to become law the identical legislation needed to be passed in the Senate before proceeding to the President for signature into law. Because of this quirk of history, the official record shows the legislative history of HR-6933 as the legislative history of Bayh–Dole, not the legislative history of S. 414, which could be problematic if a court is ever called on to divine what the intent of Congress was when it passed Bayh–Dole.

The rules of lame duck sessions are harsh. There is no time for debate, so bills can only be passed by unanimous consent and a single Senator can block a piece of legislation by simply placing a "hold" on the bill, meaning that they object to it being considered for passage. By now there were only a few days of the lame duck session left.

Allen's first concern was Russell Long who had been an implacable opponent of Bayh–Dole. He could now, by himself, kill the bill and, given the duration, extent and passion of Long's opposition, Allen was not optimistic. Wiley Jones, Long's staffer, met with Allen in the final days of the session and asked him two questions:

First he asked a question from Long: "Does Birch really want this?" Allen answered quite simply "Yes, he really wants it." The next question was more difficult. With Bayh defeated, Allen was also out of a job. If the bill was defeated in the current Congress, Allen could use his intimate knowledge of the issue to get hired by a returning Senator who would then reintroduce the bill in the next Senate. Jones asked Allen his own question, staffer to staffer, friend to friend, "Is this bill good for you, Joe, and do you really want it?" Allen didn't blink. "Yes, I really want it." "OK", said Jones, "As a farewell present to Birch, you've got it." The U.S. Senate is rightly proud of its tradition of Senatorial courtesy, and Long's willingness to yield on an issue on which he felt so strongly is a stunning example of this courtesy. It is hard to imagine an act of such Senatorial courtesy in the current climate in Congress.

Allen thought he was home free. However, on November 21, 1980, as the 96th Congress ground to a close, Allen found that Majority leader Robert Byrd's staff (D., WV) had received a hold on considering the bill from a Democratic Senator. The identity of the dissenter was not revealed to Allen, but he worked out that it had

through a network of federally funded technology development centers. In his Presidential Memorandum on Patent Policy of 1982, Reagan backed the Bayh–Dole approach. Whether this was the result of blind adherence to political philosophy, inspired government insight or simply the easier choice for a young administration fighting another oil price shock by avoiding the need to create a whole new bureaucracy will probably never be known.

Acknowledgments

This article is based on a talk given by Joseph Allen, President of the National Technology Transfer Center at the AUTM Directors' Forum in Naples, Florida in December 2002 and on an extensive interview with Joe at the 2003 AUTM Annual Meeting in Orlando, FL. I thank Joe for his time and for reviewing the draft of the manuscript to make sure that my slow longhand had kept up with his impassioned account of these events, a passion undiminished by the passage of 25 years. My thanks to Janine Anderson for proof reading the manuscript. I submit nothing for publication without her imprimatur.

References

'Innovation's Golden Goose' December 12th 2002 *The Economist* 'Technology Quarterly'.

See, for instance, Richard Nelson, 2001, 'Observations on the Post Bayh–Dole Rise of Patenting at American Universities,' *Journal of Technology Transfer* **26**, 13–19; Avital Bar-Shalom and Robert Cook-Deegan, 2002, 'Patents and Innovation in Cancer Therapies: Lessons from CellPro,' *Milbank Quarterly* **80** (4); and Derek Bok, 2003, in *Universities in the Market Place*, Princeton University Press, April.

Etzkovitz, H. 2002, 'MIT and the Rise of Entrepreneurial Science,' MIT Press, p. 119.

Increased Federal funding of R+D after WWII brought with it the ~~establishment of~~ a patchwork of agency patent different policies covering the ownership of inventions resulting from this funding. ~~Outside the Department of~~ In the civilian agencies, ~~Defense,~~ the policies were heavily weighted in favor of government ownership, ~~resulting in either dedication~~ to ~~the public or non-exclusive licensing of~~ the ~~government's patent rights.~~

By the 1960's, ~~it was clear to~~ the science management at the National Institute of Health began to question the ~~that their Department's title~~ government ownership policy ~~was~~ an impediment to industry development of ~~the~~ life science inventions ~~resulting from N.I.H. funding.~~

~~In 1963, Dr. Endicott, the Director of the National Cancer Institute vigorously pursued the Department until it amended its regulations to provide for industry ownership of new uses of industry compounds submitted to the Institute's cancer chemotherapy screen.~~

Dr. Endicott, the director of the NCI and Dr. Shannon, the director of N.I.H were vocal ~~and outspoken critics of the~~ HEW ~~Department~~ policy.

Dr. Shannon, the N.I.H. Director, emphasized before Congress that NIH's research effort was complementary to that of other elements of society and that it was in the best interests of the American people to assure that the various interests of the medical research community can interact and suggested that the Department's patent policy impeded this interaction.

The problem was dramatized by increasing numbers of invention ownership disputes involving inventions assigned to industrial developers by NIH grantee investigators without notice to NIH.

In the case of Gatorade, Dr. Cade of the University of Florida, frustrated by the Department's failure to timely respond to his request for patent rights to Gatorade, assigned the invention to Stokely-VanCamp, who thereafter sued the Department for clear title.

NIH took the lead IN licensing ownership of Gatorade from the U. of Fla.

~~Florida~~ under conditions which were later adopted in ~~the Department~~ HEW's ~~Institutional Patent Agreements~~ (IPA's) SPIN OUT and then later in the Bayh-Dole Act.

Earlier, in another notorious situation, Dr. Heidelburger and the University of Wisconsin, after being publicly accused by Sen. Long's staff of confiscating ownership of 5FU, a breakthrough cancer chemotherapy drug and licensing it to an industry developer, successfully convinced the Department that minimal government funds were involved in its conception.

Further, Dr. Guthrie, a Department grantee and the inventor of the then preferred test for PKU being marketed by an industrial developer under license, after being publicly pilloried by Sen. Long's staff for confiscating the invention, assigned ownership to the Department.

These ~~cases~~ disputes had a further chilling effect on industry involvement as they asserted that any amount of government funding touching an industry invention as it was argued that any could ~~result in a similar~~ claim of right by the Government.

~~Thereafter~~ In 1968, the G.A.O. ~~added~~ confirmed additional urgency to resolving the problem, by ~~reporting that due to Department Patent Policy~~ confirming that the HEW's policy impeded industry support inventions resulting from all of NIH's medicinal development of N.I.H. involvement chemistry grants could not find the necessary industry support to continue development of identified science inventions.

Finally, in 1969, ~~responding to these situations, the Department~~ Under pressure HEW changed its patent policy in 1969 by establishing and established a uniform institutional patent agreement policy that left ownership to grantee institutions who agreed to ~~staff~~ identifying a technology transfer manager office to manage and license these rights. ~~The~~ Under which conditions attached to these agreements reflected the

practices of Research Corporation and WARF. ~~The NSF followed with similar changes in 1972.~~

In 1974, ~~the newly established IPA holders~~ formed the Society of Patent Administrators to enhance outreach to industry so as to overcome industry's continuing resistance to development of government funded inventions because they were not made in the company's laboratories. (Ironically, this impediment was called the NIH or not-invented-here syndrome).

In that same year, members of the Society found their political legs by assisting in preventing the inclusion in legislation creating the Energy Research and Development Agency of a requirement for government ownership of inventions resulting from its funding.

By 1976, 75 IPA's had been ~~negotiated and~~ executed with institutions who received well over 50% of ~~the annual~~ DHEW extramural funding.

Also in 1976, Dr. Frederickson, the Director of NIH, agreed with the consent of other Federal research agencies to permit the University of California and Stanford to administer the Cohen-Boyer gene splicing patent under their IPA's. Stanford's non-exclusive licensing of Cohen-Boyer to dozens of commercial concerns sparked the start of the biotech industry.

Notwithstanding the clear record of increasing successful licensing by IPA holders, the Secretary of the DHEW, HHS, Calif. Agency instituted a 1977 "reassessment" of the Department IPA policy which stopped further invention processing on the ground that the introduction of new technology into the marketplace was escalating the price of healthcare which required Department oversight. Legislation was introduced in the Senate to provide the Department with this oversight authority at the same time.

Simultaneously, Sen. Nelson of Wisconsin initiated hearings to discuss the legality of IPA's HHS's

the GSA regulations expanding their use to all government agencies not otherwise covered by statute.

These actions served as the flashpoint for organizations having IPA's to pursue legislation to assure continuance of the 1969 Department policies and its further expansion to other federal agencies having conflicting policies. Led by the University of Wisconsin, Stanford University, the University of California, and Purdue, the IPA community were so successful in making their views know to the Congress that Bayh-Dole passed the Senate by a vote of 91-4.

Some suggest that the primary purpose for Bayh-Dole is the production of income for those that participate in the conception and delivery of inventions to the marketplace. I do not believe that was the primary intent of the Act's architects. Income, which was a distant possibility at the time of enactment, was viewed only as a collateral benefit of success. The Act is structured so as to assist

During these early years of the century, the services of Research Corporation and WARF were clearly limited by their resources. The majority of investigators were left to determine on their own whether to pursue moving their discoveries into practical life.

For example, in 1929, Fleming discovered the utility of penicillin, but unlike Pasteur or Ehrlich, made no identifiable effort to bring it into practice beyond its publication. Patent protection was not pursued.

Absent a champion, the benefits of penicillin languished until Florey and Chain devised a method to produce it economically in volume and, promoted by World War II, the Department of Agriculture began manufacture and distribution in 1941.

The huge increase in funding of research and development by the Federal agencies following World War

Time does not permit me to convey the intensity of the debate between the adversaries leading to the changes in policy in 1969 and passage of Bayh-Dole. However, I would note that the present day critics of Bayh-Dole have added nothing not considered at that time. Other than the monetary rewards, their unhappiness with

earned by the collaboration between inventors, their institution and industry in delivering discoveries to practical life which to my mind pales to what the public has gained,

successfully

reward

Institute as a clinic for rabies treatment, and a research center ~~for infectious disease and a teaching~~ center, with Pasteur as director, which is still following his ~~Today's Pasteur Institute continues its~~ research to bring its new discoveries into practical life, ~~research, funded in part through royalty returns from discoveries made in their laboratories.~~

~~Among the few examples of investigator driven application of their discoveries, the practices leading to the discovery and application of Salvarsan, the first cure for syphilis discovered by Paul Ehrlich comes closest to present day practice.~~

In 1906, ~~at~~ Paul Ehrlich ~~founding~~ was able to establish, the Georg-Speyer-Haus ~~Research~~ Institute for chemotherapy ~~was established with its own staff~~ with private funding, under Ehrlich's direction. ~~The Institute was an interdisciplinary institute formed to define problems to be attacked through exchange of ideas among biochemists, pharmacologists, clinicians and other scientists~~ interdisciplinary research of

~~own makeshift laboratory and then pursued its marketing through the incentive of his patent position. Edison's hundreds of patents helped fund the reduction to practice and the licensing of a flood of new every day products from his Menlo Park laboratory.~~

~~But as~~ the early and fundamental discoveries in the life sciences evolved, it became clear that the resources necessary to bring them to practical life exceeded what their investigator could provide through ~~their own effort.~~

In 1885, Pasteur saved a young boy with rabies in his laboratory. Patients flocked from all parts of the world but his office was too small to receive them all. The next year, before the Academy of Sciences, Pasteur declared that "There is a need for prophylactic measures against rabies. An anti-rabies vaccine should be created." This plea resulted in an extensive, international public subscription generating a fantastic burst of generosity that built the Pasteur

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March 24, 2004

VIA TELEFACSIMILE

Ashley J. Stevens
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Boston, MA 02215

Dear Ashley,

Thank you for your kind words. They act as an incentive to keep involved.

I have a growing concern about the populist attack on Bayh-Dole by dimwits like Ms. Rai. I'm attaching her latest pronouncement. Here again she fails to recognize that her "dedication" concept destroys the inventor's incentive to pursue involvement in moving to the marketplace.

I think it's important to document the 1970's debate leading to passage of the Act (notwithstanding my involvement) as it should act to put those suggesting inconsistent positions on the defensive.

At any rate, I would very much like to assist your efforts anytime you wish.

Best Regards,

Norman J. Latker

NJL:jab
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Subject: Norm FYI
From: "Latker, Carole (NIH/NIGMS)" <LATKERC@nigms.nih.gov>
Date: Wed, 24 Mar 2004 09:43:45 -0500
To: "Latkerc@bellatlantic.net" <Latkerc@bellatlantic.net>

THE WASHINGTON FAX
WEDNESDAY, MARCH 24, 2004

Open, collaborative research models can avoid intellectual property problems, Duke's Rai says

Biomedical research approaches modeled on the qualities of the open source software movement can avoid problems associated with having intellectual property rights on research products, such as increased transaction costs, Duke University Law School professor Arti Rai maintained at a Health Policy Forum hosted by Duke March 19.

The forum, co-hosted by Sen. Elizabeth Dole (R-N.C.) and Rep. David Price (D-N.C.), examined the impact of intellectual property rights on the innovation process. Rai discussed her research on the ways open, collaborative research production processes -- such as distributed genome database annotation efforts, the Human Genome Project, the Haplotype Map Project and the Alliance for Cell Signaling -- work in biomedical research.

Characteristics of these kinds of research approaches include promotion of free and immediate access to data and receiving contributions from a coordinated, decentralized network of researchers.

Rai explained the movement toward open and collaborative research efforts seems to be driven by the increasing prevalence and importance of computational biology, where work can be divided, completed remotely and integrated later, as well as systems biology, which requires multiple groups to tackle research problems too complex for a single laboratory.

Patents on biomedical research intellectual property often have been overly broad, the Duke professor said, creating a situation where innovation may be stifled by the hurdles of securing licenses to perform research in an area where patents are held.

Rai said her research has indicated the "open source" biomedical research approach is "promising" in some areas, asserting NIH efforts to encourage this type of research production should be supported.

She specifically mentioned the large-scale collaborative research project awards, known as "glue grants," in several NIH institutes, for example the National Institute of General Medical Sciences. The grants are intended to support collaborative activities and resources for groups of researchers working on the same complex biological problem.

Rai also mentioned the NIH policy requiring investigators seeking more than $500,000 in funding to include a plan for data dissemination in their application. A final rule on that policy was announced in February 2003, and it went into effect in October.

In addition to the argument that "open source" research models could avoid patent-related problems, Rai also commented the open, collaborative model would have other advantages, including increasing overall progress through enhanced research coordination.

Also speaking at the forum was fellow Duke Law School professor James Boyle, co-director of the university's Center for the Study of the Public Domain.

Boyle said the last 25 years have seen an "unparalleled expansion" in the scope of intellectual property rights, through both legislative and judicial action. While he asserted intellectual property systems are needed to promote innovation when set up in the correct way, Boyle presented a group of "mistaken beliefs" that are weakening the positive effects of the IP rights system.

For example, he warned against moving toward a situation where concepts such as business methods could be patented. The extension of IP rights into the realm of facts and ideas is "particularly worrisome" for science, Boyle noted. "The worst example of this is the increasing tendency to drive intellectual property rights down into the data layer -- the layer of facts," he said. Boyle cautioned against the wisdom of allowing patents on gene sequences and criticized current legislation aimed at protecting databases.

The Database and Collections of Information Misappropriations Act (H.R. 3261) is an "unparalleled assault on the idea that IP rights never descend into the realm of facts," Boyle said. The bill has been considered by the House Judiciary and Energy and Commerce Committees, but has not seen a floor vote. (see Washington Fax 11/26/03b)

The idea that additional property rights necessarily give rise to more prosperity also is false, Boyle said, explaining

too much protection of IP rights could lead to more difficult access to the "raw materials" of innovation -- "upstream" data and research tools. Striking a proper balance between enough IP rights to promote innovation, but not too many to stifle access to upstream tools, is critical, Boyle indicated.

-- Scott C. Jenkins

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March 23, 2004

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Norman Latker, Esq.
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Dear Norm

Thanks for your call this afternoon. I wish the answer had been the opposite, but the facts are the facts!

It was truly great seeing you at AUTM. You are looking GREAT! I had been meaning to write and follow up, so your call made me turn intentions into deed.

I'd like to come and visit with you sometime this summer, probably on a weekend (since this activity will have to remain a hobby as long as I need to maintain my gainful employment) and talk about a follow-up article on the administration role in Bayh-Dole and more specifically, to make sure that your role is fully documented and credited.

With every best wish,

In the attached article Ms. Bai makes the same mistake I pointed out at the San Antonio session)

At any rate I would very much like to assist your efforts any time you are able.

Dear Ashley

Thank you for the kind words, they act as an incentive to keep involved. I have a growing concern about the populist attack on Bayh-Dole by chemists like Ms. Bai (see attached) and believe it is very important to document the debate leading to the Act. It does [illegible] the opposition to address the arguments that resulted in the Act's passage.

Science
19 March 2004

INTELLECTUAL PROPERTY: NIH Roils Academe With Advice on Licensing DNA Patents

The National Institutes of Health urges universities not to strangle the goose laying the golden biotech eggs

SAN ANTONIO, TEXAS--When academic scientists Stanley Cohen and Herbert Boyer successfully spliced a functioning foreign gene into a bacterium in 1973, the discovery helped launch the biotechnology revolution--and ultimately produced a blockbuster patent that earned the inventors and their universities some $300 million. Since then, U.S. universities have patented more than 4500 DNA-based discoveries. Although few have paid off like Cohen and Boyer's, the patents have helped attract the type of massive private investments needed to move campus discoveries into the clinic.

Critics, however, argue that academia's eagerness to patent genomic inventions is having some negative side effects. Some campuses have licensed discoveries exclusively to a single company, for instance, reducing competition that might spur innovation and drive down prices. And some experts worry that a growing thicket of patent-related legal restrictions--especially on research tools--could strangle future biomedical research.

This month the National Institutes of Health (NIH) offered a proposal aimed at clearing out some of the patent undergrowth. But the draft guidelines, unveiled here at a meeting of university patent experts,* are being criticized as premature and based on anecdote rather than evidence. Meanwhile, academic researchers and the U.S. National Academies have launched studies of DNA-based patents intended to inform the debate. "There is often more rhetoric than data," says Robert Cook-Deegan, a policy specialist at Duke University in Durham, North Carolina.

Gene king. The University of California has patented more DNA discoveries than the government or any company has.
SOURCE: L. WALTERS/KENNEDY INSTITUTE OF ETHICS/GEORGETOWN UNIV.

NIH officials emphasize that their draft guidelines, labeled "best practices for the licensing of genomic inventions," is a work in progress. NIH technology transfer specialist Jack Spiegel advised the gathering of patent administrators that federally funded researchers should seek to patent DNA-based inventions only if the inventions will need "significant" private sector investment to become products. And any patented inventions should be licensed as widely as possible, with owners giving nonprofit researchers and public health agencies easy access. "An exclusive [licensing] arrangement may not be the most beneficial one for the public," the draft concludes.

Although the draft has not yet been circulated widely, university officials who have seen it say much of it is not controversial. "Many of us are already doing these things," says Thomas Ittelson, who handles technology transfer issues for the Massachusetts Institute of Technology's (MIT's) Whitehead Institute in Cambridge. For instance, making sure that licenses allow academics and public health agencies to freely use patented technologies has become standard practice at major institutions, he says. Still, he and others worry that NIH, although well-intentioned, may be moving too quickly. In particular, they are concerned that the guidelines could harden into regulations accompanying grants--as happened with earlier NIH guidance on licensing biomedical research tools.

Growth curve. The number of U.S. patents on DNA products took off in the 1990s.
SOURCE: L. WALTERS/KENNEDY INSTITUTE OF ETHICS/GEORGETOWN UNIV.

That could codify some language that troubles university officials. The draft suggests, for example, that exclusive licensing of gene-related patents is having "detrimental short-term and long-term effects on both the quantity and quality" of health care. University-based technology transfer officers contacted by

Science described that concept as "annoyingly half-baked ... overly simplistic." One wondered, "Where did that come from?" Several noted that small biotechnology companies often need to have exclusive rights to a nascent technology to raise sufficient venture capital. "The vibrancy of the biotechnology industry is dependent on these exclusive licenses," says Ittelson, adding that he "was dismayed that NIH would even think about drafting guidelines before we had all the facts."

NIH officials were somewhat surprised by the negative reaction. "I'm not sure we realized the impact that some of the language would have," says one. The draft had been circulating within the agency for months, the official said, and was intended to reflect NIH's own approach to patenting and licensing. The NIH officials reassured critics that they have no timetable for finalizing the guidelines and welcome all comments.

NIH is also sponsoring several studies aimed at providing new data on the scope and impact of university gene patents. One is a nine-scholar effort led by former MIT licensing specialist Lori Pressman, Cook-Deegan, and ethicist LeRoy Walters of Georgetown University in Washington, D.C. The team has begun to analyze the nearly 4400 DNA-based patents held by 30 top universities to determine what discoveries academia is patenting and how they are licensed. Some preliminary findings--including that very few of the patents have been licensed to more than 10 users and nearly one-third have never been licensed at all--may surprise some people, notes Walters. "The data may help us get past the anecdotes," he says. The project should be completed later this year.

In the meantime, Walters's team has been sharing some of its numbers with a new National Research Council panel on gene patents that began work earlier this month. Led by Princeton University President Shirley Tilghman, the panel aims to identify where intellectual property is either creating problems for genomic research or helping fuel new discoveries. It hopes that the result will inform all sides of the debate over how universities should handle DNA-based patents.

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Date: Monday, March 29, 2004 5:56PM
Subject: First Draft - Rebuttal of James Love's March-In Requests

I'm attaching a requested first draft of a rebuttal of James Love's march-in requests to DHHS which in most part is also a rebuttal of the Tulane Law Review article which serves as the basis for the requests. Any suggested changes would be welcome either orally or by e-mail.

Norm Latker

From: <jallen@nttc.edu>
To: "Robert Hardy" <rhardy@cogr.edu>
Date: 5/12/04 1:32PM
Subject: Re: Fwd: Six Reps. Sign letter to Barton on Norvir

Norm Latker is invited. Any idea who's on the other side?

"Robert Hardy" <rhardy@cogr.edu>
05/12/2004 12:08 PM

To
<jallen@nttc.edu>
cc

Subject
Re: Fwd: Six Reps. Sign letter to Barton on Norvir

Joe,

COGR and AAU are the only associations that were asked to testify, at least that's my understanding.

We will be represented by Andrew Neighbour, who's Associate Vice Chancellor for Research at UCLA, and Chair of our COGR IP Committee. I believe AAU may be represented by Ted Poler, who's VP for Research at Johns Hopkins.

Besides our speakers and Sen. Bayh, the only other speaker that I've heard is the Abbott rep.

Bob

>>> <jallen@nttc.edu> 05/12/04 11:50AM >>>
thanks, do you know if any of the university associations are speaking at the NIH meeting on May 25? In fact, do you have any idea who's speaking on the other side?

"Robert Hardy" <rhardy@cogr.edu>
05/12/2004 11:30 AM

To
<jallen@nttc.edu>
cc

Subject
Fwd: Six Reps. Sign letter to Barton on Norvir

Joe,

Here it is.

Bob

----- Message from "White, Pat" <pat_white@aau.edu> on Mon, 10 May 2004 18:37:09 -0400 -----
To:
"Harpel, Richard" <RHarpel@nasulgc.org>, "Jacob, Richard" <richard.jacob@yale.edu>, "Crowley, John C." <jcrowley@mit.edu>, "Lyon, Kamala" <kamala.lyon@ucdc.edu>, "Norsetter, Rhonda D." <norsetter@bascom.wisc.edu>, "Smith, Toby" <toby_smith@aau.edu>, "Vaughn, John" <john_vaughn@aau.edu>, "Casey, Kevin" <kevin_casey@harvard.edu>, "Lokken, Pamela" <lokken@hilltop.wustl.edu>, <rhardy@cogr.edu>, <jon.soderstrom@yale.edu>, "Ellen Smith" <ess9@columbia.edu>
cc:
"Steinbach, Sheldon E." <sheldon_steinbach@ace.nche.edu>, <Michael.Remington@dbr.com>
Subject:
Six Reps. Sign letter to Barton on Norvir
Colleagues:

Ellen Smith alerted me to the attached letter on the Essential Inventions website.

Patrick White
Director of Federal Relations
Association of American Universities
202-408-7500
pat_white@aau.edu

CC: <njl@browdyneimark.com>

Dr. Mark Rohrbaugh
Director of the Office of Technology Transfer
Office of Intramural Research
National Institutes of Health
6011 Executive Boulevard, Suite 325
Rockville, MD 20852

Dear Dr. Rohrbaugh:

The Association of American Universities is comprised of 60 of the leading research universities in the United States. We understand that the National Institutes of Health is currently considering two petitions to exercise the "march-in rights" provision of the Bayh-Dole Act.

March-in rights are retained by the government only as a means to ensure the prompt commercialization of inventions that result from federally-supported research and to prevent companies from slowing, for commercial or competitive advantage, the development of new inventions. Under Bayh-Dole, the government has neither rights nor a role in the licensing or commercialization of new technologies developed in whole or in part with federal research support—so long as that commercialization occurs.

To be sure, there are serious issues regarding the accessibility and affordability of pharmaceuticals, but appealing to the march-in right provision of the Bayh-Dole Act is a misapplication of the statute and would likely have serious unintended and adverse consequences for future therapeutic development. We respectfully request that NIH deny the pending petitions.

Sincerely,

Dear Dr. Rohrbaugh:

The Council on Governmental Relations (COGR) is an association of 150 of the leading research universities in the United States and several affiliated hospitals and research centers. COGR focuses on understanding federal policies and complying with federal regulations pertaining to sponsored research at universities. Among the most important policies and regulations of interest to our members are those pertaining to the transfer of federally funded research results at universities to the private sector under the Bayh-Dole Act of 1980 (P.L. 96—517; 35 USC 200--212).

The Bayh-Dole Act plays a critical role in enabling university innovations that have been crucial to U.S. economic growth and competitiveness. Bayh-Dole established the major mechanism for successfully transferring federally funded research results from the laboratory to products and services, which benefit all Americans. Bayh-Dole's success is derived from its consistency with America's commitment to free market principles and incentives.

Many studies have demonstrated the phenomenal success of the Bayh-Dole Act. For example, according to an article in the Dec. 12, 2002 *The Economist*, "The Bayh-Dole Act of 1980 is perhaps the most inspired piece of legislation to be enacted in America over the past half-century....this unlocked all the inventions and discoveries that have been made in laboratories throughout the United States with the help of taxpayers' money...." The Bayh-Dole Act plays a critical role in enabling university innovations that have been crucial to U.S. economic growth and competitiveness.

We understand that NIH has been asked to answer recently submitted petitions for exercise of march-in rights that, according to the authors of the legislation, Senators Birch Bayh and Robert Dole, are based on a fallacious premise. March-in rights accrue to the government only for the purpose of ensuring prompt commercialization of federally funded inventions and to avoid the possibility of companies stifling the development of new products. The legislation does not empower the government in any way to influence or to dictate licensing or commercialization terms for technologies. NIH itself has confirmed this interpretation (NIH Plan to Ensure Taxpayers' Interests are Protected, July 2001).

NIH may feel challenged to review its long-standing interpretation of the conditions under which the government may exercise march-in rights. Given the critical role played by the Bayh-Dole Act in the continuing success of university technology transfer, COGR believes that any proposed change to such a long-standing interpretation should be subjected to searching scrutiny. If this were to become necessary, all stakeholders in the continuing success of technology transfer from universities should participate fully in the consideration of the scope of government march-in rights to ensure that the public-private partnership in innovation is maintained.

COGR is concerned that a substantial reinterpretation of the Bayh-Dole's march-in

provisions could undermine the ability of universities to make their federally funded technologies available for public use. Any such change in march-in authority or in expanding their exercise by government agencies could result in the loss of the very delicate balance of rights and obligations between the three partners – government, universities and industry - which has been the basis for the success of this legislation. History has proven how important incentives are for encouraging technology transfer from the universities. It would be ironic, indeed, if a change in the current understanding of march-in rights were to impair the dissemination of, and public benefit from, university research results.

For these reasons, COGR urges the NIH to make a strong statement in support of the proper exercise of march-in rights as stated by Senators Bayh and Dole, which was recently reconfirmed in their letter dated April 11, 2002 in the Washington Post. NIH surely is aware of the importance of the Bayh-Dole Act to public-private partnerships in innovation. We see no reason to tamper with this proven platform for promoting government investment in discovery and its application for public use and benefit.

Sincerely,

April 8, 2004

17015/063598
DC\401969\1

Dr. Mark Rohrbaugh
Director of the Office of Technology Transfer
Office of Intramural Research
National Institutes of Health
6011 Executive Boulevard, Suite 325
Rockville, MD 20852

Dear Dr. Rohrbaugh:

On behalf of the American Council on Education ("ACE") and the National Association of State Universities and Land-Grant Colleges ("NASULGC"), two of this country's leading associations of institutions of higher education, we are writing to share our views about a petition filed by Essential Inventions, Inc. (Mr. James Love, President) ("Essential Inventions") to exercise Bayh-Dole march-in rights to require Abbott Laboratories to lower the price of several drugs developed from NIH extramural research. Essential Inventions, a non-profit organized under the laws of the District of Columbia, is organized to "promote the creation and distribution of essential inventions and other works that support public health, nutrition, learning, and access to information and cultured life. See <http://www.essentialinventions.org>.

The petition is rooted in the proposition that march-in rights can be exercised to maintain the accessibility and affordability of an essential medical invention. Neither the plain meaning nor the public policies that undergird the Bayh-Dole Act permit a march-in based on affordability. March-in is not a surrogate for government price controls on products that result wholly or in part from federally-funding. March-in is reserved only for the purpose of prompt commercialization of federally-funded inventions and to avoid the possibility of the stifling of new product development.

The subject of delivering affordable health care to the American public is a serious one, worthy of policy debate, which is ongoing in the Congress in the context of Medicare reform and drug reimportation. Debate about the quality and accessibility of health care is especially worthwhile when life-saving drugs involving potentially fatal diseases, such as HIV-AIDS, are involved. However, the Bayh-Dole Act is not the proper forum for this debate. The Act does not confer regulatory authority on the NIH to impose price controls either globally or on a case-by-case basis. Nor should the Patent Act, in which the Bayh-Dole Act resides, be used as a compulsory mechanism for reasonable drug pricing.

Stated differently, the public policy debate is one worthy of attention. But, the solution is not a regulatory one within the NIH.

If, per chance, the NIH were to interpret its authority so as to exercise march-in, the Bayh-Dole Act, one of this country's most successful statutes, would be subjected to a litany of

unintended consequences. The willingness of universities to request federal funding for research activities could be chilled. The ability of universities to make their federally-funded technologies available for public use might be questioned. The necessity for universities to transfer technology to the private sector for commercial exploitation might be affected. In the final analysis, the equilibrium between federal funding, university research and private sector exploitation might be disturbed.

In short, the Bayh-Dole Act has become a driving force for successful research activities. The U.S. economy and the American public have benefited. Any administrative action taken by the NIH must recognize the success of the Act and its limitations as a price-control mechanism. We trust that you will do so.

Sincerely yours,

Sheldon E. Steinbach
American Council on Education

Richard Harpel
National Association of State
Universities and Land-Grant Colleges

17015/063598
DC\401969\1

April 22, 2004

Dr. Mark Rohrbaugh
Director of the Office of Technology Transfer
Office of Intramural Research
National Institutes of Health
6011 Executive Boulevard, Suite 325
Rockville, MD 20852

Dear Dr. Rohrbaugh:

On behalf of the National Association of State Universities and Land-Grant Colleges ("NASULGC"), the Association of American Universities (AAU), and the American Council on Education ("ACE"), we are writing to share our views about the two petitions filed with the National Institutes of Health (NIH) to exercise Bayh-Dole march-in rights to require Abbott Laboratories to lower the price of several drugs developed from NIH extramural research.

The petitions are rooted in the proposition that march-in rights can be exercised to maintain the accessibility and affordability of an essential medical invention. Neither the plain meaning nor the public policies that undergird the Bayh-Dole Act permit a march-in based on affordability. March-in is not a surrogate for government price controls on products that result wholly or in part from federal funding. March-in is reserved only for the purpose of prompt commercialization of federally funded inventions and to avoid the possibility of the stifling of new product development.

The subject of delivering affordable health care to the American public is a serious one, worthy of policy debate; it is ongoing in Congress in the context of Medicare reform and drug reimportation. Debate about the quality and accessibility of health care is especially worthwhile when life-saving drugs involving potentially fatal diseases, such as HIV-AIDS, are involved. But, the Bayh-Dole Act is not the proper forum for this debate. The Act does not confer regulatory authority on the NIH to impose price controls either globally or on a case-by-case basis. Nor should the Patent Act, in which the Bayh-Dole Act resides, be used as a compulsory mechanism for reasonable drug pricing.

If the NIH were to interpret its authority so as to exercise march-in rights, we are deeply concerned that the Bayh-Dole Act, one of this country's most successful statutes, could be subjected to a litany of unintended consequences. The ability of universities to make their federally funded technologies available for public benefit would be undermined, and the incentive for the private sector to invest in federally funded discoveries would be removed. In the final analysis, the synergy between federal funding, university research and the private sector

for product development could be lost.

Dr. Rohrbaugh
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April 22, 2004

In short, the Bayh-Dole Act has become a driving force for successful research activities from which the U.S. economy and the American public have benefited. Any administrative action taken by the NIH must recognize the success of the Act and its limitations as a price-control mechanism.

Cordially,

C. Peter Magrath
President, NASULGC

Nils Hasselmo
President, AAU

David Ward
President, ACE

CPM/rh