Statement of

E. Jonathan Soderstrom, Ph.D.

Before the

House Energy and Commerce Committee
Subcommittee on Health

On

"National Institutes of Health: Moving Research from the Bench to the Bedside"

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Mr. Chairman, thank you for the opportunity to testify before your Subcommittee on the important topic of translating research from the bench to the bedside.

My name is Jon Soderstrom. I am the Managing Director of the Office of Cooperative Research (OCR) at Yale University. The Office of Cooperative Research is the patent management organization for Yale University. I also serve as the Vice President for Public Policy the Association of University Technology Managers known as AUTM. AUTM is a nonprofit organization created to function as a professional and educational society for academic technology transfer professionals involved with the management of intellectual property. AUTM was founded in 1974 as the Society of University Patent Administrators. That group laid the foundation for the association that exists today - more than 3,000 members strong representing over 1,500 institutions and companies across the globe. Neither Yale nor AUTM have received any federal grants, or engaged in any federal contracts or subcontracts that require reporting under House rules.

Translating University Inventions into Commercial Products

In the course of fulfilling our research and educational missions, university faculty often create intellectual assets that have the potential to benefit society and further the university's educational goals. These assets may include patentable inventions, copyrightable works or ideas that form the basis for commercializable intellectual property. As they initially emerge from the university's laboratories, these inventions are not mature commercial products. Rather, they require significant investment of time, energy and financial resources to unlock their potential.

This process is best realized through a strategy of attracting commercial sector involvement. Under the protection of a license agreement, companies can confidently invest in transforming these intangible assets into tangible products. Prior to the enactment of the Bayh-Dole Act (P.L. 96-517), the "Patent and Trademark Act Amendments of 1980" on December 12, 1980, companies faced significant hurdles in negotiating such agreements with universities.

The Bayh-Dole Act created a uniform patent policy among the many federal agencies that fund research. The Act enables small businesses and nonprofit organizations, including universities, to retain ownership of inventions resulting from federally funded research and to manage the licensing of them to industry for commercial product development in the public interest. Prior to the Act, ownership of patents resulting from university discoveries was largely controlled by the federal agencies that sponsored the research. Because the Government lacked the resources and links with industry needed for development and marketing of the inventions, hundreds of valuable patents were sitting unused on the shelf. Government policy at that time was generally to offer non- exclusive licenses under all inventions that it owned – a licensing stance administered under some 24-26 different non-uniform agency policies, which proved to be highly unsuccessful. Under these conditions, U.S. industry was not inclined to brave government bureaucracy to license patents. Thus, technology transfer from universities was accomplished primarily by the publishing of research results, training of students for the workforce and some extension programs established by the land-grant universities. The benefit to U.S. industry of such an unstructured process is undocumented and highly speculative. As the authors of the Act, former Senators Birch Bayh and Robert Dole, recently noted[1]:

[1] Birch Bayh and Robert Dole, "Our Law Helps Patients Get New Drugs Sooner," Letter to the Editor, Washington Post, April 11, 2002; Page A28

> Government alone has never developed the new advances in medicines and technology that become commercial products. For that, our country relies on the private sector. The purpose of our act was to spur the interaction between public and private research so that patients would receive the benefits of innovative science sooner.

The ability to retain title to and license their inventions has been a healthy incentive for universities to become involved in transfer of technology from their laboratories to the marketplace. Such incentive is needed, since participation in patent and licensing activities is time consuming for faculty, and must be done in addition to our primary research and teaching missions. University patenting and licensing efforts under the Bayh-Dole Act have fostered the commercialization of many new technological advances that impact the lives of millions of people across the nation. Numerous pharmaceutical and medical products, environmentally friendlier manufacturing technologies, inventions which improve public safety, and information technology services have resulted from the transfer of federally supported research results from academic laboratories to the business community and, ultimately, consumers. In many instances, these products and processes would not have reached the public without the incentives and procedures afforded to higher education institutions by the Act. As a recent article in *The Economist* noted[2]:

> Possibly the most inspired piece of legislation to be enacted in America over the past half-century was the Bayh-Dole act of 1980. Together with amendments in 1984 and augmentation in 1986, this unlocked all the inventions and discoveries that had been made in laboratories throughout the United States with the help of taxpayers' money. More than anything, this single policy measure helped to reverse America's precipitous slide into industrial irrelevance.

[2] *The Economist*, "Innovation's golden goose," December 14, 2002

A recent national survey conducted by AUTM[3] reports that 70% of the active licenses of responding institutions are in the life sciences - yielding products and processes that diagnose disease, reduce pain and suffering, and save lives (Attachment 1: AUTM Licensing Survey, FY 2001). Most of these inventions involved were the result of federal funding from the National Institutes of Health. While it would be impossible to list all such inventions, a few examples of technologies and products originating from federally funded university discoveries include:

- Artificial lung surfactant for use with newborn infants, University of California
- Cisplatin and carboplatin cancer therapeutics, Michigan State University
- Citracal® calcium supplement, University of Texas Southwestern Medical Center
- Haemophilus B conjugate vaccine, University of Rochester
- Neupogen® used in conjunction with chemotherapy, Memorial Sloan Kettering Cancer Institute
- Process for inserting DNA into eucaryotic cells and for producing proteinaceous materials, Columbia University
- Recombinant DNA technology, central to the biotechnology industry, Stanford University and University of California
- TRUSOPT® (dorzolamide) ophthalmic drop used for glaucoma, University of Florida

These examples of successful new technologies demonstrate that a strong national infrastructure to support technology transfer has been established at academic institutions across the nation since passage of the Bayh-Dole Act. The royalties received from the licensed inventions support such an infrastructure. The Act requires that royalties received by universities from federally-funded inventions be reinvested for research and education purposes, after payment of a share to the inventor and payment of incidental legal expenses associated with

[3] The Association of University Technology Managers, "AUTM Licensing Survey, FY 2001: A Survey Summary of Technology Licensing (and Related) Performance for U.S. and Canadian Academic and Nonprofit Institutions, and Patent Management Firms." AUTM: Northbrook, IL, 2002.

patenting and licensing of the invention.

University use of royalty income is complex and diverse. Most frequently royalty income is used for research and educational expense of graduate students, start-up research costs for new or junior faculty, seed money for innovative new projects or initiatives (often provided through an intramural research competition), computer equipment and laboratory facilities renovation. Universities have used royalty income for a variety of innovative programs or initiatives. Examples include summer programs for female undergraduate students interested in science careers, technical assistance programs which provides high technology urban planning and architectural visualization services to inner city communities based on the agricultural extension service model, and new laboratory buildings to support the demands of 21st century medical research.

For most universities royalty income does not represent a significant source of revenue when compared with their federal funding or sponsored research expenditures. The Council on Government Relations (COGR) estimates that overall the aggregate university share of royalty revenues is in the range of 3% of total federal funding and of total research expenditures[4]. Some universities do better than others in terms of royalty income received. Most universities, however, do not derive substantial revenue from royalties by almost any standard of comparison. For those universities that derive substantial income from royalties, that success often tends to be associated with one particular invention. There is considerable annual fluctuation in income received, and one-time occurrences (e.g. settlement of a legal dispute over rights to an invention) can result in very large perturbations in income amounts. Thus, relatively

[4] Letter from Katharina Phillips, President, Council on Government Affairs to Dr. Wendy Baldwin, Deputy Director Extramural Research, National Institutes of Health, June 5, 2001.

few universities derive substantial revenues from royalties, and universities as a whole are not reaping "windfall profits."

Nevertheless, in 1980 there were approximately 25-30 universities actively engaged in the patenting and licensing of inventions. It is estimated that there has been close to a ten-fold increase in institutional involvement since then. The AUTM survey reflects the impact of this growth in activity:

- Over 4,000 new license and option agreements were executed with nearly 23,000 such agreements currently active.
- Nearly 360 new commercial products were brought to the market under license to a commercial partner. Since 1998, more than 1,500 new products have been introduced to the marketplace.
- 494 new companies were formed based on a license from an academic institution. Since 1980, over 3,800 such ventures have been created.
- Approximately $30 billion of economic activity each year, supporting 250,000 jobs can be attributed to the commercialization of new technologies from academic institutions.

Technologies licensed from academia have been instrumental in spawning entirely new industries, improving the productivity and competitiveness of companies, and creating new companies and jobs. In summary, the Bayh-Dole Act and its subsequent amendments created incentives for the government, universities, and industry to work together in the commercialization of new technologies for the public benefit. The success of this three-way partnership cannot be overstated.

Yale's Experience

Yale's Office of Cooperative Research was created in 1982 in response to the passage of the Bayh-Dole Act that encouraged universities to seek commercial partners to move their discoveries out of the laboratory and into the marketplace. The OCR was charged with

extending and expanding Yale University's interaction with the private sector. The duties of the OCR include oversight for patenting and licensing activities, as well as development of university inventions. OCR staff work with Yale researchers to identify inventions that may ultimately become commercial products and services useful to the public.

In FY 2002, approximately $335 million or 80% of Yale's sponsored research and training was supported federal agencies such as the National Institutes of Health (NIH), National Science Foundation (NSF), Department of Defense (DOD) and Department of Energy (DOE). The largest federal sponsor is the NIH, which provided $257 million of grants and contracts during 2002. The result of this support has been a wealth of new knowledge that has led to discoveries that are transforming our understanding of human disease. Translating this knowledge into new means of diagnosis, prevention and treatment has yielded new inventions with the potential for a profound and positive effect upon the welfare, health and safety of humankind. Researchers in the Department of Pharmacology of the Yale School of Medicine, for example, together with their research collaborators at other institutions, have played significant roles in developing two key ingredients of the so-called drug cocktail: the reverse transcriptase inhibitor d4T, known commercially as Zerit, and 3TC, known as Epivir. These medicines have fundamentally changed the nature of AIDS therapy during the past decade.

William Prusoff, Ph.D., Professor Emeritus of Pharmacology, has spent a 45-year career at Yale investigating potential antiviral and anticancer compounds, part of the traditional, small-molecule approach. In the late 1950s he synthesized idoxurine, an analog of thymidine, which was the first antiviral compound approved by the FDA for therapy in humans. It was used to treat herpes infection of the eye. Dr. Prusoff and his long-time collaborator, the late Tai-Shun Lin, Ph.D., discovered in the 1980s that a thymidine analog, reported in scientific literature by

researchers from Wayne State University as a poor anticancer agent, was very effective in slowing the production of HIV. This compound is known as d4T or stavudine. Bristol-Myers Squibb developed the drug under the trade name Zerit and brought it to market in 1994.

Yung-Chi (Tommy) Cheng, Ph.D., the Henry Bronson Professor of Pharmacology, has worked on a parallel course. While Drs. Prusoff and Lin found drugs that work against AIDS, Dr. Cheng has sought ways to reduce their toxicity. Long-term usage of anti-retroviral AIDS drugs leads to a decline in the mitochondrial DNA of certain organs, impairing their ability to function properly. After a month or two of use, these agents can cause problems in nerves, the pancreas, muscles and the liver. Dr. Cheng's laboratory team studies drugs that will be active against the virus but will have no toxicity to the mitochondrial DNA.

One such drug turned out to be 3TC, a compound with positive and negative forms that mirror one another. Originally synthesized by a Canadian researcher and identified as an antiviral agent, samples were sent to Dr. Cheng for study of the drug's toxicity. He found that 3TC's negative form reduced side effects when used in combination with AZT. The combination increases 3TC's efficiency at inhibiting an enzyme HIV uses to reproduce its genetic material. Dr. Cheng identified 3TC as an agent that would be less toxic to mitochondrial DNA than other retroviral drugs.

A new approach to combating AIDS may grow out of work led by John K. Rose, Ph.D., Professor of Pathology and Cell Biology. The agent he developed, based on a common virus found in cattle, has killed HIV-infected cells in culture. He also sees the possibility of developing an AIDS vaccine, using recombinant form of the virus as a vaccine vector. Researchers hope the vaccine will stimulate both parts of the immune system: antibodies to neutralize any free-floating HIV and specialized immune cells to kill any cells that HIV does

manage to infect. Early results using a form of the engineered virus showed promise against SIV, the simian form of HIV, for use in animal trials. Dr. Rose is working together with scientists at Wyeth Pharmaceuticals in conducting further animal tests. If it is proven safe and effective in animals, human trials could follow.

These are only a few examples of the life-changing discoveries resulting from Yale's scientific endeavors. Currently, Yale's has licensed eight (8) novel therapeutic drugs being tested in thirteen (13) different clinical trials for such life-threatening diseases as various types of cancer, Hepatitis B and AIDS (see attachment 2: Yale Pharmaceutical Pipeline). The benefit to the public derived from these and other inventions created through the research at Yale and other academic research institutions is incalculable.

The Impact on Local Economic Development

In many communities around the country, the scientific research undertaken by universities has been a powerful engine of local economic development. As President Richard C. Levin recently pointed out[5], without critical mass in electrical engineering and computer science, Yale - and consequently New Haven - missed out on the technological revolution that spurred the development of Silicon Valley and Boston's Route 128. But Yale has impressive strength in biomedical sciences with unexploited potential to build a biotechnology industry in and around New Haven. With the administration of President Levin, which started in 1993, Yale heightened its involvement in community economic development through specific operations backed by financial investments and increased professional staffing. The results include:

[5] Richard C. Levin, "Universities and Cities: The View from New Haven," Inaugural Colloquium, Case Western Reserve University, January 30, 2003.

- A commitment to spend over $500 million to renovate every science laboratory on campus as well as construct 5 new state-of-the-art research and educational buildings.
- A commitment to spend an additional $500 million to renovate the laboratories at the Medical School including the construction of a recently opened 457,000 square foot building for disease-based research that increased the total lab space by 25%.
- Twenty-five new biotechnology companies have been established in the greater New Haven area, seventeen within the city limits. These firms have attracted over $1.5 billion in capital and together they now employ 1300 people.
- Attracting Winstanley Enterprises of Concord, Massachusetts to purchase the 550,000 square foot former headquarters of the Southern New England Telephone Company one block from the Medical School that it transformed into the George Street Technology Center housing eight biotechnology spin-offs from Yale.
- Working with the State of Connecticut and City of New Haven to attract Lyme Properties (the developers of Kendall Square in Cambridge, Massachusetts) to convert 1 million square feet of former factory space at Science Park into labs, offices and restaurants for additional spin-offs from Yale.

Although these results are just from New Haven, Connecticut, similar scenarios are being replicated at numerous sites across the country. On a nation-wide basis, the results support the conclusion that the Bayh-Dole Act has promoted a substantial increase in technology transfer from universities to industry, and ultimately to the public. There has been a tremendous acceleration in the introduction of new products through university technology transfer activities. These benefits have been significantly enhanced by the adoption of federal policies encouraging technology transfer. Such policies have led to breathtaking advances in the medical, engineering, chemical, computing and software industries, among others. The licensing of new technologies has led to the creation of new companies, thousands of jobs, cutting-edge educational opportunities and the development of entirely new industries. Today, the Vice Chairman of the NASDAQ Stock Market, Alfred Berkeley III[6] estimates that 30% of the

[6] Personal communication with Alfred Berkeley III.

companies listed owe their value to the results of government sponsored research and development. Accordingly, the Bayh-Dole Act continues to be a national success story, representing the foundation of a successful union among government, universities, and industry.

Mr. Chairman, thank you again for your time and attention. If there are any questions, I will be pleased to answer them.

Attachment 2: YALE PHARMACEUTICAL PIPELINE

AGENT	LICENSEE	INDICATION	STAGE	PATENT EXPIRATION
Zerit®	Bristol-Myers Squibb	HIV / AIDS	Marketed	June 2008
Coviracil®	Triangle Pharmaceuticals	Hepatitis B	Phase III	January 2010
Pexelizumab™	Alexion Pharmaceuticals	Cardiopulmonary Bypass	Phase III	Pending
Troxatyl®	Shire Pharmaceuticals	Acute Myelogenous Leukemia	Phase II	April 2017
Troxatyl®	Shire Pharmaceuticals	Solid Tumors (pancreatic cancer)	Phase II	April 2017
Triapine™	Vion Pharmaceuticals	Leukemia	Phase II	January 2011
Triapine™	Vion Pharmaceuticals	Metastatic Breast Cancer	Phase II	January 2011
Clevudine™	Triangle Pharmaceuticals	Hepatitis B	Phase II	December 2013
Elvucitabine™	Achillion Pharmaceuticals	Hepatitis B	Phase II	May 2014
Elvucitabine™	Achillion Pharmaceuticals	HIV / AIDS	Phase II	May 2014
TAPET™	Vion Pharmaceuticals	Anticancer	Phase I	March 2013
TAPET-CD	Vion Pharmaceuticals	Anticancer	Phase I	March 2013
VNP40101M	Vion Pharmaceuticals	Anticancer (Solid Tumors)	Phase I	March 2010
VNP40101M	Vion Pharmaceuticals	Anticancer (Leukemia)	Phase I	March 2010
IoddU	Achillion Pharmaceuticals	Epstein-Barre Virus	Pre-clinical	Pending
ACH0630	Achillion Pharmaceuticals	Hepatitis B and C	Pre-clinical	Pending
VSV Vaccine	Wyeth Pharmaceuticals	HIV / AIDS	Pre-clinical	Pending