

COMMENT***ALLIANCES FOR THE FUTURE: CULTIVATING A COOPERATIVE ENVIRONMENT FOR BIOTECH SUCCESS******Gina A. Kuhlman*****TABLE OF CONTENTS****I. INTRODUCTION****II. COOPERATION IS NECESSARY TO ACHIEVE TECHNOLOGY TRANSFER.**

A. Overview of the Biotechnology Industry.

B. Neither Academia Nor Industry Can Individually Transfer Technology to Commercial Applications Efficiently.

III. EMERGENCE OF RESEARCH ALLIANCES BETWEEN ACADEMIA AND INDUSTRY.

A. The Nature of The Industry Inherently Requires Cooperation to Sustain It

B. Federal Laws Enable University-Industry Cooperation.

IV. COOPERATION HAS PRODUCED SERIOUS CONCERNS REGARDING CONFLICTS OF INTEREST.

A. Inadequate Policing Mechanisms Permit Researchers to Defect from Scientific Obligations.

B. The Self-Policing Mechanism of Reciprocity.

V. BENEFICIAL EFFECTS OF UNIVERSITY-INDUSTRY COOPERATION.

A. Federal Laws Encouraging Cooperation Have Resulted in Exponential Growth in the Biotechnology Industry.

B. Social and Economic Benefits.

VI. THE FEDERAL GOVERNMENT MUST REJECT PROPOSALS TO ENACT LAWS THAT COULD THREATEN COOPERATION.

A. The Federal Government Should Not Adopt the Proposed NIH Guidelines Because They Lower the Payoffs of Investing in Biotechnology Research.

B. The Federal Government's Proposal to Set Price Controls on Breakthrough Biotechnology Drugs Would Lower the Payoffs for Investment in Innovation.

VII. CONCLUSION**I. INTRODUCTION**

Breakthroughs in biotechnology have the potential to enhance quality of life and spur the national and local economies throughout America. Biotechnology holds promise for developing cures and treatments for currently untreatable afflictions and for enhancing

agricultural products. As a result, the exploding biotechnology industry holds the potential to create jobs and to become this nation's most important source of economic development, leading America to the forefront of this young but exploding industry. The vitality of biotechnology is critical to combating diseases, to job creation, to economic development nationally, and to the maintenance of America's competitiveness in the world economy. Biotechnology's potential to develop life-saving drugs and help power America's economy requires sustained development in this field of endeavor, which can best be achieved through cooperation between universities and industry.

Cooperation between universities and industry has historically produced advancements in technology unachievable by independent institutions. Laws and research funding that encourage university-industry cooperation have played important roles in the development of biotechnological breakthroughs. Promoting this cooperation in the biotechnology industry is particularly important because the industry is young and characterized by long-term and capital-intensive research. The federal government can play a vital role in encouraging such cooperation by increasing investment incentives, rather than by imposing strict regulatory mechanisms or controlling product prices, which would only discourage cooperation by increasing the risk and uncertainty that investors face in the biotechnology industry. Proposed price controls on biotechnology products,¹ for example, would reduce the incentives necessary to induce cooperation. These proposed restrictions by the federal government only threaten to increase the cost and uncertainty of biotechnological research by imposing an additional layer of bureaucracy

However, there are potential pitfalls to university-industry cooperation. Where this relationship has been too integrated, researcher misconduct has at times resulted. However, for the most part, sufficient mechanisms are in place to deter researcher misconduct. Thus concerns of conflict-of-interest-generated misconduct on the part of researchers have largely not materialized, and additional federal restrictions are unnecessary.

This article has the following structure: in part II, I discuss the need for cooperation between universities and companies for the translation of the results of basic research into marketable products. Part II provides a brief overview of the biotechnology industry and describes why neither universities nor biotechnology companies can individually promote the development of marketable biotechnology products efficiently. In part III, I relate how cooperative relationships between academia and industry have emerged. Part III also contains a discussion of such relationships in reference to a specific model for cooperation and how such relationships confer advantages. Finally in part III, I discuss Congressional actions that have promoted technology transfer. Part IV lists conflicts-of-interest concerns that can arise in a cooperative environment and indicates that, for the most part, such fears have not been realized and why this is so. Part V describes how university-industry cooperation has fueled growth in the biotechnology industry and has promoted social benefits. Part VI indicates why the federal government should resist the temptation to stifle cooperation through over-regulation. Lastly, part VII summarizes important points.

II. COOPERATION IS NECESSARY TO ACHIEVE TECHNOLOGY TRANSFER

Biotechnology is at the forefront of producing therapies and treatments that have the potential to save lives, protect the environment, and enhance overall quality of life. However, fulfillment of this potential requires the transfer of the results of biotechnological research to society. Industry is motivated to invest in biotechnology research, which has the potential to produce high returns through sales of breakthrough products; however, the high risks associated with such investments offset the incentives. Without university-industry cooperation to offset the long-term, capital-intensive risks of the young biotechnology field, such technology transfer will not occur.

A. Overview of the Biotechnology Industry

Biotechnology is the application of engineering and technological principles to living organisms or their components to produce new inventions or processes.² The field of biotechnology comprises the following groups: university and federal research laboratories and biotechnology/pharmacology companies. University and federal laboratories typically conduct basic research, which is research geared toward increasing scientific knowledge of fundamental systems or mechanisms relevant to an organism's physiological, biochemical, or molecular biological processes. This type of research is not directed toward commercial applications, although such applications could result. On the other hand, while biotechnological and pharmacological companies also conduct basic research, their focus is more toward developing products that form the basis of the biotechnology and pharmacology industries. In the medical world, biotechnology is at the cutting edge of research on cancer and other deadly and costly diseases.³ As of 1994, "twenty-three genetically engineered drugs and vaccines were commercially available to prevent or treat such diseases as AIDS, diabetes, dwarfism, hepatitis, heart attacks, anemia, leukemia, renal cancer, organ transplant rejection, and Kaposi's sarcoma."⁴ Drugs and vaccines are being developed that "will treat such intractable diseases as cancer, arthritis, Alzheimer's, and genetic disorders such as cystic fibrosis."⁵ The biotechnology industry is also producing diagnostic materials for such medical conditions as pregnancy, cancer, hypercholesterolemia, and AIDS.⁶

Biotechnology is also likely to spur an economic revitalization of the agricultural industry.⁷ Biotechnology is already beginning to provide improved crops, better pest control and new agricultural products.⁸ Agricultural technology promises to improve food quality, while reducing farm input costs, and to offer benefits to the environment.⁹ Advances in agricultural biotechnology may "provide the only impetus for agricultural self-sufficiency and economic stability in developing countries."¹⁰ The United States currently leads the world in this developing industry.¹¹

Other countries, however, have begun targeting biotechnology as a growth industry, thereby challenging the dominance of the United States in this area.¹² This fact, plus the prospect of breakthrough products through biotechnology research, has fostered recognition by the White House that biotechnology represents a "national critical technology," one that is "essential for the United States to develop further the long-term national security and economic prosperity of the United States."¹³

The long-term, capital-intensive nature of the biotechnology industry necessitates cooperation because it involves continuing or repeat interaction between universities and industry. Since biotechnology is a relatively new science, one characterized by the concentration of researchers in academia and by the need for sophisticated research equipment, the ability to share research talent, equipment, information and financial resources through cooperation increases the likelihood that research findings in academia will lead to the development by industry of treatments and therapies that benefit society. The prospect of utilizing knowledge derived from the research findings serves as a natural motivation for cooperation.

B. Neither Academia Nor Industry Can Individually Transfer Technology to Commercial Applications Efficiently

The long-term and capital-intensive nature of biotechnology make research investment in this field an expensive and high-risk endeavor. Thus cooperation between academia and industry is necessary to spread the costs and lower each party's risks.¹⁴ Cooperation would involve industry funding of basic university research, thus reducing the risk that such research will go unfunded, and in return companies would gain access to the findings of basic research. Unlike traditional pharmaceutical companies, which focus on incremental improvements to existing compounds, biotechnology firms are geared toward discovering "breakthroughs"¹⁵ by concentrating on producing more or better naturally occurring compounds.¹⁶ The average time it takes to market a drug from the time of discovery is ten to twelve years.¹⁷ Moreover, according to a recent report, this average length of time to the development of biotechnological products may be understated because the biotechnology industry is both young and consists of products that require long periods for development and market approval.¹⁸

The length of time and costs required to develop a product, coupled with the risks of its never achieving market approval, act to force universities to rely on corporate sponsors for support of their research initiatives. Also, whereas pharmaceutical companies are able to finance research with the revenue streams from the hundreds of products they market, biotechnology firms must rely on outside financing because they are often developing only a single target breakthrough compound.¹⁹

Carl B. Feldbaum, President of the Biotechnology Industry Organization (BIO)²⁰ has identified the biotechnology industry as being "one of the most capital intensive and research intensive industries in the history of civilian manufacturing."²¹ The cost of developing and bringing a product to market is phenomenal.²² Harry Penner, President and CEO of Neurogen Corporation, notes that "the Office of Technology Assessment finds that the average cost per new chemical entity (NCE) is \$359 million."²³ In a 1993 survey conducted by Business Week, seven of the top ten firms in the United States in terms of research expenditures per employee were biotechnology firms.²⁴ According to Carl B. Feldbaum, President of the Biotechnology Industry Organization, biotech firms average research expenditures of \$59,000 per employee on research; the corporate average in the U.S. was \$7,106.²⁵

The large amounts of capital needed to develop a product through research in biotechnology necessarily affects a university's ability to conduct research. Since biotechnology derives from basic research,²⁶ which can consume years of development time, and since biotechnology requires sophisticated lab equipment, universities require outside funding to maintain a research program in biotechnology.²⁷

University-industry cooperative relationships can yield the transfer of technology from university labs to the marketplace; otherwise, university researchers may discover important biotechnology products and have no means to develop the discoveries into usable products.²⁸ A prime example of a university's failure to develop marketable products without industry support is Johns Hopkins Medical School's inability to find a company to produce its patented cardiopulmonary resuscitation (CPR) device²⁹ until the university amended its long-standing no-stock policy in 1993. In spite of the potential benefits of the Johns Hopkins patented device, large companies were not interested in it, and entrepreneurs who wanted to build a new firm around the invention did not have the money for a significant licensing fee. Once the university changed its policy to allow its schools to make deals for stock, its medical school

was able to enter into a joint venture with Baltimore's business community, forming CardioLogic Systems Inc., to market the CPR device.³⁰

Historical evidence demonstrates that university-industry cooperation can surpass the independent abilities of universities, industry, and government to develop and transfer technology into the marketplace. Such evidence indicates that cooperation is often needed to reduce the costs of advancing breakthrough technology and to encourage investment in research. Cooperation therefore fosters American industrial growth through the sharing of knowledge, equipment and other resources that aid in the transfer of technology to the marketplace. When demand for technological advancements increases, university-industry alliances, funded by the government, have historically met the demand that independent institutions are unable to fill. The reason that university-industry cooperation is preferable to independent research in technological fields is that sharing of resources reduces the costs of innovation. When technological advancements are made, the supply of researchers knowledgeable in the particular development is limited, particular lab equipment may be scarce, and future return streams are unpredictable. Cooperation therefore effectuates technological advancement, where independent institutions may be unable to support research.

Industrial sponsorship of university research is not a recent development. Corporate sponsors have funded a significant portion of university research since long before World War II.³¹ For example, university and industry collaboration existed as early as 1861, with the founding of Massachusetts Institute of Technology (MIT).³² Under collaborative agreements, university faculty, staff, and students gained access to a wide variety of corporate research and development projects, and individual companies gained a window to state-of-the-art research and resources of academic laboratories.³³ In other words, cooperation became more profitable than competition in the area of research, given the payoffs of sharing resources that were unavailable without cooperation.

University-industry collaboration has also historically led to technology transfer. As early as 1925, the University of Wisconsin Alumni Research Foundation (WARF) was founded to organize patenting and licensing.³⁴ This was in response to the inability to transfer new discoveries to the market where they could be utilized. WARF successfully established an arm's-length relationship between academia and industry.³⁵ Prior to the founding of WARF, neither the university nor the attorney general wanted to take the risks or incur the costs of patent applications for innovative research methods. The cooperative arrangement returned over \$100 million from patent royalties to the university for research grants, professorships, traveling fellowships, and student support through the university.³⁶ Cooperation promoted the transfer of research innovations to industry where competition with industry had failed. The rewards were significant for the university, as well for industry and consumers, demonstrating the advantages of university-industry cooperation.

Land-grant colleges are another example of institutions serving as technology-transfer mechanisms. The Land Grant College Act (Morrill Act) of 1862³⁷ created cooperation between the agricultural industry and state and private universities. The federal government recognized the need for technology transfer through relationships between universities and industry and provided the incentives to enter such relationships. The cooperation among government, universities and industry, through the vehicle of land-grant colleges, accelerated America's leadership in agriculture.³⁸

The Department of Defense has also long functioned as a national technology-transfer service and in such capacity has heavily contributed to the development of the modern chemical and computer industries in America.³⁹ The catalyst for such government-industry-university relationships was the federal government's interest in national defense during World War II. The federal government sought major assistance from university scientists because the limited research programs of the armed services proved insufficient for wartime demands.⁴⁰ The framework for the government-industry-university relationships was established in 1941 with President Roosevelt's creation of the National Defense Research Committee (NDRC) and expanded in 1942 with the creation of the Office of Scientific Research and Development (OSRD).⁴¹

The foregoing examples demonstrate that cooperation between universities and industry, coupled with federal support, has historically stimulated research and transferred technological developments to the market. Cooperation has evolved over time as a response to lack of resources, inability to transfer technology to the market, and the increased demand for innovation (such as during wartime). As a result of the arrangements, specific industries became globally competitive, universities gained access to industrial resources, and consumers obtained access to beneficial inventions.

III. EMERGENCE OF RESEARCH ALLIANCES BETWEEN ACADEMIA AND INDUSTRY

Cooperation has resulted from the long-term, capital-intensive nature of biotechnology and, more significantly, from laws passed by Congress to encourage cooperation in order to promote technology transfer of biotechnology innovations. The laws are successful because within biotechnology, they have promoted what economist Robert Axelrod regards as the five essential factors for

cooperation.⁴²

- (1) enlarging the shadow of the future in which each player will continually meet;⁴³
- (2) changing the payoffs of cooperation and defection (non-cooperation);⁴⁴
- (3) teaching the players to care about the welfare of the other;⁴⁵
- (4) teaching reciprocity in interactions;⁴⁶ and
- (5) improving each player's ability to recognize the features of each other from past interactions.⁴⁷

The establishment of these essential factors ensures that universities and industries will engage in continuing relationships based on reciprocity. Cooperation in this strategic setting ensures that each party will benefit from the relationship.

A. The Nature of The Industry Inherently Requires Cooperation to Sustain It

1. Long-term relationships create an enlarged shadow of the future to support cooperation between universities and industry

The long-term, capital-intensive nature of the biotechnology field promotes and requires cooperation because it increases the shadow of the future for continuing or repeat interaction between universities and industry. This characteristic of the biotechnology field precisely mirrors one aspect of the strategic setting identified in the Axelrodian model of cooperation as a long shadow of the future. This notion is based on the premise that when a relationship between parties extends over a period of time, or when parties will interact repeatedly over time, the parties will tend to cooperate in reliance of that relationship in the future. For example, if two parties interact on one occasion with no prospect for meeting in the future, defection (non-cooperative behavior) on the part of the first party will provide higher benefits for the defecting party than mutual cooperation on that one occasion. But if the parties interact again in the future, the other party will likely defect, given the first party's prior defection, and both parties will be worse off through mutual defection.⁴⁸

The biotechnology industry inherently involves an elongated shadow of the future for the parties involved. Although research relationships in biotechnology involve long-term investments rather than repeat encounters, the lowered probability of defection is similar to the repeat-encounters model. Since the parties invest significant resources to the relationship over a long period of time, each party's reliance on the other increases over time. In other words, the long-term nature of biotechnology research and development, as opposed to the potential for repeat relationships, enlarges the shadow of the future and increases the tendency of the parties to cooperate.⁴⁹

2. Cooperation Increases the Payoffs for Both Universities and Industry Due to the Demand for Resources

A second factor supporting the emergence of cooperation between parties is increased payoffs for cooperation.⁵⁰ In the context of biotechnology research, universities and industry achieve higher rates of returns per investment when they cooperate than they would independently.

a. Increasing the payoffs for industry

Cooperation increases the payoffs for industry because of the high demand for, and low supply of, research talent in biotechnology, such talent being located primarily in academia. Precisely because biotechnology is in a critical stage of innovative basic research,⁵¹ which requires sophisticated lab equipment, the biotechnology industry is more dependent on universities for basic research than are other industries.⁵² Dr. Charles Muscoplat of Molecular Enectics explained the unique dependence of industry on academia for biotechnology research, as it existed in 1982:

[A] chemical company may have hundreds of organic chemists working for them, and if they need an outside consulting organization they will go and retain organic chemists at some university to help them solve a particular problem. However, if a large industrial company wants to do research in biotechnology today, *they don't have the in-house skills*. They either have to go to small biotechnology companies or to universities to acquire many of the skills relevant to do that type of work.⁵³

Industry's development in biotechnology is extremely dependent upon industry's ability to combine research efforts with academia to lower research and development costs.⁵⁴ The costs of R&D in biotechnology are inflated by the sophistication of laboratory equipment and materials involved, the concentration of scientists skilled in biotechnology within academia, and the need for long-term focus that are characteristic of the biotechnology industry.⁵⁵ By combining the research efforts with the knowledge base and resources of academia, both parties are able to lower costs associated with the development of applied and marketable technology.

Industry not only benefits by avoiding costs of developing its own basic-research departments, it is able to draw on the collective talents of academic and company scientists in the field of biotechnology.⁵⁶ This situation enables companies to obtain access to the most skilled researchers in the field, from "Nobel laureates to talented graduate students." It also enables industry sponsors to obtain a "window on the technology" and a broader perspective on potential developments from researchers in academia, who have less of a commercial orientation in performing initial research.⁵⁷ By collaborating with academia, companies are also able to draw on a university's interdisciplinary faculty.⁵⁸ The variety of specialties that can be accessed is particularly important, since biotechnology research impacts many different industries, such as the "pharmaceutical industry, the health industry, the agriculture, mining and chemical industries, and even waste management."⁵⁹

b. Increasing the payoffs for universities

Universities benefit by receiving funds that fill the federal-funding gap.⁶⁰ Surveys of university faculty suggest that university-industry relationships have become an important alternative to government funding in the emerging field of biotechnology, with companies supporting up to 16 percent of university research in this area.⁶¹ University-royalties revenues, generated from, e.g., licenses granted to industry, were \$130 million in 1991 and \$172 million in 1992.⁶² Responding to concerns about industry funding of academic research, in 1982 Terry Sanford, then President of Duke University, commented, "[u]niversities should do all that is reasonably possible to earn returns on inventions, and should not be timid in making prudent business arrangements to assure the largest fair return," since the promotion of the technological applications of science concerns "the well-being of all people."⁶³

Universities also stand to benefit from collaboration with industry as a means of retaining the relatively scarce numbers of leading scientists in biotechnology, instead of losing them entirely to industry.⁶⁴ Biotechnology has changed science in that researchers now know that they may be able to make breakthrough discoveries within their own lifetimes. Academia is forced to realize that scientists will naturally want to develop their discoveries, and the only way they can do that is by interacting with the commercial sector.⁶⁵

University-industry collaboration has also been shown to enhance research and to promote the publication of research findings. A survey of biotechnology companies found that university investigators working with industrial funds enjoyed higher rates of innovative findings, publication in peer-reviewed journals, and service in administrative roles.⁶⁶ University relationships with industry have also been shown to enhance educational experiences for university students and fellows.⁶⁷

B. Federal Laws Enable University-Industry Cooperation

To encourage cooperation between academia and industry, Congress passed laws that promote technology transfer. The federal government's focus on technology transfer transformed the strategic setting in which the parties interact, which translates into incentives for university-industry cooperation under the Axelrodian model by resting one party's utility on the other's welfare, increasing each party's ability to recognize defection and increasing the payoffs from investment in cooperative agreements.⁶⁸ The recognition of the benefits of cooperation between government, universities and industry has developed consistently over the years, as the private sector alone has been found to be unable to transfer beneficial technology to society.

The following table illustrates the laws Congress passed specifically to encourage university-industry cooperation, including the year each law was passed, and indicates its key features.

TABLE: Federal Laws Passed to Encourage Cooperation

Law	Year Passed	Key Features

Bayh-Dole Patent and Trademark Act ⁶⁹	1980	<ul style="list-style-type: none"> •Permits universities, nonprofit organizations and small businesses to retain the intellectual property rights to inventions resulting from research supported by federal grants.
Stevenson-Wydler Technology Innovation Act ⁷⁰	1980	<ul style="list-style-type: none"> •Created the Office of Technology Transfer at the National Institute of Health (NIH) to investigate projects for use by government or private industry. •Created the Center for the Utilization of Federal Technology to provide industry with information on federally developed technology with potential for commercial application.

Federal Technology Transfer Act ⁷¹	1986	<ul style="list-style-type: none"> •Amends the Stevenson-Wydler Technology Innovation Act •Permits agreements between Federal laboratories and private firms, known as CRADAs. •Requires the Federal laboratories to share royalties from patents with the investigating scientists. •Allows the Federal government to offer exclusive licenses to private research partners.
Orphan Drug Act ⁷²	1983	<ul style="list-style-type: none"> •Grants biotechnology companies a seven year monopoly on medications developed for rare diseases. •Provides biotech companies with tax credits up to fifty percent of annual testing expenses on medications developed for rare diseases.

The Bayh-Dole Act and the Federal Technology Transfer Act have provided significant federal incentives for university-industry cooperation in general. The laws require the parties involved in the cooperative agreements to make certain trade-offs while benefiting from the relationship. In effect, cooperation is able to flourish because one party's utility is legally dependent on another party's welfare. At the same time, the Stevenson-Wydler Technology Innovation Act has provided for the establishment of government agencies that investigate the commercial viability of technology. The government agencies provide a mechanism for interacting parties to recognize defective behavior, which further fosters cooperation. Federal tax credits for orphan drugs add an additional incentive for cooperation by lowering investment costs and therefor increasing the payoffs per investment dollar.

1. Teaching each of the parties to care about the welfare of the others

Robert Axelrod describes one factor contributing to the emergence of cooperation as teaching players to care about the welfare of others.⁷³ Axelrod suggests supplying motives that will cause people to act altruistically, which he defines as "the phenomenon of one person's utility being positively affected by another person's welfare."⁷⁴ The federal government has created the "altruistic" motivation for universities to cooperate with industry by establishing laws that allow parties to benefit from the welfare of other players involved in the relationship.

The development of federal laws encouraging university-industry cooperation came in response to the private sector's inability to transfer technology to the marketplace adequately. For example, in the period immediately following the first major biotechnological discovery, recombinant DNA, the rights to many federally funded biotechnological inventions, which were assigned to the federal government, were not being commercialized.⁷⁵ Congress's concern about the United States' competitiveness led to the enactment of the most important government policy to encourage the transfer of technology from academia to the marketplace, the Bayh-Dole Patent and Trademark Act of 1980.⁷⁶ This law focuses attention on the importance of identifying, protecting, and commercializing discoveries growing out of research by giving universities, nonprofit organizations, and small businesses the intellectual property rights to inventions resulting from research supported with federal grants.⁷⁷ In return, the Bayh-Dole Act requires the research institutions to share any royalties from the patents with the scientists responsible for the inventions. In this respect, research institutions are encouraged to promote the development of inventions for the benefit of being able to profit from patents obtained for such inventions. In other words, research institutions will receive benefits when they pay the "welfare costs"-the costs of acting generously in return for benefits.⁷⁸ Researchers, in turn, are motivated to develop inventions and perform diligent work that will benefit both the university and themselves.

The Bayh-Dole Act also requires universities to make good-faith efforts to seek patents on discoveries and to secure licensees for those patents. The universities are to give preference to small businesses that agree to manufacture any products resulting from the license in the United States.⁷⁹ Universities are thus motivated by potential profits to transfer technology into the marketplace while acting in ways that will benefit American business. At the same time, American businesses are motivated to invest in university research by the legally imposed assurance that those companies that invest will be given preference when the university licenses its patents. Ultimately, both industry and universities benefit from promoting the welfare of each other.

In addition to the Bayh-Dole Act, Congress passed the Federal Technology Transfer Act of 1986,⁸⁰ amending the Stevenson-Wydler Technology Innovation Act of 1980, to facilitate the transfer of scientific discoveries from federal laboratories, such as the National Institutes of Health (NIH), to the marketplace.⁸¹ The Federal Technology Transfer Act permits agreements between federal laboratories and private firms, known as CRADAs (Cooperative Research and Development Agreements).⁸² Under a CRADA, the public and private parties collaborate to provide the resources for research. According to the provisions of the Act, the federal agencies participating in research agreements with private parties must share at least fifteen percent of royalties from licensed inventions with the investigating scientists.⁸³ Additionally, the Federal government can offer in advance exclusive licenses to the collaborating partner on any invention resulting from joint research efforts.⁸⁴ The incentives for cooperation are similar to those of the Bayh-Dole Act; however, the Federal Technology Transfer Act additionally allows federal researchers to enter into direct agreements with corporate sponsors.

2. Improving the recognition abilities of the parties

Axelrod proposes that cooperative interaction between parties requires one party to recognize the other party from past interactions and to remember relevant features of those interactions.⁸⁵ The recognition ability involves being able to detect defection when it occurs.⁸⁶

The federal government has provided universities and industry with some ability to detect defection by passing the Stevenson-Wydler Technology Innovation Act of 1980.⁸⁷ The Act created such offices as the Office of Technology Transfer at NIH to provide a

mechanism for investigating projects for use by government or private industry.⁸⁸ The Act also created the Center for the Utilization of Federal Technology within the National Technical Information Service to provide industry with information regarding federally developed technology with potential for commercial application.⁸⁹

By establishing agencies to investigate technology with commercial potential, the government has also supplied one way for universities and industry to detect misdirected or fraudulent research and to avoid interacting with non-cooperative parties. In other words, these agencies could provide information that can enable cooperatives to evaluate the directives of the involved parties. The agencies also serve as constant players, increasing the likelihood that industry and universities will detect non-cooperative behavior by the federal government.

3. Changing the payoffs

The federal government has additionally transformed the strategic setting in which universities and industry interact by changing the payoffs of cooperation and non-cooperation. For example, Congress has increased the payoffs for cooperation by passing a series of laws that provide significant tax breaks to companies investing in academic research. A decline in federal funding for research has conversely increased the negative payoffs (the punishment) to universities for not cooperating, forcing universities to rely on industry for resources needed to continue conducting research. The Supreme Court's affirmation of biotechnology patents has further increased the payoffs of cooperation and has effectively lowered the risks of investment.⁹⁰

Congress has also increased the payoffs for cooperation and created incentives for industry to cooperate with universities and invest in academic research by passing a series of laws giving corporations tax credits for investing in university research. For example, companies that invest in "orphan drugs" for diseases afflicting less than 200,000 patients receive a fifty-percent tax credit for expenses related to formulating the drugs.⁹¹ These laws ensure that breakthroughs resulting from academic research are quickly developed into marketable products.⁹² The tax credits increase the payoffs for industry investment in university research by lowering investment costs.

Current Congressional attitudes, led by Speaker of the House, Newt Gingrich, and Chairman of the House Committee on Science, Robert S. Walker, favor a permanent tax credit for research and development expenses in industry.⁹³ Walker expects that the tax credit, if enacted, would encourage industry to cooperate with universities in building research facilities.⁹⁴ A permanent tax credit would further increase the payoffs to industry for investing in university research and therefore encourages cooperation.

Through the decrease in federal funding, the federal government has additionally reshaped the strategic setting in which universities and industry interact, in effect increasing the incentive for cooperation in biotechnology research.⁹⁵ With academia less able to provide the basic research upon which the development of marketable products ultimately depends, industry is driven to form cooperative relationships with university laboratories. Corporate sponsorship increases the payoffs of cooperation for universities by filling the federal funding gap.

However, despite the decline in federal funding, support of research by the federal government remains significant.⁹⁶ Roger C. Herdman, Director of the Office of Technology Assessment, reports that the federal government spent almost \$12 billion on health R&D (which includes spending on biotechnology research), roughly 39 percent of all health R&D conducted in the country. In explaining the decline in federal funding for health R&D, the Director stated that federal contribution was more important when biotechnological techniques were first developed.⁹⁷

Nonetheless, the decline in federal funding coupled with the long-term, capital-intensive nature of biotechnology research has created a gap that industry must fill. The Director of the Office of Technology Assessment acknowledged that federal funding has declined while total health R&D has increased almost 90 percent over the last ten years in constant dollars.⁹⁸ Notwithstanding the decline in federal funding, biotechnology remains a uniquely capital-intensive endeavor. Its inherent risks and long-term nature do not favor non-cooperative vehicles for technology transfer in biotechnology.

The Supreme Court has provided further incentives for university-industry cooperation in the biotechnology industry. The 1980 Supreme Court decision in *Diamond v. Chakrabarty*, approving a biotechnology-based patent, effectively encourages the commercialization of biotechnology through collaborative agreements between universities and industry, or between federal research laboratories and industry.⁹⁹ The *Diamond* case had this effect because it increased the probability that research in biotechnology would be patentable, hence profitable. The increased patentability of biotechnology subject matter creates a greater potential for commercialization, thereby spurring industry to invest in university biotechnology research in the hope that something profitable will result.

IV. COOPERATION HAS PRODUCED SERIOUS CONCERNS REGARDING CONFLICTS OF INTEREST

Though cooperation spurs economic development, it also raises the specter of serious conflicts of interest. Cooperative ventures between academia and industry necessarily involve profit motivation, which can affect the nature of university research.¹⁰⁰ Short-term product objectives of a company could run counter to imaginative or farsighted research at the university level.¹⁰¹ Also, cooperation between university researchers and their funders in industry could introduce secrecy into the scientific process. Profitable research findings may be kept confidential, remain unpublished, or be significantly delayed in publication in response to industry's demand for privacy and security of proprietary data.¹⁰²

Another troubling scenario involves companies that might exploit taxpayer-funded research without providing adequate returns to the public.¹⁰³ In such a scenario, taxpayers who bankroll federal funding to institutions involved in agreements with industry are hit twice when they are forced to pay exorbitant prices for products developed with their tax dollars.¹⁰⁴

In sum, the different goals of universities and industry could inevitably lead to problems of conflict of interest, a situation complicated by federal funding. Where there are no negative repercussions for researchers who defect from scientific goals of openness, the profit motive may predominate to the detriment of basic university research. The "defection" in such case refers to defection from the scientific and societal goals of research and not to defection between the cooperating parties; collusive behavior may actually strengthen cooperation between universities and corporate sponsors, but such cooperation would be socially undesirable.

A. Inadequate Policing Mechanisms Permit Researchers to Defect from Scientific Obligations

Axelrod suggests that defection from cooperation will occur when there is no threat of reciprocity for defecting behavior in an interaction.¹⁰⁵ Axelrod proposes that cooperation can be fully realized when the actors adopt a virtual "eye-for-an-eye" theory of interaction. The factors that will avoid continuous conflict include: 1) "paying back" slightly less than the amount of defection, and 2) creating a policing mechanism to enforce "paybacks" and subsequently reduce defection.¹⁰⁶ The conflict-of-interest issues that arise in university-industry cooperative arrangements in the biotechnology industry suggest that policing mechanisms may be inadequate to completely deter defective behavior.

There are significant concerns of conflicts of interest and research integrity in a profit-driven research environment involving university-industry collaboration. Michael Wilkes, professor of medicine at UCLA, has articulated these concerns as follows: "In the past, people did research and had high ethical standards. Today, everybody is hoping to make big money."¹⁰⁷ Thus the concern arises that companies will require research that is potentially profitable to be kept confidential, thereby subverting the tradition in science of open communication of research findings.¹⁰⁸ Data developed by the Harvard Project on University-Industry Research in Biotechnology (Harvard Project) validate such concerns. The survey found that biotechnology faculty with industry support were more than four times as likely as colleagues without such funding (12 percent versus 3 percent) to report that trade secrets had resulted from their research.¹⁰⁹ The former were also nearly five times as likely as the latter (24 percent versus 5 percent) to report that they had conducted research that generated findings that were the property of the sponsors and could not be published without the sponsors' consent.¹¹⁰

Another concern is that researchers who are motivated by financial rewards may distort research priorities and outcomes to conform with commercial aims. Among respondents to a survey conducted by the Harvard Project, 30 percent of biotechnology faculty with industry support said that their choice of research topics had been influenced by the likelihood that the results would have commercial applications.¹¹¹

Daryl Chamblee, acting Deputy Director for Science Policy and Technology Transfer at NIH, has expressed concern over the government's ability to protect the public against non-use or unreasonable use of inventions.¹¹² Opponents of university-industry relationships have also charged that NIH itself endangers public health through that agency's inability to regulate against fraud in research.¹¹³ Furthermore, since all agreements made under the Bayh-Dole Act are confidential, the public "is denied even knowledge of [such agreements], much less scrutiny or oversight."¹¹⁴

Some specific examples of investigator misconduct arising out of industry-sponsored research include instances of distorting research discoveries, keeping negative findings secret, and conducting unnecessary tests on patients. One example of a loss of objectivity in research occurred under a CRADA agreement. Researchers who discovered Retin-A touted the acne medication as a wonder drug that could erase wrinkles, a claim published in the *Journal of the American Medical Association (JAMA)*.¹¹⁵ Subsequent contradictory findings indicated that the authors of the *JAMA* article prematurely released their positive findings.¹¹⁶ In the interim, Ortho, a subsidiary of Johnson & Johnson, made millions in Retin A sales, which increased as a result of the prematurely publicized claim that

the medication could erase wrinkles.¹¹⁷

An example of a profit-motivated research cover-up, occurring solely within one company's laboratory, involves the failure of Dow Corning to disclose its in-house scientists' concerns that silicon breast implants leaked and ruptured. The serious health problems caused by silicone gel breast implants came to light only after a decade of sales. Dow Corning experienced a high rate of implant sales, with approximately 150,000 women receiving the implants each year.¹¹⁸ For an entire decade, Dow reaped the profits while many women paid the price for the company's silence regarding the safety of the implants.

One instance of a physician-researcher compromising the rights of a patient is the subject of the 1990 California case, *Moore v. Regents of the University of California*.¹¹⁹ John Moore suffered from hairy cell leukemia, a rare condition. The cells found in his blood and bodily substances were unique, even in comparison with such cells in other hairy cell leukemia patients, and they were commercially valuable because his cells "overproduced certain [proteins], thus making the corresponding genetic material easier to identify."¹²⁰ Without obtaining adequate consent, Dr. Golde solicited Moore for continuous testing under the guise of treatment.¹²¹ Subsequently, Dr. Golde produced a patentable cell line from Moore's cells and negotiated agreements with two biotechnology companies from which he received a consulting contract, 75,000 shares of common stock, and payments to the Regents and himself totaling \$440,000.¹²² The court concluded that the research conducted by Dr. Golde constituted an invasion of Moore's legally protected interest in determining the use of his body.¹²³

B. The Self-Policing Mechanism of Reciprocity

While conflict-of-interest issues have raised valid concerns regarding cooperation in the biotechnology industry, the feared occurrences of blatant research misconduct have not materialized. The self-policing mechanisms developed by universities, pursuant to federal policy, are effective in deterring misconduct because they monitor research motives and provide for reciprocity of defective behavior.

1. Unallayed defective behavior has not materialized

The existence of competition and confidentiality in university research, even in the absence of industry funding, suggests that fears that conflicts of interest will lead to excessive research confidentiality and outcome secrecy may be unwarranted.¹²⁴ To promote university-industry relationships while avoiding the tendency to excessive secrecy, several universities have adopted policies restricting a sponsor's right to review findings prior to their submission for publication. Such policies may limit the sponsor's right to that of reviewing for patentable results.¹²⁵ Daryl Chamblee of NIH publicly stated that an NIH survey found no occasions of unreasonable restrictions, publication delays, or constraints on university researchers stemming from collaborating with industry.¹²⁶

Governmental mechanisms are already in place to protect against the commandeering of basic research by industry. For example, NIH and the National Science Foundation (NSF) already exercise considerable control over the direction of much scientific research by choosing to fund certain kinds of projects over others. The competition for federal funding is fierce and many grant applications are denied.¹²⁷ Grant proposals undergo a two-tiered review to ensure that the proposed research is scientifically worth supporting in light of funding priorities and public policy.¹²⁸ Researchers have argued that the government exerts greater control over the direction of research than does industry.¹²⁹

In response to concerns over "corporate welfare" and government presence in industry, amidst the budget proposals in Congress, a joint committee of the NRC has concluded a report that encourages Congress to maintain funding of basic research, but to give priority to academic research.¹³⁰ The Committee's recommendations include the following:

- (1) Fund projects and people rather than institutions to promote research quality and flexibility;
- (2) Utilize competitive merit reviews as the basis for allocating funds;
- (3) Grant priority funding to academic research to encourage flexibility and quality control via grant competition and rigorous peer review;
- (4) Have the government refrain from directly funding the development of private-sector technology, except when such is in pursuit of the government's own goals (for example, weapons development and space flight);
- (5) Force existing federal laboratories to undergo renewed scrutiny, holding open the possibility of redirecting or

By utilizing these concepts in funding basic research, the government can foster the flexibility of academic research and the continuance of scientific integrity, without removing the incentives researchers and industry currently possess to invest time and money in developing research into commercially viable products. As a result, the profit motivation driving industry should not affect the integrity of government-funded research.

Concerns over public accountability for research conducted under university-industry reliances may also be exaggerated. While it is true that the biotechnology industry directly affects public health, a company's own interest in producing safe and effective drugs is a "built-in fail-safe."¹³² As a matter of economy, a bad drug triggers a costly public-relations disaster and subjects a company to a series of lawsuits. For example, Dow Corning's distribution of unsafe silicone gel breast implants ultimately proved a costly mistake due to associated liability costs, which have been substantial. Products liability laws can provide a significant deterrent to the distribution of faulty products when a company is truly aware of the defects.

Additionally, the Bayh-Dole Act provides that universities may maintain title to research inventions discovered under industry sponsorship. Universities' retaining title to inventions would tend to ensure that research results will benefit the public.¹³³ The rationale for this assertion is that the invention will be developed rather than merely patented by a sponsor in an attempt to suppress an area of technology that is potentially valuable to competitors. By retaining title to inventions, universities are also able to expand on existing findings and perform follow-up research without incurring risk of patent infringement.¹³⁴

Another reason that university ownership of patent rights benefits the public is that it enables universities to license inventions that are supported by sponsored research to the companies that will utilize them best, as opposed to granting all the rights to a company that may be unable or unwilling to develop all portions of the invention.¹³⁵ Even if a single company were willing to pay a premium for exclusive title to a particular invention, a university would likely reject the offer if the university's researchers believed the invention had broad applications and development potential. In such a case, the university would consider whether relinquishing the rights to develop related inventions and to sell licenses on any additional, related patents in the future is worth the price the company is willing to pay now for exclusive title. Conversely, if the usefulness of an invention is believed to be limited to a narrow use, it may be in all the parties' best interest to grant title to a single company that can actively develop the invention. The narrower the potential applications of an invention, the lower the threat that corporate ownership of title will restrain biotechnological developments.

While Daryl Chamblee acknowledged concerns of researcher misconduct in recent testimony before the Senate Subcommittee on Patents, Copyrights and Trademark, Chamblee's final conclusion was that feared adverse effects have not materialized and that the technology-transfer mechanism established by the Bayh-Dole Act appears to be working effectively.¹³⁶ In fact, the Journal of the American Medical Association concludes that scientific misconduct has rarely, if ever, been demonstrated in association with or as a result of a university-industry relationship.¹³⁷ Additionally, physician misconduct, such as that engaged in by Dr. Golde to further his biotechnology research in the *Moore* case, may be no more frequent than other occurrences of scientific misconduct, since, because of its implications for public health, it is likely that physician misconduct will be reported more often than other research misconduct.¹³⁸

In the midst of concern over conflicts of interest arising from the motivation for profit, it is important to acknowledge that profit incentives can spur development in biotechnology. Financial ties to industry do implicate conflict of interest, without profit incentives, medical products essential to the public health may never reach the public.¹³⁹ Indeed, in the United States' market economy, fostering the application of new knowledge requires that academic institutions form relationships with private, for-profit concerns.¹⁴⁰ Even if the prospects of financial reward from royalties on the sale of products were not so remote as to be ineffective,¹⁴¹ "there is nothing inherently wrong with profiting from the results of scientific work and achievements."¹⁴² Profit motives are not inherently evil, and personal gain may help propel scientific advances.¹⁴³ In turn, profiting from government funding is not unique to science.¹⁴⁴ In the view of Skolnick, founder of Myriad Genetics: "In order to encourage private investment, you have to tolerate a certain amount of managed conflict. In life there are often trade-offs-one of the trade-offs is that some people with good ideas are going to get wealthy."¹⁴⁵

2. Reciprocity mechanisms police conflicts of interest

While the conflict-of-interest issues are a significant concern in collaborative agreements in the area of biotechnology, regulatory mechanisms for deterring defective behavior presently exist. In the Axelrodian Cooperation Model, in instances where the strategic setting makes cooperation socially beneficial, interacting parties develop the self-policing mechanism of reciprocity.¹⁴⁶ In the biotechnology setting, the interacting parties control defection by reciprocating exploitative behavior by punishing the defecting party or by avoiding future interaction with that party. This type of self-policing can be effective in the biotechnology setting because none

of the researchers, universities, or companies want to risk public stigmatization; none of the parties can afford to be outcasts from university-industry circles.

Specific external policing mechanisms in place to reciprocate (and thereby deter) exploitative behavior include guidelines proffered by the federal government, the American Medical Association, and prominent medical journals. Internal policing mechanisms include university guidelines and review procedures for researchers involved in corporate-sponsored projects. As evidenced above, defective behavior is not prevalent within university-industry cooperative arrangements, as opponents of the agreements claim, and the existing policing mechanisms provide the reciprocity of behavior needed to sustain cooperation.

External policing mechanisms have arisen in reaction to concerns over conflicts of interest, with various institutions establishing guidelines to prevent misconduct. On the federal level, the Public Health Service (PHS) adopted a general policy requiring institutions to develop conflict of interest guidelines as a condition of federal funding.¹⁴⁷ Institutions such as the American Medical Association (AMA) have adopted their own guidelines in compliance with the PHS guidelines. The AMA guidelines provide that "all medical centers should develop specific guidelines for their clinical staff on conflicts of interest."¹⁴⁸ The AMA guidelines prohibit clinical investigators from buying or selling company stock, once they become involved in a research project for that company, until the involvement ends and the results of the research are published.¹⁴⁹ Corporate payments to a researcher are approved by the AMA; the AMA then requires the receipt of such payments be disclosed to the research institution, the research sponsor, and medical journals.¹⁵⁰

Universities have begun to respond to conflict-of-interest concerns by adopting their own conflict of interest guidelines, similar to those mandated by PHS and the AMA. Many universities require researchers to disclose outside financial interests.¹⁵¹ This disclosure gives private and public authorities a chance to review existing relationships so that their benefits and risks can be assessed, and it encourages individual faculty to evaluate their own relationships with companies. A number of academic institutions have also banned or provided special regulations for equity holdings in company stock by faculty.¹⁵²

Additionally, the more prestigious medical publications are imposing disclosure requirements on scientists when publishing their results. The Journal of the American Medical Association and the New England Journal of Medicine, for example, now detail researchers' financial ties to industry in order to alert readers to any possible bias.¹⁵³

V. BENEFICIAL EFFECTS OF UNIVERSITY-INDUSTRY COOPERATION

The federal laws encouraging university-industry cooperation have resulted in growing numbers of cooperative arrangements in the biotechnology industry that significantly contribute to the steady increase in the number of biotechnology patents sought by universities. This growth in the biotechnology industry has had a substantial impact on the public health and the regional and national economies, and it has the potential to increase with continued cooperation.

A. Federal Laws Encouraging Cooperation Have Resulted in Exponential Growth in the Biotechnology Industry

The incentives under federal law to increase cooperation that cause one party's utility to rest on another party's welfare have increased cooperation in the biotechnology industry. A variety of university-industry relationships have developed since the enactment of the Bayh-Dole Act.¹⁵⁴ Examples of such relationships include the following: industry sponsorship of university research, university ownership or interest in biotechnology firms, and commercial joint ventures or research consortia between universities and private industry.¹⁵⁵ Additionally, relationships between individual scientists conducting federally funded research and companies that purchase licenses in the research have become commonplace.¹⁵⁶ For instance, university researchers may enter into consulting agreements or research contracts in return for company stock, a percentage of sales, positions on company boards of directors or positions on scientific advisory boards for the industry.¹⁵⁷

Since the enactment of the Bayh-Dole Act, cooperation has resulted in the increase of technology transfer in general, as evidenced by the increase in patents issued to universities. Before implementation of the Act, relatively few patents were issued to universities annually.¹⁵⁸ A recent survey conducted by the Association of University Technology Managers reported that universities and other research institutions filed 2,700 patents in 1992 and granted over 1,500 licenses to industry.¹⁵⁹ As a demonstration of the increase in patents awarded since the enactment of legal incentives, the number of patents awarded to academic institutions in 1991 totaled 1,324, representing an increase of more than 200 percent over the 437 granted in 1980.¹⁶⁰ In contrast, cooperation and resulting technology transfer under the Stevenson-Wydler Act and the Federal Technology Transfer Act (governing agreements entered into by federally employed researchers) have increased since enactment of the laws, but not as successfully as under the Bayh-Dole Act. Of the 100 highest selling drugs on the market, 94 are based on patents filed by private companies, not by NIH, which sponsors research and retains intellectual property rights under CRADAs formed under the Act.¹⁶¹ The number of patents obtained under CRADAs may be

relatively low because the government retains intellectual property rights to the discoveries made under CRADAs, thus making such arrangements less attractive to industry than arrangements with universities.¹⁶² While the number of new CRADAs has suddenly increased by 37% in 1993, for a total of 206 such agreements, the number of CRADAs remained relatively stagnant at about 110 during the late 1980s and early 1990s and is still small in comparison to the number of university-industry relationships.¹⁶³

While not all of these patents represent biotechnology patents, the effect that university-industry cooperation has had on the increase in patents awarded under the respective Acts demonstrates the desirability of university-industry cooperation. It has been theorized that fewer patents have been awarded under the Stevenson-Wydler and Federal Technology Transfer Acts due to the fact that the federal laboratories may claim ownership to intellectual property rights under CRADAs formed under the Acts.¹⁶⁴ In comparison to the greater increase in patents awarded under the Bayh-Dole Act, which may be licensed to industry, it becomes evident that industry has greater incentive to invest in university research than to invest in CRADA agreements with federal laboratories. The greater incentive to invest in university research under the Bayh-Dole Act could prove crucial to the increased development of patentable biotechnological products.

B. Social and Economic Benefits

While universities and biotech companies benefit from cooperating with one another, society's benefits provide perhaps the most compelling rationale for encouraging university-industry cooperation. Society benefits from the introduction of new, lifesaving applications of biotechnology that are able to be introduced into the market because of university-industry collaboration.¹⁶⁵

University-industry relationships hold the promise of transferring biotechnological products essential to the public health more efficiently than academia or industry do individually. Discoveries and patents obtained under these relationships can profoundly enhance the quality of life for many individuals. For example, Genetech, Inc., secured approval on December 30, 1993 for Pulmozyme, the first new therapy for cystic fibrosis in 30 years.¹⁶⁶ Other ongoing research and patented therapies are focused on breakthrough treatments for many serious diseases, treatments that traditional science has not been able to provide.¹⁶⁷

Economic growth is also a substantial benefit of university-industry cooperation in the field of biotechnology. Biotechnology has involved breakthrough technology, which in turn has created markets and jobs.¹⁶⁸ In fiscal year 1992, sales and employment attributable to university-industry relationships formed under the Bayh-Dole Act were estimated to be between \$9 and \$13 billion in sales and 50-100,000 jobs, with an annual increase of between 25 and 30 percent.¹⁶⁹ The biotech industry currently represents a significant number of good-paying jobs, 87,000 directly and perhaps 100,000 more indirectly, with the potential for creating over a million jobs within the next 10 years.¹⁷⁰ By the year 2000, total biopharmaceutical sales are expected to reach \$100 billion, up from the \$16 billion achieved in 1992.¹⁷¹ The growing sales and employment figures represent growing tax revenues as well.¹⁷²

In the United States, university-based research provides an information base that fosters biotechnological innovation. New products and processes developed through that innovation and supported by capital formation and entrepreneurship are essential for real economic growth.¹⁷³ Such biotechnological innovations have made the U.S. the preeminent site of biotechnology research and manufacture in the world.¹⁷⁴ The ability to transfer basic research from universities to private companies for commercialization is indeed vital to American competitiveness globally.¹⁷⁵

VI. THE FEDERAL GOVERNMENT MUST REJECT PROPOSALS TO ENACT LAWS THAT COULD THREATEN COOPERATION

Proposals currently before the federal government create uncertainty and a perception of risk on the part of investors in biotechnology. Thus, such proposals could threaten the viability of biotechnology. Proposed national guidelines and regulation of university-industry cooperative agreements, as well as proposed profit caps or price controls on biotechnology breakthroughs, directly counter the objective of the Bayh-Dole Act and would seriously deter biotechnology research investment and innovation. Discouraging cooperation in the biotechnology industry would have repercussions not only on the competitiveness of American industry but also on the development and availability of life-saving drugs.

Despite the anti-industrial policy climate in Congress, and the call for budgetary cuts for biotech and scientific research in general, the Congressional majority is likely to maintain a commitment to basic research, particularly in the area of biotechnology.¹⁷⁶ Speaker of the House Newt Gingrich has demonstrated an allegiance to biotech interests in his support of the continuance of the tax credits for orphan drugs and his leadership in supporting the reform of the Federal Drug Administration (FDA) approval process.¹⁷⁷ Current legislation with respect to the biotech industry focuses on overhauling the FDA approval process to reduce the costs involved in transferring biotech products to the commercial sector.¹⁷⁸ While governmental involvement in private research will be seriously

examined, the current Congress is likely to view favorably current NRC recommendations to focus on basic research with priority funding to academia; the present Congress espouses a commitment to basic research, international competitiveness, and developing a budget which will be responsive both to interests in research and to interests in reducing the amount of government funding being dispersed directly to corporate laboratories.¹⁷⁹ Therefore, Congress is likely to reject the following proposals to increase regulation and to lower profitability potential of biotechnology research. However, because they are currently before the Congress and forces that led to their introduction will persist, I will analyze their potential impact on the biotechnology industry.

A. The Federal Government Should Not Adopt the Proposed NIH Guidelines Because They Lower the Payoffs of Investing in Biotechnology Research

Currently, proposals for a national NIH policy on conflicts of interest are being discussed before the Joint Economic Committee.¹⁸⁰ The NIH proposal includes the following: a reasonable delay of 30 days for disclosure of research findings, a limit of six months on a corporate sponsor's option to enter licensing agreements with universities after research results are found, a mandate that products developed with federal funds be substantially manufactured in the United States; a mandate of disclosure of inventions to the NIH prior to publication, a mandate that licensing rights be limited to the amount of funding the sponsor contributes to the research; and a provision that licensing rights may not be granted to sponsors without NIH approval.¹⁸¹

Reactions to the proposed NIH guidelines have not been supportive. Recent comments on the PHS proposal from seven hundred fifty-one respondents, representing various interested parties,¹⁸² are to the effect that the proposed guidelines would impose undue burdens on funded institutions and would impede mutually beneficial research collaborations between universities and industry.¹⁸³ The additional costs and burdens of the proposed guidelines would stem from the additional level of scrutiny of the university/industry relationships, as well as from the imposition of arbitrary time frames for publication and licensing that may not be responsive in all contexts. In addition to adding direct costs to collaborative arrangements, the proposed guidelines increase uncertainty related to the already high-risk nature of developing marketable biotechnology inventions, thus increasing the cost of-and deterring-investment in the industry.¹⁸⁴ The imposition of such uncertainty would significantly undermine the government's effort under the Bayh-Dole Act to encourage the transfer of technology into the market.

The current NIH proposal does not cure the problems of a previous set of guidelines proposed and rejected in 1989. The previous draft included such stringent measures as requiring that NIH-participating researchers have no financial interests in organizations that produce the inventions studied in a federally funded clinical trial.¹⁸⁵ The guidelines caused so much controversy that they were withdrawn within a matter of months by then-Secretary of Health and Human Services, Louis Sullivan.¹⁸⁶ The criticisms were focused on the restrictiveness of the guidelines, their prevention of fair remuneration to scientists, and their chilling effect on cooperative ventures between university researchers and corporate sponsors.¹⁸⁷ While the new NIH Proposed Guidelines relax restrictions on remuneration, the criticisms against restrictiveness and probable chilling effect remain.

The guidelines that NIH proposed would impose unnecessary restrictions and burdens, since policies originated at the cooperative-agreement level already adequately combat conflict-of-interest problems. The incentives in the biotechnology industry have caused the development of long-term cooperation, and the parties have thus developed their own policing mechanism of reciprocity through university policies and review standards, as well as university-imposed limitations on industry rights over inventions. Industry has accepted the university-imposed limitations in return for access to researchers and facilities. The self-imposed regulating mechanisms can be effective, given the long-term nature of the university/industry agreements and the likelihood of future encounters between universities and corporate sponsors.¹⁸⁸ Biotechnology inventions take years to develop, requiring the university/industry relationship to last over a significant period of time. At this relatively early stage in the biotechnology industry, stable biotechnology companies are still few in number, and so a university may realistically anticipate going to a given company or set of companies multiple times for research sponsorship. Additionally, internal incentives operate to maintain the integrity of research and development under such agreements. Universities that allow researcher misconduct and the publishing of fraudulent research results will inevitably harm their own reputations and abilities to attract learned researchers. Similarly, corporate sponsors are deterred from encouraging the development of fraudulent or unsafe products by the internal incentives to establish good reputations and avoid future product liability suits. Existing securities laws prohibiting insider trading deter both universities and corporate sponsors from mishandling research results and participating in bribery.¹⁸⁹

The NIH guidelines should be rejected because universities have implemented their own policies; moreover, universities are better equipped than external regulators to protect the integrity of university research.¹⁹⁰ Universities can most easily access information about conflicts of interest by requiring faculty to document and report any industry-sponsored research activities to department heads or to university administration. University faculty are better equipped to evaluate research proposals because they have the easiest access to information within the university and possess a case-by-case expertise that external regulatory agencies may lack.¹⁹¹ Universities are also better equipped to formulate policies concerning collaboration with industry that are acceptable to both faculty

and university administrators, since they can consider faculty preferences and concerns and thus gain the respect and support of the faculty for university policies.¹⁹²

Current governmental regulation of federally funded research sufficiently monitors conflicts of interest and ensures funding disclosure. The Public Health Service (PHS), which includes NIH, currently requires that "[t]he source and amount of costs and/or the value of third party in-kind contributions proposed by the applicant or recipient to meet a matching requirement must be identified in the application."¹⁹³ In addition, PHS guidelines already require institutions receiving PHS funds to implement policies regarding conflicts of interest and to provide safeguards against the appearance of financial motivation on the part of researchers, or risk losing PHS funding.¹⁹⁴

Under the current federal policy, control is left with the party most able to police defecting researcher conduct: the universities. Attempts by the federal government to control conflicts of interest through national policy guidelines for federally funded research would only discourage cooperation between universities and industry by increasing the cost of cooperation by adding another layer of bureaucracy. As discussed, the AMA, universities and medical journals have established policy guidelines on their own initiative to counter potential conflict of interest problems relating to delayed publication, falsification of findings and profit-influenced direction of research.

B. The Federal Government's Proposal to Set Price Controls on Breakthrough Biotechnology Drugs Would Lower the Payoffs for Investment in Innovation

The federal government proposes implementing price controls with the stated purpose of making breakthrough drugs more available to patients. In reality, price controls threaten to reduce the availability of breakthrough drugs by undercutting incentives to invest in research from the start. Investment in biotechnology research, in particular, is already a high-cost, high-risk venture where future profits are uncertain. Price controls lower the potential profitability of biotechnological research and therefore increase the risk that investors will not recover their investments. Price controls therefore reduce the incentives for companies to provide financial support for biotechnology R&D, whether they cooperate with universities or conduct their own research. Fewer incentives for companies to cooperate with universities result in fewer biotechnological discoveries and fewer life-saving drugs available to patients.

1. The federal government's price control proposal

Proposed price caps would limit the potential profitability of technology transfer from academic researchers to commercial industry.¹⁹⁵ The proposed caps are indirect, in that agencies and legislatures would insert a "reasonable price clause" into each cooperative agreement among or between government, academia and industry.¹⁹⁶

President Clinton's proposed health-care plan also threatened investment and innovation incentives; Congress should avoid reviving such a threat. Clinton's health care plan proposed de facto price controls for breakthrough drugs.¹⁹⁷ The proposal included a "special rebate" provision, which is a classic price control mechanism. Such a price control would be undesirable because it would permit unfettered governmental discretion to set the rebate at whatever amount it wished, since the drugs would be blacklisted if the producer rejected the rebate.

Price controls are directly counter to cooperative-agreement incentives embodied in the Bayh-Dole Act, the Stevenson-Wydler Act and the Federal Technology Transfer Act. Senator Birch Bayh (D-Ind), co-author of the Bayh-Dole Act, testified in an April 1994 oversight hearing of the Senate Subcommittee on Patents, Copyrights and Trademarks, that legislative proposals to impose price controls on cooperative research and development agreements would "discourage industry and not-for-profit institutions from participating in these CRADAs," given the impossibility of predicting the ultimate cost of products resulting from such agreements.¹⁹⁸

2. Price controls would reduce the availability of breakthrough drugs by increasing the cost of investment in innovative research

While biotechnology revenues are expected to reach the \$100 billion mark by the year 2000, up from the \$16 billion in 1992,¹⁹⁹ the financial outlook for profits is uncertain. As of 1993, fewer than one percent of the 1300 biotechnology companies in the United States were profitable.²⁰⁰ The biotechnology industry as a whole has never had a profitable year. Net losses for the industry totaled \$3.6 billion in 1993, an increase of six percent over 1992.²⁰¹ Most individual biotechnology companies have less than 18 months of funding left. In fact, many of them have less than 12 months of remaining funding and dozens have less than six months of funding.²⁰² Ernst & Young reports that biotech companies are raising capital now at 25 percent of their burn rate (the rate at which capital is being expended).²⁰³ The report indicates that the burn rate reflects the large amount of capital invested in research, as biotechnology

companies spent \$5.7 billion on research in 1992. With the average cost per new chemical entity (NCE) equaling \$359 million,²⁰⁴ threats by the federal government to implement price controls on biotechnology products severely limits potential profits needed to maintain investment in biotechnology research.

Opponents of university-industry collaboration in the biotechnology industry cite the initial \$10,000 annual price of AZT, the treatment found to thwart the HIV virus, as evidence that the government should impose price controls on breakthrough drugs.²⁰⁵ While the price for breakthrough drugs may initially be astronomical, the free market quickly lowers their price.²⁰⁶ This held true for AZT, as other companies developed the drug, and the price of AZT dropped precipitously within two to four years of its introduction into the market.²⁰⁷

Additionally, biotechnology companies that sell orphan drugs have voluntarily established programs to ensure that patients can receive needed drugs despite an inability to pay. Eligible patients are those who do not have private health insurance and who are not covered by Medicare or Medicaid. Of the patients receiving biotech orphan drugs, "[a]s many as 10% . . . receive them under these programs."²⁰⁸ These programs lower the profitability of biotechnology companies, but the companies have imposed them on themselves to ensure accessibility of the drugs to needy patients. Federally imposed price controls would simply lower profitability unnecessarily since the market and the individual companies are effectively making the drugs accessible to the patients that need them.

The initial prices for breakthrough therapies in the United States appear high but are actually consistently lower than the prices for the same drugs in other countries. Prices for the leading biotech drugs are often three times higher in Japan, where the government sets the prices.²⁰⁹ The Biotechnology Industry Organization (BIO) "is aware of only one case in which a biotechnology company charges a lower price for its drugs in a major developed country than does any company based in the United States."²¹⁰

Japan adopted its high-pricing policy precisely to encourage innovation and to compete with the United States.²¹¹ The United States government threatens to do precisely the opposite by imposing price controls below current prices, which would discourage innovation and lower America's global competitiveness. With Japan providing incentives for innovation, the United States should seriously consider the implications of penalizing innovation. Discouraging innovation through price controls will likely inhibit university-industry cooperation, which the federal government has up to now encouraged. This in turn would stifle innovation and product development. The end result could be that desperate patients are deprived of the very life-sustaining drugs that proponents of price controls are arguably trying to make more accessible. One doctor explained that "price controls would quite literally pull out the underpinnings of the biotech industry and cause it to self-destruct. Setting pricing is often put under the guise of 'helping' the patients when, in fact, it will deprive them of lifesaving new treatments."²¹²

The argument that price controls on breakthrough drugs will lower total health care costs is misplaced. In reality, the price of breakthrough drugs constitutes only one-fifth of one percent of the total costs of the health care system.²¹³ For example, "[o]nly 7% of the cost of health care in America comes from the cost of drugs, \$56.1 billion out of \$823 billion. Only 3.4% of this 7% comes from the breakthrough biotech drugs, \$1.9 billion out of \$56.1 billion."²¹⁴ Carl Feldbaum, President of BIO, argues that eliminating the total cost of every drug would have a "trivial and imperceptible impact on total health care costs."²¹⁵

More importantly, breakthrough drugs are the most cost-effective means to combat health care costs. Biotechnology therapeutics contribute substantially to a reduction in total health care costs by:

shorten[ing] or eliminat[ing] the need for hospitalization, help[ing] to avoid emergency room visits, serv[ing] as substitutes for expensive surgeries, and keep[ing] people out of nursing homes. . . . Biotechnology therapeutics are also in many cases more cost-effective than the products they are taking the place of. For example, granulocyte colony-stimulating factor (G-CSF) helps restore the blood's immune cells in patients with small-cell lung cancer, thereby reducing the number of days of hospitalization by approximately 50 percent compared with the number of patients were hospitalized if they received no G-CSF treatment. The drug costs \$1,000 per course of treatment, but by preventing infections it can save roughly \$7,000.²¹⁶

Price controls enacted in other countries are evidence that such controls stifle investment and innovation in research. In the United Kingdom, price controls on innovative medicine has reduced the number of the country's top ten best-selling products worldwide from three out of the ten in 1988 to only one in 1992. In 1989, the German Health Ministry designed a plan to control drug costs which limited the price public health plans could pay for drugs and limited which drugs would be eligible for reimbursement. A five percent reduction in drug prices was mandated by the government in 1993. Out of over 126 pharmaceutical firms in Germany, 40 percent have cut their R&D investment by 10-30 percent, 22 percent of the firms have cut R&D by a third or more, and two German companies made no investment in 1994. The Ministry of Health in France controls the price of each individual product at the time of introduction

as well as subsequent price increases. This price-control practice contributes to France's status as one of the least globally competitive countries in terms of developing innovative products.²¹⁷

The mere threat of price controls has already had a negative impact on investment in the biotechnology industry. The American Stock Exchange Biotechnology Index lost 32.6 percent in 1993²¹⁸ when public investors were deterred by the de facto price controls in the president's health care plan. The investors feared that they would not be able to recoup their investment in companies that were close to bringing a product to market.²¹⁹

The refusal to invest in companies that may be subject to price controls is evidenced by the lower number of CRADAs formed in 1993 compared to the number formed in 1992. According to Conte, "1993 was the worst year for new CRADAs in the history of the program," with only 26 new CRADAs created compared with 47 new CRADAs in 1992.²²⁰ The lower investment in CRADAs exemplifies the negative impact that "reasonable price" clauses may have on investment, as the NIH has already been inserting a "reasonable price clause" into its CRADA agreements over the last few years.²²¹ The evidence of how investors are responding to existing and potential profit caps via reasonable price clauses strongly indicates that reasonable price proposals should be rejected to salvage investment and cooperation in the biotechnology industry. This ideology has already been accepted by the NIH, which now promises to eliminate the "reasonable price" clause from CRADA agreements. NIH Director Harold Varmus has announced that the clause is being eliminated because "a year-long analysis of technology transfer at the NIH has revealed that the clause has driven industry away from collaboration with NIH and produced no gain to the public."²²² The lessons learned by NIH should prove to be a significant deterrent to Congress against enacting price controls over the broad spectrum of biotechnology breakthroughs resulting from collaborations between government, industry and universities.

Biotechnology therapies are especially important for enhancing the quality of life for patients with otherwise terminal diseases. For example, ALFA-interferon saves the lives of patients afflicted with hairy cell leukemia, and ceredase treats Gaucher's disease (a rare genetic disease), providing patients with the "opportunity to live somewhat of a normal life."²²³ Price controls would have a deleterious effect on the advancement of much needed therapies and cures by reducing research and innovation, as summed up by one cancer patient's plea:

My own conclusion, after looking at the facts, is that price controls on drugs would not serve the public well. Those patients who are fortunate enough to have a drug for their disease would be able to buy their drug a little cheaper. Other patients for whom there are no good drugs, such as myself, would go without and die. The reason is that R and D for new drugs depends on the cash flow from existing products. Price controls, price caps, or the setting of reasonable prices by a government agency threaten R and D investment, making it less likely that there will ever be a good drug for my kidney cancer.²²⁴

If the goal of the proposed price controls and extensive regulatory guidelines is to improve America's health care system, the foregoing proposals are simply misguided. Fewer hospital stays, better treatments, earlier diagnoses, and improved outcomes would reflect improvements in the health care system. However, such improvements are unlikely if the federal government remains preoccupied with the input costs of drug development and ignores the potential for outcome savings. In other words, improvements to the present health-care system in the United States are contingent upon the development of biotechnological products, which has the potential reduce the need for complex and expensive health-care services.

VII. CONCLUSION

Biotechnology has great potential to provide critical breakthrough drugs for the treatment of serious and previously non-treatable diseases. The benefits of biotechnology can also extend beyond the development of life-saving drugs to the solution to world-wide agricultural and environmental problems. University-industry cooperation is necessary to drive such development.

The infrastructure for supporting such cooperation is already in place. The high-risk and capital-intensive nature of the biotechnology industry creates a setting in which parties will interact repeatedly over long-periods of time. The elongated shadow of the future, under the Axelrodian model for cooperative behavior, closely models this setting. For example, because biotechnology is a new field, research talent and sophisticated research equipment are relatively scarce, and sophisticated research equipment required in the field is often prohibitively expensive. The sharing of resources by universities and private companies, where the former supply the equipment and expertise and the latter supply research funding, increases the financial payoffs for each party in the development of breakthrough drugs. The public clearly benefits from the increased availability of such drugs. University-industry cooperation is preferable to an alternative setting characterized by independent research and development because it allows the parties involved to share resources and improve the payoffs to universities, industry and society by reducing investment costs and spreading risks.

Even though the government provides a substantial amount of funding to support biotechnology research, it cannot provide enough. This is particularly so in the present deficit-reduction political climate. Therefore, universities can find themselves strapped for funding for biotechnological research unless they can obtain corporate sponsorship. For their part, biotechnology companies typically are unable to raise sufficient capital for independent basic research in this field. Therefore, university-industry cooperation is needed to sustain basic research in biotechnology.

Even if federal government had adequate resources to support university research in biotechnology, neither the federal government nor universities have historically been as effective as university-industry cooperative ventures in transferring technology to the marketplace. However, such cooperation raises the specter that the profit motive will unduly influence the nature of basic research efforts. However, the fact that universities often retain patent rights over inventions goes against this fear. That is because in holding patent rights, universities are not foreclosed from conducting research related to the patented subject matter, whereas they are still able to license the patented subject matter to companies that can actively develop the product. This situation enables the creation of an arm's length relationship between universities and industry, one that promotes technology transfer without concomitantly providing to the companies power to impede all related research.

Researcher misconduct could potentially arise in university-industry cooperation agreements, but concerns over such misconduct should not lead to actions that inhibit cooperation between these entities. Private monitoring mechanisms, characterized by reciprocity, are already in place, and these have proven successful in managing potential conflicts of interest. Researcher misconduct is monitored and punished through university policies and financial-disclosure requirements of various universities and journals, as well as through federal policy. Companies have further incentives to be honest about research findings due to the threats of product liability and harm to business reputation. The effectiveness of these mechanisms is evidenced by the fact that conflicts of interest have generally not arisen to the detriment of basic research in biotechnology.

The federal government has acknowledged that biotechnology is a crucial field, and the legislature passed the Bayh-Dole Act specifically to specifically foster such university-industry cooperation agreements. Through the Stevenson-Wydler Technology Innovation Act, which established agencies to investigate potentially viable technology, universities and industry necessarily develop the ability to recognize the characteristics of other parties in the field. Through the Bayh-Dole Act and the Federal Technology Transfer Act, the government has provided an altruistic motivation for universities to cooperate with industry. The welfare of each party rests on the ability of the other parties to make scientific strides and to increase their own welfare.

The recent federal proposal to institute strict regulatory guidelines over research conducted through university-industry cooperation substantially undermines the goals of the Bayh-Dole Act. An additional layer of regulation not only discourages cooperation but is unnecessary to protect against researcher misconduct since there presently exist disincentives to such misconduct. The price the proposed regulations would exact is an increase in the cost of development of breakthrough products by delaying their marketability. That is because the proposed regulations would disincentive university-industry cooperative agreements by increasing the cost of maintaining such cooperative arrangements.

Proposed price controls on breakthrough drugs likewise lower the incentive for cooperation in the field of biotechnology by increasing uncertainty as to whether returns will be made on the investment. Although price controls are intended to increase the availability of drugs by limiting their cost to consumers, they would actually decrease their availability by reducing investment in necessary underlying research. Data show that the mere proposal of price caps has already exerted an adverse effect on investment in biotechnology. Cooperation is the key to the development and transfer of biotechnological inventions, not federal regulations that unduly burden such cooperation.

Rather than imposing disincentives to cooperation, the federal government should focus on maintaining support for biotechnology research. Such focus would be consistent with Congress's current plan to encourage cooperation and reduce the government's own research costs by redistributing funding primarily to research institutions. Federal funding is essential to the development of biotechnology and is beneficial to society as a whole. Federal funding in the area of biotechnology increases the likelihood and imminence that innovations such as life-saving drugs will be developed. However, another real benefit to taxpayers is that the federally funded university-industry cooperation agreements positively impact economic growth. Federally funded cooperative agreements have been responsible for the explosion of biotechnology. As a result, more biotechnology companies have entered the industry and new jobs are continually being created. Local economies experience growth, and the United States as a whole enjoys a competitive edge in the global biotechnology industry.

Cooperation in the field of biotechnology will facilitate the development of products that benefit society. Developments in biotechnology promise to improve public health and enhance quality of life. At the same time, biotechnology could stimulate the national and local economies, raising the overall economic position of the United States.

1996 Gina A. Kuhlman.

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1. The federal government proposes to impose reasonable price clauses in cooperative agreements among or between government, academia, and industry and to instate de facto price controls for breakthrough drugs. These proposals are discussed in Section VI. B. *supra*.

2. *Competitiveness of the U.S. Biotechnology Industry: Hearing Before the Subcomm. on Science, Technology, and Space of the Senate Comm. on Commerce, Science, and Transportation*, 103rd Cong., 2d Session 18 (1994) (statement of Lisa Conte, President and CEO, Shaman Pharmaceuticals) [hereinafter Conte]. Biotechnology is fundamentally a technology that either improves on, or increases the quantity of, natural products. *Biotechnology: Part of the Solution: Hearing Before the Subcomm. on Technology, Environment and Aviation of the House Comm. on Science, Space and Technology*, Cong. (1993), available in LEXIS, Legis Library, CMTRPT File (statement of Marc E. Goldberg, President, Massachusetts Biotechnology Research Institute) [hereinafter Goldberg]. Beginning with the discovery of DNA, biotechnology has been responsible for developing such treatments as gene therapy, which is potentially the most effective and longest-term treatment for mankind's most severe and previously untreatable diseases. *Hearing Before the House Comm. on Science, Space and Technology*, Cong. (1994), available in LEXIS, Legis Library, CMTRPT File (statement of Robert T. Abbott, President and CEO, Viagene, Inc., on behalf of the Biotechnology Industry Organization) [hereinafter Abbott]. See also, Goldberg, *supra* (The production of healthier food products in the past involved years of selective breeding; today, biotechnology has helped produce food products superior in nutrition which thrive under a wider range of growing conditions and are organically more resistant to insects.).

3. *Hearing Before the Subcomm. on Technology, Environment and Aviation of the House Comm. on Science, Space and Technology*, Cong. (1994), available in LEXIS, Legis Library, CMTRPT File (statement of Carl B. Feldbaum, President of the Biotechnology Industry Organization) [hereinafter Feldbaum].

4. Conte, *supra* note 2.

5. *Id.*

6. Goldberg, *supra* note 2.

7. *Competitiveness of the U.S. Biotechnology Industry: Hearing Before the Subcomm. on Science, Technology, and Space of the Senate Comm. on Commerce, Science, and Transportation*, 103rd Cong., 2d Session 39 (1994) (statement of Barry Jacobsen, Dean, College of Agriculture, Montana State University-Bozeman) [hereinafter Jacobsen]. Applications of biotechnology in agriculture can be divided into three basic areas: improved plants, improved animals, and bioprocessing in the industrial sector. It is the production and processing of food, and ultimately its marketing, that employs approximately one in five people in the United States today. *Id.* at 40. This accounts for roughly 19 percent of the gross domestic product. In 1993, it accounted for approximately \$42 billion in export surplus for this country. *Id.* at 36.

8. *Id.* at 39.

9. Conte, *supra* note 2. Not only is biotechnology vital to the medical world, but it is now also of vital importance to world-wide progress in improving agriculture and cleaning the environment. Lisa Conte testified before the Senate Subcommittee on Science, Technology and Space that "[a]gricultural biotechnology promises to improve the nutrition, taste and yield of our food crops while lowering farm input costs and offering environmental benefits over existing agricultural technologies through the net reduction of chemical pesticide use." For example, the development of biopesticides-organically produced, nontoxic proteins which strengthen the resistance of crops to destruction by insects-has created a practical and important alternative to the use of synthetic chemical pesticides. *Id.*

10. Conte, *supra* note 2 at 21.

11. *The Biotechnology Industry: Hearing Before the Joint Economic Committee*, Cong. (1994), available in LEXIS, Legis Library, CMTRPT File (statement of Roger C. Herdman, Director of the Office of Technology Assessment) [hereinafter Herdman]. The manufacture of technology-intensive products contributed significantly to the growth experienced by the world's leading market economies during the past decade as evidenced by its growing share of total manufacturing output: United States-30.4% in 1990, up from 20% in 1980; Japan-35.1% in 1990, up from 20% in 1980; and EC-12-20% in 1990, up from 15.2% in 1980. *Supra* note 1. Recent data show that "United States bio-pharmaceutical companies have 70% of all biotechnology based drugs on the market and 70% of all biotechnology drugs in development. . . . The United States discovered 47% of world class drugs between 1990-1992, which far outpaces any other country's share. The U.S. received 140 patents in the biotechnology driven field of gene engineering in 1992. . . . The next country, Japan, had sixteen." Feldbaum, *supra* note 3.

12. Conte, *supra* note 2, at 18. Lisa Conte, president and CEO of Shaman Pharmaceutical, testified before the Senate Subcommittee on Science, Technology, and Space that: "In 1991, the Office of Technology Assessment (OTA) found that Austria, Brazil, Denmark, France, South Korea and Taiwan (Republic of China) all had targeted biotechnology as an enabling technology. Furthermore, in 1984, the OTA specifically identified Japan as the major potential competitor to the U.S. in biotechnology commercialization." *Id.* (citing U. S. Congress, Office of Technology Assessment, *Biotechnology in a Global Economy* 243 (October 1991)). The United States' preeminence in biotechnology is particularly threatened by Japan, which has mounted a challenge in biotechnology "in the same way that it earlier targeted the semiconductor and consumer electronic industries." The President's Council on Competitiveness, *Report on National Biotechnology Policy* 5 (February 1991).

13. Conte, *supra* note 2 (citing White House Office of Science and Technology Policy, *Report of the National Critical Technologies Panel* 7 (1991) (the National Critical Technologies Panel was established in 1989 pursuant to the National Competitiveness Technology Transfer Act, Pub. L. No. 101-189, 103 Stat. 1352 (42 U.S.C. §6681 et seq.)).

14. *H.R. 4160, Legislation to Amend the Orphan Drug Act: Before the Subcomm. on Health and the Environment of the House Energy and Commerce Comm.*, June 16, 1994, available in LEXIS, Legis Library, CMTRPT File (statement of Thomas Wiggans, President of Connective Therapeutics) [hereinafter Wiggans] Speaking on behalf of the Biotechnology Industry Organization (BIO), Wiggans stated that the reason the biotechnology industry has not seen a profitable year is because of the immense capital and time required to develop breakthrough drugs into marketable products, coupled with the long odds against a biotechnological drug surviving the hurdles associated with the regulatory process. *Id.*

15. Breakthroughs are defined as "therapeutic products capable of delivering benefits never before available." Goldberg, *supra* note 2.

16. Goldberg, *supra* note 2.

17. Kenneth J. Wigger, *Why the Biotech Industry is in Peril*, SAN DIEGO UNION TRIBUNE, June 20, 1993, at G-3.

18. Brigitta Bienz-Tadmor and Jeffrey S. Brown, *Biopharmaceuticals and Conventional Drugs: Comparing Development Times*, BIOPHARM, at 44, 48 (March 1994).

19. *Id.*

20. BIO is the predominant organization of the biotechnology industry. The organization "represents more than 500 biotechnology companies, universities, state biotechnology centers and service organizations in 47 states." Feldbaum, *supra* note 3.

21. *Id.* Private investment is the lifeblood of the industry because the industry is characterized by not yet having a base of revenue from existing product sales with which to reinvest into research and development. Feldbaum argues that private investors "rightly expect a return on their investment commensurate with the risk they are taking," and that the risks are worth taking and the rewards are worth giving to the investors because society is in desperate need of the high-risk research in the combat against its gravest diseases. *Id.*

22. Genzyme and Amgen, two member companies of BIO, raised \$328 and \$406 million, respectively, in equity before bringing their first products to market. Wiggans, *supra* note 14 at 11. One biotech company, NeoRx, currently awaits approval of its first product, 10 years and \$100 million after its founding. Abbott, *supra* note 2. NeoRx is a public biotechnology company founded by Robert Abbott,

who is now president and CEO of Viagene, the country's largest gene therapy company. NeoRx's research centers on pharmaceutical applications of monoclonal antibodies. *Id.*

23. *Hearing Before the Senate Small Business Comm.*, May 26, 1994, available in LEXIS, Legis Library, CMTRPT File (statement of Harry Penner, President and CEO, Neurogen Corporation, representing the Biotechnology Industry Organization) (citing U.S. Congress, Office of Technology Assessment, *Pharmaceutical R&D: Costs, Risks and Rewards*, OTA-H-522 (Washington, DC: U.S. Government Printing Office, February 1993)). Viagene is arguably the most financially stable of the gene therapy companies in existence today, and is a startling example of the amount of capital a company must tie up in the development of marketable products. The company employs over 160 persons, including about 40 Ph.D.s and M.D.s, and spends approximately \$25 million per year in gene therapy research and development. Viagene focuses primarily on developing treatments for such serious diseases as AIDS and cancer. Abbott, *supra* note 2.

24. Peter Coy et al., *In the Labs, the Fight to Spend Less, Get More*, BUSINESS WEEK, (June 28, 1993), 102, According to the survey, expenditures per employee are as follows: Biogen, \$178,168; Genentech, \$115,893; Centocor, \$105,291; Amgen, \$78,072; Chiron, \$76,554; Genetics Institute, \$66,572; and Immunex, \$55,034. *Id.*

25. Feldbaum, *supra* note 3. Ernst & Young reports that biotechnology firms spent \$5.7 billion on research in 1993, a 14 percent increase over 1992. ERNST & YOUNG, BIOTECH 94 LONG TERM VALUE SHORT TERM HURDLES, EIGHTH ANNUAL REPORT ON THE BIOTECH INDUSTRY, VIII (1993).

26. Feldbaum, *supra* note 3. The high cost of biotech research is attributable to the fact that it is in the critical stage of basic research, i. e., the development of fundamental knowledge required so that such knowledge can eventually be utilized in applied research, which focuses on developing therapies for specific diseases. The prevalence of basic research in the biotechnology industry is evidenced by the fact that all of the latest Nobel prizes for Medicine and Chemistry were for biotechnology. *Id.*

27. David E. Korn, *Patent and Trade Secret Protection in University-Industry Research Relationships in Biotechnology*, 24 HARV. J. LEGIS. 191, 195 (1987).

28. *Id.* "Technology transfer," as used in this Article, is the process by which research innovations are developed into marketable products and transferred into the commercial market where they become available for consumer use. In the field of biotechnology, transferring technology to consumers is critical because the developments treat society's deadliest diseases.

29. The CPR device is an inflatable chest wrap that promised to double the 15% survival rate achieved by manual CPR. *Owning Hearts and Souls*, MEDICINE & HEALTH, February 8, 1993.

30. *Id.*; see also Sandy Sugawara, *Cashing in on Medical Discoveries: Hopkins's Corporate Ties to Help Fund Research*, WASHINGTON POST, Jan. 4, 1993, at F-01.

31. Korn, *supra* note 27, at 191.

32. MIT has had the explicit mission to establish close research ties with industrial interests. BERNARD D. REAMS, JR., UNIVERSITY-INDUSTRY RESEARCH PARTNERSHIPS: THE MAJOR LEGAL ISSUES IN RESEARCH AND DEVELOPMENT AGREEMENTS (1986), at 34.

33. Collaboration with industry through, e.g., MIT's Industrial Associates Program developed after World War I, inherently provided incentives to cooperate by reducing the payoffs for competition. *See id.*

34. *Id.*

35. As a result of the relationship formed, patent applications were filed on behalf of Professor Harry Steenbock for methods he developed for irradiating milk to activate vitamin D. *Id.*

36. *Id.*

37. *Act donating Public Lands to the Several States and Territories which may provide Colleges for the benefit of Agriculture and*

Mechanical Arts, ch. CXXX, 12 Stat. 503 (1862) (the Act provided assistance to state and private education institutions through the sale of federal government land). The purpose of the Morrill Act "was sufficiently broad and general to include all the varied concepts of industrialists: ' . . . the endowment, support, and maintenance of at least one college where the leading object shall be . . . to teach such branches of learning as are related to agriculture and the mechanic arts . . . in order to promote the liberal and practical education of the industrial classes in the several pursuits and professions of life.'" REAM, *supra* note 34 at 24 (citing EARLE D. ROSS, *DEMOCRACY'S COLLEGE: THE LAND-GRANT MOVEMENT IN THE FORMATIVE STYLE* (Ames, Iowa: Iowa State College Press, 1942) at 47).

38. REAMS, *supra* note 32, at 25.

39. Goldberg, *supra* note 2.

40. REAMS, *supra* note 32, at 27.

41. Order by the Council of National Defense Establishing the National Research Committee, 5 Fed. Reg. 2446 (1940); Exec. Order No. 8807, 3 C.F.R. 959 (1938-1943) (*amended by* Exec. Order No. 9309, 3 C.F.R. 1256 (1939-1943.)) With the conclusion of World War II in 1945, OSRD went out of existence.

42. ROBERT AXELROD, *THE EVOLUTION OF COOPERATION* (BASIC BOOKS) at 124-141. Axelrod proposes that the emergence of cooperation develops through the transformation of the strategic setting in which players interact. Axelrod's model emphasizes that a party's own self-interest can best be served through cooperation when the strategic setting is arranged so that "the same two individuals will meet each other again, be able to recognize each other from the past, and to recall how the other has behaved until now." *Id.* at 125. This continuing interaction is the key in Axelrod's model in making cooperation based on reciprocity possible. *Id.* Axelrod's premise is that "if the strategic setting allows sufficiently long interactions to occur between parties, even the egoist will cooperate where there is a short-term incentive not to cooperate." *Id.* at 124.

43. "Enlarging the shadow of the future" refers to increasing the durability or the frequency of the interactions between parties. Enlarging the shadow of the future promotes cooperation by increasing the significance of the future in relation to the present. *Id.* at 126. Where the probability of frequent meetings between parties in the future is high, each party will have an incentive to cooperate in the present because the payoffs in the future will be greater given past cooperation between the parties.

Axelrod uses an iterated Prisoner's Dilemma, in which he refers to the interactions as "TIT FOR TAT," to illustrate the payoffs of mutual cooperation in a setting which makes the future more important than the present by enlarging the shadow of the future. Axelrod's numerical example of the payoffs for cooperation or defection (non-cooperation) is as follows: "the temptation to defect while the other is cooperating gives $T = 5$, the reward for mutual cooperation is $R = 3$, the punishment for mutual defection is $P = 1$, and the sucker's payoff for cooperating when the other defects is $S = 0$." Supposing the next move (in a subsequent interaction) is worth 90% of the current move, making w (the discount parameter) = .9, it does not pay to defect on the current move because the other party will be encouraged to use TIT FOR TAT, or reciprocate the defection. While the payoff in the first move may be $T = 5$ for defecting while the other party cooperates, a TIT FOR TAT strategy will only create mutual defection in each subsequent interaction, making the maximum payoff for each subsequent move amount to $P = 1$. Numerically, never defecting when meeting TIT FOR TAT will result in a score of R on each move. A total expected score will be $R + wR + w^2R . . .$ i.e. $R/(1-w)$. For $R = 3$ and $w = .9$ this is 30 points. Always defecting results in a first time score of $T = 5$, but subsequent mutual defection accumulates to only a score of 14 points. Even if a player alternates defection and cooperation, repeatedly exploiting TIT FOR TAT at the cost of being exploited herself, the maximum total points obtainable equals 26.3. *Id.* at 127.

One example of cooperation emerging from the durability of an interaction is the live-and-let-live system developed during the trench warfare of World War I. *Id.* at 129. Enemies were often engaged in static combat, in which the enemies fought the same opposing units over substantial periods of time. The enemies developed a system of mutual restraint, whereby soldiers on the front lines, for example, would not engage in combat during the each other's meal times. This system of non-aggression emerged because the payoff for mutual restraint-life-was much greater than the punishment for mutual defection-death. *Id.*, at 77.

An example of enlarging the shadow of the future by increasing the frequency of future interactions is the concentration of players so that they must interact with each other. For example, store clerks and customers in a small town will have an easier time developing cooperative relationships because of repeat interactions than store clerks who only see repeat customers at long and unpredictable intervals. *Id.* at 130. Even if a majority of the interactions of the parties will be with the general population, cooperation will develop and stabilize where the parties have a non-trivial proportion of their interactions with each other. *Id.* at 131.

44. Increasing each player's payoffs requires that payoffs be altered so that the long-term incentive for mutual cooperation becomes greater than the short-term incentive for defection (non-cooperative behavior). This can be effected by either increasing the short-term payoff for cooperation or increasing the short-term punishment for defection, relative to the duration and frequency of interactions (i. e., relative to the discount parameter, w). *Id.* at 134. A common example of laws that provide incentives to cooperate by changing the payoffs is the tax laws. The direct benefits of paying taxes are so diffuse that no one wants to pay taxes; however, each person will be better off by cooperating in paying taxes because he will share in the benefits of the collective goods such as roads and schools. Conversely, the tax laws decrease the incentive for defection-not paying taxes-because if detected, the punishment is a jail sentence. *Id.* at 133.

45. Axelrod suggests supplying motives that will cause people to act altruistically, which he defines as "the phenomenon of one person's utility being positively affected by another person's welfare." The premise is that one party will receive benefits when it pays welfare costs-the costs of acting generously in return for benefits-to achieve the desired benefits. The classic example is that "[a] mother who risks her own life to save several of her offspring, can increase the odds that copies of her genes will survive." *Id.* at 135.

46. Cooperation is best achieved when interacting parties practice a system of "TIT FOR TAT," which is generally a system implementing the "eye for an eye" strategy. This is more effective than practicing unconditional cooperation because inevitably that strategy will be exploited by others. As indicated in the illustration of the iterated Prisoners' Dilemma, the short-term payoff for defection where the other interacting party attempts to cooperate is higher than the short-term payoff for mutual cooperation. See *supra*, note 45. Reciprocating defection elicits cooperation in subsequent interactions because it results in a lower short-term payoff for the initial defecting party. In other words, a strategy that guarantees the "punishment of any individual who tries to be less than cooperative renders the deviant strategy unprofitable." *Id.* at 138. Additionally, a reciprocating party benefits when other parties, with whom she may never interact, reciprocate as well. This is because the other's reciprocity functions as a police mechanism to deter those parties who try to be exploitive. In turn, this decreases the likelihood that non-exploitive parties will deal with uncooperative parties in the future. *Id.* at 139.

47. Cooperation can only be sustained in settings where each party is able to recognize the other players and their features from past interactions. Axelrod provides a biological illustration of birds that are able to "distinguish among a number of neighboring birds by their songs. This ability allows birds to develop cooperative relationships-or at least avoid conflicting ones-with several other birds." *Id.* at 140. Inherent in the recognition ability required to sustain cooperation is the ability to recognize defection when it occurs. *Id.*

48. *Id.* at 124-41; see *supra* note 43 for a detailed analysis of Axelrod's concept of an elongated shadow of the future as required for cooperation to emerge and be sustained.

49. It should be noted that the enlarged shadow of the future created by the long-term nature of biotech research relationships is only one factor that fosters university-industry cooperation. University-industry cooperation is unlikely to emerge without federal funding and federal laws that encourage cooperation. The capital-intensive nature of biotechnology research is such that without federal funding, important biotechnology research may suffer due to lack of capital. Even if universities and corporations could raise enough capital to perform biotechnology research independently of one another, the length of time required to raise such capital coupled with the high risk of investment in biotechnology would significantly delay research. While Federal funding has contributed significantly to biotechnological developments, a funding gap exists that requires universities to cooperate with industry to attract needed funds. Additionally, even if Federal funding was sufficient, history has shown that universities alone do not have adequate mechanisms to transfer technology into the marketplace without corporate sponsorship. Federal laws allowing universities to retain patents, and therefore to retain rights and control over research developments, provide an additional incentive for universities to cooperate with industry. The federal laws likewise provide incentives for industry to cooperate with universities by permitting industry to share resources with federally sponsored research universities, thus lowering corporate investment costs in the long-term, high-risk field of biotechnology research. As a result, an enlarged shadow of the future fosters university-industry cooperation, whereas federal support provides the initial incentives to cooperate.

50. See, generally AXELROD, *supra* note 43, at 133. Axelrod's Prisoner's Dilemma model suggests that increasing the payoffs for cooperation reduces the likelihood of either party defecting. In contrast, increasing the payoffs for cooperation in biotechnology research increases the benefits achieved through cooperation over those that can be achieved without cooperation.

51. Feldbaum, *supra* note 3.

52. *Id.* at 3.

53. Korn, *supra* note 27, at 196 (citing *University/Industry Cooperation in Biotechnology: Hearings Before the Subcomm. on Investigations and Oversight and the Subcomm. on Science, Research and Technology of the House Comm. on Science and Technology*, 97th Cong., 2nd Sess. 90 (1982) (statement of Dr. Charles Muscoplat of Molecular Enetics)) (emphasis added.) Talent within the biotechnology research field is located primarily in academia because biotechnology research originated in universities and remains a fairly new science. *Id.* at 197.
54. Korn, *supra* note 27, at 198.
55. *Id.* at 196-198.
56. See Claire T. Maatz, Comment, *University Physician-Researcher Conflicts of Interest: The Inadequacy of Current Controls and Proposed Reform*, 7 HIGH TECH. L.J. 137, 138 (1992) (cooperation reduces total industry costs, which allows for "rapid technology transfer, thereby facilitating the development of new products.")
57. Korn, *supra* note 27, at 200.
58. *Id.* at 201.
59. *Id.* at 200 (citing N. Wade, *The Science Business: Report of the Twentieth Century Fund Task Force on the Commercialization of Scientific Research* (1984)).
60. *Industry, Researchers Say NIH Should Not Get More Involved in CRADAs*, BIOTECHNOLOGY NEWSWATCH, March 1, 1993, at 5. In the midst of the exploding demand for biotech research, a gap in funding has been created because the federal funding available for research grants has diminished. Maatz, *supra* note 56 at 138.
61. David Blumenthal, *Relationships in the Life Sciences: Extent, Consequences, and Management*, 268 JAMA 3344(6) (1992).
62. *Bayh-Dole Act Has Met its Tech Transfer Goal, Witnesses Tell Panel*, BNA PAT. TRADEMARK & COPYRIGHT DAILY, April 21, 1994, at 1 (survey conducted by Association of University Technology Managers). According to NIH data for the period 1980 to 1990, total funding for United States health research and development (including biotechnology research and development) increased dramatically from \$7.94 billion in 1980 to \$20.57 billion in 1989. In that same period, NIH's proportion of total funding dropped from 40% to 33%, while industry's contribution rose from 31% to 45%. Other public funding sources dropped from 25.6% in 1980 to 18% in 1989. Likewise, NIH's awards for new grants decreased from a record high of 6446 in 1987 to only 4600 in 1990. Many of the 1987 NIH grant awards spanned longer terms than had been customary. As a result, NIH has had less funding available for new grants in recent years. John Carey, *NIH Is Not the Institution It Was*, BUS. WK. Nov. 5, 1990, at 145, 148.
63. REAMS, *supra* note 32, at 8 (statement by Terry Sanford, President of Duke University).
64. Sugawara, *supra* note 30, at F-01.
65. *Id.*
66. Blumenthal, *supra* note 61, at 3345.
67. In the survey cited by Blumenthal, 89 percent of responding trainees with industrial support rated their training and educational experiences as very good or excellent, compared with 87 percent without such funding. Eighty-three percent of students and fellows with industry support reported that the benefits of such funding outweighed any risks, as did 74 percent without industrial support. *Id.* (citing David Blumenthal, M. Bluck, S. Epstein, K.S. Louis and M.A. Stoto, *University Relationships in Biotechnology: Implications for Federal Policy: Final Report*, 1987, U.S. Dept. of Health and Human Services Grant 100A-83, unpublished).
68. Robert Axelrod proposes that "one of the primary functions of government [is] to make sure that when individuals do not have private incentives to cooperate, they will be required to do the socially useful thing anyway." AXELROD, *supra* note 42, at 133.
69. Publ. L. No. 96-517; 94 Stat 3015 (1988 & Supp II 1990) (codified at 15 U.S.C. §§ 3701-3714 (1988 & Supp II 1990)).

70. Publ. L. No. 96-480, 94 Stat 2311 (1980) (codified at 15 U.S.C. § 3701).

71. Publ. L. No. 99-502; 100 Stat 1785 (1986) (codified at 15 U.S.C. §§ 3701, 3711-3714, 3710a).

72. Orphan Drug Act, Publ. L. No. 97-114, 96 Stat. 2049 (1983) (codified as amended in scattered sections at 21 U.S.C.A. (West Supp. 1993), 26 U.S.C.A. (West 1988 & Supp. 1993), and 42 U.S.C.A. (West 1991 & Supp. 1993)) (granting biotech companies a seven-year monopoly and tax credits up to 50% of the annual testing expenses on medications developed for rare diseases), and Health Promotion and Disease Prevention Amendments of 1984, Publ. L. No. 98-551, 98 Stat. 2815 (codified in 21 U.S.C.A. § 360ee(b)(2) (West Supp. 1993)) (defining "orphan drug" to be one with a patient population of less than 200,000).

73. AXELROD, *supra* note 42, at 135.

74. *Id.* at 135. The premise is that one party will receive benefits only when it pays welfare costs; i.e., the desired benefits reward the costs of acting generously. The classic example is of a mother who risks her own life to save her offspring, which increases the odds of her own genes' survival. *Id.*

75. *Hearing Before the Joint Economic Comm.*, Cong. (1994), available in LEXIS, Legis Library, CMTRPT File (statement of Daryl A. Chamblee, Acting Deputy Director, Science Policy and Technology Transfer, National Institute of Health, Department of Health and Human Services) [hereinafter Chamblee]. Research results of inventions assigned to the federal government were made available to the public through publication. This approach naturally stifled commercialization of research results as evidenced by the fact that in 1976, less than four percent of the approximately 28,000 patents in the Federal government's patent portfolio had been successfully licensed. At the same time, universities that offered licenses were licensing about one-third of their patent portfolios. *Id.* (referring to evidence introduced before the 1976 subcommittee on Domestic and International Scientific Planning and Analysis of the House Committee on Science and Technology)

76. Public Law 96-517; 94 Stat 3015 (1988 & Supp. II 1990) (codified at 15 U.S.C. §§ 3701-3714). Under this Act, universities and other research institutions that receive federal funding are permitted to retain title to federally funded inventions.

77. Herdman, *supra* note 11 (stating that the commercialization resulting from permitting private research institutions to retain patent rights on federally-funded research has been "extraordinary"). Over 1000 licenses and options were executed in 1992, for example, and over 5,000 licenses were already active in 1992. *Id.* (citing a survey of 260 academic institutions as reported in Blumenthal, et al., *University-Industry Relationships in Biotechnology: Implications for the University*, 232 SCIENCE: 1361-1366, (1986)).

78. *See* AXELROD, *supra* note 44.

79. *Id.* *See* Public Law 96-517, 94 Stat 3015 (1988 & Supp II 1990) (codified at 15 U.S.C. §§ 3701-3714).

80. Public Law 99-502, 100 Stat 1785 (1986) (codified at 15 U.S.C. §§3701, 3711-3714, 3710a).

81. The Act is similar to the Bayh-Dole Act in that it allows government researchers to cooperate directly with industry, just as university researchers do under the Bayh-Dole Act. Linda Marsa, *Unhealthy Alliances: Scripps Research Institute and Sandoz Medical Research Commercializing Agreement*, OMNI, Feb. 1994, at 36 (permitting government researchers to retain patents enables these researchers to attract corporate dollars in exchange for exclusive licensing agreements in the same manner in which federally-funded university researchers are able to do under the Bayh-Dole Act).

82. Public Law 99-502, *supra* note 80.

83. Herdman, *supra* note 11.

84. Herdman, *supra* note 11. In one CRADA, for example, the NIH collaborated with Genzyme Corporation for the production of the first successful drug to treat Gaucher's Disease. An NIH laboratory "isolated the crucial enzyme that is missing in patients" who have this life-threatening and crippling inherited disease. Genzyme Corporation agreed to "produce research quantities of the enzyme," and the NIH agreed to pay for the "clinical trials supporting its FDA approval. The Genzyme Corporation applied for orphan drug status for the drug and developed it for the market. Today, the Genzyme Corporation has the exclusive right to sell the drug in the United States." *Id.*

85. AXELROD, *supra* note 47, at 139.

86. For example, defection from a cooperative agreement to ban all testing of nuclear weapons can be detected through the ability to distinguish explosions from earthquakes; without that detection ability, there would be no way to determine whether cooperation existed. *Id.* at 140.

87. Pub. L. No. 96-480, 94 Stat. 2311 (1980) (codified at 15 U.S.C. §3701 *et seq.*). The Act was passed specifically to "stimulat[e] improved utilization of federally funded technology developments by state and local governments and the private sector." Pub. L. No. 96-480, 3 (1980) (codified at 15 U.S.C. §3702(3)).

88. Pub. L. No. 96-480, 94 Stat. 2311 (1980) (codified at 15 U.S.C. §3701 *et seq.*).

89. *Id.*

90. *Diamond v. Chakrabarty*, 447 U.S. 303 (1980).

91. *See Orphan Drug Act*, *supra* note 72.

92. Marsa, *supra* note 81. Marsa criticizes the tax credits as merely providing a "free lunch for private corporations" which "erode[s] the public's ownership or control over important technology." *Id.* (quoting Ralph Nader).

93. The permanent tax credit proposal is aimed at reducing the government's research role where private industry is capable of performing the research independently. *If it Ain't Broke, Don't Fix It: GOP Should Go Slow on Science Policy Revision*, LOS ANGELES TIMES, April 3, 1995, at B-4.

94. *Id.* The Republican agenda remains focused on governmental support of basic research and attempts to limit governmental involvement in applied research. The policy of Congress is the driving force behind reducing funding to industry as a form of "corporate welfare." *Id.*

95. Since the enactment of the Bayh-Dole Act and the Stevenson-Wydler Act in 1980, federal funding for academic research and development fell from 67.5 to 55.5% in 1993. During that same time period, industry sources increased from 3.9% of funds for academic R&D to 7.3%. *Hearing on the Bayh-Dole Act: Hearing Before the Senate Subcomm. on Patents, Copyrights and Trademarks*, Cong. (1994), available in LEXIS, Legis Library, CMTRPT File (statement of Gary M. Munsinger, Ph.D., President, Research Corporation Technologies) [hereinafter Munsinger].

96. *See supra* note 95.

97. In 1983, for example, federal funding amounted to 50% of all health R&D, with industry funding equaling 39%. Herdman, *supra* note 11 (citing U.S. Department of Health and Human Services, Pub. No. 93-1261, NIH Data Book (1993)).

98. *Id.* In addition, the technology transfer function of the Defense Department has virtually ceased in the post-Cold War era. *See Munsinger, supra* note 92 (citing Science & Engineering Indicators, 1993) (Federal funding for research and development fell from 67.5 percent in 1980 to 55.5 percent in 1993).

99. *Diamond v. Chakrabarty*, 447 U.S. 303 (1980). The Supreme Court held that a new bacterium, capable of consuming oil spills, was markedly different from any natural occurring bacteria, *id.* at 310, and should not be denied patent protection simply because the subject matter of the patent was alive. *Id.* at 312-313.

100. One commentator advocates that profit motives in academia preclude universities from researching for the "truth:" "Government and business are not wholly disinterested in their approaches to the universities: they are not seeking the truth, but are hiring universities to promote the ends they have in view. If the truth serves these ends, it is merely a coincidence." REAMS, *supra* note 32, at 7 (citing ROBERT M. HUTCHINS, *THE HIGHER LEARNING IN AMERICA* (Yale University Press, 1936 (2d printing 1962)), at x-xi.

101. *Commercialization of Academic Biomedical Research: Hearings before the Subcomm. on Science, Research, and Technology of the House Comm. on Science and Technology, 97th Cong. 1st. Sess. 14 (1981)* (statement of Donald Kennedy, then President of Stanford University) [hereinafter Kennedy] (noting that industry focus may contaminate basic research as well as present conflicts of interest on the part of university researchers between their obligations to the universities to research new areas and their obligations to corporate sponsors to develop specific products).
102. Maatz, *supra* note 56, at 138 (charging that researchers may compromise scientific goals to accommodate industry objectives and to capitalize exponentially on the profits that can be obtained through commercialization of research).
103. Industry's influence, control, monitoring and approval power over federally funded research threatens the government's ability to protect the public against non-use or unreasonable use of potentially beneficial inventions. Reginald Rhein, *NIH Finds Scripps-Sandoz Deal Unusual for Sponsored Research Agreement*, BIOTECHNOLOGY NEWSWATCH, February 7, 1994, at 1.
104. Marsa, *supra* note 81. Marsa cites the example of the discovery and marketing of AZT, the drug that thwarts the HIV virus. AZT research was funded by grants from the National Cancer Institute (NCI), a federal research institution; the British pharmaceutical company, Burroughs Wellcome, has produced and marketed the drug with earnings of \$1.4 billion dollars since its introduction, and, in the meantime, the federal agency received no royalties while patients originally were charged a \$10,000 annual price for the drug. *Id.*
105. See AXELROD, *supra* note 46, at 136-37. See *infra* note 50 for a discussion on the need for reciprocity to maintain mutually beneficial payoffs in interactions.
106. See *Id.* at 137-38.
107. Marsa, *supra* note 81.
108. Blumenthal, *supra* note 61. Daryl Chamblee, acting deputy director for science policy and technology transfer at NIH, voiced concerns at a 1994 Senate hearing that technology transfer may stifle the free exchange of knowledge in the academic community and promote secrecy. Chamblee, *supra* note 75.
109. Blumenthal, *supra* note 61, at 3364 (trade secrets are defined as information kept secret to protect its proprietary value).
110. *Id.*
111. *Id.* (citing H.T. Shapiro, *The Research University and the Economy*, presented at the National Academy of Engineering Symposium: The Role of Universities in National Economic Development, December 6, 1990, Washington, D.C.)
112. "The potential to protect the public is threatened when research is influenced, controlled, monitored and approved by a biotech company." Statement by Daryl Chamblee, quoted in Rhein, *supra* note 103.
113. Marsa, *supra* note 81 (charge made by Ted Weiss, New York Congressman, following a three-year inquiry into researcher conduct).
114. *Id.* (statement by David Noble, professor of history at York University in Toronto and a founder of the National Coalition for Universities in the Public Interest). See also *Bayh-Dole Act Has Met Its Tech Transfer Goal, Witnesses Tell Panel*, *supra* note 62.
115. *Id.* After an article appeared in a January 1988 issue of the Journal of the American Medical Association, demand for the anti-aging elixir skyrocketed-nearly 1 million tubes were sold in February of 1988 alone. Scientists never duplicated the results of the original study. *Id.*
116. Maatz, *supra* note 56.
117. Marsa, *supra* note 81.
118. *Id.* The substantiality of this example as an argument against cooperation may be insignificant since Dow Corning has incurred

serious liability for its conduct. For a further discussion of actual controls over accountability, *see infra*, Part IV. B.

119. *Moore v. Regents of the Univ. of Cal.*, 793 P.2d 479 (Cal. 1990), *rev'g* 249 Cal. Rptr. 494 (Ct. App. 1988).

120. *Id.* at 482.

121. *Id.* at 481.

122. *Id.* at 482.

123. *Id.* at 483.

124. Researchers often keep their results confidential until publication, to ensure that they will receive due credit for the results of their research. This is important to researchers since a scientist's reputation is often measured by peer review of published research results. Korn, *supra* note 28, at 205. One example of intense competition in non-industry-funded research was the race to discover the structure of DNA. *Id.* (citing James Watson, *The Double Helix* (1968)) (the DNA "run to glory" led to an extremely competitive environment until an official public announcement could be made).

125. *See* Burke, *University Policies on Conflict of Interest and Delay of Publication*, 12 J.C. & U.L. 175, 189 (1985).

126. Rhein, *supra* note 98.

127. Korn, *supra* note 27, at 203. For example, in fiscal year 1989 only 27.5% of the grant proposals submitted by research institutions actually received federal funding through NIH. Tammy L. Lewis and Lisa A. Vincler, *Storming the Ivory Tower: The Competing Interests of the Public's Right To Know and Protecting the Integrity of University Research*, 20 J.C. & U.L. 417, 422 (1994).

128. U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH, *ORIENTATION HANDBOOK FOR MEMBERS OF SCIENTIFIC REVIEW GROUPS* 4 (1989). The review boards consist of university and industry scientists, and therefore subject research proposals to peer review before federal funding is granted. *Id.*

129. Barbara J. Culliton, *Biomedical Research Enters the Marketplace*, 304 NEW ENG. J. MED. 1195, 1197 (May 14, 1981).

130. Marjorie Shaffer, *NRC Issues First Recommendations on Post-Cold War Science Funding*, BIOTECHNOLOGY NEWSWATCH, December 4, 1995, at 1 (the committee members represented industry and academic scientists, government officials, and leading educators) [hereinafter Shaffer].

131. *Id.*

132. Marsa, *supra* note 81.

133. Korn, *supra* note 27, at 224.

134. *Id.* at 225.

135. *Id.*

136. *Bayh-Dole Act Has Met Its Tech Transfer Goal, Witnesses Tell Panel*, *supra* note 62; *see, e.g.,* M.B., *Investigation Clears Medarex, Dartmouth of Scientific Misconduct*, BIOTECHNOLOGY NEWSWATCH, Feb. 15, 1993 at 14. Lyle Bivens of the Office of Research Integrity of the Public Health Service reports that his office is involved with about 70 cases of alleged misconduct by individual scientists at any given time. Of those allegations, Bivens estimates that 50 to 60% of even the allegations that require an investigation result in a finding of no misconduct. *Id.*

137. The specific conflict of interest cases cited in Part IV. A, *infra*, did not involve university-industry agreements made under the Bayh-Dole Act. The Retin-A case involved government scientists and industry; the silicone breast implant case involved solely in-

house scientists with Dow-Corning; the *Moore* case involved patient consent laws and occurred in 1976, before the enactment of the Bayh-Dole Act.

138. *Are Scientific Misconduct and Conflicts of Interest Hazardous to Our Health?: Hearing Before the House Comm. on Gov't Operations*, 101st Cong., 2d Sess. 6 (1990).

139. Michael D. Witt & Lawrence O. Gostin, *Conflict of Interest Dilemmas in Biomedical Research*, 268 JAMA 547(5) (1994).

140. Blumenthal, *supra* note 61.

141. Munsinger, *supra* note 96, at 21.

142. Witt & Gostin, *supra* note 139, at 548.

143. ROGER J. PORTER & THOMAS E. MALONE, *BIOMEDICAL RESEARCH: COLLABORATION AND CONFLICT OF INTEREST* (1993).

144. Witt & Gostin, *supra* note 139, at 548.

145. Christopher Anderson, *Genome Project Goes Commercial: Includes Related Article on Patent*, 259 SCIENCE 300-302 (1993).

146. Axelrod defines one criterion for achieving sustained cooperation as "teaching reciprocity." By guaranteeing the punishment of any party that tries to be less than cooperative, deviant strategies are made unprofitable. AXELROD, *supra* note 42 at 138. For a complete discussion of the element of reciprocity under the Axelrodian Cooperation Model, see *supra* note 46, at 136-39.

147. The policy, strengthened in 1991, requires "[r]ecipient organizations . . . [to] establish safeguards to prevent employees, consultants, or members of governing bodies from using their positions for purposes that are, or give the appearance of being, motivated by a desire for private financial gain. . . . These rules must also indicate the conditions under which outside activities, relationships, or financial interests are proper or improper, and provide for notification of these kinds of activities, relationships, or financial interests to a responsible and objective institute official. The institutional guidelines must specify the administrative action taken for violations." U.S. DEP'T OF HEALTH & HUMAN SERVS., DHHS PUB. NO. (OASH) 90-50,000, PHS GRANTS POLICY STATEMENT at 8-19 (rev. 1991) [hereinafter PHS GRANTS POLICY].

148. *Id.*

149. *Code of Medical Ethics: Annotated Current Opinions*, American Medical Association (1992) at §§8.031, 8.031(1) (hereinafter AMA GUIDELINES). Presumably, a "clinical investigator" is someone conducting clinical trials and not a researcher engaged in basic research.

150. *Id.* at §8.031(2)-(3).

151. A survey of 35 universities conducted by the General Accounting Office in 1992 found that "21 of the universities required either annual disclosure of outside financial interests by at least a portion of their faculty (9 respondents) and/or disclosure of such relationships at the time an application is approved for submission (14 respondents)." Blumenthal, *supra* note 61 at 3346 (citing U.S. GENERAL ACCOUNTING OFFICE, *CONTROLLING INAPPROPRIATE ACCESS TO FEDERALLY FUNDED RESEARCH RESULTS* (1992)).

152. *Id.* at 3347. Examples of institutions that have adopted special policies concerning faculty stock holdings include Harvard Medical School, Johns Hopkins University, Massachusetts Institute of Technology, Cambridge University, and the University of Illinois, Urbana-Champaign.

153. Marsa, *supra* note 81.

154. Some specific examples of this type of relationship: (1) Stanford University reached a license agreement with Cohen-Boyer for

the recombinant DNA patent. Stanford will receive a total of \$87 million when the patent expires in 1997. *At the Edge of Cohen-Boyer Patent 'Cliff,' Stanford Seeks \$15 M Cushion*, BIOTECHNOLOGY NEWSWATCH, June 21, 1993, at 12-13. (2) Diasense, Inc., an affiliate of Ciocontrol Technology, Inc., acquired exclusive license to a patent for a new modified insulin. Diasense entered into a joint-venture agreement with the Biomedical Research Institute at Indiana University of Pennsylvania, Indiana, PA, through a \$1 million federal appropriation. Diasense expects to capture a solid portion of the well established \$2 billion/year world insulin market. *Diasense, Inc. Signs Exclusive License Agreement for a New Insulin*, PR NEWSWIRE, February 1, 1994. (3) Johns Hopkins University entered into a three-year agreement with Oncor Inc. of Gaithersburg, MD, to research a specific oncogen for \$400,000/year. One-fourth of the funding will be paid in Oncor stock. In return, Oncor receives first options on licensing discoveries that come out of the research. *Owning Hearts and Souls*, MEDICINE & HEALTH, February 8, 1993. (4) Massachusetts General Hospital's \$70 million agreement with Hoechst A.G. created a new department of molecular biology at the hospital to perform a wide spectrum of research. Herdman, *supra* note 12.

155. Maatz, *supra* note 56, at 138.

156. See Witt & Gostin, *supra* note 139, at 547-48 (citing M.E. Hoppin, *A University Perspective on Pharmaceutical and Industry Support of Research*, 46 AM. J. CLIN. NUTR., at 226-228; D. Blumenthal, *University-Industry Research Relationships in Biotechnology: Implications for the University*, 232 SCIENCE at 1361-66); Maatz, *supra* note 56.

157. See *supra* notes 13 and 47.

158. *Bayh-Dole Act Has Met Its Tech Transfer Goal, Witnesses Tell Panel*, *supra* note 62 at 1.

159. *Id.*

160. Science & Engineering Indicators-1993.

161. Feldbaum, *supra* note 3.

162. *Bayh-Dole Act Has Met Its Tech Transfer Goal, Witnesses Tell Panel*, *supra* note 62 at 1.

163. Herdman, *supra* note 11. While the numbers of patents obtained by CRADAs are significantly lower than in university-industry relationships, the research performed under CRADAs has resulted in such developments as the drug taxol to treat ovarian and breast cancer, a patent application for a diagnostic test for Alzheimer's disease, a Hepatitis A vaccine, and other current research for treatments for AIDS-related symptoms and various cancers. Chamblee, *supra* note 75.

164. *Bayh-Dole Act Has Met Its Tech Transfer Goal, Witnesses Tell Panel*, *supra* note 64.

165. BNA PATENT, TRADEMARK & COPYRIGHT LAW DAILY, *supra* note 62 at 1. For a discussion on the impact of the Bayh-Dole Act, the Stevenson-Wydler Technology Innovation Act and the Federal Technology Transfer Act on the number of patents filed by research institutions, see *infra* Part III.B.

166. Penner, *supra* note 23. The drug, Pulmozyme, breaks down the thick, infected secretions afflicting cystic Fibrosis patients, significantly reducing the risk of serious respiratory tract infections, making breathing easier, and improving quality of life. *Id.*

167. See *infra* Part II.

168. Feldbaum, *supra* note 3.

169. Chamblee, *supra* note 75 (source of data: Dr. Ashley J. Stevens, Director, Office of Technology Transfer, Dana-Farber Cancer Institute, Association of University Technology Managers Winter Meeting, 1994).

170. Ann Thayer, *Opinion: Why the Biotech Industry is in Peril*, SAN DIEGO UNION-TRIBUNE, June 20, 1993, at G-3.

171. Herb Lass, *Biotech Revenues to Top \$100B by 2000*, BIOTECHNOLOGY NEWSWATCH, January 18, 1993 at 2.

172. Goldberg, *supra* note 2. In Massachusetts alone, biotechnology companies raised over \$1 billion, supporting a growing workforce of over 15,000 employees. Massachusetts Biotechnology Research Institution itself has created 2,200 jobs and represents \$120 million in research through the founding of 15 new companies during the period from 1984 to 1993. *Id.*

173. Munsinger, *supra* note 96.

174. U.S. OFFICE OF TECHNOLOGY ASSESSMENT, BIOTECHNOLOGY IN A GLOBAL ECONOMY, OTA-BA-494 (Washington, D. C.: U.S. Government Printing Office, May 1990).

175. Abbot, *supra* note 2. Having emerged from a "premier scientific and technology base," fueled by the United States' venture capital and public market system, the biotechnology industry ranks second only to the computer industry in market valuations created among high-technology companies. "However, the National Research Council's Committee on Japan questions whether biotechnology will go the way of semiconductors and lose its lead, or remain competitive and reap profits from its investments." Thayer, *supra* note 170.

176. An example of government's commitment to fund basic research conducted through cooperative agreements with industry is the increasing tendency of NASA to collaborate with industry and university research projects. NASA maintains "Centers for Commercial Development of Space" (CCDS) programs, which are co-funded by industry and currently target biotechnology and biomedicine. NASA and industry funding has continually increased since 1985, and as a result, 218 technologies were commercialized by the end of 1995. *NASA Consortia Go Commercial for Low-Cost Space Systems*, TECHNOLOGY TRANSFER WEEK, October 17, 1995, at 41.

177. See Karen Southwick, *Don't Take the Republicans for Granted*, BIOVENTURE VIEW, November 1, 1995 (reporting that BIO President Carl Feldbaum is encouraged by the support Gingrich has given to biotech interests, but is skeptical whether the Republican Congress will in actuality create better outcomes for the biotech industry; Feldbaum espouses the need to gain bipartisan support for lobbying efforts aimed at the maintenance of the R&D tax credit, support of NIH funding and FDA reform).

178. FDA's Center for Biologics Evaluation and Research (CBER) announced revisions to FDA rules that would shrink product marketing applications from 21 forms to one and focus on reorganizing decision making to simplify the analysis of biotech products. *Regulations Overhaul Starts with Definition of "Well-Characterized" Biotech Products*, *BIO WORLD TODAY*, December 13, 1995.

179. See Shaffer, *supra* note 130 (summarizing the NRC recommendations on science funding).

180. Notice of Proposed Rulemaking, 59 Fed. Reg. 33,242, at 33,243 (June 28, 1994) (notice of proposed rule: Policies on Conflict of Interest in the NIH Guide for Grants and Contracts (Volume 18, Number 32)) [hereinafter Proposed NIH Policies].

181. Penner, *supra* note 23.

182. The respondents include individuals associated with medical schools, other academic and research institutions, local governments, non-profit organizations, biotechnology companies, venture capitalists, attorneys, biomedical journal editors, federal employees, contractors at government facilities, and others. Proposed NIH Policies, *supra* note 180 at 33,243.

183. *Id.*

184. Munsinger, *supra* note 92.

185. National Insts. of Health & Alcohol, Drug Abuse & Mental Health Admin., Request for Comment on Proposed Guidelines for Policies on Conflict of Interest, NIH GUIDE FOR GRANTS & CONT., Sept. 15, 1989, at 1 [hereinafter NIH Proposed Guidelines 1989]. The guidelines also required federally funded research institutions to maintain records of disclosure for three years, including disclosure of all funding for laboratory activities, services, consultancies, honoraria, and other benefits. Witt & Gostin, *supra* note 139, at 547(5).

186. Witt and Gostin, *supra* note 139.

187. *Id.*

188. "The evolution of cooperation requires that individuals have a sufficiently large chance to meet again so that they have a stake in their future interaction." See AXELROD, *supra* note 47, at 20. Additionally, reciprocity for non-cooperative behavior is effective in policing university-industry relationships. If one party should exploit the cooperative arrangement, the other parties will react equally by punishing the exploitation; thereafter, fewer parties will invest in a relationship with the known, deviant party. *Id.*, *supra* note 47, at 138.

189. *NIH Conflict-of-Interest Guidelines Target Clinicals, Not Basic Research*, BIOTECHNOLOGY NEWSWATCH, Dec. 17, 1990, at 5 (statement by Alan Goldhammer, director of technical affairs for the Industrial Biotechnology Association) (agreeing that federal guidelines must have "broad flexibility").

190. Maatz, *supra* note 56.

191. *Id.* (referring to a telephone interview with Richard P. Seligman, then Associate Director of the Office of Contract and Grant Administration, UCLA (February 1992) in which Mr. Seligman espoused the concern that external monitors may develop "a rigid list of acceptable and unacceptable arrangements without fully assessing individual proposals.").

192. *Id.*

193. PHS GRANTS POLICY, *supra* note 147 at 6-11. PHS also requires a detailed cost analysis of every grant application, which includes "the process of obtaining cost breakdowns, verifying cost data, evaluating specific elements of cost, and examining data to determine necessity, reasonableness, and allowability of the cost reflected in the grant budget." *Id.* at 4-15. Grants Management Officers may require applicants to submit:

1. Grantee administrative directives, organization charts, manuals, etc.
2. Corporate charters and bylaws, financial statements, IRS Tax Exemption Certification, etc.
3. Grantee accounting manuals, charts of accounts, procedures, etc.
4. Grantee personnel policies and directives.
5. Grantee travel policies.
6. Grantee procurement procedures and property management instructions.
7. Overall institutional audit reports affecting an individual grant or a number of grants.
8. Information on indirect cost rates, items included in indirect cost pools, etc.

9. Copies of, or references to, awards with special conditions (including awards from other agencies), terminations, and any other useful background information. *Id.*

194. PHS requires that "[r]ecipient organizations . . . establish safeguards to prevent employees, consultants, or members of governing bodies from using their positions for purposes that are, or give the appearance of being motivated by a desire for financial gain for themselves or others such as those with whom they have family, business, or other ties. Therefore, each institution receiving financial support must have written policy guidelines on conflict of interest and the avoidance thereof. These guidelines should reflect State and local laws and must cover financial interest, gifts, gratuities and favors, nepotism, and other areas such as political participation and bribery." *Id.* at 8-19.

195. Goldberg, *supra* note 2. Goldberg explains that however well intentioned, limiting profits "[f]ar from address[ing] [the] perceived wrong-industry exploitation of 'pure' research funding in part or in its entirety by public funds-will only remove the incentive to commercialize research, leading a downward spiral of less research, less new business development, loss of American leadership in a vital new industry and, critically for the public, fewer beneficial products reaching the market." *Id.* at 5.

196. Economist Peter Arno of Albert Einstein College of Medicine proposes, for example, that a price-review board for drugs

developed by federal researchers may be the best way to ensure that drug prices are "reasonable". R.R., *Industry, Researchers Say NIH Should Not Get More Involved in CRADAs*, BIOTECHNOLOGY NEWSWATCH, March 1, 1993, at 5.

197. Feldbaum, *supra* note 3 at 15-17. *See also, The Pricing of Breakthrough Drugs: Hearing Before the Senate Comm. on Labor and Human Resources*, 1993, available in LEXIS, Legis Library, CMTRPT File, statement of Mitchel Sayare, Chairman and Chief Executive Officer of Immunogen, Inc. Sayare described the proposals as embodied in the proposed Health Security Act, §§ 1572, 2003(c)(1) and 2003(c)(3): Without explicitly imposing price controls, he stated that Clinton's plan provided for the following:

(1) the review by an 'Advisory Council on Breakthrough drugs' and the Secretary of health and Human Services (HHS) of the 'reasonableness' of the launch prices of 'breakthrough' therapeutic drugs; (2) the authority of the Secretary to negotiate a 'special rebate' or discount for all 'new' drugs sold to Medicare patients; and (3) the authority of the Secretary to deny reimbursement for, i.e. to blacklist, 'new drugs' where she cannot negotiate a 'special rebate' that yields a 'reasonable price.')

198. *Bayh-Dole Act Has Met Its Tech Transfer Goal, Witnesses Tell Panel*, *supra* note 62. Both Senators Bayh and Dole testified that they would likewise caution against enabling the federal government to share in royalties earned by the sale of licensed products, commenting that this type of scheme may be justified only where the licensee's profits are "exorbitant." In any event, both of the Act's original drafters adamantly dissent from proposals that would establish an up-front "user" fee payable to the federal government by licensees.

199. Lass, *supra* note 171, at 2.

200. Conte, *supra* note 2, at 18 (citing Ernst & Young, BIOTECH 94 LONG TERM VALUE SHORT TERM HURDLES, EIGHTH ANNUAL REPORT ON THE BIOTECH INDUSTRY 45 (1993)).

201. *Id.*

202. Abbott, *supra* note 2 (calculating that a "staggering" 975 of 1,300 U.S. biotech companies will be forced to raise capital through public offerings by the end of 1996; otherwise they will be forced to go out of business, or merge or sell rights to larger companies).

203. The overall "burn" rate just for the biotechnology industry is nearly \$3 billion per month and the net burn rate (counting income and additional capital) is \$760 million. Ernst & Young, BIOTECH 94, LONG TERM VALUE, SHORT TERM HURDLES, EIGHTH ANNUAL REPORT ON THE BIOTECH INDUSTRY 45 (1993).

204. Feldbaum, *supra* note 3, at 7-8.

205. Marsa, *supra* note 81.

206. It should be noted that the patentability of biotechnological inventions confers a short-term monopoly to the patent holder which temporarily prevents free market competition; however, as innovations continue and patents expire, the price-lowering effect of free market competition takes effect.

207. *Competitiveness of the U.S. Biotechnology Industry: Hearing Before the Subcomm. on Science, Technology, and Space of the Senate Comm. on Commerce, Science, and Transportation*, 103rd Cong., 2d Session 59 (1994) (statement of Mark Skaletsky, President and CEO of Geltex Pharmaceuticals, Inc.) [hereinafter Skaletsky].

208. Wiggans, *supra* note 14.

209. "In 1992, the investment bank of Robertson Stephens & Company performed a study that compared international prices for the leading biotechnology drugs in the United States and Japan. Specifically, the study revealed the following price differences: Human Growth Hormone is priced at \$14 in the U.S. and \$53 in Japan; G-CSF is priced at \$112 in the U.S. and \$375 in Japan; EPO is priced at \$40 in the U.S. and \$99 in Japan and Alpha Interferon is priced at \$8.75 in the U.S. and \$25 in Japan." *Id.*

210. The drug sells for nine percent less in Europe, for the same price in Canada, and for 65 percent more in Japan. *Id.*

211. Skaletsky, *supra* note 207, at 54.

212. Wiggans, *supra* note 14 (citing Robert J. Beall, Ph.D., excerpt from *Regarding Research on Cures and Therapies for Cystic Fibrosis*, May, 1994).

213 Feldbaum, *supra* note 3.

214. *Id.*

215. *Id.*

216. *Id.*

217. *Id.*

218. Wiggans, *supra* note 14. The difficulties in obtaining commercial capital is further evidenced by the decreased size of public offerings in 1993 to \$23 million, from \$28.2 million in 1992. Initial public offerings (IPOs) fell from \$26 million in 1992 to \$22 million in 1993. *Id.*

219. Jennifer Van Brunt, *1993 Tops Out at \$2.9 Billion-And It's Stiff Coming*, BIOWORLD FINANCIAL WATCH I, January 10, 1994.

220. Conte, *supra* note 2 at 22.

221. *Id.*

222. *NIH Ends R&D Price Requirements*, MEDICINE AND HEALTH, April 17, 1995, at 16.

223. Feldbaum, *supra* note 3.

224. Wiggans, *supra* note 14 (quoting Eugene Schonfeld, Ph.D., excerpt from his preface to *A Cancer Patient to a U.S. Senator*, February, 1993).