UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

ASSOCIATION FOR MOLECULAR PATHOLOGY; AMERICAN COLLEGE OF MEDICAL GENETICS; AMERICAN SOCIETY FOR CLINICAL PATHOLOGY; COLLEGE OF AMERICAN PATHOLOGISTS; HAIG KAZAZIAN, MD; ARUPA GANGULY, PhD; WENDY CHUNG, MD, PhD; HARRY OSTRER, MD; DAVID LEDBETTER, PhD; STEPHEN WARREN, PhD; ELLEN MATLOFF, M.S.; ELSA REICH, M.S.; BREAST CANCER ACTION; BOSTON WOMEN'S HEALTH BOOK COLLECTIVE; LISBETH CERIANI; RUNI LIMARY; GENAE GIRARD; PATRICE FORTUNE; VICKY THOMASON; KATHLEEN RAKER,

Plaintiffs,

-against-

UNITED STATES PATENT AND TRADEMARK OFFICE; MYRIAD GENETICS; LORRIS BETZ, ROGER BOYER, JACK BRITTAIN, ARNOLD B. COMBE, RAYMOND GESTELAND, JAMES U. JENSEN, JOHN KENDALL MORRIS, THOMAS PARKS, DAVID W. PERSHING, and MICHAEL K. YOUNG, in their official capacity as Directors of the University of Utah Research Foundation,

Defendants.

No. 09 Civ. 4515 (RWS)

ECF Case

DECLARATION OF DR. PHILIP R. REILLY

I, Philip R. Reilly, hereby declare that:

I. EDUCATION AND BACKGROUND

1. I currently hold the position of Venture Partner at Third Rock Ventures in Boston, Massachusetts. Third Rock Ventures is a venture capital company whose mission is to create transformational life science companies through close collaboration with members of the scientific and business communities. My qualifications, experience, and a list of my publications are set forth in my *curriculum vitae*, attached hereto as Exhibit 1.

2. I am Adjunct Professor of Law at Suffolk University School of Law in Boston, Massachusetts where I teach a seminar in Biomedical Policy and Law. I previously held teaching positions at Cornell University, Tufts University School of Medicine, Harvard Medical School, and Brandeis University. I am a member of the Board of Trustees of Cornell University.

3. I am trained in and have been board certified in both internal medicine and clinical genetics. I have also been a member of the Massachusetts Bar since 1973.

4. I received my J.D. in 1973 from Columbia University in New York, New York and practiced as an attorney from 1975 to 1977 at the law firm of Powers & Hall in Boston, Massachusetts. For a number of years thereafter, I had a part-time practice at Powers & Hall.

5. I received my M.D. in 1981 from Yale University in New Haven, Connecticut and completed my internship and residency in the Department of Medicine at Boston City Hospital in Boston, Massachusetts. From 1982 to 1983, I was a Professor of Law at the University of Houston. Between 1983 and 1985, I completed my residency. Thereafter, I became a Staff Physician and then, ultimately, Executive Director of the Eunice Kennedy Shriver Center for Mental Retardation, Inc., which was at the time affiliated with Massachusetts General Hospital, in Waltham, Massachusetts.

6. From 2000 to 2006, I was Chairman of the Board and CEO of Interleukin Genetics, Inc. in Waltham, Massachusetts. During the same time, I was also Director of Clinical Genetics. Interleukin Genetics was then and still is a publicly traded company with a focus on developing DNA-based risk assessment tests and preventative and therapeutic products to reduce or ameliorate those risks.

7. I chaired the social issues committee of the American Society of Human Genetics during the 1990's. I also served for three years on the Board of Directors of the American

Society of Human Genetics. In my capacity as chair of the social issues committee, I authored or co-authored numerous position papers on important public policy issues related to human genetics that were adopted by the American Society of Human Genetics.

8. I was president of the American Society of Law and Medicine and Ethics (at the time, including about 3,000 members) in 2002 and 2004. I also served on its Board of Directors.

9. In the 1990's, I was heavily involved in advising leading companies in developing and/or commercializing gene-based diagnostics and therapeutics, including diagnostic tests. This was a time when the field of biotechnology was rapidly developing and a period when many genes were being associated with risk for disease. In particular, many companies turned to me for advice regarding the ethical and legal issues they needed to consider in connection with the new gene based diagnostic tests they were creating. Such companies included, for example, Myriad Genetics, Genzyme Corporation, Collaborative Research, Inc., and Vivigen, Inc. for which I served as a member of the Board of Directors. I further advised biotechnology companies such as Millennium Pharmaceuticals, Inc., GlaxoSmithKline, and Pharmacia.

10. I have served as a member of several advisory boards, including the SmithKline Beecham Genomics Advisory Board, and was Chair of the SmithKline Beecham Clinical Genetics, Ethics and Public Policy Advisory Board. From about 1995 to 2000, I was a member of the Clinical Advisory Board of Myriad Genetics. I assisted Myriad in identifying ethical considerations related to the *BRCA1* and *BRCA2* genetic tests that were developed, and played an important role in developing Myriad's patient consent forms. It was my experience during those years that the entire scientific and clinical team at Myriad showed deep concern for the best interest of patients. For example, Myriad tried to ensure that as many patients as possible had

access to the test. Importantly, Myriad also strived to ensure that patients were given the results of their genetic tests in a responsible and compassionate manner.

11. For several years, I was an advisor to the Biotechnology Industry Organization ("BIO"). BIO is well-regarded and the world's largest biotechnology organization, providing advocacy, business development and communications services for more than 1,200 members worldwide. In my capacity as an advisor, I helped to develop a number of position statements for BIO including in areas such as genetic testing.

12. I am an author of numerous peer-reviewed academic articles and books on topics such as the ethical, legal, and social issues related to genetics. From the 1990's to about 2003, I was frequently a public speaker on the topic of genetics, the future of medicine, and bioethics. I have given approximately 500 speeches on these topics during my career.

13. In my capacity as CEO at Interleukin Genetics, I became familiar with the workings of the United States patent system. I was also involved in drafting or reviewing some of the company's patent applications.

14. I keep apprised of the literature regarding the impact of United States intellectual property law and policy on the development and commercialization of science and technology, particularly with respect to biotechnology.

II. BASIS OF OPINION

15. In preparing this declaration, I have been provided and considered the following: (1) the Complaint filed in connection with this proceeding; (2) Plaintiffs' Memorandum of Law in Support of Motion for Summary Judgment; (3) Plaintiffs' Rule 56.1 Statement of Material Facts; (4) the Declaration of Dr. Mildred Cho, dated August 17, 2009 ("Cho"); (5) Cho, MK *et al.*, 2003, Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services, *J. Mol. Diagnostics* 5(1):3-8 (cited in paragraph 11 of the Cho Declaration) (Exhibit 2; "Cho

2003"); (6) Merz and Cho, 2005, What are gene patents and why are people worried about them?, *Community. Genet.* 8(4):203-08 (Exhibit 3; "Merz and Cho"); (7) Declaration of Dr. Wendy Chung, dated July 30, 2009 ("Chung"); (8) BIO 2009 Member Survey: Technology Transfer and the Biotechnology Industry, located at http://bio.org/ip/techtransfer/PDF.TECH.TRANSFER.PRESENTATION.10.25.pdf (last printed on December 11, 2009) (Exhibit 4; "BIO Survey"); (9) The Economic Impact of Licensed Commercialized Inventions Originating in Research, 1996-2007: Final Report to the Biotechnology Industry Organization, September 3, 2009, located at http://www.bio.org/ip/techtransfer/BIO_final_report_9_3_09_rev_2.pdf (last printed on December 11, 2009) (Exhibit 5; "BIO Study"); (10) Walsh et al., 2005, "View from the Bench: Patents and Material Transfers" *Science* 309:2002-03 (Exhibit 6; "Walsh"); and (11) Bremer *et al.*, August 14, 2009, The Bayh-Dole Act and Revisionism Redux, Patent, Trademark & Copyright Journal (Exhibit 7; "Bremer").

III. PATENTS PROVIDE THE ESSENTIAL INCENTIVE FOR THE DEVELOPMENT AND COMMERCIALIZATION OF NEW TECHNOLOGIES

16. Patents provide a *bona fide* net social benefit. First, patents are essential in obtaining capital investment in the development and commercialization of technological breakthroughs. Second, patents encourage the sharing of technological advances through the disclosure requirements of the applicable patent laws and regulations, thus enabling the public to take advantage of these developments after the patents expire.

17. The net social benefit provided by patents is especially striking for patents in the life sciences arena. Numerous biotechnology-based clinical applications, especially, gene-based applications, would not be available today without patents. There are many diagnostic tests based on patented isolated DNA molecules or methods of detecting mutations therein. Examples

of such tests include the DNA tests for cystic fibrosis (a severe lung disease) which are based on the *CFTR* gene, and for Fragile X syndrome (a leading cause of inherited mental retardation), which is based on the *FMR1* gene. There are today many other DNA based diagnostic tests secured by patents. Similarly, there are many therapeutic products based on patented isolated DNA molecules or their recombinant protein products, including recombinant erythropoietin ("EPO") to treat anemia, and recombinant human granulocyte colony-stimulating factor ("G-CSF") to treat cancer patients receiving chemotherapy and bone marrow transplants.

18. The patent system is essential to attract investors. Without the incentive provided by the patent system, investors would be much less likely to invest in new and potentially life-saving technologies. Patents, through the promise of a limited period of market exclusivity, provide investors with an opportunity to recoup their initial investment and ultimately, derive commercial benefit therefrom.

19. Indeed, Dr. Mildred Cho has recognized that "[p]atents are clearly seen as a necessary stimulus for the infusion of venture and risk capital in the bio-technology industry . . .." Merz and Cho at p. 6.

20. As Venture Partner of Third Rock Ventures, my work includes the analysis and valuation of intellectual property portfolios and, most importantly, patent portfolios in the life sciences sector. I have come to understand that intellectual property protection is essential to biotechnology and pharmaceutical companies that must invest up to hundreds of millions of dollars in research and development over many years to bring their diagnostic and therapeutic products to market. Patents enable these companies to acquire the capital needed for diagnostic and drug development testing by providing a necessary period of market exclusivity.

21. In the case of genetic testing companies, the limited period of exclusivity provided by a patent is almost always required to secure sufficient capital needed to establish testing capability on a clinical scale. As CEO of Interleukin Genetics, I personally found this to be the case.

22. I recently reviewed a survey published in 2009 by BIO of 150 biotechnology member companies in the therapeutic and diagnostic healthcare industry. (*See* Exhibit 4, BIO Survey). The survey revealed that the majority of companies (61%) stated they generally in-license projects that are in the pre-clinical or Phase I stage of development, and thus still require substantial R&D investment and commercialization risk by the licensee (*See* Exhibit 4, BIO Survey at 13). A substantial majority (77%) of the respondents without approved products indicated that they expect to spend 5-15 years and over $100 million developing a commercial product (*See* Exhibit 4, BIO Survey at 25, 28). These expenditures far exceed most initial research funding by the federal government.

23. The net social benefit of the patent system accrues both to the biotechnology sector and to the patients it hopes to serve. This is true with regard to patents related to isolated DNA molecules.

IV. PATENTS PROMOTE INFORMATION DISCLOSURE

24. The patenting of human isolated DNA molecules is not in conflict with the notion that science would advance more rapidly if researchers are allowed to take advantage of free access to knowledge. Part of the *quid pro quo* of the patent system is that inventors, in exchange for a limited period of patent exclusivity, must provide a sufficient description of the patented invention so that others may improve upon it.

25. Moreover, patents do not necessarily operate as an absolute monopoly. Although a patent grants the right to exclude others from making, using, and selling or importing into the

United States the patented invention for a limited term, the patent holder must still respect the intellectual property rights of third parties in the same field of the invention. Thus, the patentee may not be able to practice the invention covered by the patent without a license from the third party.

26. In addition, the patent system promotes more disclosure than otherwise might occur if, for example, trade secrets were the only means to exclude competitors, at least in the commercial sector. For example, one of the most well-known products sold throughout the world is Coca-Cola (or "Coke"). It is generally known that although various formulas have been introduced since the 1880's, the various formulas have and still are protected by trade secrets. This period of time far exceeds the limited period of market exclusivity that a patents can provide.

V. THE PATENT SYSTEM WORKS AS THE FOUNDING FATHERS INTENDED

27. The Constitution recognizes the need "[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries." United States Constitution, Article 1, Section 8, clause 8.

28. A historical example of the success of the patent system comes from the area of federally funded research. In 1980, in response to concerns about U.S. competitiveness in the global economy, Congress enacted the Bayh-Dole Act.

29. In 1980, Congress enacted Bayh-Dole to address concerns regarding barriers to commercial development affecting non-governmental entities such as universities and small business firms. Some of the stated objectives of the Act include: (1) utilization of inventions arising from federally supported research or development; (2) to promote collaboration between commercial entities and nonprofit organizations, including universities; and (3) to promote the

commercialization and public availability of inventions made in the United States by United States industry and labor. 35 U.S.C. § 200.

30. As reported in the BIO Survey discussed above, the vast majority of the surveyed biotechnology companies license technology from universities (76%) (Exhibit 4, BIO Survey at 17). Moreover, half of the companies surveyed reported that they were founded on the basis of obtaining an in-licensing agreement (Exhibit 4, BIO Survey at 28).

31. Patents also have a significant and positive influence on the United States economy. A 2009 study released by BIO illustrates the importance of university-industry research and development partnerships based on in-licensing of patents. (*See* Exhibit 5; BIO Study). The study reports that university-licensed products commercialized by industry created more than 279,000 new jobs across the United States during the 12-year period between 1996 and 2007 (*See* Exhibit 5, BIO Study at p. 8). Further, the study states that "[w]ithout accounting for product substitution effects, we estimate that over the period 1996 to 2007, university licensing agreements based on product sales contributed at least $47 billion and [possibly] as much as $187 billion to the U.S. GDP. A moderately conservative estimate based on 5% royalty rates yields a total contribution to GDP for this period of more than $82 billion." (Exhibit 5, BIO Study at p. 32).

32. In a 2009 article published by Bremer and colleagues the authors concluded that "[r]eams of objective data exist supporting the conclusion that the Bayh-Dole Act greatly improved the commercialization of federally-funded research . . . and that the public sector-private sector partnerships which were generated under the [Bayh-Dole] Act are essential both to the well being and the competitive position of the United States." (Exhibit 7, Bremer Article).

33. It is my understanding that the University of Utah Research Foundation, an owner or part-owner of at least some of the patents at issue in this case, obtained federal funding in connection with *BRCA1* and *BRCA2* research. I further understand that Myriad, the exclusive licensee of the patents at issue in this case, developed and commercialized its breakthrough diagnostic tests through the investment of a significant amount of venture and risk capital. The *BRCA1* and *BRCA2* story is just one of the many positive examples of the impact of the Bayh-Dole Act.

34. Further, I believe that the incentives of the patent system were instrumental in Myriad's discovery of the correct *BRCA1* and *BRCA2* sequence and characterization of its true structure, which has enhanced *BRCA1* and *BRCA2* research by its disclosure to the public.

35. Finally, from my experience in industry, post-invention development costs far exceed pre-invention and research expenditures. In the case of the *BRCA1* and *BRCA2* genes, for example, although the U.S. Government may have granted millions of dollars in the initial research that led to the patents at issue in this case. Myriad almost certainly spent far more in development and commercialization in order to bring its groundbreaking sequencing tests rapidly to the market.

36. Given the immense importance of the existing patent portfolio to the biotechnology industry, it would be far wiser to have any important policy shifts be made prospectively by Congress after sustained public debate. I believe that the policy arguments are better left to the parts of government where they are better addressed—in Congress and in the U.S. Patent and Trademark Office.

VI. PATENTS ON ISOLATED DNA PROMOTE RESEARCH AND ADVANCE CLINICAL DEVELOPMENT

37. Plaintiffs have voiced the concern that gene patents impede scientific research and clinical development by creating an atmosphere of apprehension of patent infringement in the research community. Underlying such concern appears to be the assumption that such patents cover the genes as they are found in the human body.

38. Patents such as the patents-in-suit have served to advance research and the practice of medicine and benefit patients. I am not aware of any credible evidence that Myriad's patents impede or have impeded basic research.

39. Isolated and purified DNA molecules are chemically, structurally, and functionally different from genes in their native states as they exist in the human body.

40. Thus, the notion that genes and their mutations, alterations, or variations are naturally occurring substances that should not be patented is misplaced. Genes as they are found in the human body are not patentable subject matter.

41. Data cited to support the notion that patents impede research or diagnostic test development is at best inconclusive. This conclusion is echoed in part by an article co-authored by Dr. Mildred Cho. In the article, the authors conclude that "[l]ittle is known about how gene patents are being used and whether they are having a net beneficial or detrimental effect on scientific research and commercial product development." (Exhibit 3, Merz and Cho at p. 6). The authors also state that "[t]here is little evidence that early fears about gene patenting placing substantial restraints on research and clinical medicine have come to fruition." (Exhibit 3, Merz and Cho at Abstract, p. 1).

42. Further, in a 2005 article published in the journal *Science*, John P. Walsh and colleagues report the findings from a survey conducted on 414 biomedical researchers in

universities, government, and nonprofit institutions to determine the effect of patents on biomedical research and material transfers. (Exhibit 6, Walsh at p. 2002). The researchers found that "few academic bench scientists currently pay much attention to the others' patents." *Id.* Moreover, of the "32 respondents who were aware of relevant IP, four reported changing their research approach and five delayed completion of an experiment by more than one month. No one reported abandoning a line of research. Thus, of 381 academic scientists . . . none were stopped by the existence of patents, and even modifications or delays were rare." *Id.*

43. The sheer volume of scientific publications on BRCA1/2 genes and their gene products belies the purported impediment in basic research. On December 10, 2009, I performed a search using the term "BRCA1" in the PubMed database[1] which retrieved almost 7,000 references. A similar PubMed search conducted using the term "BRCA2" retrieved over 4,000 references.

44. Moreover, the *BRCA1* and *BRCA2* patents at issue in this case do not appear to have impeded clinical research. A search on the website ClinicalTrials.gov[2] on December 19, 2009 using the term "BRCA1" retrieved 77 clinical trials that have been completed, are ongoing, or are actively recruiting subjects. Using the search term "BRCA2," 58 clinical trials were retrieved that have been completed, are ongoing, or are actively recruiting subjects.

45. From my experience, the sharing of research tools was not inhibited by IP protection. For example, during my tenure as Executive Director at the Eunice Kennedy Shriver Center for Mental Retardation, an institute that focused on neuroscience research, the scientists

[1] PubMed at the website pubmed.org is a free search engine for accessing citations, abstracts and some full text articles on life sciences and biomedical topics. PubMed is maintained by United States National Library of Medicine at the National Institutes of Health.

[2] ClinicalTrials.gov is a registry of federally and privately supported clinical trials conducted in the United States and around the world. It is a service provided by the National Institutes of Health.

with whom I had the privilege to work routinely acquired valuable substances, materials, and information under material transfer agreements from both academe and industry.

46. I note that in her declaration, Dr. Cho concludes that "patents on genes used for clinical diagnostics inhibit the conduct of research to further the development of improvements to genetic tests." Cho ¶ 24. I strongly disagree. I would be curious to see how Dr. Cho herself would reconcile her statement quoted above with her own article published just a few years ago, which states that "[t]here is little evidence that early fears about gene patenting placing substantial restraints on research and clinical medicine have come to fruition." (Exhibit 3, Merz and Cho at p. 6).

47. Moreover, I note that the surveys conducted by Dr. Cho and cited in her declaration included many clinical geneticists who were involved in or overseeing genetic testing laboratories that were intended to generate a profit. Thus, many of these geneticists charge for genetic testing themselves. For example, in her 2003 article, Dr. Cho and colleagues performed a telephonic survey of all laboratory directors in the United States who were members of the Association for Molecular Pathology ("AMP") or who were listed on the GeneTest.org website. (Exhibit 2, Cho 2003 at p. 3). I further note that AMP is a plaintiff in the present proceeding. I believe that the study was biased towards individuals or laboratories many of whom stand to gain should the patents at issue become invalidated.

48. The results obtained through Dr. Cho's telephonic survey published in 2003 at most represent a snapshot of opinions of a 122 laboratory directors at that time. (Exhibit 2, Cho 2003 at p. 3). Dr. Cho was clearly aware of the limitations of her own study. She concluded that "our data do not directly address the question or whether patents and restrictive licensing

practices have affected the cost and quality of genetic tests, or hindered new research." (Exhibit 2, Cho 2003 at p. 8).

49. Based on the above, any concerns that human "gene" patents impede basic scientific and/or clinical research are not supported by the evidence. The sheer amount of research being conducted and the number of scientific articles being published regularly on the *BRCA1* and *BRCA2* genes and their protein products, for example, provide strong evidence that research is not impeded.

VII. PATENTS ON ISOLATED DNA PROMOTE ADVANCES IN MEDICINE AND ENHANCE THE QUALITY OF PATIENT CARE

50. Another concern voiced by Plaintiffs is that "gene" patents impede advancements in medicine and clinical development. Again, Dr. Cho was clearly aware of the limitations of her own study. She concluded that "our data do not directly address the question or whether patents and restrictive licensing practices have affected the cost and quality of genetic tests, or hindered new research." (Exhibit 2, Cho 2003 at p. 8).

51. The reality is quite the opposite. As discussed above, without the promise of a period of market exclusivity provided by patents and the infusion of venture and risk capital derived therefrom, companies that capitalize on innovation simply would not be created. Their products would not be brought to market, to the clinic, and most importantly, to patients. This of course, holds true for companies such as Myriad and its *BRCA1/2* diagnostic tests.

52. Intellectual property is essential to innovation in health care. In my capacity as venture partner, I help to start companies that develop treatments for rare genetic disorders for which there is no adequate current therapy. An example is a company to develop a recombinant protein to treat a rare genetic disorder, namely X-linked hypohidrotic ectodermal dysplasia. The decision to fund this company with significant capital was critically dependent on an assessment

of the quality of the relevant intellectual property. Without the promise of a period of market exclusivity provided by the patent law, this investment would not have been made.

53. Without strong patent protection, the many biotechnology-based medical advances, such as Myriad's *BRCA1/BRCA2* genetic based testing, would not be developed.

54. Yet another concern voice by the Plaintiffs about "gene" patents is that they harm patients by interfering with their ability to get a second opinion and to make informed decisions about their health and medical care. I disagree. Indeed the term "second opinion" is not used properly. In the clinic, the term "second opinion" is used to refer to the interpretation of diagnostic tests and their implications for treatment. It would be quite unusual to have a patient's DNA sequenced a second time in a second laboratory. If, however, there were any doubts regarding the accuracy of the test, re-sequencing with the proper controls would normally be performed by the original provider. The term, second opinion, generally refers to the interpretation of a test result and which therapeutic options to follow based thereon.

55. As an internist and clinical geneticist, it is my understanding that once a patient has his or her genes sequenced, *e.g.*, the *BRCA1* and/or *BRCA2* genes, the patient generally does not get his or her genes re-sequenced. In the absence of any doubts regarding the accuracy of the original test, re-sequencing of the patient's genes would be an unnecessary use of resources.

56. The situation is analogous to a person who obtains an MRI and whose physician then diagnoses a disorder and subsequently recommends a course of treatment. The patient is free to take the MRI images to another physician for a second opinion. Again however, obtaining another MRI just a short time thereafter would be an unnecessary use of resources, and it is unlikely that an insurance plan would cover a second MRI.

VIII. TEST RESULTS GENERATED IN RESEARCH LABORATORIES SHOULD NOT BE COMMUNICATED TO PATIENTS

57. Plaintiffs have complained that because of the patents at issue in this case, they are unable to share the results of any genetic testing performed and that this goes against their ethical obligations. In particular, Dr. Chung in her declaration states the following: "[a]s a researcher, I believe I have an ethical responsibility to offer my test subjects access to information about their genes. In order to meet this ethical responsibility, I offer my research subjects the option of finding out their results. As a result of the patents, I can only do that by sending samples to Myriad Genetics to test the sample [*sic*] so I can communicate that information to the patients." Chung ¶14.

58. While I respect Dr. Chung's eagerness to help her "test subjects," Dr. Chung appears to confuse information generated during the course of research with information generated within a legally certified diagnostic laboratory. I believe it would be illegal to provide results of genetic testing for clinical use if the laboratory is not Clinical Laboratory Improvement Amendments ("CLIA")-certified. In order for a laboratory to provide a clinical test result to a patient, it must be CLIA-certified. In addition, New York State, where Dr. Chung operates her research laboratory, imposes additional licensing requirements on DNA testing, which could take, in my personal experience, a year or more to satisfy.

59. It is my impression, based on many years of interacting with academic researchers, that the majority of academic researchers operating laboratories (as opposed to CLIA-certified laboratories) do not believe that they should share test results with subjects outside of the standard clinical setting.

IX. PATENTS SUCH AS THE ONES AT ISSUE ARE CRITICAL TO A NASCENT AND BURGEONING INDUSTRY

60. I believe that the emerging field of personalized medicine promises dramatic improvements in health care. The opportunity to develop new therapies based on the genetic dissection of complex disorders raises the realistic hope for individualized treatment plans.

61. The future of personalized medicine will require understanding the biological and physiological significance of variations in genes like *BRCA1* and *BRCA2*, and designing ways to use them in preventative and therapeutic interventions. By identifying and targeting faulty genes before they wreak havoc in the cells of the human body, medicine has the chance to save countless lives.

62. Patents upon the Myriad inventions, and similar ones, have had and will continue to have a positive impact on clinical practice and research. The granting of patents in this area has not had a negative impact on breast or ovarian cancer research and clinical practice, and clinical practice has not been harmed. To the contrary, patents on these isolated molecular diagnostic tools are important, indeed essential, to create the incentives for the immense effort involved in their discovery, and for the expense involved in bringing them to market. The incentives provided by patents fuel discovery and commercialization in emerging technologies such as medical diagnostics, resulting in social and health benefits for future generations.

The views expressed herein are my own and should not be construed in any way to represent the views of Third Rock Ventures.

Pursuant to 28 USC § 1746, I declare under penalty of perjury that the foregoing is true and correct.

Executed on December 21, 2009

Philip R. Reilly

LIST OF EXHIBITS

1	*Curriculum vitae*
2	Cho, MK et al., 2003, Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services, J. Mol. Diagnostics 5(1):3-8
3	Merz and Cho, 2005, What are gene patents and why are people worried about them?, Community. Genet. 8(4):203-08
4	BIO 2009 Member Survey: Technology Transfer and the Biotechnology Industry, located at http://bio.org/ip/techtransfer/PDF.TECH.TRANSFER.PRESENTATION.10.25.pdf (last printed on December 11, 2009)
5	The Economic Impact of Licensed Commercialized Inventions Originating in Research, 1996-2007: Final Report to the Biotechnology Industry Organization, September 3, 2009, located at http://www.bio.org/ip/techtransfer/BIO_final_report_9_3_09_rev_2.pdf (last printed on December 11, 2009)
6	Walsh et al., 2005, "View from the Bench: Patents and Material Transfers" Science 309:2002-03
7	Bremer et al., August 14, 2009, The Bayh-Dole Act and Revisionism Redux, Patent, Trademark & Copyright Journal

CERTIFICATE OF SERVICE

This is to certify that on December 23, 2009, a true and correct copy of the foregoing document has been served on all counsel of record via the court's ECF system.

/s/ Brian M. Poissant
Brian M. Poissant

EXHIBIT 1

CURRICULUM VITAE

Name:	Philip Raymond Reilly
Address:	145 Monument Street, Concord, MA 01742
Date of Birth:	October 3, 1947
Place of Birth:	Albany, NY
Citizenship:	United States of America
Marital Status:	Married (Nancy), three children (Thomas, Sarah, Christopher).

Education:

1965-1969	B.A.	Cornell University
1970-1973	J.D.	Columbia University
1973-1975		University of Texas (Human Genetics)
1977-1981	M.D.	Yale University

Licensed to practice both law and medicine in Massachusetts.
Board Certified in Internal Medicine and Clinical Genetics

Current Positions

Venture Partner, Third Rock Ventures, Boston, MA;
(I work to start companies to treat rare genetic disorders.)
Adjunct Professor of Law, Suffolk University.
(I teach a seminar in biomedical policy and law).

Prior Positions

2000-2006	CEO, Interleukin Genetics, Inc.
2000-2006	Chairman of the Board, Interleukin Genetics, Inc.

I was responsible for all aspects of running personalized medicine company that focused on the genetics of inflammation. I oversaw a growing patent portfolio, raised multiple rounds of capital, supported shareholder relations, re-listed the company on a stock exchange (AMEX), and played in key role in complying with Sarbanes-Oxley requirements. I oversaw the build-out of a state of the art DNA testing laboratory, as well as the successful effort to gain CLIA certification. Between 2000 and 2003, I rebuilt the company, hiring each of the first 20 employees.

1990-2000	Executive Director, Eunice Kennedy Shriver Center For Mental Retardation, Inc., Waltham, MA 02452
1985-1990	Director, Primary Care Program, Shriver Center;
1987-1998	Director, UAP, Shriver Center

Internships and Residencies:

1973	Summer intern (Fellowship award) Institute for Society, Ethics and the Life Sciences, Hastings-on-Hudson, New York
1981-1982	Intern, Department of Medicine, Boston City Hospital, Boston, MA
1983-1985	Resident, Department of Medicine, Boston City Hospital

Research Fellowships:

1973-1975	Research Associate, Medical Genetics, University of Texas Graduate School, Houston, Texas (Dr. Margery Shaw)

Licensure and Certification:

1973	Massachusetts Bar Association
1981	Certified to practice medicine in Massachusetts (#49965)
1983	Board Certification in Internal Medicine
1990	Board Certification in Clinical Genetics
1993	Founding Fellow, American College of Medical Genetics

Academic Appointments:

1985-1992	Instructor in Neurology, Harvard Medical School
1992-1998	Assistant Professor of Neurology, Harvard Medical School
1992-1995	Adjunct Professor of Legal Studies, Brandeis University
1998-2000	Assistant Professor, (Genetics) Tufts Medical School
Fall 2008	Visiting Professor, Cornell University
2008-2009	Adjunct Professor of Law, Suffolk Las School

Hospital Appointments:

1984-1986	Emergency Room Staff Physician (part-time), Leonard Morse Hospital, Natick, Massachusetts
1985 –2000	Physician, Shriver Center for Mental Retardation, Waltham, Massachusetts
1986-1988	Medical Director, Shriver Center for Mental Retardation, Waltham, Massachusetts
1987–1992	Clinical Assistant, Department of Neurology, Massachusetts General Hospital, Boston, MA;
1992-1999	Assistant Professor, Department of Neurology, Harvard Medical School

Other Professional Positions and Consulting (Selected):

1975-1976	Attorney, Powers & Hall, Boston, MA
1976-1977	Fellow, Program in Law, Science and Medicine, Yale Law School, New Haven, Connecticut
1978-1990	Legal editor, Medical Liability Monitor (140 Published columns)
1984-1992	Consultant, Vivigen, Inc. Santa, Fe, NM
1985 -1990	Attorney, Powers & Hall, Boston, Massachusetts
1985-1986	Joseph P. Kennedy, Jr. Foundation Fellow in Geriatrics and Mental Retardation, Shriver Center, Waltham, Massachusetts
1990-1992	Member, Vivgen Board of Directors
1986-1993	Consultant, Collaborative Research, Inc., Bedford, Massachusetts
1993 - 1995	Consultant, Integrated Genetics, Inc., Framingham, Massachusetts
1994 - 1999	Member, SmithKline Beecham Genomics Advisory Board
1995 - 1999	Chair, SmithKline Beecham Clinical Genetics, Ethics and Public Policy Advisory Board
1995 - 2004	Consultant, Myriad Genetics, Inc., Salt Lake City, Utah
1995 - 2002	Consultant, Millennium Pharmaceuticals, Inc., Cambridge, MA

Awards and Honors:

1977	American Bar Association Gavel Award “in recognition of a distinguished contribution to public understanding of the American system of law and justice” bestowed for my book, Genetics, Law and Social Policy (Harvard University Press, 1977)
1981	Book Award for scholastic excellence, presented upon graduation from Yale University School of Medicine
1984	Offered Chief Residency, Medicine, Boston City Hospital

Major Committee Assignments (Selected):

National, and Regional:

1976-1977	Member, NAS/NRC Committee on Public Information in the Prevention Of Occupational Cancer
1990-1992	Member, NAS/NRC Committee on DNA Typing and Forensic Science
1991-1992	Member, Advisory Committee to the National Museum of Health and Medicine on DNA Testing of President Lincoln's Tissue
1991-1993	Member, Task Force on Genetic Information and Insurance of the NIH-DOE Working Group on Ethical, Legal, and Social Implications of Human Genome Research
1991-1993	Member, Liaison Panel to the Institute of Medicine Committee on Assessing Genetic Risks
1987 -	New England Regional Genetics Group Prenatal Testing Committee
1995 -	Member, Federal Bureau of Investigation, DNA Advisory Board

Hospital:

1986-1988	Member, Massachusetts General Hospital Committee for Presymptomatic Huntington's Disease Testing.

Memberships, Offices and Committee Assignments in Professional Societies (Selected):

1982-1989	Member, Social Issue Committee, American Society of Human Genetics
1988-1989	Chair, Ad Hoc Committee on Individual Identification by DNA Technology, American Society of Human Genetics
1989-1993	Chair, Social Issues Committee, American Society of Human Genetics
1990-1993	Ad Hoc Committee on Cystic Fibrosis Testing, American Society of Human Genetics
1994 -1997	Member, Public Policy Committee, American Society of Human Genetics
1994 -1997	Member, Ad Hoc Genome Database Committee, American Society of Human Genetics
1994 -1997	Bylaws Committee, American Society of Human Genetics
1996 -1999	Board of Directors, American Society of Human Genetics

Major Career Interests:

Genetic Screening, Genetic Counseling, Legal Medicine, Prevention of Mental Retardation, DNA Forensics, Science and Public Policy, History of Genetics, Education of Physicians about Genetics

Teaching Experience:

1973-1975	Adjunct Assistant Professor of Law, Bates College of Law, University of Houston
1977-1978	Visiting Lecturer, University of North Carolina School of Medicine, Chapel Hill (Summer Terms)

1981	Visiting Associate Professor, Institute for the Inter-Professional Study of Health Law, University of Texas Health Science Center (Feb.1-May30)
1981-1982	Director Health Law Institute, University of Houston Law Center and University of Texas health science Center Houston Texas
1985 -1999	Instructor, Department of Neurology, Harvard Medical School
1987-1993	Lecturer, Genetics Course, Harvard Medical School
1992 -1995	Adjunct Professor in Legal Studies, Brandeis University (Seminar on "Genetics, aw and Social Policy" offered to masters degree students in genetic counseling)

Major Administrative Responsibilities:

1987 -1990	Director, University Affiliated Program, Shriver Center for Mental Retardation, Waltham, Massachusetts
1990 -2000	Executive Director, Shriver Center for Mental Retardation, Waltham, MA

Editorial Responsibilities:

1987-1993	Editorial Board, American Journal of Medical Genetics
1990 -1993	Editorial Board, Genetic Resource
1990 -1993	Editor in Chief, Exceptional Physician Newsletter

Reviewer for: Am J Human Genetics, Am J Med Genetics, JAMA, Science

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Other Articles (Selected):

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2. Reilly P. There's Another Side to Genetic Screening. Prism. 1976; pp.55-57.

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4. Reilly P. The Case Against Countersuits. Impact in Am Med New. 1977; pp.3-6.

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6. Reilly P. A Lawyer Goes to Medical School. Impact in Am Med News. 1978; pp. 16-18.

7. Reilly P. How Legal is Laetrile? Osteopath Phys. 1978; pp.38-39.

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9. Reilly P. Defining Brain Death. Osteopath Phys. 1978; p. 44.

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11. Reilly P. The Bakke Case: Who Really Won? Osteopath Phys. 1978; p.43.

12. Reilly P. Columnist for Malpractice Lifeline, A Monthly Newsletter. 144 Columns Written for this Newsletter. 1978-1990.

13. Reilly P. Nurse is Acquitted after Controversial Mercy Killing Trial. Am Med New. 1981; p. 3:40-41.

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15. Reilly P. Injection Laws Latest Ground in Death Penalty Fight. Am Med News. 1982; p. 32.

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19. Reilly P. The Verdict Prompts Painful Memories. Am Med News. 1983; pp 4-6, 16.

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EXHIBIT 2

Journal of Molecular Diagnostics, Vol. 5, No. 1, February 2003

Special Article

Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services

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The growth of patents that include genetic sequences has been accompanied by concern about their impact on the ability of physicians to provide clinical genetic testing services and to perform research. Therefore, we conducted a survey of clinical laboratory directors that perform DNA-based genetic tests to examine potential effects. We performed a telephone survey between July and September in 2001 of all laboratory directors in the United States who were members of the Association for Molecular Pathology or who were listed on the *GeneTests.org* website. One hundred thirty-two of 211 (63%) laboratory directors were interviewed. Ten of these were excluded because they did not conduct DNA-based genetic tests. Almost all performed genetic tests for clinical purposes. Half performed tests for research purposes as well. Twenty-five percent of respondents reported that they had stopped performing a clinical genetic test because of a patent or license. Fifty-three percent of respondents reported deciding not to develop a new clinical genetic test because of a patent or license. In total, respondents were prevented from performing 12 genetic tests, and all of these tests were among those performed by a large number of laboratories. We found 22 patents that were relevant to the performance of these 12 tests. Fifteen of the 22 patents (68%) are held by universities or research institutes, and 13 of the 22 patents (59%) were based on research funded by the United States Government. Overall, respondents reported that their perceptions of the effects of patents on the cost, access, and development of genetic tests, or data sharing among researchers, were negative. In contrast, most respondents felt that patents did not have an effect on the quality of testing. We conclude that patents and licenses have had a significant effect on the ability of clinical laboratories to develop and provide genetic tests. Furthermore, our findings suggest that clinical geneticists feel that their research is inhibited by patents. The effects of patents and licenses on patients' access to tests, and the costs and quality thereof, remains to be determined. *(J Mol Diagn 2003, 5:3–8)*

Patents were created to provide incentives for the production of innovative products that could benefit the public. It is argued that patents have been critical to the growth and maintenance of the pharmaceutical industry.[1,2] In this industry particularly, patents are seen as necessary to enhance an inventor's ability to recoup the substantial investments of many years and hundreds of millions of dollars necessary to bring a new drug or device to market. However, it has been proposed that patents are not necessarily an effective incentive for the development of clinical genetic diagnostic tests.[3] For example, it may only take weeks or months to go from a research finding that a particular genetic variant is associated with a disease to a clinically validated genetic test.[4] Furthermore, the need to license multiple patents for the development of a multigenic genetic test may inhibit the development of such tests. Thus, some have suggested that patents and their associated licenses may be inhibitory to the translation of genetic findings into diagnostic tests.[3]

An increase in the number of patents that cover genetic sequences has raised concerns about the impact of these patents on the ability of physicians to provide clinical genetic testing services and perform research necessary to refine or develop new tests or therapeutics.[4,5] Some of the concerns are that patents and restrictive licensing practices for genetic tests may decrease access to testing services, increase test costs, or decrease the quality of testing. On the other hand, others are concerned that, without intellectual property protection, re-

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search would not be done to make the discoveries on which genetic tests are based, and the test would not be developed after the discovery was made.

Previously, we conducted a pilot study to examine the effects of patents and licenses on the practice of clinical genetic testing.[5] To conduct a more comprehensive study and update our previous findings, we conducted a systematic survey of clinical laboratory directors in the United States that perform DNA-based genetic tests to examine the impact of patents and licenses on the provision of clinical genetic testing services.

Materials and Methods

Sampling

Our sampling frame was all laboratories in the United States who were members of the Association for Molecular Pathology or who were listed on the *GeneTests.org* website. We identified directors or the representative of each laboratory most knowledgeable about impacts of patents and licenses on the laboratory's practice. Laboratory directors were identified from the 1998 printed Association for Molecular Pathology Test Directory (the most recent directory available), and from the *GeneTests.org* website on June 18, 2001. (GeneTests is a website maintained by the University of Washington and funded by the National Institutes of Health, the United States Department of Energy, and the Health Resources and Services Administration. The website lists laboratories in North America and elsewhere that perform genetic tests if they request inclusion on the website.) The Association for Molecular Pathology Directory identified 95 laboratory directors who perform genetic tests. The search of *GeneTests.org* identified 127 laboratory directors. An additional 6 laboratory directors were added from a comprehensive updated listing of clinical laboratory directors provided by GeneTests, for a total of 133. We combined this sample of 133 directors from GeneTests with the sample of 95 from Association for Molecular Pathology and eliminated 17 duplicates for a final sample of 211 laboratory directors.

Survey

We conducted a telephone survey of the selected laboratory directors between July and September in 2001. We attempted to contact each director by phone up to approximately three times, followed by one e-mail contact to establish an interview time. A small proportion (~10 people) was contacted by e-mail because their staff indicated this as their preferred method of communication.

The survey consisted of 95 closed-ended questions that addressed the following topics: the setting in which the respondent worked; the categories of tests performed by the respondent's laboratory (eg, genetic, paternity, infectious diseases, and so forth); whether the respondent held any patents or licenses for procedures, devices, or reagents used in clinical testing; whether the laboratory had been prevented from performing or had decided not to develop a clinical test because of a patent or license; and the respondent's perception of how strongly patents had affected access to, quality, and costs of testing, or the ability to do research. The survey included one open-ended question asking whether participants thought there were any ethical issues raised by patents on genetic tests and another to allow participants to add any additional comments. For the purposes of the survey, respondents were told that we defined genetics tests as DNA-based tests to predict or diagnose disease (not including tests to detect infectious agents).

Table 1. Institutional Affiliation of Respondents*

Institutional affiliation	*n* (%)
Company	19 (16)
University	73 (60)
Federal	16 (13)
Nonprofit	80 (66)
Private hospital	64 (52)
Other	10 (8.2)

*Totals do not add up to 100% because response options were not mutually exclusive.

Analysis

Our analysis included descriptive summary statistics on respondent characteristics (eg, role in the laboratory, type of testing performed) and proportion of respondents reporting particular effects of patenting on the laboratory.

Results

Response Rate and Respondent Characteristics

Of 211 laboratory directors contacted, 132 responded, yielding a total response rate of 63%. Of these, 10 were not included for further analysis because they reported that they did not perform DNA-based genetic tests. The final number of responses analyzed was 122 (58%). Respondents did not differ significantly from nonrespondents in the likelihood of being from a for-profit or nonprofit institution (chi-square test, $P = 0.37$).

The majority of respondents were directors of university laboratories. The institutional affiliation of respondents is shown in Table 1. Sixty-one respondents (50%) were from laboratories that conducted clinical laboratory tests only, 60 (50%) were from laboratories that conducted laboratory tests for both research and clinical purposes, and 1 laboratory conducted tests for research purposes only. One hundred fourteen respondents (93%) were laboratory directors, and the remainder were laboratory supervisors, technologists, or other laboratory staff.

Licensing Practices

Ninety-one respondents (75%) said that their laboratories held a license to use a patented method, device, or reagent, and 90 of the 91 said that they had a license to

conduct the polymerase chain reaction. Twenty-five laboratories (27%) had a license to perform a genetic test. These licenses were for tests to detect a wide variety of conditions, including hereditary breast and ovarian cancer (BRCA1/BRCA2), Canavan disease, hereditary hemochromatosis, and fragile X syndrome, among others. Eighty-four respondents (69%) said that they paid royalties to use a patented method or reagent.

Effects of Patents and Licenses on Clinical Genetic Testing Services

Seventy-nine respondents (65%) said that their laboratories had been contacted by a patent or license holder regarding the laboratory's potential infringement of a patent by performance of a genetic test. These notifications were for several different genetic tests, including Apolipoprotein E genotyping, hereditary hemochromatosis, fragile X syndrome, BRCA1/BRCA2, Canavan disease, Charcot-Marie-Tooth disease, spinocerebellar ataxia, and Duchenne muscular dystrophy, among others. Twenty laboratories had received notification for one test, and 51 had received notifications for up to three tests, but 26 labs had received notifications for four or more tests.

Thirty respondents (25%) answered yes to the question, "Has notification from a patent holder or licensee ever prevented you from continuing to perform any clinical test or service that you had developed and were offering?" The 12 tests that laboratories had reported ceasing to perform are shown in Table 2. In searching the US Patent and Trademark database of patents on January 15, 2002, we found 22 patents that were relevant to the performance of these 12 tests. Fifteen of the 22 patents (68%) are held by universities or research institutes, one by an individual, and the rest by for-profit companies. Thirteen of the 22 patents (59%) were based on research funded by the United States Government. The patents were issued from October 1994 to June 2001. The research leading to these patents was published between December 1988 and August 1996 in research articles that we found in *MEDLINE*.

To put these 12 tests into context, we searched the GeneTests database and found that, in June 2001, 461 genetic tests were offered as a clinical service. The vast majority of the tests was for rare disorders and not performed by many laboratories; 394 of the tests were performed by 10 or fewer laboratories, whereas 67 of the tests were done by 11 or more laboratories. However, all of the 12 tests that laboratories had stopped performing were performed by 11 or more laboratories, as reported by GeneTests in June 2001. The number of laboratories performing these tests ranged from 11 (for Charcot-Marie-Tooth disease) to 97 (for fragile X syndrome).

Of the 30 laboratories that reported being prevented from performing a test, 17 reported being prevented from performing one test and 12 laboratories had been prevented from performing more than one test (one laboratory director did not respond to this question). Of those who had reported being contacted by patent or license holders, laboratory directors at companies were significantly more likely to report being prevented from providing a test (10 of 14, 71%) than laboratory directors at universities (12 of 50, 24%) ($P = 0.001$).

Sixty-four (53%) respondents answered yes to the question, "Have you ever decided not to develop or perform a test/service for clinical or research purposes because of a patent?" Laboratory directors at companies were slightly more likely to report that they had decided not to develop or perform a test (12 of 19, 63%) than those at universities (36of 73, 49%) but this difference was not statistically significant ($P = 0.28$).

Opinions about Effects of Patents on Genetic Testing

Respondents were asked to rate the effect of gene patents on various aspects of clinical genetic tests. They were asked to provide these ratings based on their perceptions of clinical laboratories in the Unite States that provide genetic testing. Means and distributions of ratings for their perceptions of laboratories in general are shown in Table 3. Mean ratings indicate that respondents thought that patients access to testing had been decreased by patenting, costs of testing for laboratories had increased, and costs of testing for patients had increased. Respondents thought that the laboratory's ability to develop tests had been decreased, but that test quality had only been modestly affected. Respondents reported on average that information sharing between laboratories had decreased and that the ability of laboratories to do research had been decreased modestly by patents. However, analysis of the distribution of ratings (Table 3) shows that virtually all laboratory directors felt that patents have had a negative effect on all aspects of clinical testing, except on the quality of testing. A few respondents felt that patents were beneficial to test development more generally. For example, one respondent said, "I don't think that the argument that we can't research or do more testing because of patents is valid. Without patents, people wouldn't be able to test because the technology would just be published and sitting in someone's lab book. People shouldn't be complaining that they can't run tests. They should just pay." There were no significant differences between average responses of laboratory directors from companies compared to those from universities.

Discussion

Effects of Patents and Licenses on Clinical Genetic Testing Services

Our findings suggest that a substantial fraction of laboratories in the United States that provide genetic tests have been affected by patents and licenses. Almost two-thirds of the laboratory directors in our sample had been contacted by a patent- or license-holder about the labo-

Table 2. Genetic Tests that Some Laboratories Stopped Performing Because of Patents

Genetic test	No. of respondents that stopped performing this test	U.S. patent no.*	Patent filing date	Patent issue date	Patent holder	Gov't funded work leading to invention†
Apolipoprotein E (Apo E)	9	US5508167	4/13/94	4/16/96	Duke University	X
		US6027896	4/15/98	2/22/00	Duke University	X
		US5716828	2/10/98	5/15/95	Duke University	X
Hereditary breast/ovarian cancer (BRCA1/BRCA2)	9	US5753441 (BRCA1)	1/5/96	5/19/98	Myriad Genetics, Inc. (BRCA1)	
		US6051379 (BRCA2)	12/2/97	4/18/00	Oncormed, Inc. (BRCA2)	
Duchenne/Becker muscular dystrophy	5	US5541074	11/21/94	7/30/96	The Children's Medical Center Corporation	X
Hereditary hemochromatosis (HFE)	5	US5705343	2/9/96	1/6/98	Mercator Genetics, Inc.	
		US5712098	4/16/96	1/27/98	Mercator Genetics, Inc.	
		US5753438	5/8/95	5/19/98	Mercator Genetics, Inc.	
Myotonic dystrophy	4	US5955265	4/14/95	9/21/99	Massachusetts Institute of Technology; University of Wales College of Medicine	X
		US5977333	4/14/95	11/2/99	Massachusetts Institute of Technology; University of Wales College of Medicine	X
Canavan disease	4	US5679635	9/9/94	10/21/97	Miami Children's Hospital Research Institute	
Spinocerebellar ataxia (SCA1, SCA2, SCA3, SCA6)	4	US5834183 (SCA1)	6/28/94	11/10/98	Regents of the University of Minnesota (SCA1)	X (SCA1)
		US5741645 (SCA1)	6/6/95	4/21/98	Regents of the University of Minnesota (SCA1)	X (SCA1)
		US6251589 (SCA2)	5/18/98	6/26/01	SRL, Inc. (SCA2)	
		US5840491 (SCA3)			Kakizuka, A.	
		US5853995 (SCA6)	1/7/97	12/29/98	Research Development Foundation (SCA6)	X (SCA6)
Adenomatous polyposis of the colon	2	US5352775	8/8/91	10/4/94	Johns Hopkins University	X
Charcot-Marie Tooth type 1A (CMT-1A, CMT-X)	1	US5780223 (CMT-1A)	6/6/91	4/26/94	Baylor College of Medicine (CMT-1A)	X
		US5691144	6/5/96	11/25/97	Athena Diagnostics, Inc.	
Fragile X syndrome	1	US6107025	5/24/91	8/22/00	Baylor College of Medicine	X
Huntington disease	1	US4666828	8/15/84	5/19/87	The General Hospital Corporation	X
Factor V Leiden (activated protein C for thrombophilia)	1	US5874256	2/21/97	2/23/99	Rijks Universiteit	

*For patents filed with the U.S. Patent and Trademark office that were most relevant to the performance of the clinical genetic test of interest.
†As indicated in the U.S. patent.

ratory's potential infringement of a patent by performance of a genetic test. The majority of the patent holders enforcing their patents were universities or research institutes, and more than half of their patents resulted from government-sponsored research. If these patents are inhibiting commercialization of genetic tests, our findings would suggest that the Bayh-Dole Act may not enhance technology transfer of this kind of invention in the intended manner.

Table 3. Opinions about Effects of Patents on Genetic Testing

Patents have:	No. (%) indicating negative effect*	No. (%) indicating no effect*	No. (%) indicating positive effect*	Mean rating (*n*)†
Made testing more or less accessible to patients, or no effect? (less access to testing) (no effect) (more access to testing) −3 −2 −1 0 1 2 3	107 (89)	10 (8.3)	3 (2.5)	−1.8 (120)
Decreased or increased the cost of testing to labs, or no effect? (increased cost) (no effect) (decreased cost) −3 −2 −1 0 1 2 3	115 (96)	4 (3.3)	1 (0.83)	−2.2 (120)
Decreased or increased the cost of testing to the patient, or had no effect? (increased cost) (no effect) (decreased cost) −3 −2 −1 0 1 2 3	107 (91)	10 (8.5)	1 (0.85)	−2.0 (118)
Increased or decreased the ability to develop a test, or no effect? (decreased ability) (no effect) (increased ability) −3 −2 −1 0 1 2 3	105 (91)	10 (8.6)	1 (0.86)	−2.0 (116)
Increased or decreased the quality of testing services in labs, or no effect? (decreased quality) (no effect) (increased quality) −3 −2 −1 0 1 2 3	53 (45)	61 (51)	5 (4.2)	−0.8 (119)
Resulted in more or less sharing of information among researchers, or no effect? (less sharing) (no effect) (more sharing) −3 −2 −1 0 1 2 3	98 (85)	16 (14)	1 (0.87)	−1.7 (115)
Has resulted in an increased or decreased ability to do research, or no effect? (decreased ability) (no effect) (increased ability) −3 −2 −1 0 1 2 3	79 (67)	35 (30)	4 (3.4)	−1.1 (118)

*Percentages do not always add up to 100 because of rounding error.
†Not all respondents answered all questions.

As a result of patent- or license-holders exercising their intellectual property rights, one-quarter of the laboratory directors in our sample stopped performing a genetic test that they had been offering. In addition, just more than half of the laboratory directors had decided not to develop or perform a test specifically because of intellectual property considerations (eg, knowledge of the existence or possible future existence of a patent or license).

All but one of our respondents represented laboratories that performed genetic testing for clinical, as opposed to research, purposes. Thus, the implications of these results are fully applicable to the availability of genetic testing in clinical settings. These results also suggest an impact on hospital budgets, to the extent that hospitals are forced to send laboratory tests out to a licensed laboratory at a higher cost to the institution than if they were to perform the tests in-house. Although the absolute number of genetic tests that the laboratories in our sample stopped performing is not large, and the proportion of all tests offered is not high, the tests that laboratories have stopped performing seem to have high clinical relevance because they detect common alleles and/or are relatively commonly used in clinical practice.

Laboratories at companies seem to be more affected than university laboratories in their ability to continue to perform tests that they had been offering, but not necessarily more affected in their decision to develop new tests. This may indicate that companies are more likely to be challenged for patent infringement activities than universities.

These findings are virtually identical to those we obtained in a pilot study of laboratory directors conducted in November 1998,[5] suggesting that patenting and licensing practices affecting genetic tests has not changed dramatically in the last 3 years.[5] They are also generally consistent with a 1999 laboratory survey concerning testing for hemochromatosis.[4] However, with the explosion in the discovery of new genes and the likely development of many commercially viable genetic tests (including those designed to predict susceptibility to prevalent conditions and those to predict responses to drugs), these practices may change. One reason may be that intellectual property could be perceived to be more important for niche markets created by pharmacogenomics research.

Opinions about Effects of Patents and Licenses on Genetic Testing

It was striking that virtually no respondents, including those from commercial laboratories, thought that the effects of patents and licenses on the cost, access, and development of genetic tests have been positive. In contrast, most respondents thought that patents did not have a significant impact on the quality of testing (although nearly half stated that the effects were somewhat negative). Our data indicate that United States laboratory directors performing genetic tests think that gene patents hinder rather than facilitate clinical genetic testing. In addition, our data suggest that laboratory directors may feel more strongly than genetics researchers that patents have a negative effect on research; a recent survey of the members of the American Society of Human Genetics found that 46% of the respondents feel that patents have delayed or limited their research, whereas two thirds of laboratory directors in our survey felt that patents inhibit research.[6] This may point to a more pronounced effect of

patents on clinical genetic testing research than other kinds of research.

Conclusion and Limitations of the Study

We conclude that patents and licenses have a significant negative effect on the ability of clinical laboratories to continue to perform already developed genetic tests, and that these effects have not changed substantially throughout the past 3 years. Furthermore, the development of new genetic tests for clinical use, based on published data on disease-gene associations, and information sharing between laboratories, seemed to be inhibited. Our study does not address the issue of whether patents provided a major incentive for the initial research that led to the patent and development of the genetic tests that the laboratories subsequently stopped providing. However, our findings here and elsewhere[4] demonstrate that laboratories are able to quickly translate published data into clinical tests without the incentives provided by patents, and that laboratories are stopped from performing tests after patents issue. This suggests that patents are not critical for the development of an invention into a commercially viable service when the invention is the finding of an association between a genetic variant and a particular condition.

Despite the reduced number of clinical laboratories offering specific clinical genetic tests, we do not know whether patients who were denied access to these tests had testing performed by another laboratory. Furthermore, our data do not directly address the question of whether patents and restrictive licensing practices have affected the cost and quality of genetic tests, or hindered new research. Nevertheless, the practitioners in the United States who perform these tests on a daily basis overwhelmingly feel that costs, both to laboratories and to patients, have been increased. Such increases can only lead to limited access. In addition, a lower number of laboratories performing the tests could lead to lower test quality, less test method innovation, and less clinical research. Although patents may have provided incentives to conduct the basic research underlying the genetic tests, the reported inhibition of clinical testing and research does not bode well for our ability to fully and efficiently use the results of the Human Genome Project and related work.

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EXHIBIT 3

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What Are Gene Patents and Why Are People Worried about Them?

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Abstract

This article examines what it means to patent a gene. Numerous ethical concerns have been raised about the effects of such patents on clinical medical practice as well as on research and development. We describe what kinds of inventions are covered by human gene patents, give several examples and summarize the small body of empirical research performed in the US examining the effects of these patents. There is little evidence that early fears about gene patenting placing substantial restraints on research and clinical medicine have come to fruition. Nonetheless, there are areas of concern, and policy makers, physicians and the public should be alert to ensure that the net social benefits of patenting human genes are maintained.

Keywords

Gene patent; Genetic invention; Drug licensing

Introduction

Nearly 30,000 human genes have been patented in the US [R. Cook-Degan, pers. commun.]. Patents will often be secured in countries throughout the world where the patent owner thinks there may be a viable market. Patents are granted by the US government to inventors for new, non-obvious and useful inventions and discoveries, and similar standards of patentability are applied around the globe. A patent grants to its owner the right to exclude others from making, using or selling a patented machine or composition of matter, or using a patented method, typically for a period of 20 years from the date of filing a patent application. In contrast to trade secrets (which must be kept secret by their owner and do not protect against independent invention), patents require disclosure that teaches the world how to make and use an invention, rewarding the inventor with a period of exclusivity during which time profits may be earned from its commercialization.

Throughout the developed world, patents are awarded following an examination by a patent agency (e.g., the European Patent Office, the US Patent and Trademark Office). Examination procedures ensure that inventions fulfill the standards for patentability, and that the patent grants protection only for that which has been invented, and no more. The patent *claim* defines the scope of patent protection. Typically, there is a negotiation between the inventor and the patent examiner, with the former trying to get very broad protections, and the latter seeking to allow a patent narrowly restricted to the technological improvements made by an invention and disclosed in the specification. Broad claims may often be granted for breakthrough inventions, such as those on the polymerase chain reaction (PCR), recombinant technology, gene knock-out methods and even for individual gene sequences. Because broad claims to

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inventions such as a sequence or a recombinant protein are so basic, they cannot easily be invented around, and any improvements are likely to require licenses before they can be used commercially. In biotechnology, such licenses may be impossible to secure, since the owners of the dominant patents are likely to depend upon them to maintain market exclusivity [1,2]. In any technology, broad claims will create a disincentive for downstream development and improvements [3].

A patent grants what is called a negative right, i.e., the right to enjoin others from using the claimed invention without permission. A patent owner may turn to the government – through lawsuits for infringement – to use its judicial and police powers to block others from making, using or selling the invention and to collect damages from those who infringe. A patent does not grant its owner the positive right to use an invention, as its use or application may be subject to legal restraints (e.g., human cloning) or regulatory licensing requirements (e.g., drugs and medical devices). Likewise, there is no legal compunction for a patent owner to 'work' or license others to use a patented invention, and, as a general rule, a patent may even be used wholly to keep products from coming to market [4]. Exceptions have been recognized for compulsory licensing of patented inventions when deemed necessary to protect public health and welfare (such as weapons and drugs) [5]. The US Federal Government retains 'march-in' rights to patents resulting from federally funded research if the inventions are not developed for practical application or if necessary to alleviate health or safety needs which are not reasonably satisfied (although this right has never been exercised) [6].

Human gene patents result from the cloning and description of the sequence of a gene, the role or function of which is somewhat understood. As cloning and sequencing capabilities rapidly evolved in the 1980s, patent applications on human genes were filed in increasing numbers. Questions concerning the wisdom of patenting genes were highlighted by the 1991 patent application filed by the US National Institutes of Health that was subsequently amended to cover thousands of expressed sequence tags. Expressed sequence tags are unique nucleotide strings, randomly culled out of the genome, which have no known function other than as a distinctive marker. These applications were ultimately withdrawn, but in 2001, the concerns over the scope of gene patents led the US Patent and Trademark Office to clarify its patentability standard for genes, requiring that a patent applicant make a credible assertion of specific and substantial utility of the genetic invention [7,8].

Gene patents cover three distinct types of invention: (1) diagnostics, (2) compositions of matter and (3) functional uses. We discuss each in turn, providing examples, highlights of areas of concern and what is known about each. This overview is centered on US patent law and what is known about how gene patents are being used in the US. Some of the problems discussed have begun to spill over to Europe, Canada and Australia, as discussed elsewhere in this issue. This is not meant to be a comprehensive international review [9], but only an attempt to demonstrate the breadth of gene patents, discuss concerns about how they are being used and summarize relevant empirical data.

Diagnostic Uses

The first type of genetic 'invention' covers testing of genetic differences. We have referred to these types of patents as 'disease gene patents', because they claim the characterization of an individual's genetic makeup at a disease-associated locus when performed for the purpose of diagnosis or prognosis [10]. These patents typically cover all known methods of testing, including the use of hybridization, Southern analysis, PCR and even DNA chips. Since the fundamental discovery patented is the statistical observation of a genetic difference and a phenotypic difference (such as the occurrence of disease), then any method for testing for that genetic difference can be covered by the patent [11].

Well-known examples of disease gene patents include those covering genes implicated in breast and ovarian cancers (BRCA1 and BRCA2), colon cancers (HNPCC, FAP), cystic fibrosis (CFTR), hemochromatosis (HFE) and a growing number of neurological diseases including late-onset Alzheimer's disease (Apo-E), Canavan disease, Charcot-Marie-Tooth disease (CMT-1A, CMT-X), spinal muscular atrophy (SMN1), spinocerebellar ataxia (SCA1–12) and others.

There are several characteristics of genes and disease gene patents that demonstrate how the genome is being divided up by small patent claims to overlapping genetic territory. First, any one gene may have multiple patents claiming the diagnosis of different polymorphisms. Thus, several patents have been issued for testing of different mutations in the CFTR gene [12]. Further, some diseases (at least the phenotypic expressions of them) are caused by multiple genes, such as Charcot-Marie-Tooth disease [13]. Questions about ownership and access get messy when there are many hundreds of known mutations in multiple causative genes, as exemplified by BRCA1 and BRCA2, for which there are at least a dozen US patents on tests of these two genes [14]. Finally, patents can issue on the same exact molecular test when it is performed for different diagnostic or prognostic purposes. For example, an Apo-E test, in which the number of E2, E3 and E4 alleles carried by a patient is assessed, can be performed for each of the following patented uses: (1) determining whether a patient is at risk of early onset Alzheimer's disease [15]; (2) assessing an Alzheimer's disease patient's prognosis [16]; (3) determining a course of therapy based on pharmacogenetic receptivity [17], and (4) assessing a patient's prostate cancer risk [18]. Apo-E is also used for the assessment of cardiovascular risk, but this use has not been patented. In these cases, a patent thicket is created that can lead to difficulties in securing licenses and expenses in paying multiple 'stacked' royalties to multiple patent owners [19].

To the best of our knowledge, the owners of the overwhelming majority of issued gene patents have not aggressively enforced their rights against clinical molecular diagnostics laboratories. Nonetheless, a majority of genetics laboratories across the US report that they have had one or more of the above disease gene patents asserted against them [20,21]. In some cases, these patent owners have been willing to grant a license to laboratories performing a home-brew test. Per test royalties of which we have become aware include USD 2 for the ΔF508 mutation of CFTR (University of Michigan), USD 5 for Gaucher's disease (Scripps Institute), USD 12.50 for Canavan disease (Miami Children's Hospital) and reportedly more than USD 20 for HFE (Bio-Rad). In some cases, an up-front license fee (not tied to volume) has been demanded as well [22]. While these royalties arguably reduce access and create problems for laboratories, they must be examined in the context of the US commercial, profit-centered health care system.

Clinical as well as research laboratories typically pay royalties for the use of patented technologies. For example, the price of widely-used PCR machines and reagents includes a premium paid for the use of the patented technologies. In addition, a royalty of about 9% is paid for all testing done by licensed laboratories [21]. As discussed in great detail by Nicol [23], the most recent patents enforced against biotechnology companies and testing laboratories are those that claim the extremely broad uses of intronic and extra-gene sequences for generating haplotypes and identifying allelic variation [24]. Disease gene patents vary in significant ways from these more typical patented tools that are used by laboratories for testing for a variety of specific disease genes. Critically, since a disease gene patent claims all methods of testing for a specific gene, there is no plausible way of working around these patents and the patents may be used to monopolize a test.

Fortunately, in only a handful of cases, patent owners have refused to grant licenses to laboratories to allow them to perform specific tests. In a few cases, patent owners have used the patents to monopolize the testing service, requiring physicians and laboratories to send

samples for testing to the owner or its specified licensees. Thus, tests for breast and ovarian cancer genes (Myriad Genetics) and a set of neurological disorders (Athena Diagnostics) are generally available from only these commercial laboratories. SmithKline Beecham Clinical Laboratories made a brief attempt at capturing the testing market for hemochromatosis before the business unit was sold to Quest Diagnostics, which then transferred ownership to Bio-Rad [22]. Myriad has extended its reach beyond the US borders, seeking to enforce its BRCA patents in, amongst others, France [25], Canada [26] and the UK [27]. The test for Canavan disease, despite being easily included in panel assays that many laboratories can run, was restricted to selected laboratories around the US by the patent owner, Miami Children's Hospital [28].

In these cases, laboratories have been told where patient samples must be sent to have the patented tests performed and how much it will cost. Being compelled to stop providing testing services has serious implications for the ability of molecular pathologists to maintain currency in their field, to treat their patients with comprehensive medical services, to train residents and fellows, to perform research and to run their laboratories in an efficient manner. Hospital-based laboratories must often absorb part of the fixed monopoly costs of the tests which they are compelled to offer patients but for which health insurance may not cover the full price. Seen in this light, these patents raise the costs of clinical services and restrict physicians' ability to practice medicine [4,29].

Compositions of Matter

The second broad type of genetic invention relates to compositions of matter (i.e., chemicals and materials), including the isolated and purified gene (cDNA) and all derivative products (e.g., recombinant proteins or drugs, viral vectors and gene transfer 'therapies', transfected cells, cell lines and higher order animal models in which the patented gene has been inserted or knocked out). According to the Biotechnology Industry Organization, there are more than 200 biotechnology drugs and vaccines that have been approved by the US Food and Drug Administration [30], and more than 370 drugs are in clinical trials [31].

Patents on human genetic compositions of matter cover a broad array of chemicals and technologies. For example, human insulin, human growth hormone and many other proteins that can be isolated and purified from human blood or urine can be patented. Further, synthesized products can be covered by various patent claims, including (1) claims to the sequences used (both the sequence to be transcribed into RNA and proteins as well as promoter sequences); (2) the virus or other vectors containing the claimed sequence; (3) transfected cells, cell lines and nonhuman organisms created and used in these processes, and, perhaps most importantly, (4) the proteins or other therapeutic products made by these claimed processes. The last, called 'product by process' claims, allow patent owners to prohibit the use or sale of products made by the claimed processes, regardless of where the product is made.

Functional Use

Finally, a third and emerging class of gene patents is that which claims the functional use of a gene. These patents are based on discovery of the role genes play in disease or other bodily and cellular functions or pathways, and claim methods and compositions of matter (typically called 'small molecule' drugs) used to up- or downregulate the gene. Note that these drugs are not likely gene products, but rather other types of chemicals found to effect gene functioning, and the drugs are likely patentable themselves as unique chemical entities useful as therapy. For example, a patent that was recently invalidated claimed methods and compositions of matter for the selective inhibition of the Cox-2 gene, which prevents inflammation and pain. The patent was invalidated because the patentee, the University of Rochester, failed to disclose a chemical entity that would perform such selective inhibition [32]. The patent claimed the mechanism by which three drugs that later came to market work: Celebrex, which is co-

marketed by Pharmacia (of which Searle is part) and Pfizer, Pfizer's Bextra and Merck's Vioxx. Each one of these chemical entities may be patented as a new, non-obvious and useful drug for the treatment of inflammation and pain, but the Cox-2 patent attempted to claim all drugs that work by manipulating the function of the target gene.

A similar case to the Cox-2 litigation involves a patent awarded to Harvard and Massachusetts Institute of Technology and exclusively licensed to Ariad Pharmaceuticals. The patent claims the basic regulation of any genes by reducing intracellular activity of the transcription factor NF-kB [33]. Upon award of the patent, Ariad sued Eli Lilly for infringement by their osteoporosis drug Evista and their sepsis drug Xigris and has asserted the patent against numerous other companies. Lilly's patent applications for these two compounds predate the filing of the NF-kB application [34]. Ariad should have a hard time winning, both because, like the selective Cox-2 inhibition patent, the NF-kB patent fails to disclose specific agents for regulating the factor and because the company is trying to assert its patent in a way that would remove from the market chemical entities that predated the discovery and disclosure of the functional pathway by which those drugs work.

Finally, we have the case of Viagra. Pfizer, which has had its erectile dysfunction drug Viagra on the market for several years, recently received a patent claiming the molecular pathway by which Viagra works. The patent claims any selective PDE5 inhibitor used to treat impotence [35]. Immediately upon allowance of its patent in late 2002, Pfizer sued Bayer and GlaxoSmithKline for their drug Levitra and Eli Lilly and their partner Icos for their drug Cialis, while both drugs were proceeding towards the Food and Drug Administration approval (and have since been approved) [36]. The difference between the Viagra case and the Cox-2 case is that Pfizer actually has and claims a specific class of drugs that work by the claimed functional pathway. Whether this is an adequate basis on which to allow Pfizer to lay claim to all drugs that work by the same molecular mechanism is a fundamental legal question that looms over the pharmaceutical industry.

Concerns about Gene Patents and Research

One of the primary concerns about human gene patents is that they will make it more difficult to perform research, thereby delaying or impeding discovery and development of diagnostics and therapeutics [37]. In the US, there is no statutory research exemption, but only an extremely narrow court-defined exemption. As recently summarized by the Court of Appeals for the Federal Circuit in a lawsuit against Duke University, 'regardless of whether a particular institution or entity is engaged in an endeavor for commercial gain, so long as the act is in furtherance of the alleged infringer's legitimate business and *is not solely for amusement, to satisfy idle curiosity or for strictly philosophical inquiry,* the act does not qualify for the very narrow and strictly limited experimental use defense' (italics added) [38]. Duke was not excused from potential infringement of patents covering laboratory equipment simply because the equipment was used solely for research and educational purposes, which the Court found to be the core of Duke's business. A strong argument can be made that the research exemption should be much broader, encompassing research aimed at better understanding of the claimed invention, such as how it works and whether it works as taught by the patent, how to improve upon it and how to work around it. Indeed, practically speaking, this may in fact be how patents are most commonly used. As a colleague stated it, research on the invention should be exempt while research using the invention is infringement [P. Ducor, pers. commun.]. As mentioned earlier, the patent law trades a period of exclusivity for disclosure, and competitors should not have to wait for the period of exclusivity to end before learning from that disclosure and attempting to improve upon it. The fact that competition occurs is shown by a simple example: a US patent search for different combinations of PDE or PDE5 or phosphodiesterase and

erectile or dysfunction in patent claims yields 76 patents assigned to 18 different companies and 2 universities [39].

Little is known about how gene patents are being used and whether they are having a net beneficial or detrimental effect on scientific research and commercial product development. Patents are clearly seen as a necessary stimulus for the infusion of venture and risk capital in the bio-technology industry; the role patents play in motivating academic researchers is less clear. Some data have been generated about the licensing of biotechnology patents. These studies suggest that most genetic inventions are not patented, but when they are, they are being licensed on exclusive terms [40,41]. In turn, researchers and firms appear to have developed various strategies to minimize the potential detrimental effects of the patents, including taking licenses when possible, inventing around patent inventions, going offshore, using publicly available resources, litigation and infringement [42]. Nonetheless, much remains unknown about the effects of these practices on basic research and commercial competition.

Conclusion

In conclusion, we see that ‘gene patents’ cover a broad range of invention. Each type has its own potential uses and marketable products, and each raises potential problems depending on how the patents are used in the relevant marketplace. Much remains unknown, and indeed, the market is still adapting to these patents. Thus, it is extremely important to continue to study and monitor how gene patents are being used, licensed and enforced in order to develop policy interventions if deemed necessary.

Acknowledgements

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EXHIBIT 4

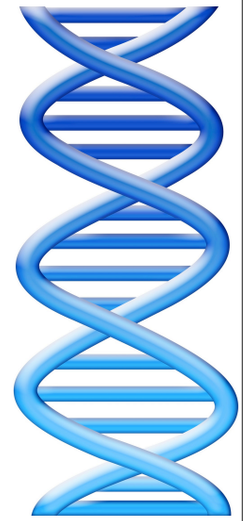
BIO 2009 Member Survey

"Technology Transfer & the Biotechnology Industry"

Bio
BIOTECHNOLOGY
INDUSTRY ORGANIZATION

BIO 2009 Member Survey
Technology Transfer & the Biotech Industry

- **GOALS**
  - **Collect Information on Biotechnology Industry's Technology Transfer Portfolios**
    - **Who Do We In-License With?**
    - **What Impact Does Bayh-Dole (Ability to In-License with Univ. and Fed. Gov.) Have on the Biotech Industry?**
    - **How are In-License Opportunities Found & Agreements Structured?**
    - **How Can We Help Ensure Effective Technology Transfer in the U.S.?**

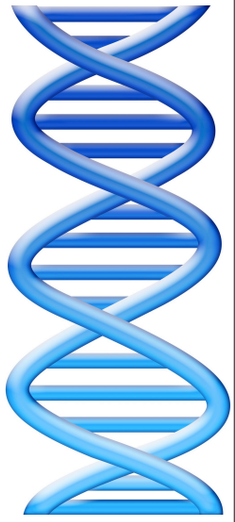


Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

BIO 2009 Member Survey
Technology Transfer & the Biotech Industry

KEY FINDINGS

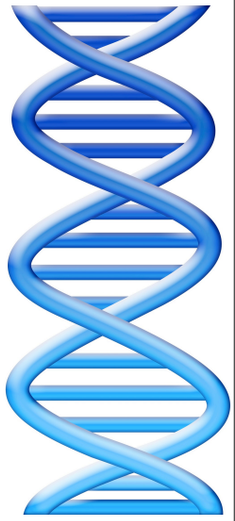
- **Majority of Companies Have License Agreements with Universities & Pharma/ Biotech Companies - Most of Which Are With U.S. Entities**
- **Majority of Companies Do Not Have License Agreements with Federal Government**
- **Half of the Companies Were Founded on the Basis of a License Agreement**
- **After Obtaining Initial License Companies' Employment Numbers Increase**
- **Companies Spend Several Years and Significant Amounts of Dollars Developing Licensed Technology Into Commercially Available Products**
- **Most University License Agreements Have Non-Commercial Research, Particular Field of Use, and Milestone Clauses Which Are Monitored to Ensure Compliance**
- **The Ability to Obtain an Exclusive License is Critical to the Ability to Research & Develop a Commercially Available Product**



Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

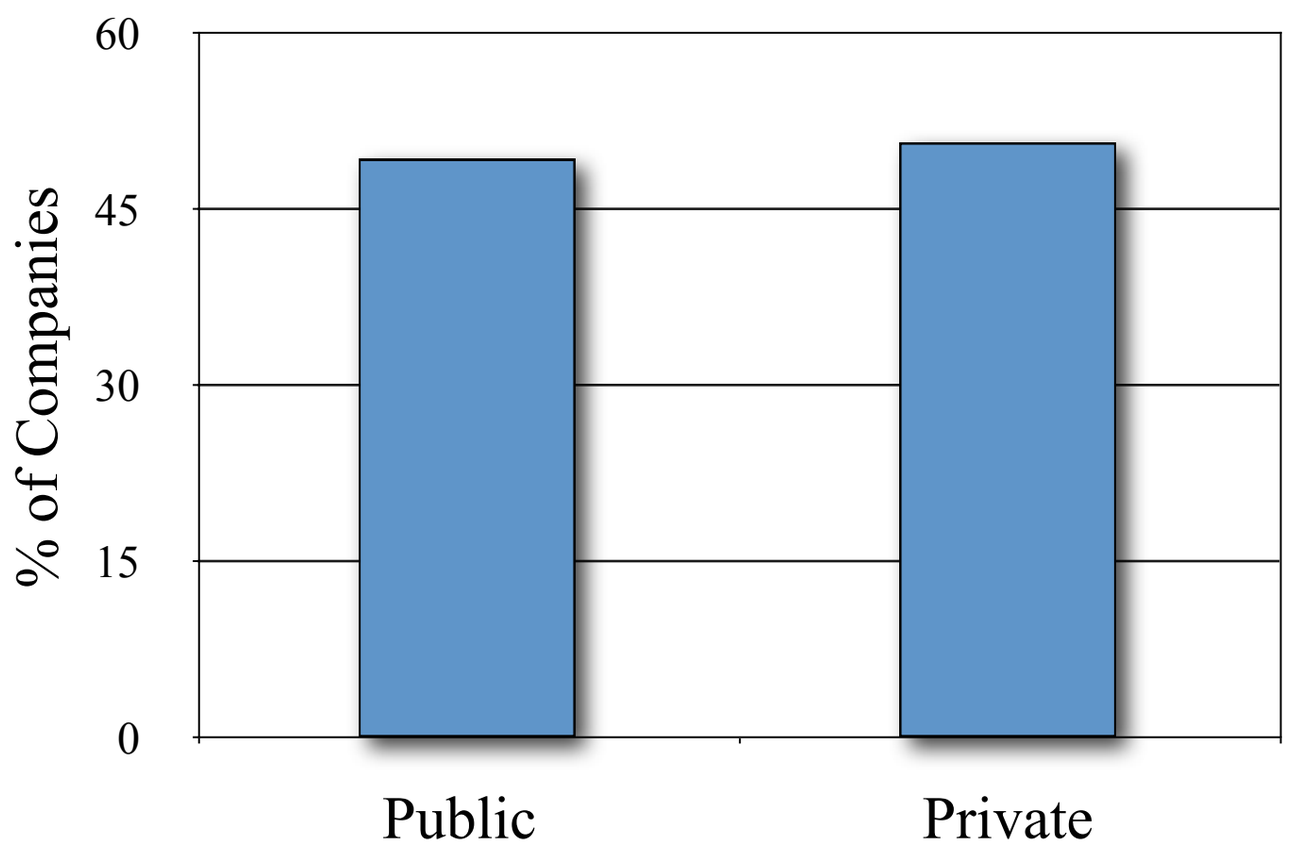
Profile of Survey Participants

- **PROFILE OF PARTICIPANTS**
  - Company Structure
  - Employees
  - Products
  - Revenues/Assets



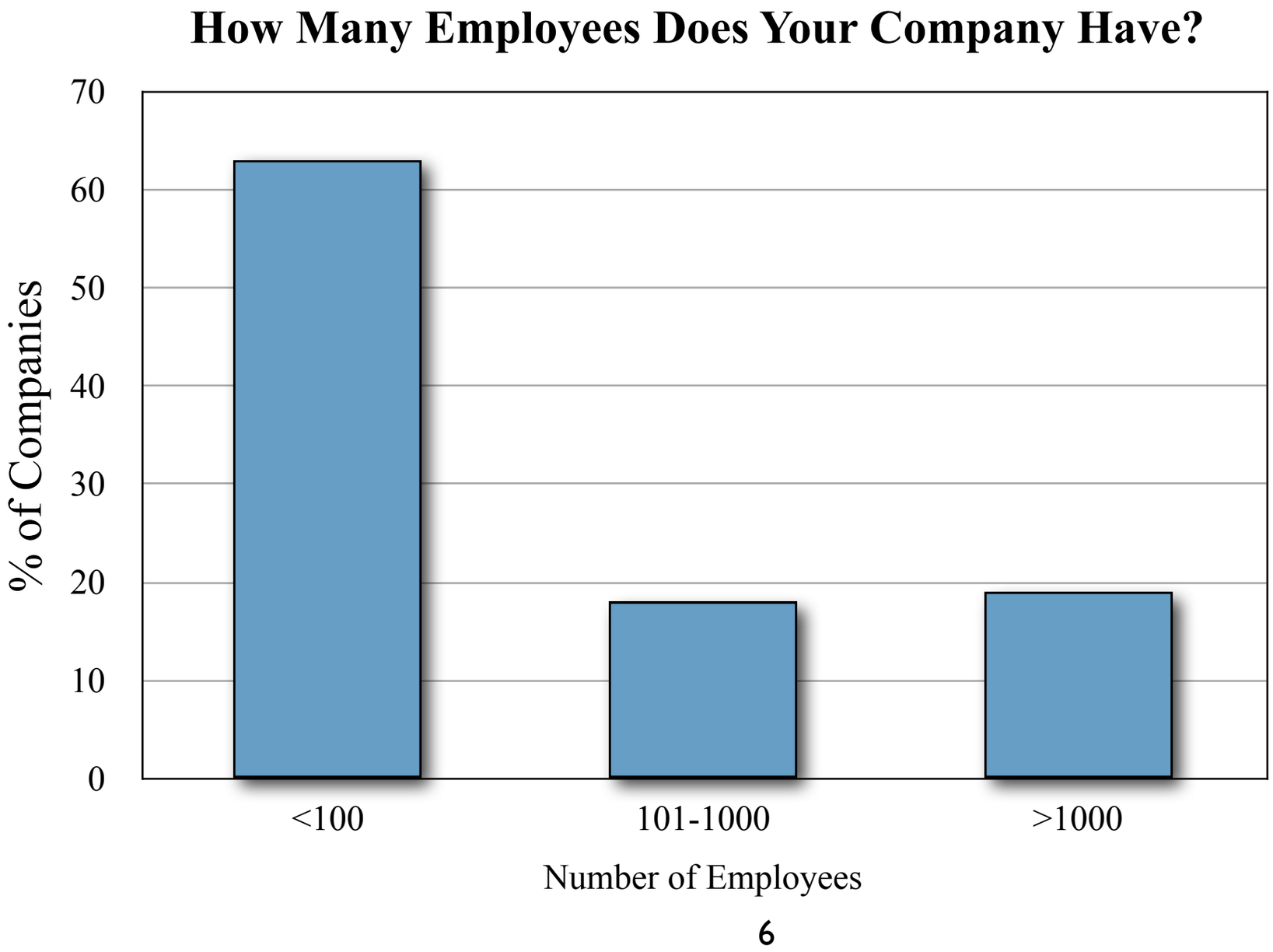
Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

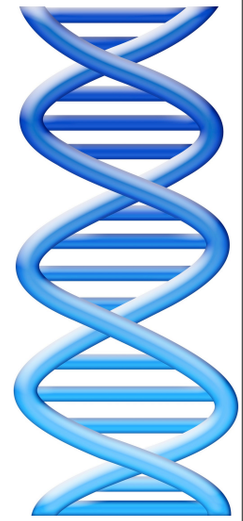
Profile of Survey Participants



150 BIO member companies participated in survey.
49% were public (N=74) and 51% were private (N=76).

Profile of Survey Participants

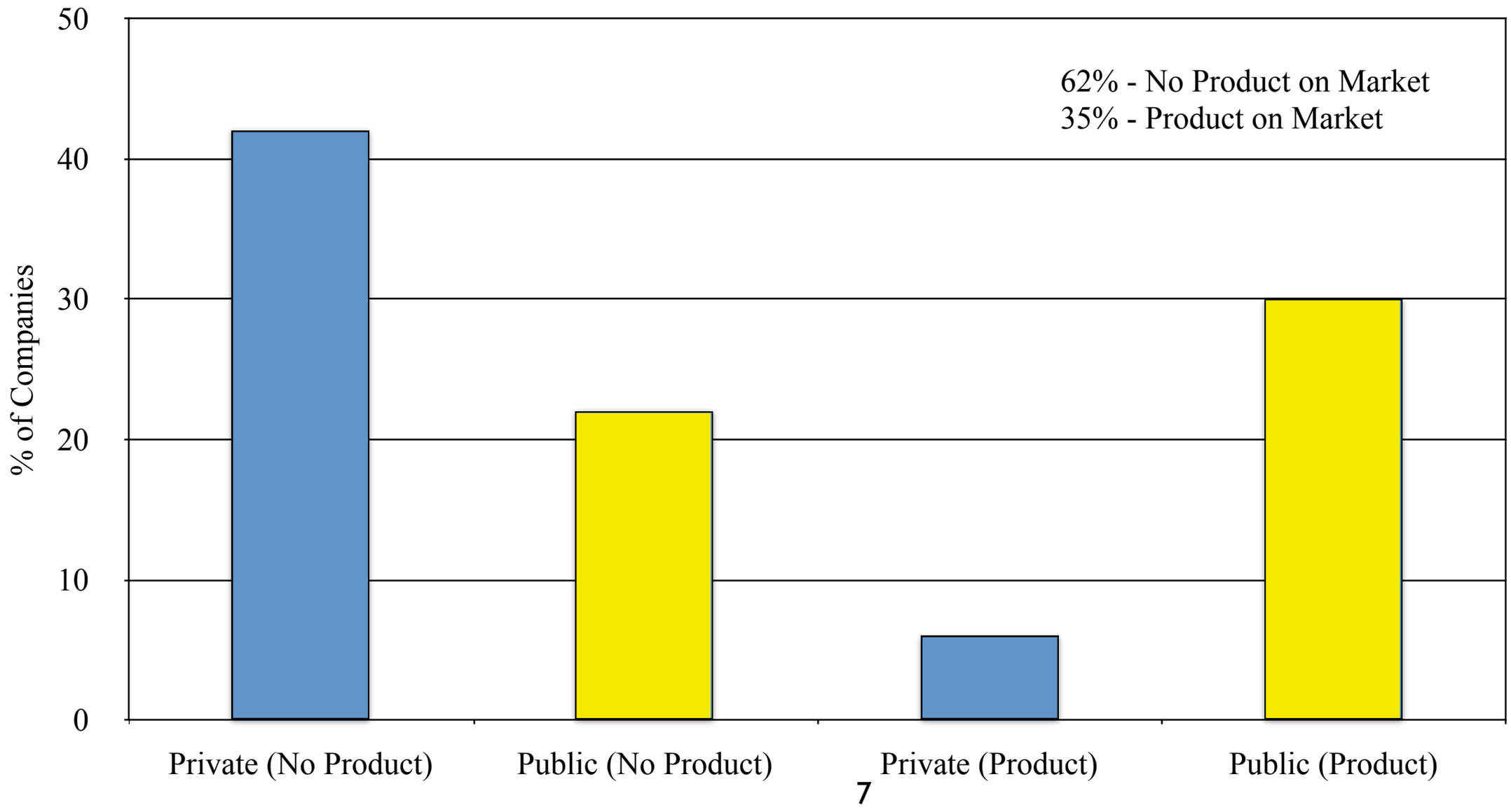




BIO BIOTECHNOLOGY INDUSTRY ORGANIZATION

The majority of these companies are small with fewer than 100 employees (63%).
54% had fewer than 50 employees.
19% had over 1000 employees.

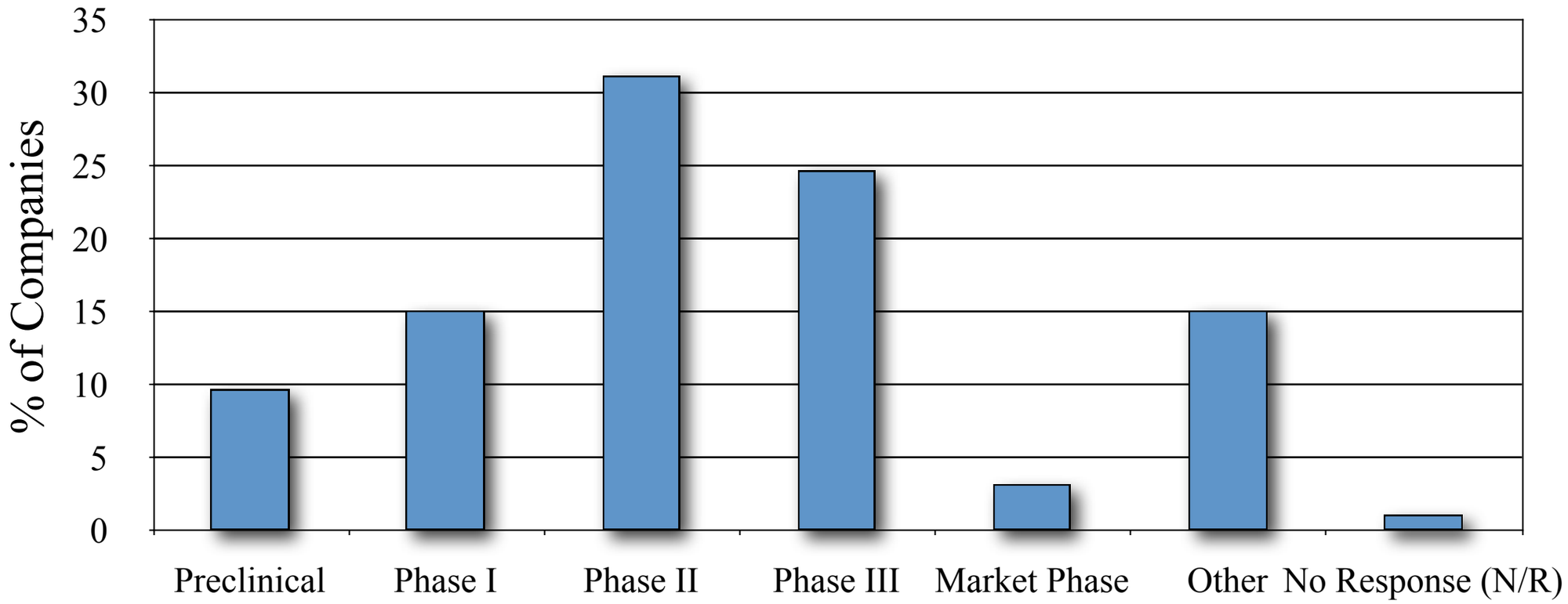
Profile of Survey Participants



Most (62%) of the these companies do not yet have a commercial product (41% were private and 21% were public.
35% have a product on the market (6% were private and 29% were private).
3% gave no response (N/R)

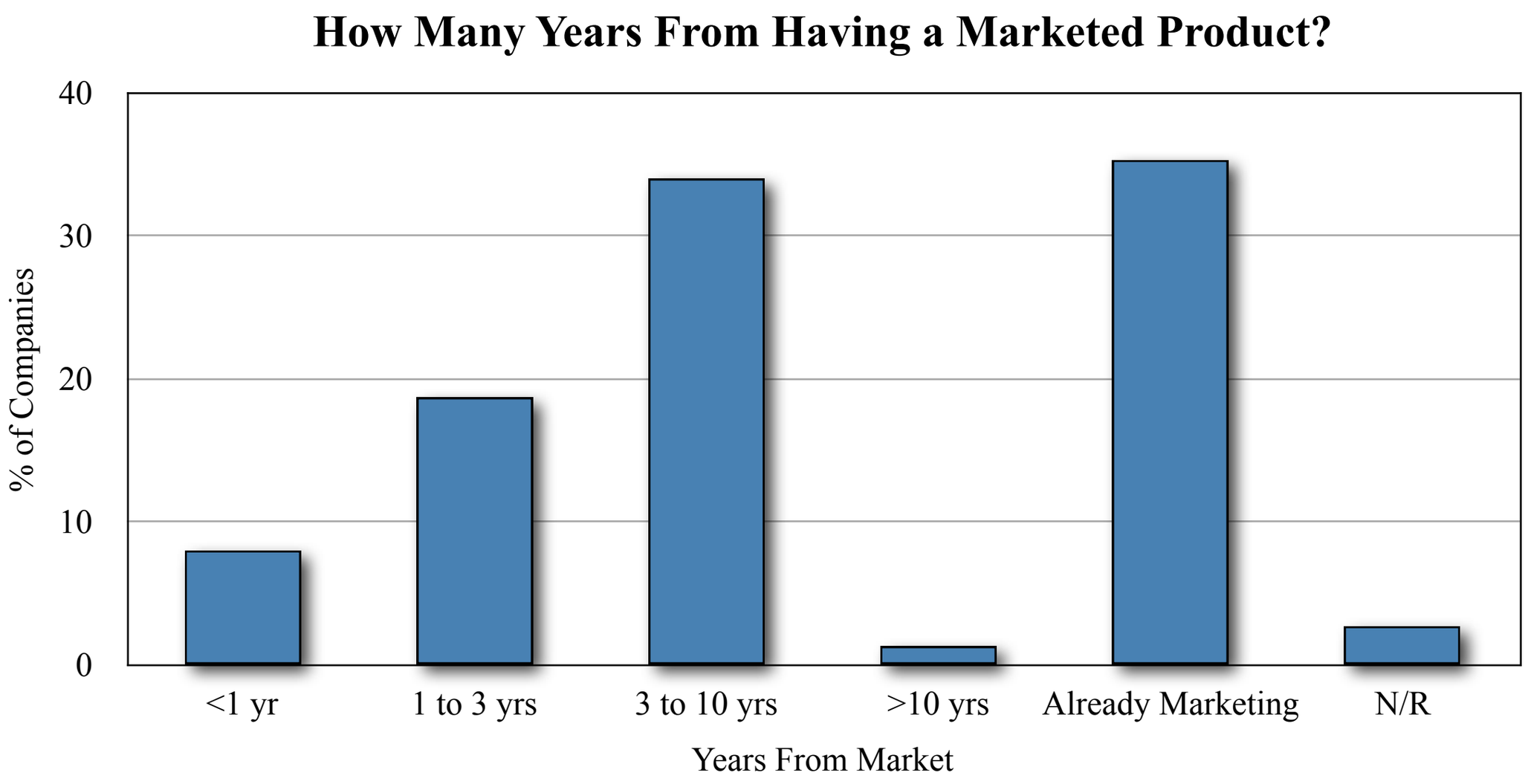
Profile of Survey Participants

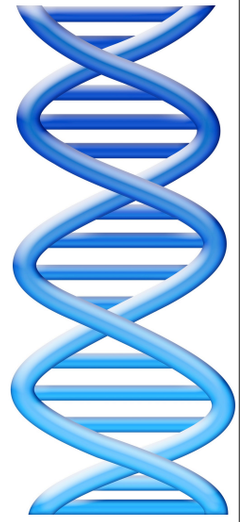
What Stage of Development is Your Lead Product In? (Companies with No Marketed Product)



56% of companies have lead products in Phase II and III stages of development.

Profile of Survey Participants





Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

9

Most companies with no marketed product are 3-10 years away from having a marketed product (34%). 35.3% of the companies surveyed have a product on the market.

Profile of Survey Participants

- **SUMMARY OF SURVEY PARTICIPANTS**
  - Represents a Mix of Public & Private Companies
  - Most are Small Companies with No Product on the Market that are 3-10 Years Away from Commercialization. Over Half of Lead Products are in Phase II or III Stage of Development.
  - Companies with Marketed Products Represent Mid and Large Biotech Companies

Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

Other Findings:
41% of companies' lead product is a small molecule and 24% have a large molecule protein lead product.
36% Have a Biologic Lead Product (Lg. Protein, Sm. Protein, Vaccine).
Majority (65.4%) have 5 or less products in development.
28.7% have more than 6 products in development.

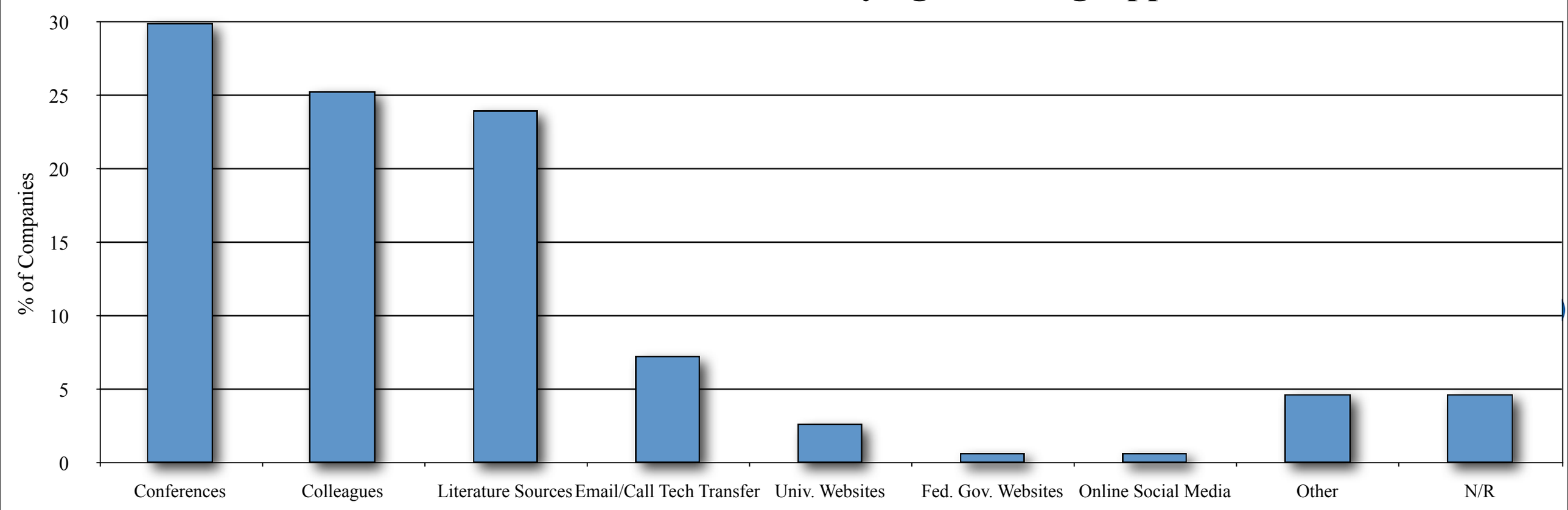
Biotechnology In-Licensing

- **BIOTECH IN-LICENSES**
  - Finding In-License Opportunities
  - Stage of Development In-Licenses Occur
  - Number of In-Licenses
  - Exclusive vs. Non-Exclusive
  - What Entities Biotech Has In-License Agreements With

Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

11

Finding Biotech In-Licensing Opportunities

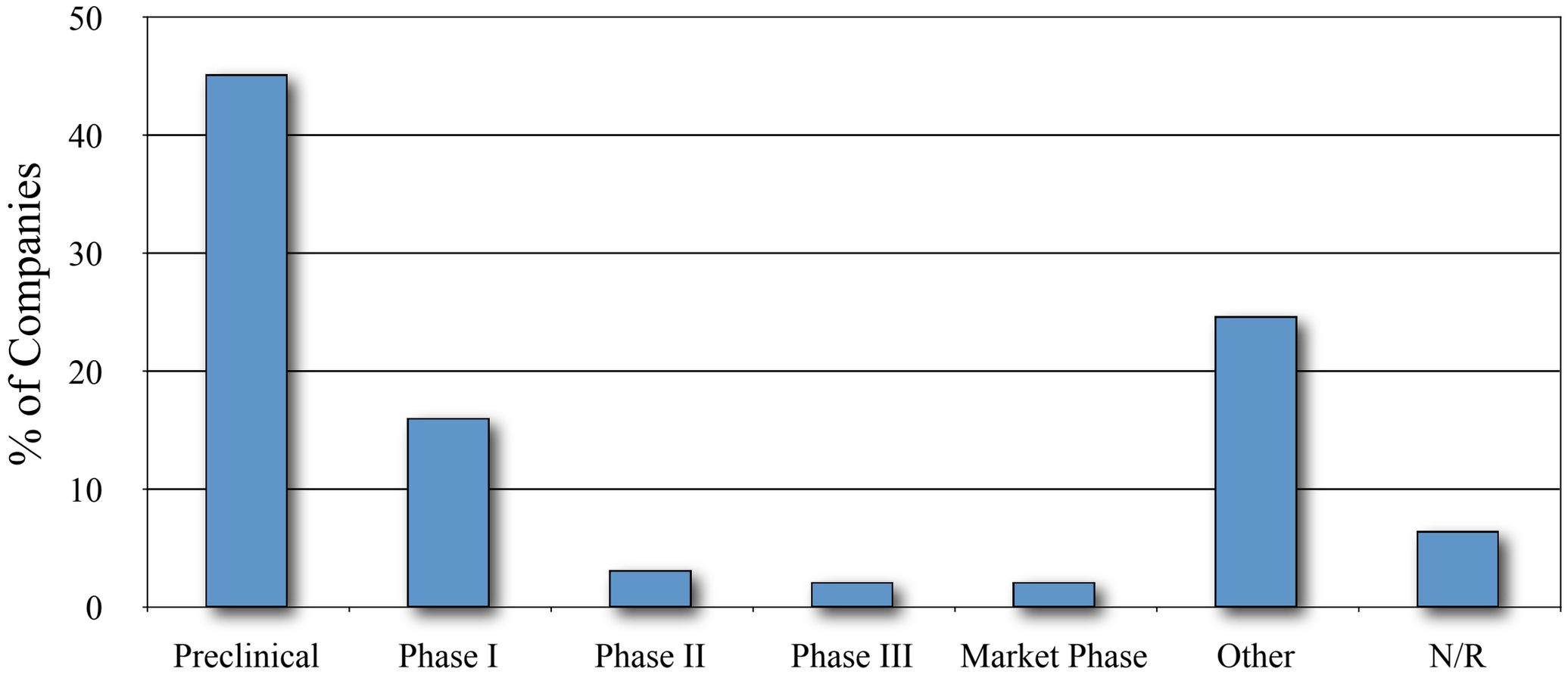


Conferences were the most common method of identifying licensing opportunities (30%) followed by colleagues (25%) and literature sources (24%).

Biotech In-Licensing

Companies with No Marketed Product

At What Stage of Development Does Your Company Generally In-License a Product?



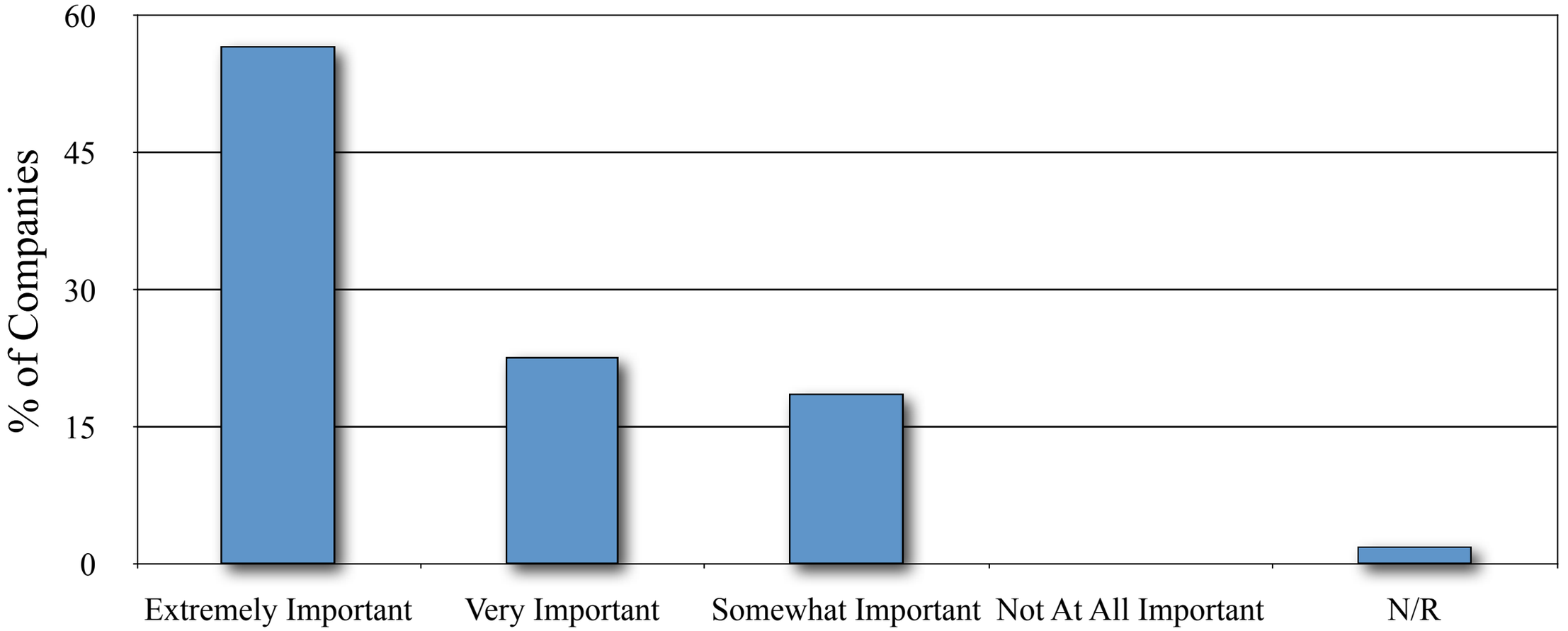
Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

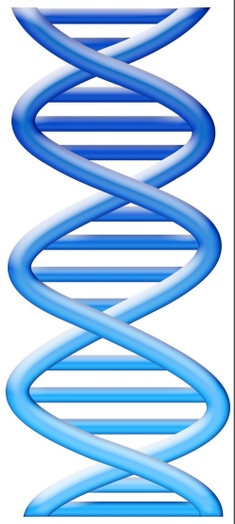
13

Almost half of the companies obtained a license in the pre-clinical stage (45%).
61% obtained license in preclinical or Phase I stage of development.
NOTE: Other may represent licenses for compounds or manufacturing processes.

Biotech In-Licensing

How Important is Ability to Obtain Exclusive License to Ability to R&D a Commercially Available Product?





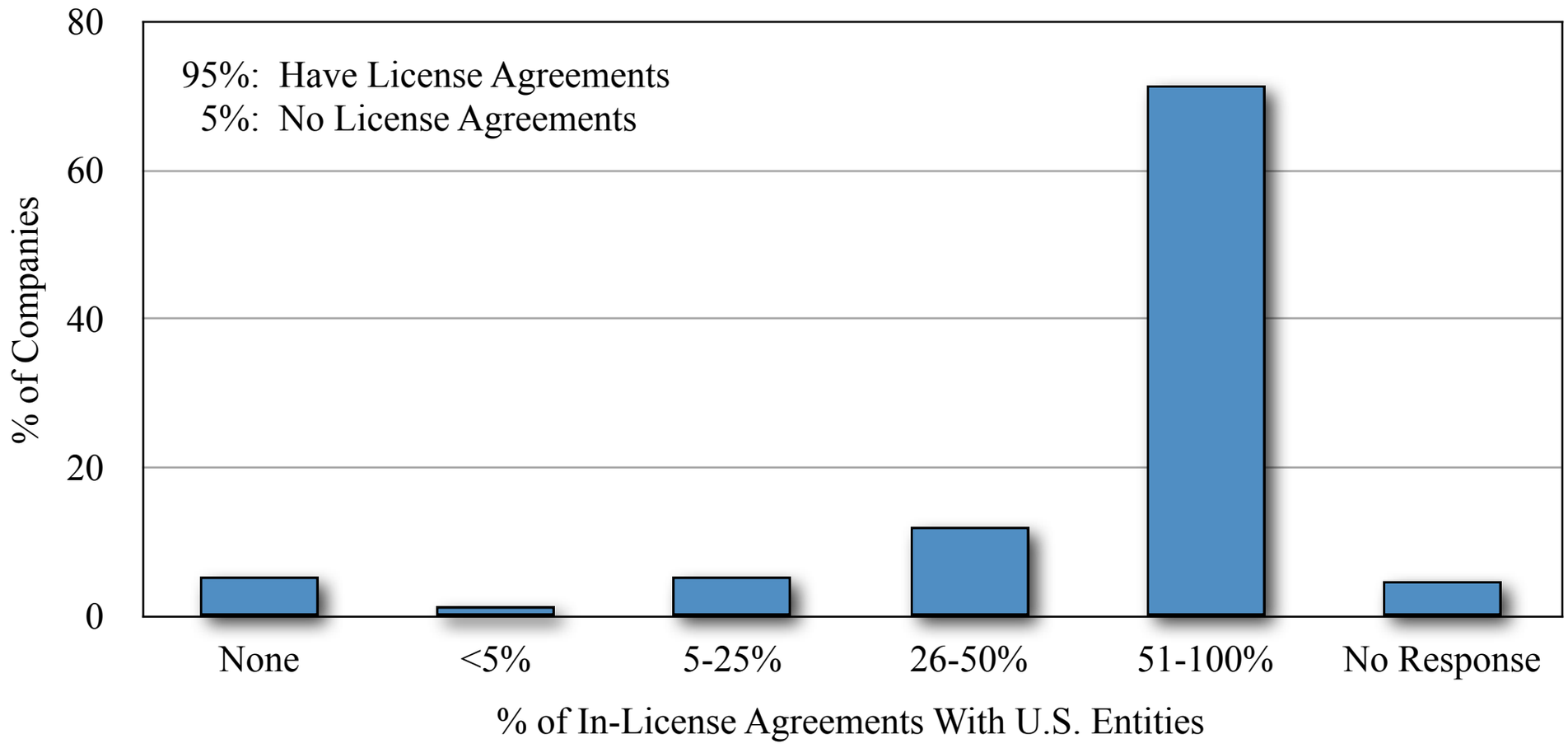
BIO BIOTECHNOLOGY INDUSTRY ORGANIZATION

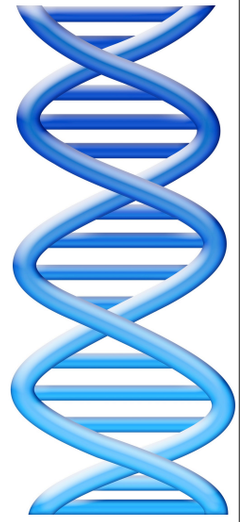
14

79% of companies surveyed said the ability to obtain an exclusive license is important to their ability to develop a commercially available product.

Biotech In-Licensing With U.S. Entities

What % of Company's In-License Agreements Are With U.S. Entities?



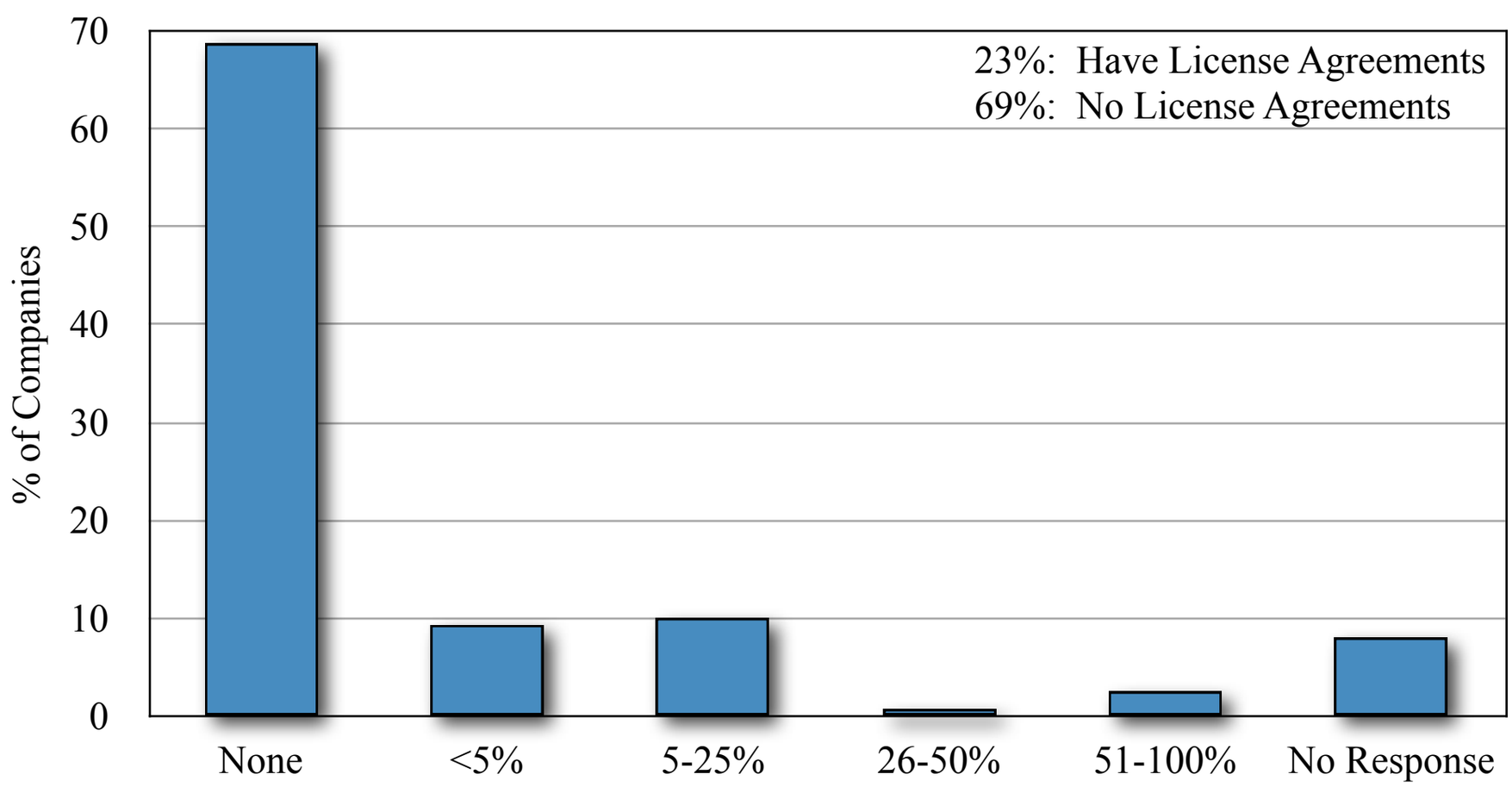


Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

15

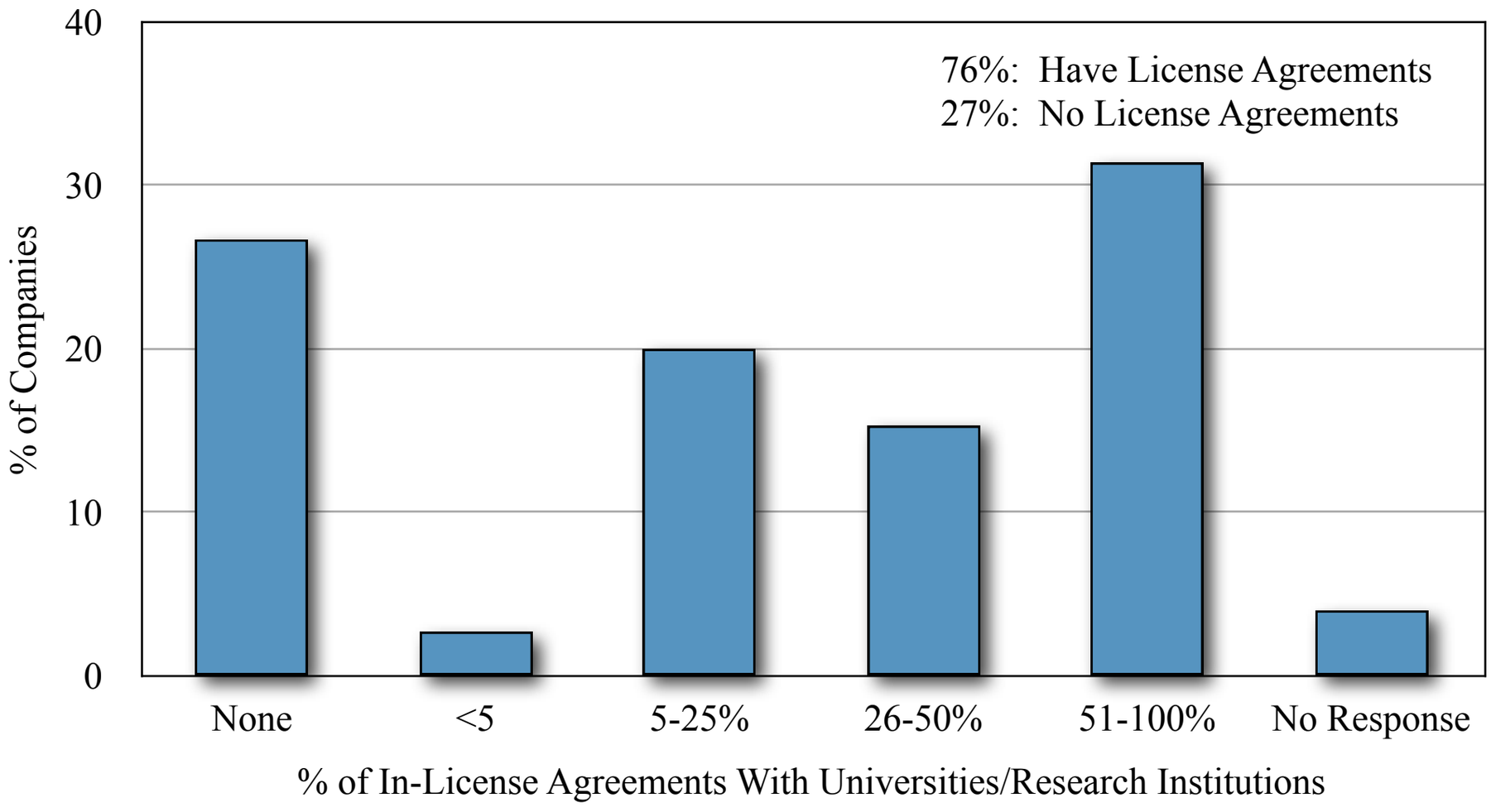
71% of companies have over half of their in-license agreements with U.S. entities.
45% have over 3/4ths of their in-license agreements with U.S. entities.

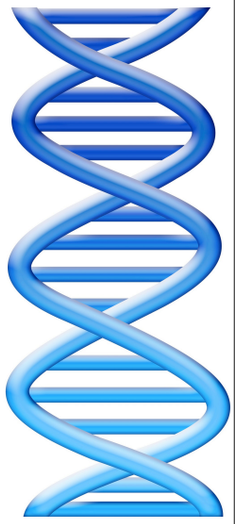
Biotech In-Licensing With Federal Government



69% of the companies surveyed do not have an in-license agreement with the federal government.
19% of companies have less than 25% of their in-license agreements with the federal government.

Biotech In-Licensing With Universities

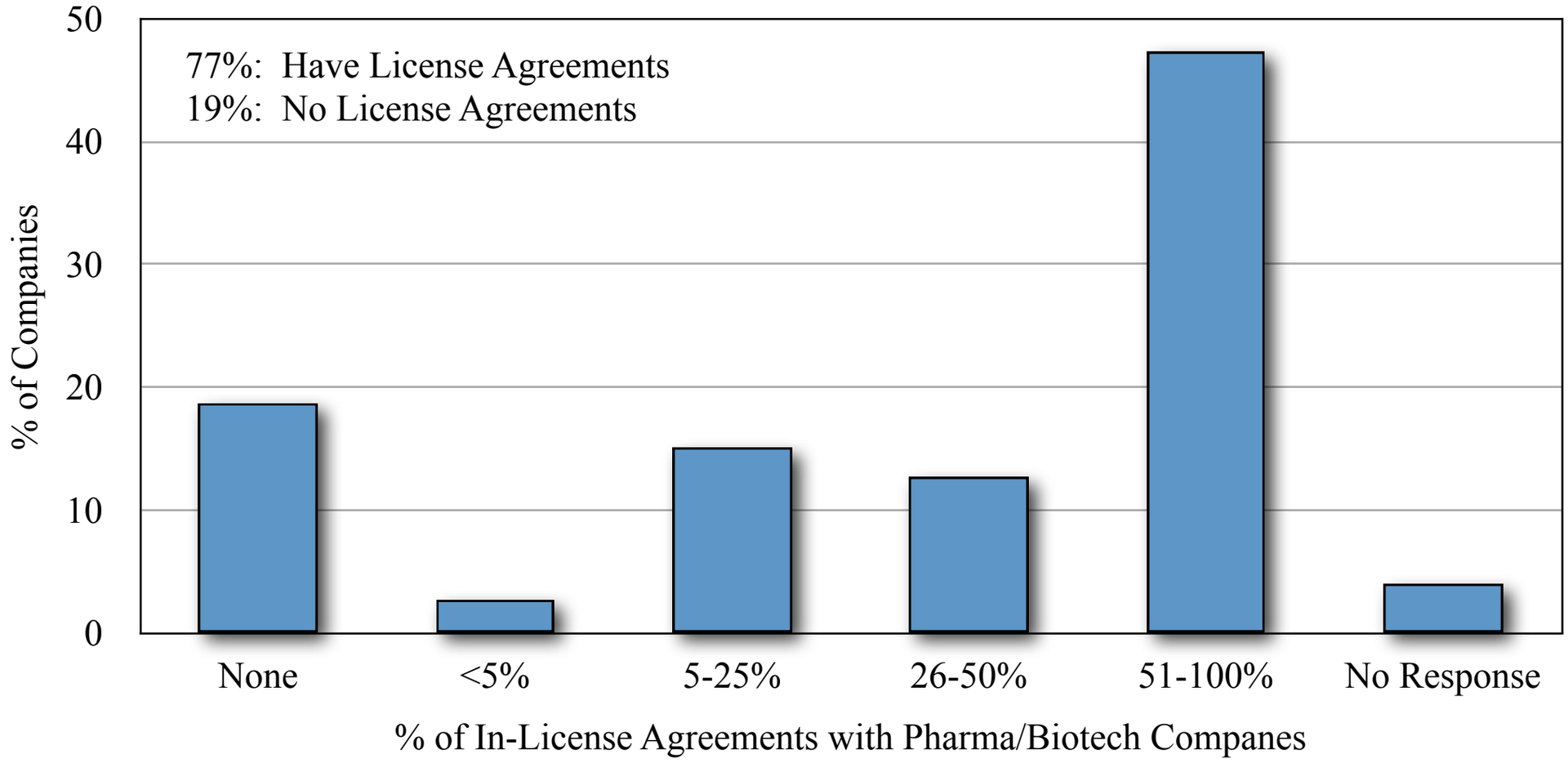




31.4% have over half of their in-license agreements with universities (19% have more than 3/4th of their in-license agreements with universities).

Biotech In-Licensing With Pharma/Biotech Companies

What % of In-License Agreements Are With Pharma/Biotech Companies?



Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

18

36% of companies stated that 3/4th of their in-license agreements are with pharma/biotech companies, 47% stated over 1/2 of their in-license agreements are with pharma/biotech companies.

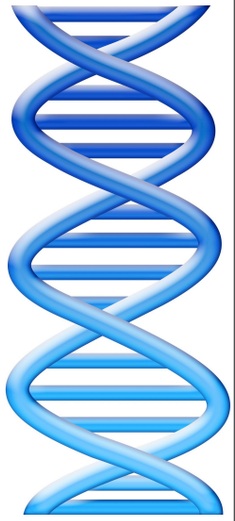
Biotech In-Licensing

- **SUMMARY OF BIOTECH IN-LICENSING**
  - Licensing Opportunities are Found at Conferences, Among Colleagues and in the Literature
  - Most Companies Obtain a License in Pre-Clinical or Phase I Stage of Development
  - Ability to Obtain Exclusive License is Critical to Ability to Research & Develop a Publicly Available Treatment or Therapy

Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

Biotech In-Licensing

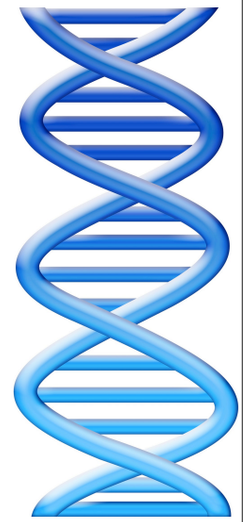
- **SUMMARY OF BIOTECH IN-LICENSE PARTNERS**
  - Most of In-License Agreements are with U.S. Entities
  - Most have In-License Agreements with Universities/Research Institutions and Pharma/ Biotech Companies
  - Most DO NOT have In-License Agreements with the Federal Government



Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

Impact of In-Licensing on Biotech Industry

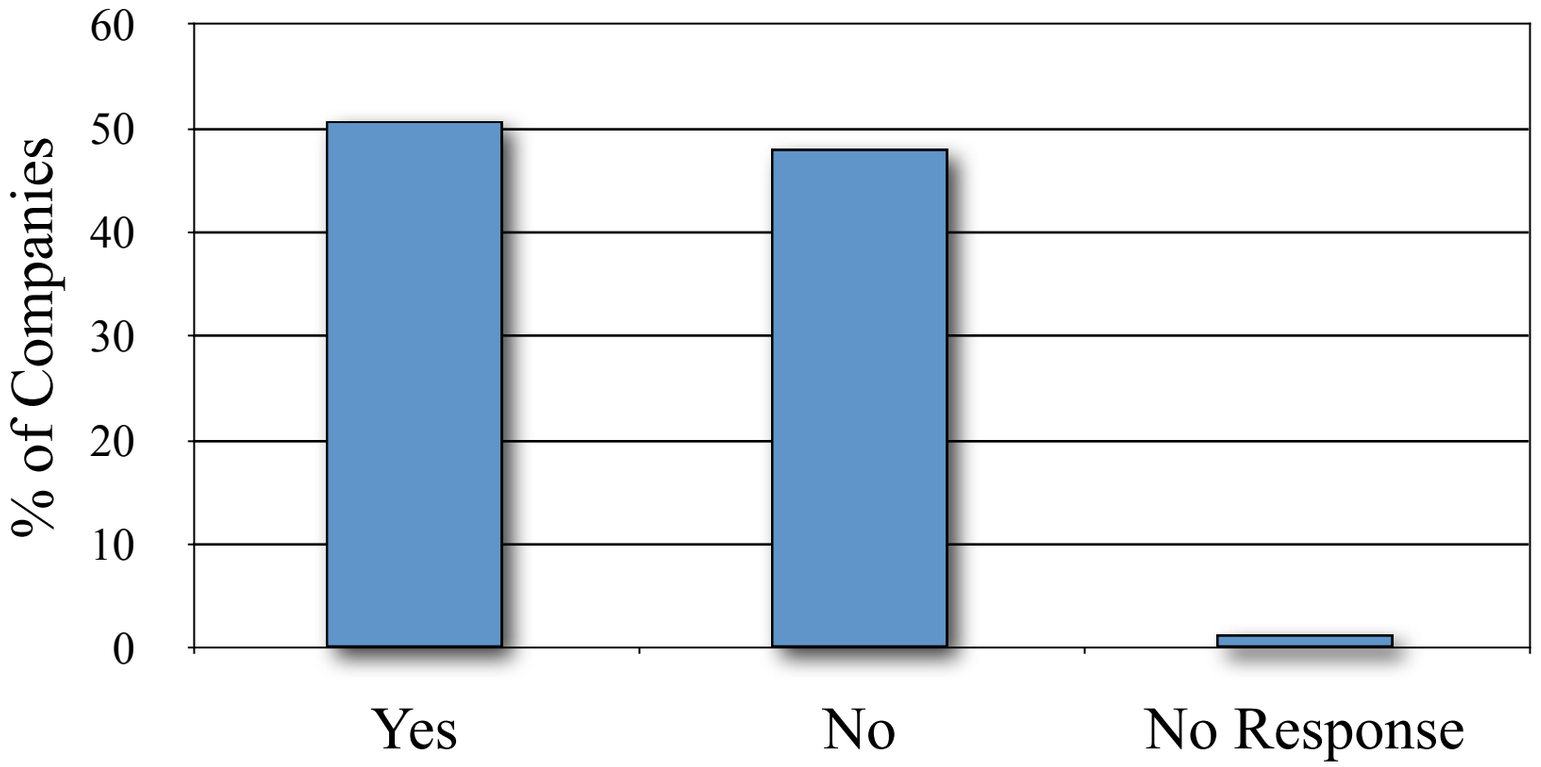
- **IMPACT OF IN-LICENSES ON BIOTECH INDUSTRY**
  - Company History
  - Company Resources

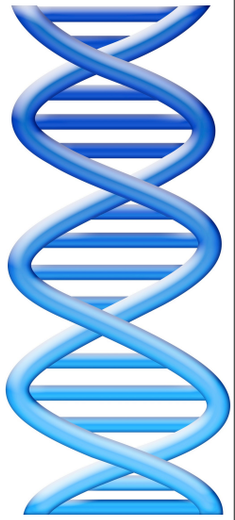


Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

Biotech In-Licensing & Company History

Was Your Company Founded On the Basis of Obtaining a License Agreement?





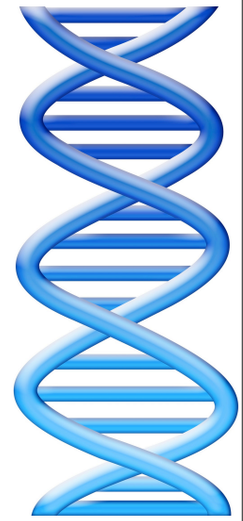
Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

50% of companies were founded on the basis of obtaining a license agreement and 48% were not.
62% of private companies were founded on obtaining a license vs. 40% of public companies.

Biotech In-Licensing & Company History

Number of Employees Prior to Obtaining 1st Tech Transfer License

# Employees	<5	<10	6-15	>15	DK/ Refused
All	51.4%	58.1%	10%	12.7%	26%
Private	68.9%	77%	12.2%	8.1%	10.8%
Public	34.2%	39.5%	5.3%	17.1%	40.8%



Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

58.1% of companies had <10 employees prior to obtaining first tech transfer license.

Biotech In-Licensing & Company History

Number of Employees Added 1-2 yrs. & 2-5 yrs. After Obtaining 1st Tech Transfer License

# Employees	<10	10-19	20-29	30-39	40-49	50-99	100-199	>200	DK/ Refused
All 1-2 yrs	28.7%	20%	8.7%	8%	1.3%	2.7%	4%	2.7%	24%
All 2-5 yrs	19.3%	10%	8%	4%	6%	12.7%	5.3%	6%	28.7%
Private 1-2 yrs.	47.3%	27%	6.8%	9.5%	1.4%	0%	0%	0%	8.1%
Private 2-5 yrs.	32.4%	17.6%	9.5%	4.1%	12.2%	6.8%	1.4%	0%	16.2%
Public 1-2 yrs.	10.5%	13.2%	10.5%	6.6%	1.3%	5.3%	7.9%	5.3%	39.5%
Public 2-5 yrs.	6.6%	2.6%	6.6%	3.9%	0%	18.4%	9.2%	11.8%	40.8%

2-5 Yrs. After Obtaining License Only 19.3% of Companies had Fewer than 10 Employees

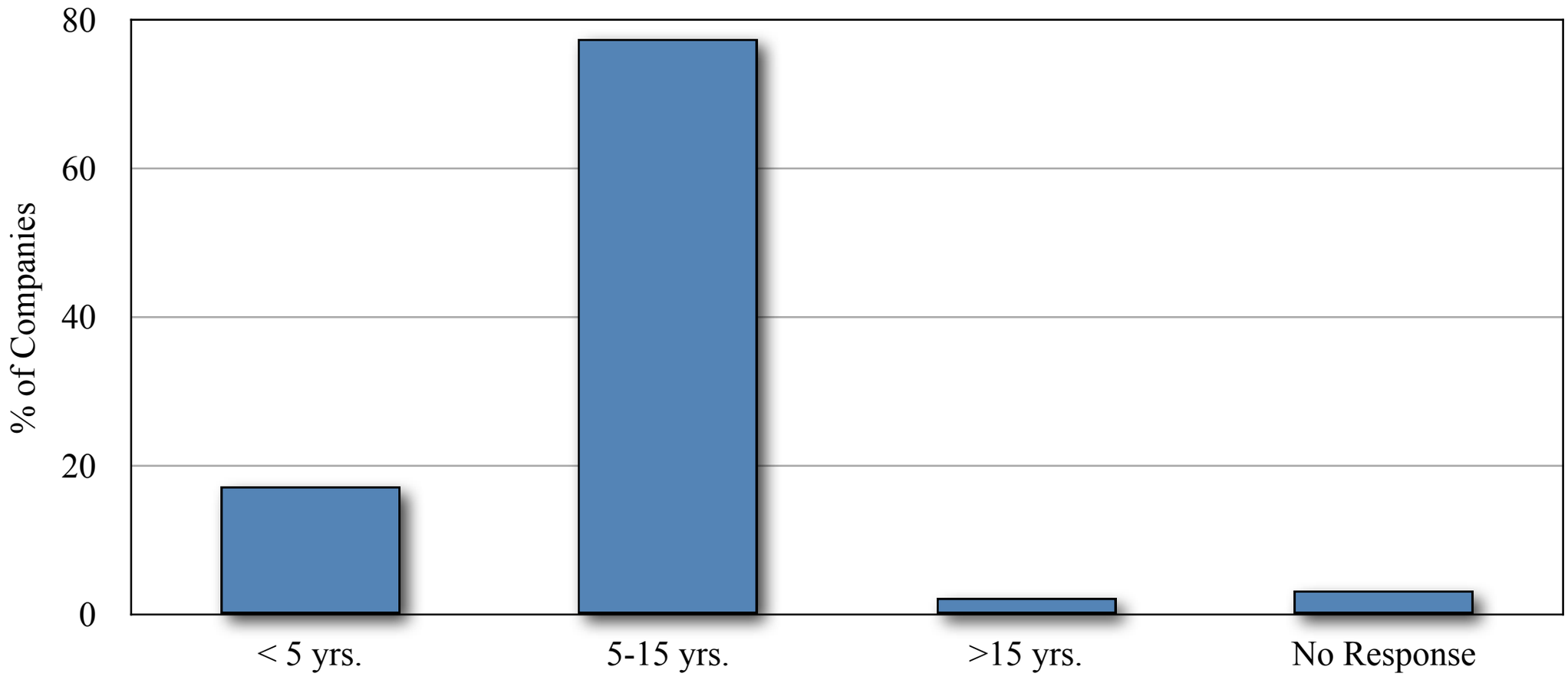
Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

2-5 Yrs. after obtaining license only 19.3% of companies had fewer than 10 employees and 42% had between 10 and 100 employees.

Biotech In-Licensing & Company Resources

Companies with No Marketed Product

Avg. # of Yrs. (Projected or Actual) Company Will Spend on R&D for Lead Product from Initial License to Commercialization



NOTE: Figures Represent Small Molecule, Large Molecule and Diagnostic Lead Products

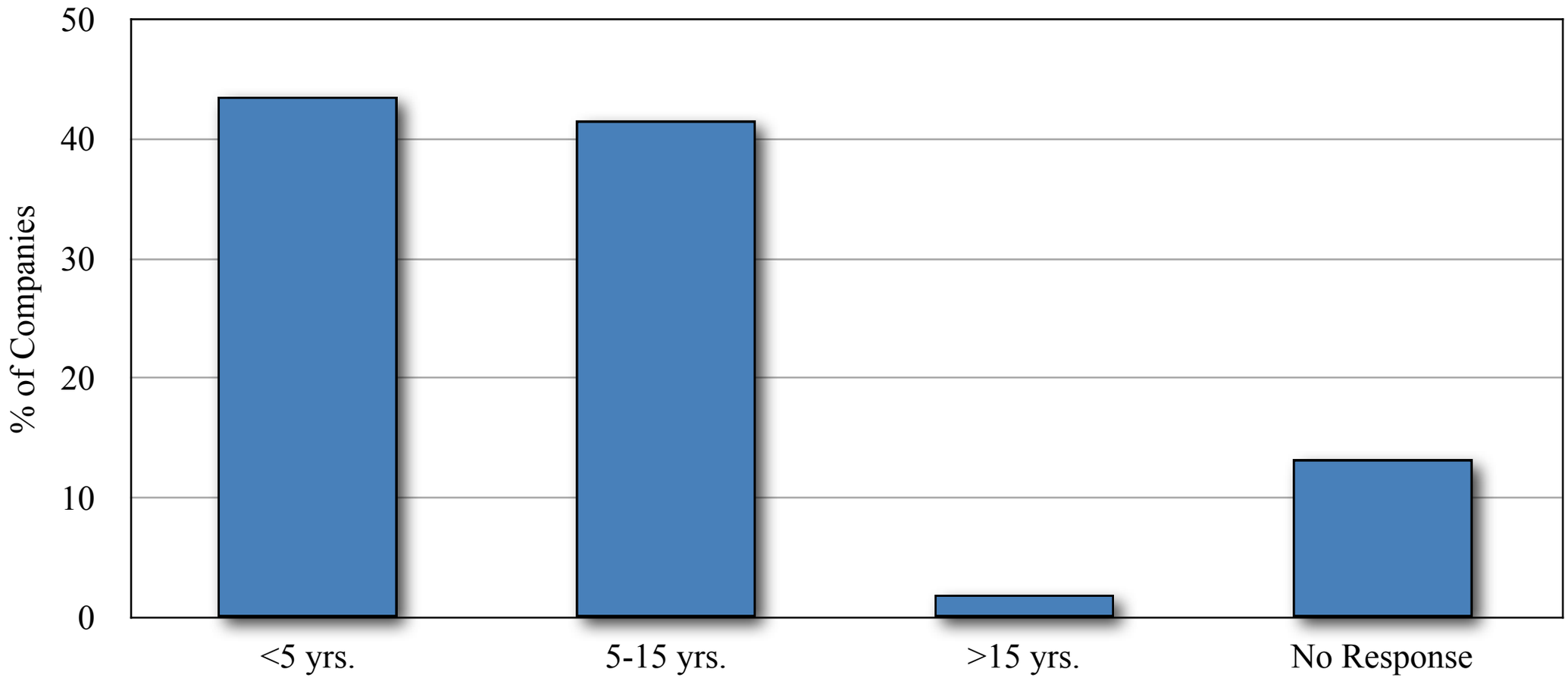
Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

77.4% of companies without a marketed product stated it will take 5-15 yrs. to develop lead product from time of initial product to commercialization.
17% said it will take 2-5 yrs.

Biotech In-Licensing & Company Resources

Companies with a Marketed Product

Avg. # of Yrs. Spent on R&D for Lead Product from Initial License to Commercialization



NOTE: Figures Represent Small Molecule, Large Molecule and Diagnostic Lead Products

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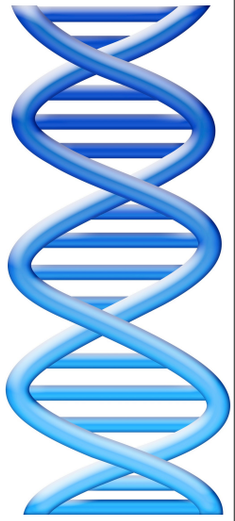
42% of companies stated it took between 5-15 yrs. to develop lead product into a marketed product
44% of companies stated it took < 5 years.
34% of companies with a marketed product stated it took 2-5 yrs.

Biotech In-Licensing & Company Resources

Companies With No Marketed Product

- 60% Project Will Spend > $100 M
- 15% Project Will Spend > $500 M



Companies With a Marketed Product

- 39% Spent > $100 M
- 21% Spent > $500 M

NOTE: Figures Represent Small Molecule, Large Molecule and Diagnostic Lead Products

Impact of In-Licensing on Biotech Industry

- **SUMMARY IMPACT OF IN-LICENSES ON BIOTECH INDUSTRY**
  - Half of Companies Were Founded on Basis of Obtaining a License Agreement
  - Prior to Obtaining a License 58% of the Companies had < 10 Employees
  - 2-5 Yrs. After Obtaining License Only 19% had <10 Employees
  - Majority of Companies With No Marketed Product Expect to Spend 5-15 Years Developing a Product and Spend > $100 M

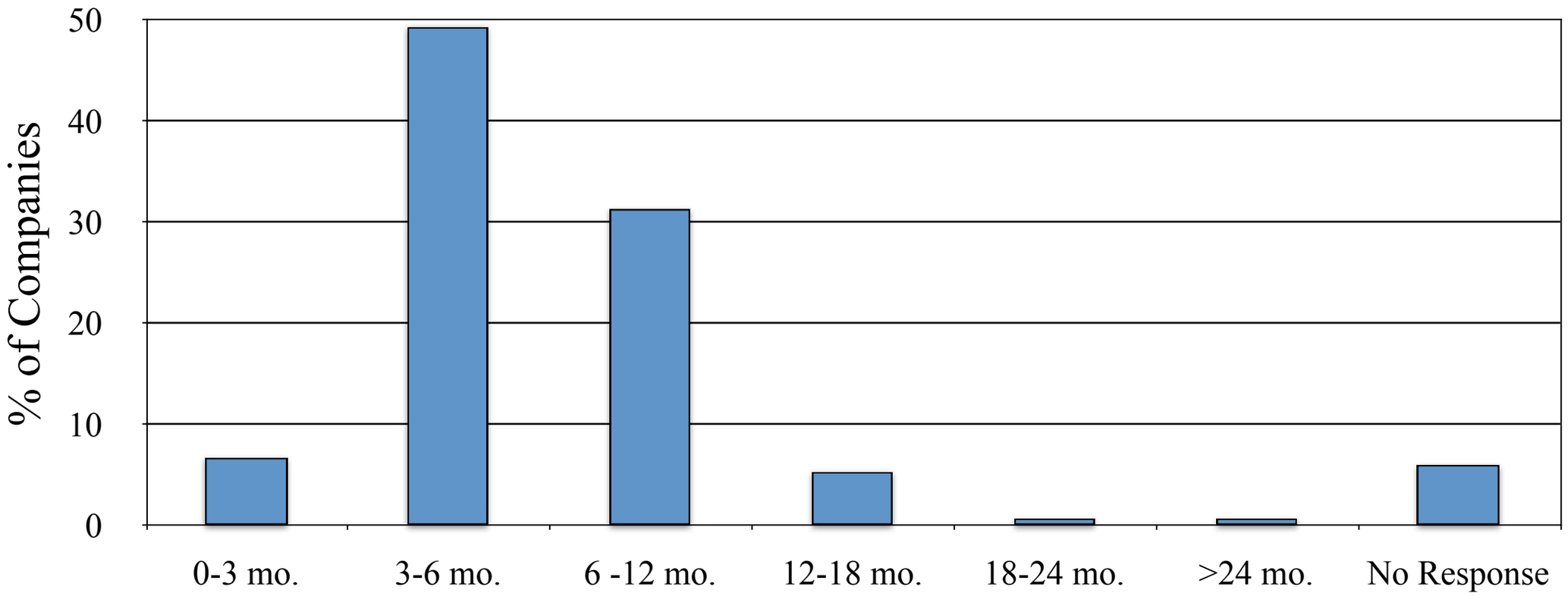
Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

Biotech In-License Agreements

- **BIOTECH IN-LICENSE AGREEMENTS**
  - Length of Time to Complete Negotiations
  - Hardest/Easiest Part of Negotiations
  - Calculating Value
  - In-License Payment Structures

Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

Biotech In-Licensing Negotiations



Bio
BIOTECHNOLOGY
INDUSTRY ORGANIZATION

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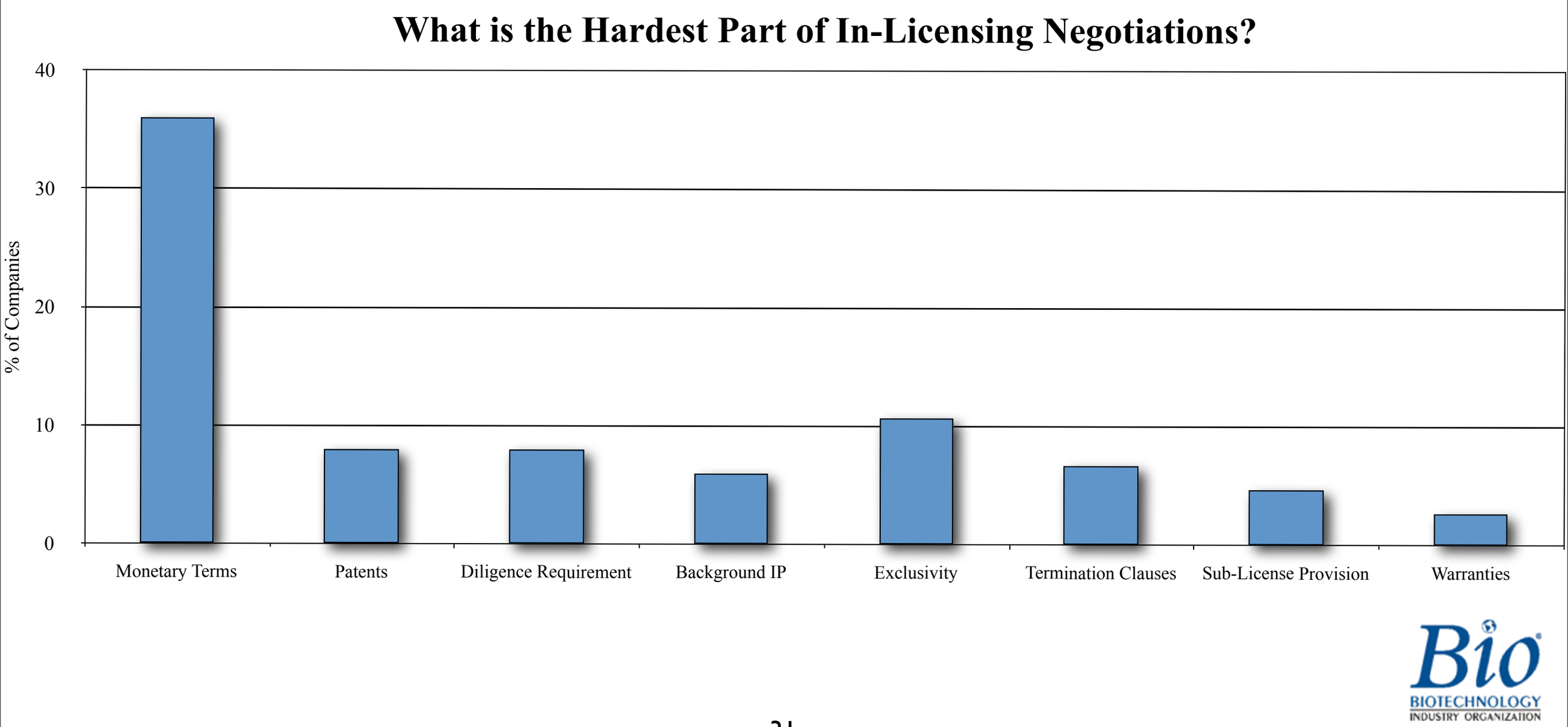
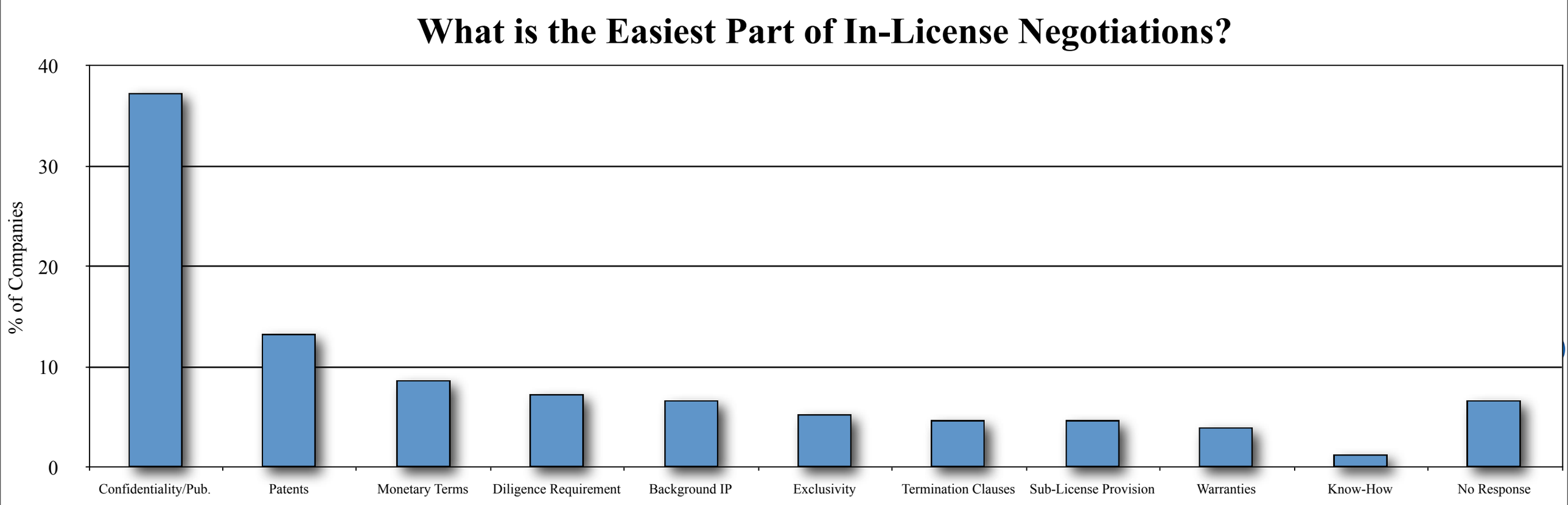
49% of companies stated it takes 3-6 mo. to complete a license agreement (31% stated it took 6-12 mo.) Same with public and private except more private companies stated it only took less than 3 mo. than public companies (12% vs. 1.3%).

Biotech In-Licensing Negotiations



36% of companies stated monetary terms are the hardest part of the negotiations. Exclusivity was second with 11% of companies id. this as the most difficult part of negotiations.

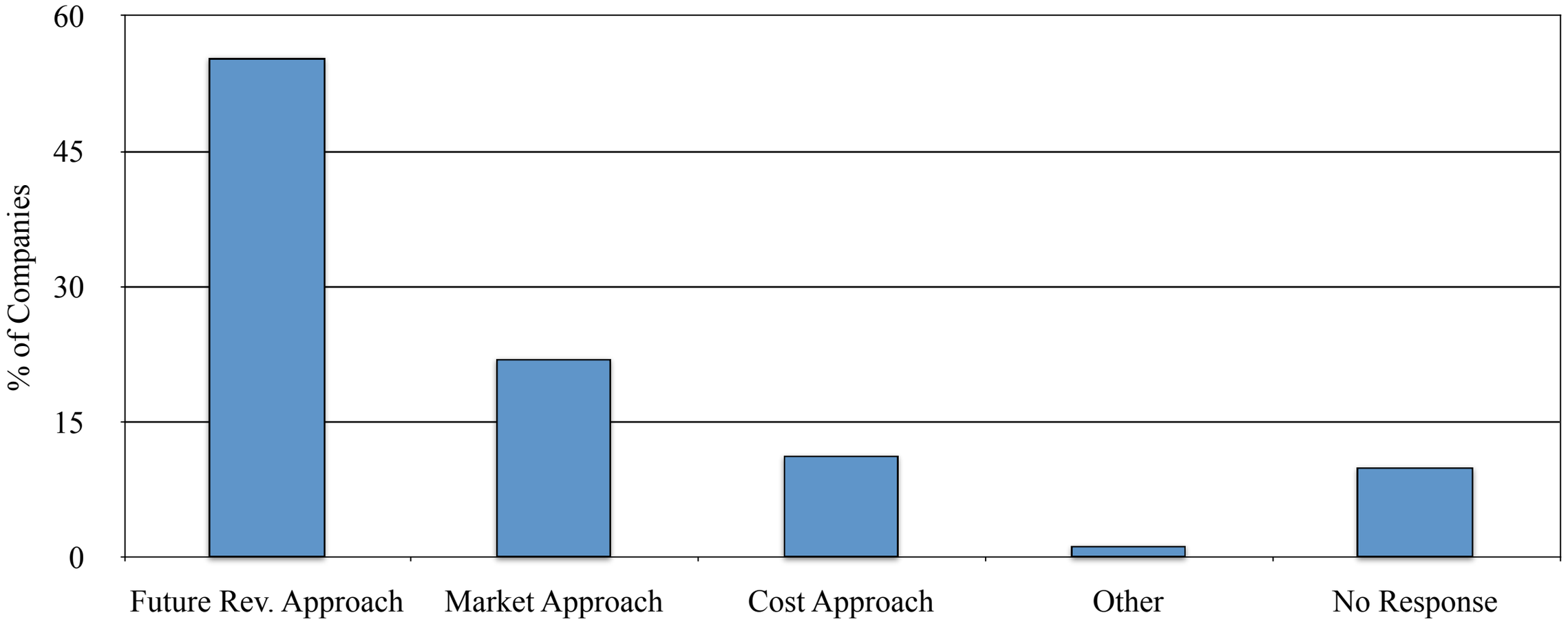
Biotech In-Licensing Negotiations



37% of companies stated confidentiality and publications were the easiest part of the negotiations followed by patents (13%).

Biotech In-Licensing Negotiations

Metric Your Company Typically Uses to Calculate Value of In-Licensing Opportunity



Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

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The majority of companies stated they use the future revenue approach to calculate value (55%). A market approach was the second most common (22%). Future Revenue Approach was defined as discount to future cash flows, market approach was defined as value of comparative technologies/assets and cost approach was defined as dollars required to bring a product to market.

Biotech In-Licensing Payment Structures

Running Royalties On Product

73% Stated Over 1/2 of Licenses Include Running Royalties

Upfront Payments

64% Stated Over 1/2 of Licenses Include Upfront Payment

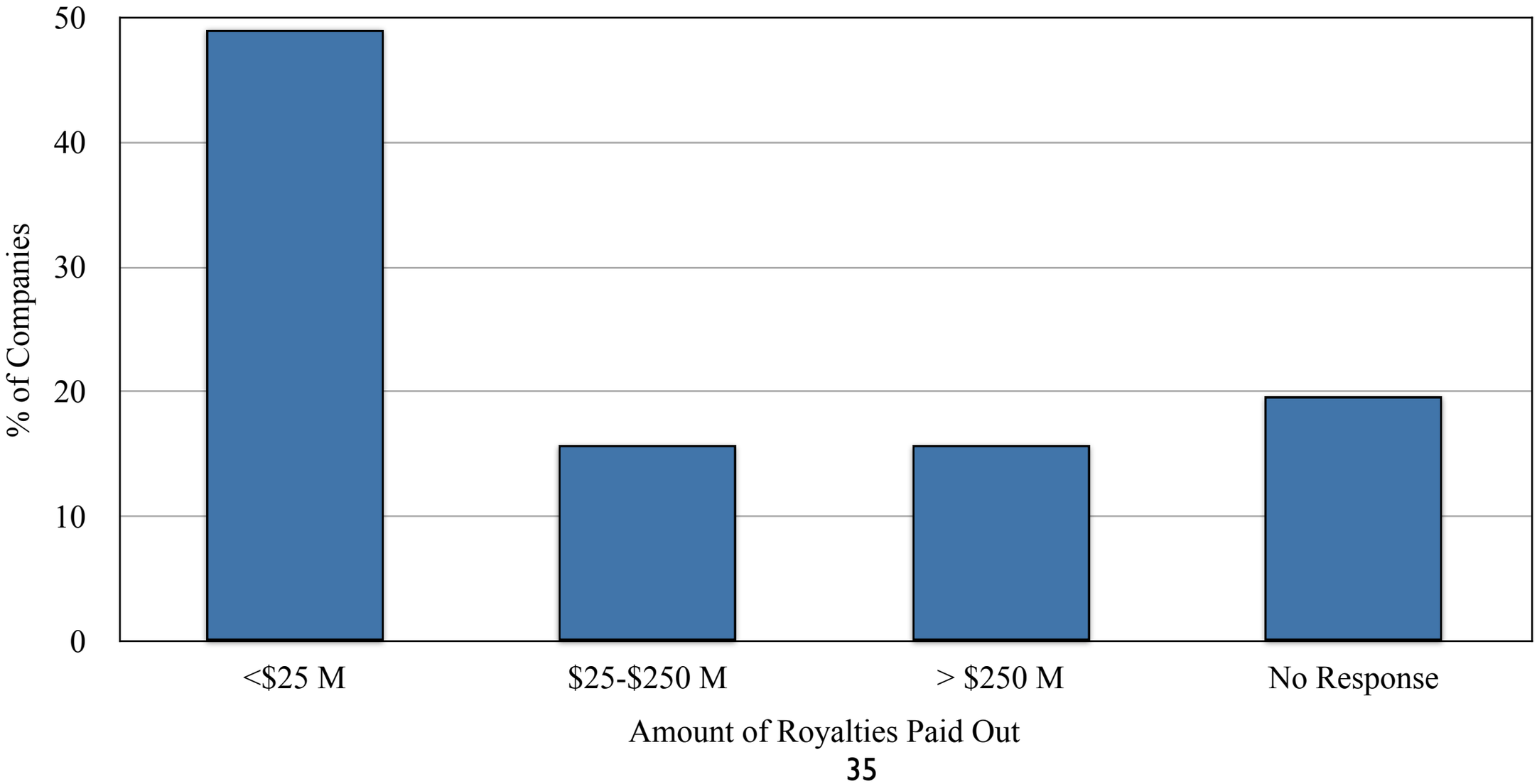
Milestone Payments

66% Stated Over 1/2 of Licenses Include Milestone Payments

Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

90% of companies have running royalties provisions.
73% stated over 1/2 of their licenses and 62% stated over 3/4 of their licenses include running royalties.
64% of companies stated that over 1/2 of their licenses and 42% stated 9/10 of their licenses included upfront payments.
66% of companies stated that over 1/2 of their licenses and 45% stated 9/10 of their licenses included milestone payments.

Biotech In-Licensing Payments



Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

35

49% of companies have paid out <$25 M, 16% have paid $25- $250 M, and 16% have paid out over $250 M.
(19% DK/Refused - all public companies.)

Biotech In-License Agreements

- **SUMMARY OF BIOTECH IN-LICENSE NEGOTIATIONS**
  - 49% of Companies Stated it Typically Takes 3-6 mo. to Complete Negotiations - 31% Stated it Takes 6-12 mo.
  - Confidentiality/Publications was Identified as the Easiest Part of Negotiations and Monetary Terms as the Most Difficult
  - 55% of the Companies Use Future Revenue Approach and 22% Use Market Approach to Calculate Value

Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

37% of companies said confidentiality was the easiest and 36% stated monetary terms was the hardest part of negotiations. Future Revenue Approach was defined as discount to future cash flows, market approach was defined as value of comparative technologies/assets and cost approach was defined as dollars required to bring a product to market.

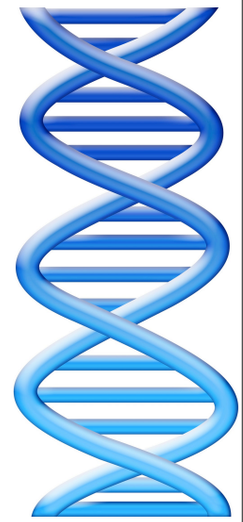
Biotech In-License Agreements

- **SUMMARY OF BIOTECH IN-LICENSE PAYMENT STRUCTURES**
  - Majority of Companies Have Payments Based on Milestones, Upfront Payments and Running Royalty Payments in Over 1/2 of License Agreements
  - 49% of Companies Have Paid < $25 M in Royalties, 16% Have Paid $25-$250M and 16% Have Paid >$250 M

Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

Biotech In-Licensing With Universities

- **BIOTECH IN-LICENSING WITH UNIVERSITIES**
  - Exclusive vs. Non-Exclusive
  - Non-Commercial Research Provisions
  - Particular Field of Use Provisions
  - Milestone Provisions
  - Oversight



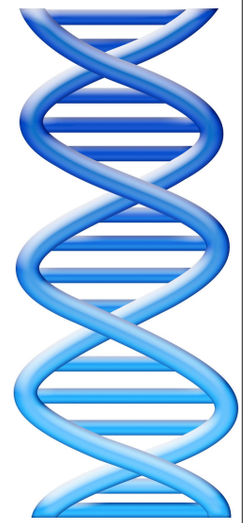
Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

Biotech In-Licensing With Universities

60% of companies surveyed stated 3/4 of their in-license agreements with universities are exclusive.

21.3% of companies stated less than 1/2 of in-license agreements with universities are exclusive.

5.8% of companies stated that none of their in-license agreements with universities are exclusive.



Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

Biotech In-Licensing With Universities

57% of Companies Stated Exclusive License Agreements With Universities Include Non-Commercial Research Provisions (46% Stated Over 1/2 Include Non-Commercial Research).

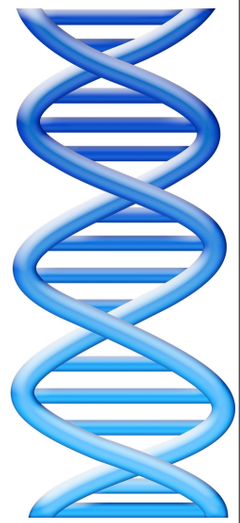
53% of Companies Stated Exclusive License Agreements With Universities Include Limited Field of Use Provisions (42% Stated Over 1/2 of License Agreements Include Limited Field of Use).

67.6% of Companies Stated Exclusive License Agreements With Universities Include Milestone With Penalty or Revocations Provisions (59% Stated Over 1/2 of License Agreements Include Milestones).

Only 17% stated they had no exclusive license agreements with universities that did not contain non-commercial research provisions (N/R=27%).
Only 31% stated they had no exclusive license agreements with limited field of use provisions (N/R=16%).
Only 13% stated they had no exclusive license agreements with milestone provisions (N/R=9%)

Oversight of Biotech In-Licensing

31% of Companies Have Had a License Revoked, Restricted, Renegotiated or Paid a Penalty Due to Non-Compliance With Milestone Clauses



BIO BIOTECHNOLOGY INDUSTRY ORGANIZATION

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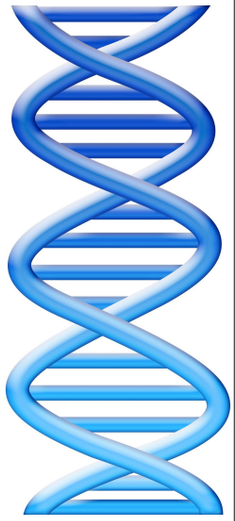
21% of companies have had a license restricted or renegotiated, 7% have had a license revoked, and 3% have had to pay a penalty due to non-compliance with milestone clauses.

Biotech In-Licensing With Universities

- **SUMMARY OF BIOTECH IN-LICENSES WITH UNIVERSITIES**
  - Majority of In-License Agreements are Exclusive But There Are Significant Numbers of Non-Exclusive Licenses
  - Majority of In-License Agreements Have Non-Commercial Research Provisions, Milestones w/Penalties and Particular Field of Use Provisions
  - 31% of Companies Have Had a License Revoked, Restricted, Renegotiated or Paid a Penalty Due to Non-Compliance With Milestone Clauses



Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

EXHIBIT 5

The Economic Impact of Licensed Commercialized Inventions Originating in University Research, 1996-2007

Final Report to the Biotechnology Industry Organization
September 3, 2009

Project Team:
David Roessner, Jennifer Bond, Sumiye Okubo, Mark Planting

Table of Contents

Project Team

This project was conducted by a small group of consultants headed by Dr. David Roessner, Professor of Public Policy Emeritus, Georgia Institute of Technology and Associate Director, Science and Technology Policy Program, SRI International. Other key project team members include Ms. Jennifer Bond, Senior Advisor for International Affairs for the Council on Competitiveness and former Director of the Science & Engineering Indicators Program at the National Science Foundation; Dr. Sumiye Okubo, former Associate Director for Industry Accounts at the Commerce Department's Bureau of Economic Analysis; and Mr. Mark Planting, former chief of research on the use and development of U.S. input-output accounts at the Bureau of Economic Analysis.

Acknowledgments

We owe substantial debts of gratitude to many people who made this project possible, especially to AUTM members and staff who helped us obtain estimates of royalty rates charged on deals based on product sales. They include Janna Tom, Anne Chasser, Pat Jones, Dana Bostrom, Lori Pressman, Ashley Stevens, John Fraser, Richard Kordal, Kevin Cullen and Richard Colman. We also thank the respondents from university technology transfer offices who provided information on the royalty rates they charge. Others who helped in a number of other ways include Patricia Cotton, Brian Wright, Maryann Feldman, and Steve Merrill. We are also grateful to Joe Allen and John Ritter, who were instrumental in moving an idea to reality, for introducing us to key staff at BIO, and for their continuing advice and encouragement. Finally, we thank Ted Buckley, Lila Feisee, Tom Dilenge, Margarita Noriega and their colleagues at BIO who provided financial support, encouragement, and hard questions that made this project better than it otherwise would have been. However, all errors of fact or interpretation in this report are ours.

EXECUTIVE SUMMARY

Study Objectives

University research and research-related activities contribute in many important ways to the national economy, notably through increased productivity of applied R&D in industry due to university-developed new knowledge and technical know-how, provision of highly valued human capital embodied in faculty and students, development of equipment and instrumentation used by industry in production and research, and creation of concepts and prototypes for new products and processes. These benefits are enabled primarily through publications, conferences, information exchange via consulting and collaborative research, and hiring of trained students. *This report develops estimates of the economic impact of just one of these research-related activities, licensing of university intellectual property, clearly an impact of major significance for the economy but by no means the largest source of the total impact of university research.*

Methods and Data

There are several relatively sophisticated methods that could be used to estimate the economic value to the nation of innovations based in university research (e.g. consumer surplus estimates for specific innovations), but most would require costly data collection and/or threaten the proprietary interests of innovating firms. This report presents the results of a modest yet rigorous approach that makes use of existing Association of University Technology Managers (AUTM) annual survey data and relatively straightforward economic calculations. Using data from annual AUTM surveys of U.S. universities, it is possible to develop systematic, conservative estimates of the economic impacts on the United States of twelve years of university-industry research collaborations. Although "deals" between university technology licensing offices and private firms take many forms, such as one-time flat fees, taking equity positions in university-based start-ups, and even in some rare cases donating intellectual property (IP) to nonprofits for charitable purposes, in many cases universities base licensing fees on the percentage of sales of new products developed using the university-based IP. Annual AUTM survey data are available on the licensing income from universities responding to the survey, typically numbering about 140. Licensing income data by reporting institution are available from 1996 through 2007. With these data as a base, we combine the AUTM survey results with other data and employ the Commerce Department's Bureau of Economic Analysis (BEA) Input-Output (I-O) model to develop estimates of the annual national economic impact of university licensed products that have been commercialized and generated sales. These impact estimates take two forms: the change in gross output of all industries due to the university

licensed products in the marketplace, and the impact on Gross Domestic Product (GDP) of university licensed products.

Figure S-1, below, provides a schematic representation of how we calculated annual estimates of the impact of university-licensed products on the U.S. GDP. Verbally, it is the sum of the estimated direct impact of university licensed products and the direct impact of university expenditures of their total (gross) licensing income. The direct impact of university licensed products is, in turn, derived from the ratio of university licensing income from "running royalties" to the royalty rates (based on percentage of product sales) charged by universities. *This ratio yields an annual estimate of the additional revenues to firms generated from sales of products based on university-licensed intellectual property.* The I-O model converts this figure into the changes in income (compensation, indirect business taxes, and gross operating surplus—i.e., profits) of companies operating under sales-based university licensing agreements, which together constitutes the contribution to GNP. Also, university expenditures attributable to licensing income have direct impacts on the economy in two ways: first, via expenditures of gross royalty income (for salaries, equipment, overhead costs, etc.) and second, via expenditures of research income from firms that contract for R&D with the university as a direct consequence of the licensing agreement. This is accounted for by the second term in the model.

Figure S-1: Estimating the Total Annual Economic Impact of University-Licensed Products

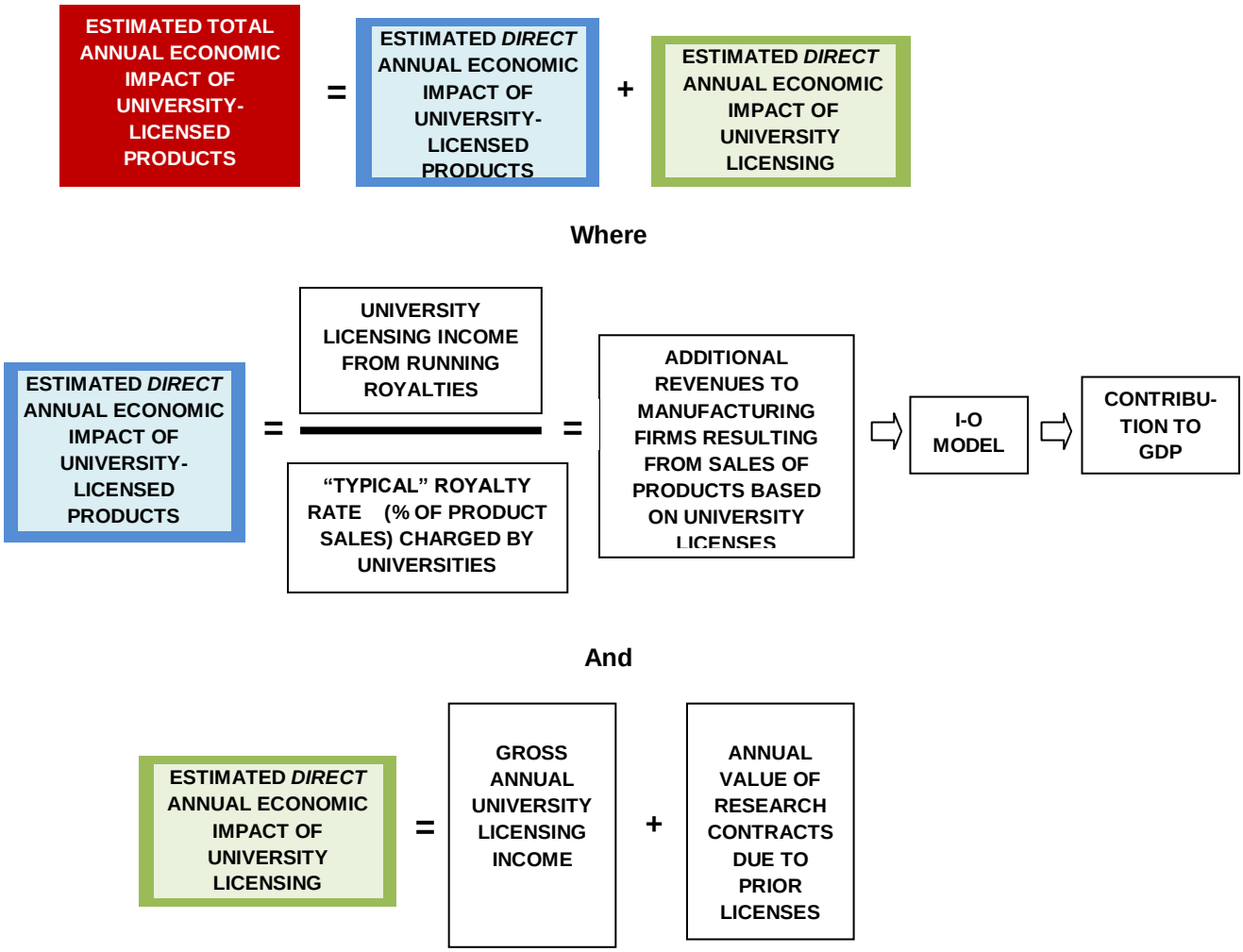
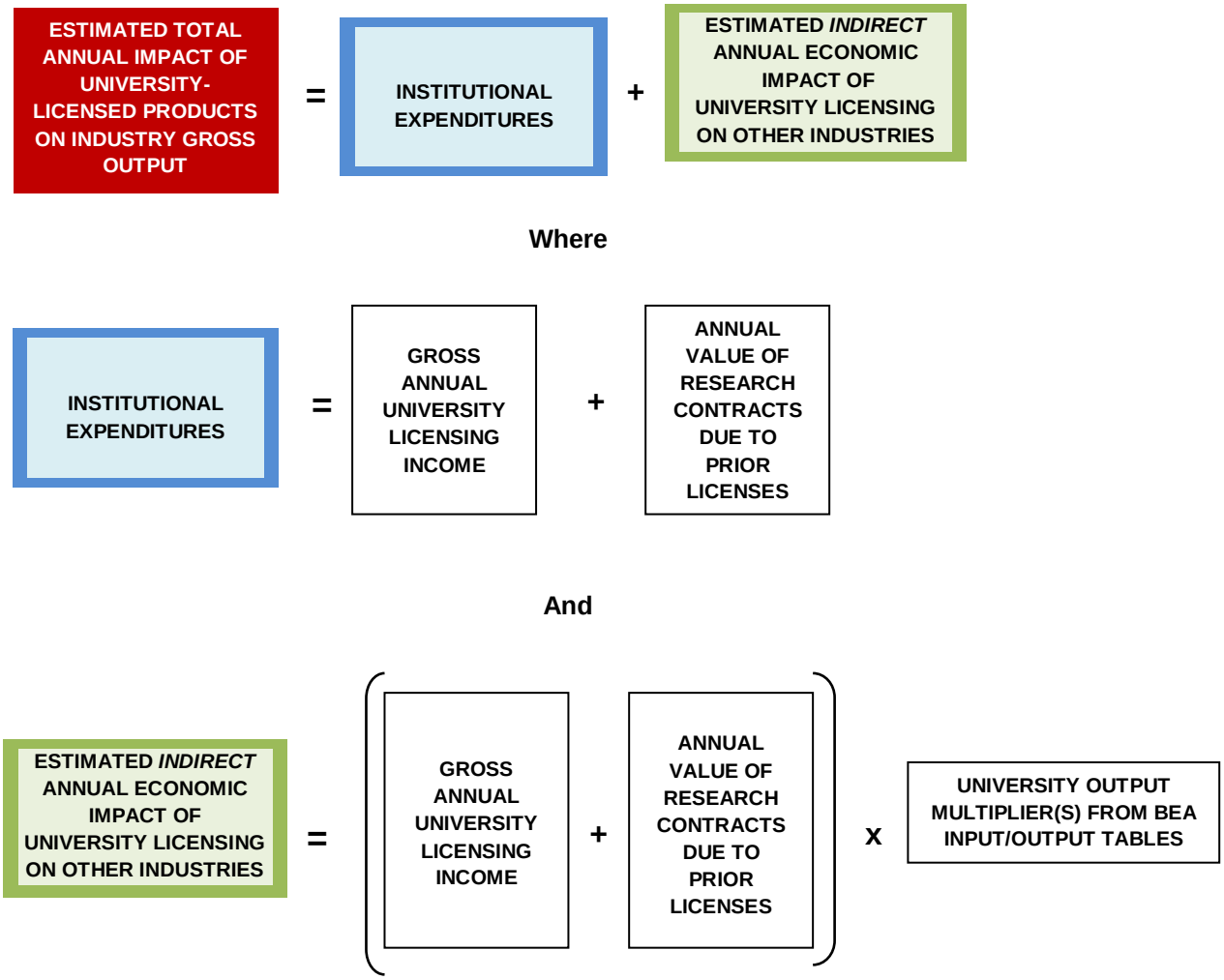


Figure S-2 shows how we estimated the change in gross output of all industries due to the university licensing of products. *Gross output is a measure of economic activity, but is not GDP.* The impact is the sum of sales of companies generated by the licensing agreements plus the change in output at universities (additional income from licensing plus additional research funds attributable to the licensing) plus the changes in gross output of all other industries that directly and indirectly provide inputs to the universities. Note that "institutional expenditures" represent university licensing income that national accountants classify as consumption expenditures.

Figure S-2: Estimating the Annual Impact of University-Licensed Products on Industry Gross Outputs

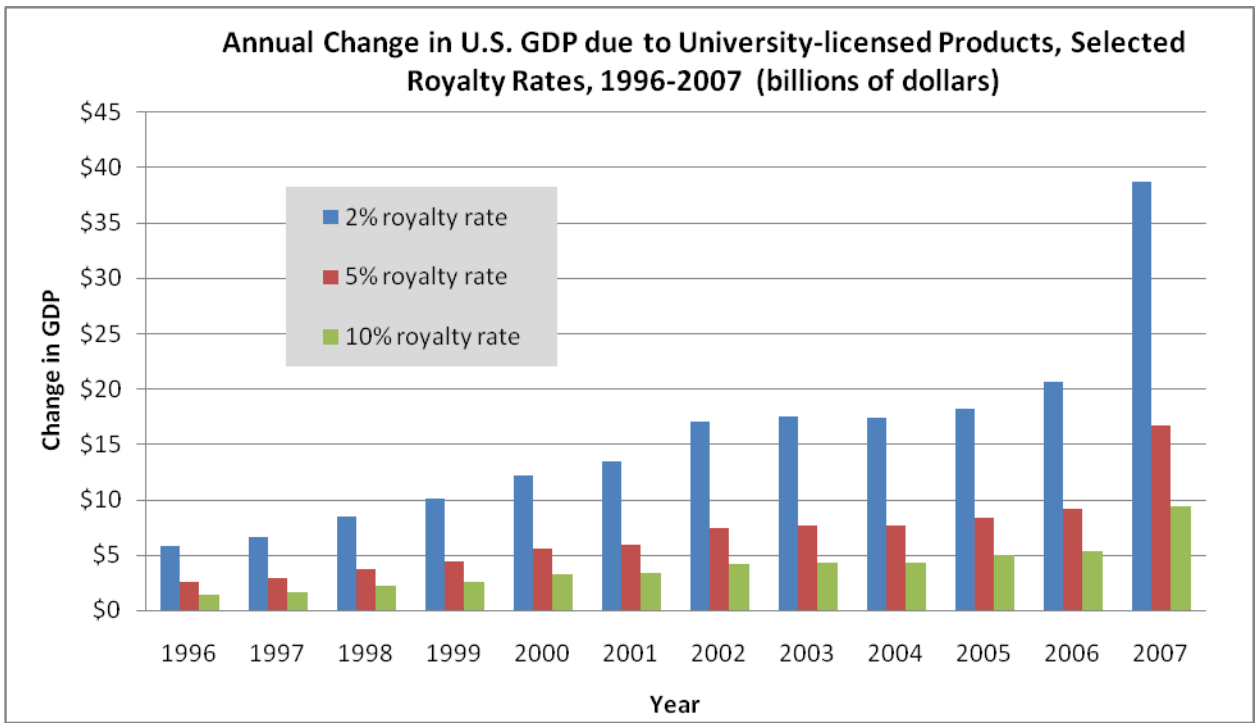


Results[1]

Impact of University Licensing on GDP. The model generates annual values for sales revenues with a range of assumptions about royalty rates: 2%, 5%, and 10%; outputs from the I-O model under these three assumptions; and estimates of the total change in GDP due to university-licensed product sales under the three royalty rate assumptions. No assumptions are made here about product substitution rates, and the additional impact generated from university income from license-related contract R&D is not included in the calculations. Under a moderately conservative assumption (conservative from the perspective of the magnitude of model's impact estimate), a 5% royalty rate, over the 12-year range of our data university licensing based on product sales contributed $2.6 billion to the U.S. GDP in 1996, and $16.8

[1] Tabulations of the data and results summarized here are presented in Tables 4 and 5, pages 32 and 34, of the full report.

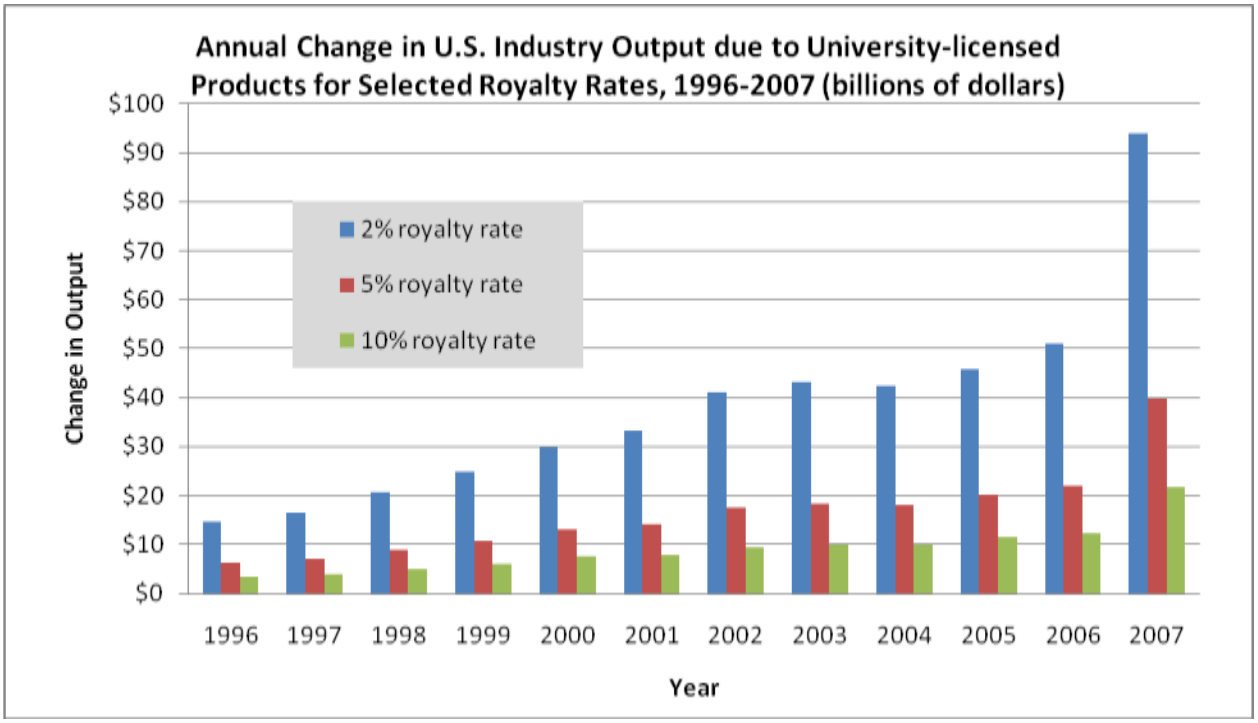
billion in 2007. Under a less conservative but realistic assumption (2% royalty rate), the annual contribution to GDP ranged from $5.9 billion in 1996 to more than $38.8 billion in 2007. ***Without accounting for product substitution effects, we estimate that over the period 1996 to 2007, university licensing agreements based on product sales contributed at least $47 billion and as much as $187 billion to the U.S. GDP. A moderately conservative estimate based on 5% royalty rates yields a total contribution to GDP for this period of more than $82 billion.*** The large range of these estimates illustrates clearly the high sensitivity of our results to assumptions about the royalty rates charged by universities on license agreements based on product sales. These results are depicted graphically below.



Impact of University Licensing on Industry Gross Output. Using the model depicted in Figure S-2, which generates estimates of the contribution to industry gross output due to university-licensed products, we calculated the total output produced annually by university licensing revenues, the direct employment generated by these revenues, and the total change in industry gross outputs due to this licensing activity. We again calculated a range of estimates based on the royalty rates charged in sales-based licensing agreements. Under a moderately conservative assumption (5% royalty rates), as a result of university licensing annual industrial output increased by $6.3 billion in 1996 and by $39.7 billion in 2007. Using a less conservative assumption (2% royalty rates),[2] the annual contribution to industry output grew from $14.7

[2] Note that because royalty rates are in the denominator of the model's calculations, a lower royalty rate yields higher estimated product sales and thus higher economic impact.

billion in 1996 to nearly $94.9 billion in 2007. ***Summing over the entire 12 years for which we have data, we estimate that the total contribution of university licensing to gross industry output at least $108.5 billion and as much as $457.1 billion (again without accounting for product substitution effects). A moderately conservative estimate based on 5% royalty rates yields an estimated impact of university licensing on total industry output over 1996-2007 of $195.6 billion.***



Impact of University Licensing on Employment. The national I-O model, based on empirical data, also calculates the number of jobs directly created per million dollars of final purchases and thus provides estimates of the total number of jobs created annually due to university-licensed products. This ranged from about 9,000 jobs in 1996 to 41,000 in 2007. ***We estimate that over the entire 12-year period, university-licensed products created more than 279,000 jobs.***

Accounting for Product Substitution Effects in the GDP Impact Estimates. In principle, product displacement effects could range from 0 percent, when the new product displaces no existing products or services, to 100 percent, when it completely displaces them. These ranges (rather than misleading "typical" or "average" values) provide a way to generate conservative estimates of the increase in GDP due to university licensing of intellectual property, accounting for the wide range of royalty rates charged by universities and for substitution effects when new products are first introduced into the marketplace. Given that there are standard ways to estimate substitution rates for a large portfolio of new products, we used three assumptions:

5%, 10%, and 50% substitution, with the latter probably excessively conservative. ***Under a conservative royalty rate assumption, 5%, the estimated total change in GDP over the 12 year period ranges from $41.1 billion to $78.1 billion, depending upon the substitution rate assumed. Using a 2% royalty rate assumption, the estimated total change in GDP ranges from $93.3 billion to $177.2 billion.*** We do not show the similar calculations for contribution to changes in total industry output or employment under these different assumptions, but of course the results are proportionately similar.

Observations

Our approach to estimating the impact of university licensing employs a number of features that we believe provide far more valid and complete estimates of national economic impact than have previously been available, while at the same time incorporating many assumptions that lead to conservative results. Our model is relatively simple and transparent, and affords users the opportunity to enter their own best estimates of appropriate royalty rates, to which the model results are highly sensitive. As far as the validity of our estimates is concerned, our approach employs a national input-output model that accounts for the fact that sales revenue estimates do not themselves represent economic impact. Sales revenue estimates, however generated, include the industry purchases of intermediate inputs; further, they do not account for the expenditures of those revenues for multiple purposes before having a final impact on value added or GDP. Our approach accounts for the fact that university expenditures of their licensing income has significant direct and induced economic impact and thus should be included in any national (or, for that matter, regional) impact estimates. Indeed, our model can be used with regional input-output models and royalty data from individual universities to generate estimates of the economic impact of individual universities. Finally, although we were unable to obtain consistent data on university income from license-related R&D contracts, these too add to the economic impact of university licensing.

Project Overview

It is widely known that university-industry research interactions and collaborations have grown substantially over the past several decades. Collaborations take many forms, ranging from university licensing of inventions based in federally funded research, to industry participation in major federally-funded university-based research consortia, to direct industry support of university-based research projects. New companies also are frequently formed around innovations based on university research. Private firms increasingly have recognized that research partnerships with universities provide a wide range of benefits, only some of which take specific economic forms such as new and improved products, processes, and services; other benefits are access to students and graduates with specialized knowledge who can be interns, employees, or consultants. While only a fraction of industry-university research collaborations result in intellectual property (IP) that is successfully commercialized by private firms, universities also own intellectual property rights to inventions derived from billions of dollars annually of federal funding. They seek to maximize the public benefits of this research by licensing these discoveries to private firms to ensure maximum access to the technology by the general public.

There are several relatively sophisticated methods that could be used to estimate the economic value to the nation of innovations based in university research (e.g. consumer surplus estimates for specific innovations), but most would require costly data collection and/or threaten the proprietary interests of innovating firms. We present here the results of a modest approach that makes use of existing Association of University Technology Managers (AUTM) annual survey data and relatively straightforward economic calculations. Using data from annual AUTM surveys of U.S. universities, it is possible to develop systematic, conservative estimates of the economic impacts on the United States of twelve years of university-industry research collaborations. Although "deals" between university technology licensing offices and private firms take many forms, such as one-time flat fees, taking equity positions in university-based start-ups, and even in some rare cases donating IP to nonprofits for charitable purposes, in many cases universities base licensing fees on the percentage of sales of new products developed using the university-based IP. Annual AUTM survey data are available on the licensing income from all U.S. universities responding to the survey, typically numbering about 140. Licensing income data by reporting institution are available from 1996 through 2007. With these data as a base, we combine the AUTM survey results with other data and employ the Commerce Department's Bureau of Economic Analysis (BEA) Input-Output (I-O) model to

develop estimates of the annual national economic impact of university licensed products that have been commercialized and generated sales. These impact estimates take two forms: the change in gross output of all industries due to the university licensed products in the marketplace, and the impact on Gross Domestic Product (GDP) of university licensed products.

The "core" of this report describes the data used to generate these estimates, the models used to develop the estimates, and the results obtained. However, it is important to place these results in context, since the economic impact of university licensing of products is only one of the many economic impacts of university research and education, and almost certainly not the largest one. In addition to placing this particular type of university output in the context of other outputs with significant economic impact, it is also necessary to place the impact of university licensing of intellectual property in historical context. Thus the next section of this report presents historical trends in university licensing of intellectual property and related outputs. The subsequent section shifts the focus to the results of empirical studies of the impact of university research generally and of university licensing particularly. Then, we present the details of our work: the data used in our model, the model itself, and the results. The final section discusses our results, noting especially the assumptions and caveats that should be kept in mind in interpreting them.

Economic Significance of University Research: History and Trends

Although the intellectual property aspects of university-industry relationships have assumed salience recently in policy debates about the appropriate role of universities in technology commercialization, university-based applied research in areas of interest to industry is not new. During the latter part of the 19th century and well into the 20th, much university research was actually oriented toward the economic interests of the states in which they resided (and from which they drew their primary support). A small number of elite, private institutions struggled to increase the amount of basic research done on campus, as their counterparts in Europe had been doing for some time. It was not until the period following World War II that American research universities assumed the role as the primary performers of the nation's basic research (Geiger, 1986; Rosenberg and Nelson, 1994; Mowery and Rosenberg, 1989; Atkinson and Blanpied, 2008).

The direct commercial value of knowledge generated from university research is only one of a wide range of outputs that have economic significance. In a synthesis of prior research, Goldstein, Maier, and Luger (1995) list eight outputs of research universities that can lead to economic impacts:

1. Generation of new knowledge;
2. Creation of human capital;
3. Transfer of existing know-how (tacit knowledge);
4. Technological innovation;
5. Capital investment;
6. Regional leadership;
7. Production of knowledge infrastructure; and
8. Influence on the regional milieu.

In their recent review of methods for assessing the economic impacts of universities, Drucker and Goldstein (2007) expand on several of the more significant (and more easily characterized) of these outputs. They note that, since their origins in the Middle Ages, universities' primary reason for existence has been the formulation and dissemination of knowledge and wisdom. Research-intensive universities have recognized that development of human capital has been an accompanying objective, difficult to separate from the research function itself. "The development of human capital is intrinsic in the process of establishing new knowledge as faculty, students, and researchers develop their own intellectual and technical skills; [it] also occurs through activities such as distance learning, industrial extension, and community

education programs." (p. 22) Knowledge and technology transfer focus on application of existing knowledge to solve problems and improvement of products and processes, functions that initially (in the U.S.) were central to land grant universities but are now recognized as highly important for all research universities, public and private. The creation of technological innovations at the university frequently leads to patenting, licensing, and the formation of start-up companies by faculty and students.

Obviously, the economic implications of some of these outputs are more easily measured and assessed than others. Traditional approaches have focused on the regional impacts of direct spending and regional investments of universities; others have extended this to include the effects of human capital creation and induced regional migration. More recent approaches have considered the effects of knowledge creation, knowledge infrastructure development, technological innovation, and technology transfer.

Sampat (2003) provides a similar but shorter list that focuses more sharply on the more readily recognized and assessed economic outputs of university research:

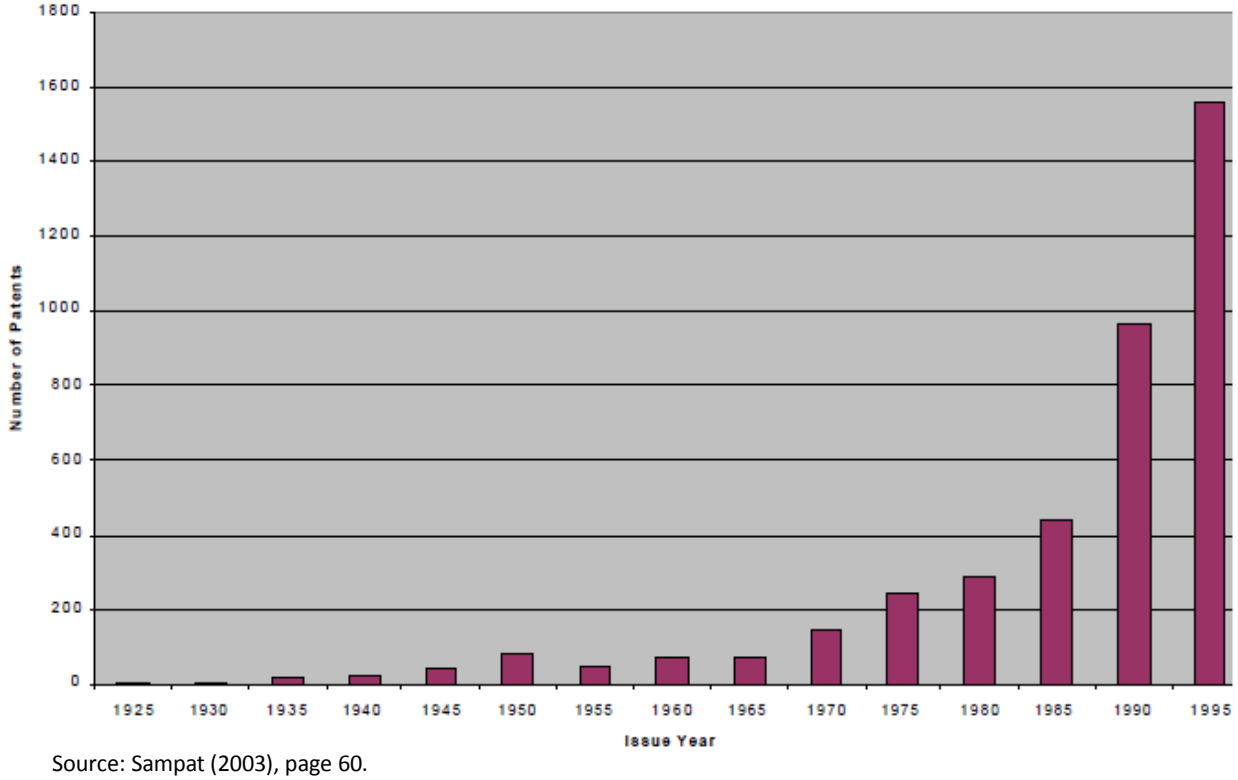
- Creation of economically useful scientific and technological information, which helps increase the efficiency of applied R&D in industry;
- Provision of skills or human capital to students and faculty members and helping to create networks of scientific and technological capabilities;
- Development of equipment and instrumentation used by firms in production or research;
- Creation of prototypes for new products and processes. (pp. 55-56)

Sampat makes several points that are relevant to the purposes of this report. He notes that the relative importance of the different channels through which these outputs diffuse (or are "transferred") to industry has varied by industry and over time. Such channels include hiring of students and faculty, consulting relationships between faculty and firms, publications, conference presentations, informal interactions with industry researchers, university start-up companies, and licensing of university patents. Recent studies show that both faculty and private firms in most industries consider the primary channels through which learning occurs to be publications, conferences, and informal information exchange (Cohen, Nelson, and Walsh, 2002; Agrawal and Henderson, 2002). Also, several studies of the benefits that companies derive from membership in National Science Foundation-funded university-industry research centers (e.g., Engineering Research Centers, Industry/University Cooperative Research Centers) show that access to students and faculty and to new ideas and research results, rather than technology *per se*, are consistently the most frequently cited benefits of center membership

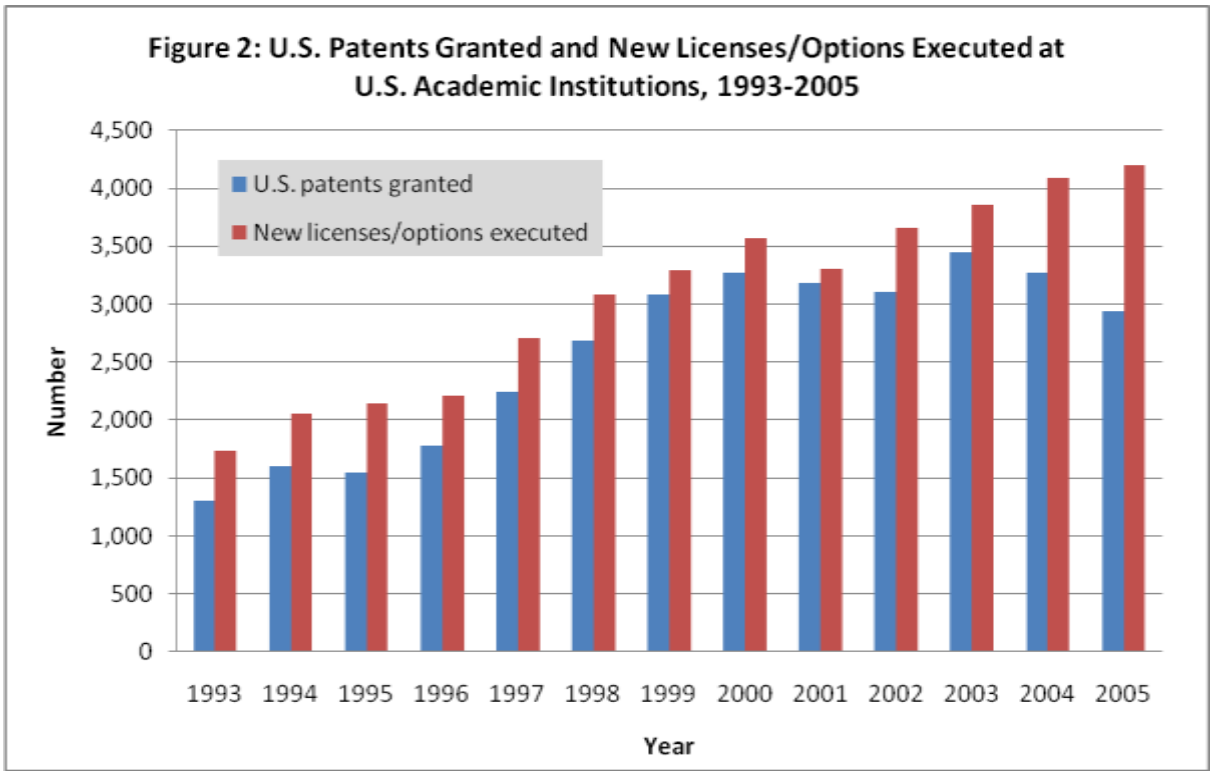
(Feller, Ailes, and Roessner, 2002; Roessner, 2000). So, although the focus of this report is clearly on the economic impact of university licensing, this represents only one of many outputs from university research that are highly valued in the economy.

Despite the "ivory tower" label sometimes attached to U.S. universities, this is now a gross misrepresentation of reality. In fact, our research universities have been among the most important economic institutions of the twentieth century (Atkinson and Blanpied, 2008). "Most economic historians agree that the rise of American technological and economic leadership in the postwar era was based in large part on the strength of the American university system" (Sampat, 2003: 56). Many other countries viewed the university-industry collaborations found in the United States as a competitive advantage and sought to duplicate the underlying conditions supporting these trends (Neal, Smith and McCormick, 2008). Patenting of university research outputs is by no means a phenomenon of the past few decades only. Although growth in university patenting accelerated dramatically beginning in the 1980s, the history of university patenting extends back to the 1920s (see Figures 1 and 2). Indicators of academic patenting are mixed in recent years. The U.S. Patent and Trademark Office reports that patent grants to universities have declined since 2002, but other indicators suggest continued expansion of activities related to patents and patent/licensing revenues, such as invention disclosures, patent applications, and revenue-generating licenses. For example, Figure 2 shows that the number of new university license agreements/options have grown steadily in recent years from 1,079 in 1991 to 4,201 in 2005.

Figure 1: Patents Issued to U.S. Research Universities, 1925-1995



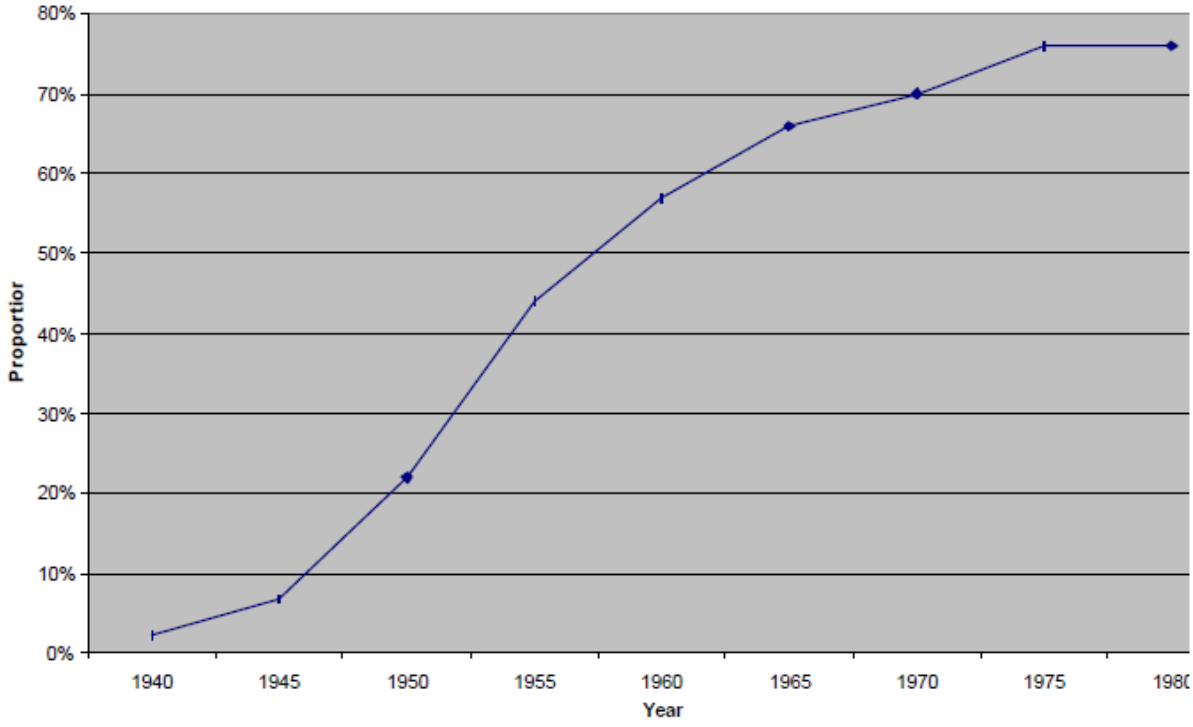
Source: Sampat (2003), page 60.



Source: AUTM annual surveys, various years, and National Science Board, 2008.

Until the latter part of the twentieth century, however, universities generally did not wish to engage directly in the patenting and licensing process, largely because they viewed such activities as possibly compromising their commitments to openness and knowledge dissemination. In these early years, most universities avoided intellectual property issues, and the few that did become involved either contracted out their patent management activities to third party organizations such as the Research Corporation (founded in 1912), or set up separate, non-profit foundations such as the Wisconsin Alumni Research Foundation (created in 1924). Beginning with MIT in 1937 and continuing into the post WWII period, universities signed "invention administration agreements" (IAA) with Research Corporation, specifying that all necessary services would be provided by Research Corporation, for which the Corporation would retain a portion of royalty income, with the remainder going to the university. Figure 3, below, shows the proportion of Carnegie research universities that had such agreements between 1940 and 1980.

Figure 3: Proportion of Carnegie Research Universities with IAAs with Research Corporation, 1940-1980

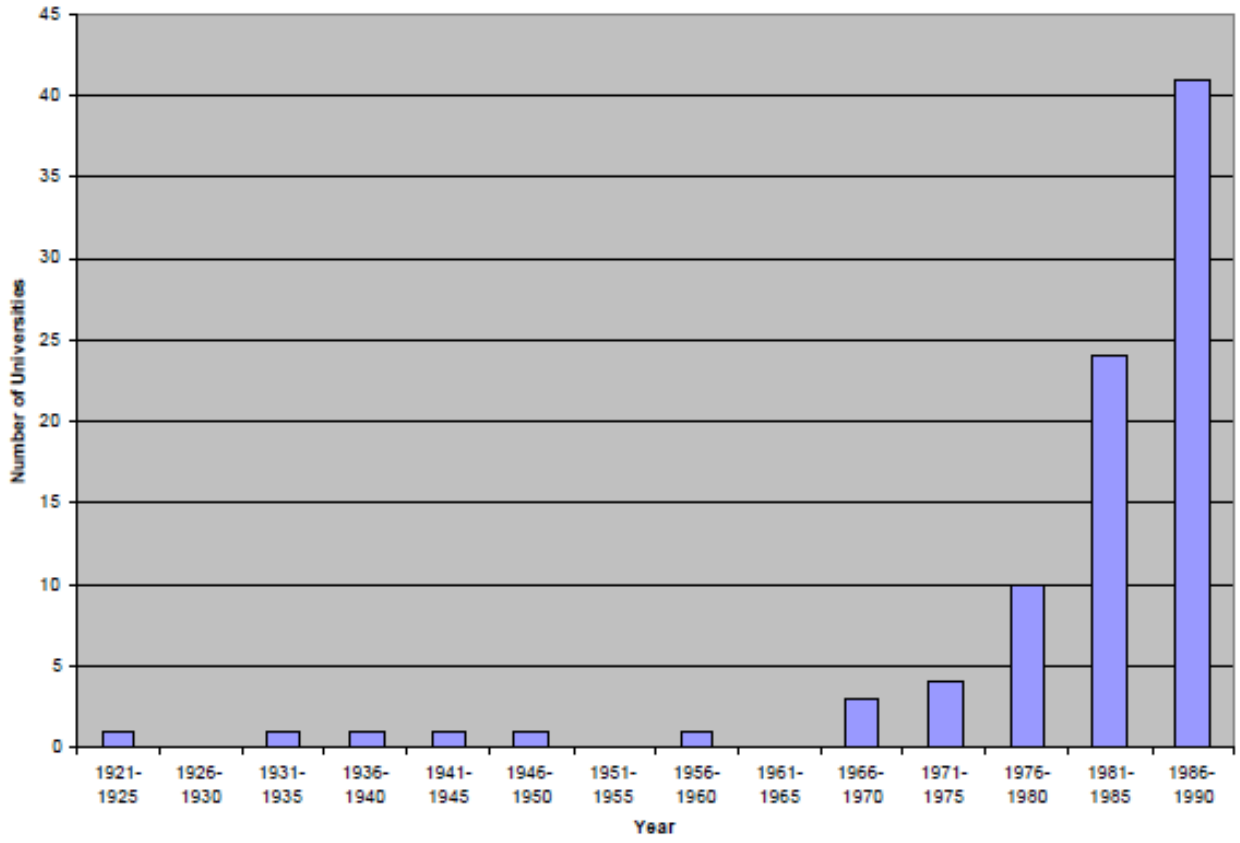


Source: Sampat (2003): page 58.

A number of forces beginning in the 1970s brought about significant changes in university patent policies, manifested most obviously in the decision by many research universities to establish internal technology transfer offices, thus internalizing the functions previously performed by the Research Corporation. Figure 4 shows the number of additional universities

"entering into" internal technology transfer activities during each five-year period between 1921 and 1990, with "entering into" defined by AUTM as having a minimum of 0.5 Full Time Equivalents (FTEs) devoted to such activities. Research Corporation noted in its Annual Report that by the mid-1970s most major research universities were considering establishing internal technology transfer offices (Sampat 2003, p. 59).

Figure 4: Year of "Entry" into Technology Transfer Activities, 1921-1990



Source: Sampat (2003), page 60.

Among the several forces at work during the 1960s and 70s, prior to passage of the Bayh-Dole Act in 1980, were:

- Commercial applications resulting from the growth of "use oriented" basic research in fields such as molecular biology;
- A decline in federal and other funding for university research;
- University frustration with Research Corporation's failure to return licensing revenues as called for in the IAAs;
- Court rulings and shifts in federal policy that made it easier to patent research results in biomedicine. (Mowery, et al., 2001; Mowery and Sampat, 2001).

According to Mowery, et al. (2001), beginning in the 1960s important federal research agencies began to allow universities to patent and license results from federally-funded research. The Department of Defense allowed universities to retain title to patents resulting from DOD research, provided that DOD retained control of the patents for military application. Both HEW and NSF negotiated Institutional Patent Agreements (IPA) with individual universities, which eliminated the need for case-by-case reviews of the disposition of individual academic inventions. The universities whose patent filings were increasing during this period were participants in these IPA agreements (J. Allen, personal communication, March 23, 2009). In addition, the Court of Appeals for the Federal Circuit (CAFC) was established in 1982 to "serve as the court of final appeal for patent cases throughout the federal judiciary . . . the CAFC soon emerged as a strong champion of patentholder rights" (p. 103). The IPAs were, in a sense, an administrative form of many of the agency-wide provisions of the Bayh-Dole Act, enacted in 1980 and implemented in 1981. In any event, as Mowery et al. (2002) note, "growth during the 1970s in patenting, licensing, licensing income, or in the establishment of independent technology transfer offices, was dwarfed by the surge in all of these activities after 1981." (p. 104)

Time-series data on a variety of indicators of the level of activities related to commercialization of university research consistently show that, while universities engaged in such actions as early as the 1920s, an enormous surge in the rate of activity took place after the Bayh-Dole Act became law in 1980. Although the trend data may suggest, *prima facie,* that Bayh-Dole is to a significant extent responsible for the economic consequences of university-based technology transfer and commercialization activities during the past twenty-five years, there is currently considerable debate about this. Mowery and his colleagues, for example, are skeptical of the causal links, arguing that there is little empirical evidence that Bayh-Dole substantially increased the contributions of university research to the U.S. economy. Based on national university patenting data and detailed historical data from Columbia, Stanford, and Berkeley, they argue that commercialization activity would have grown in the absence of Bayh-Dole, that the evidence on low rates of commercialization before passage of Bayh-Dole is weak, and that patenting and licensing frequently are not necessary for the development and commercialization of publicly funded, university-based inventions (Mowery, et al., 2004, pp. 183-184). However, these conclusions and those of other skeptics concerning the apparent economic significance of Bayh-Dole have been challenged strongly in a recently published article by Bremer, Allen, and Latker (2009). They conclude that "Reams of objective data exist supporting the conclusion that the Bayh-Dole Act greatly improved the commercialization of federally-funded research . . . and that the public sector-private sector partnerships which were generated under the Act are essential both to the well being and the competitive position of

the United States" (p. 2). Our concern here, however, is not the contribution that the Bayh-Dole Act did or did not make to the economic impact of university-based licensing of technology, but rather to estimate quantitatively the contribution that one component of the output of university-based research makes to our national economy.

Empirical Evidence of the Economic Impact of University Research and Licensing

In 2003 the National Academy of Engineering issued a report titled *The Impact of Academic Research on Industrial Performance* (NAE, 2003). The study sought to assess and document the contribution that university research made to five diverse industries: network systems and communications; financial services; medical devices and equipment; transportation, distribution, and logistics services; and aerospace. These industries illustrate the wide range of contributions of academic research to industrial performance: trained graduates; new knowledge emerging from research; and development of tools, prototypes, and products. They also illustrate different patterns of collaboration with universities and different mechanisms for taking advantage of academic contributions. The study concluded that "Academic research has made substantial contributions to all five industries, ranging from graduates at all levels trained in modern research techniques to fundamental concepts and key ideas based on basic and applied research to the development of tools, prototypes, and marketable products, processes, and services" (p. 2). The study also noted that quantitative evidence of the impact of university research on industrial performance was largely lacking. A number of efforts are ongoing to improve metrics of innovation outputs, technology transfer, and commercialization of R&D results including those at the National Science Foundation (NSF), the Association of Public and Land-Grant Universities (APLU—formerly NASULGC), the Association of American Universities (AAU), AUTM, and the Organisation for Economic Co-operation and Development (OECD). In response to the need to provide qualitative as well as quantitative information on the economic and social contributions of university R&D, AUTM has also launched The Better World Project, which provides case studies of examples such as Taxol, Alegra, Google, holograms, etc. The latest report, *2009 Better World Report*, focuses on health (AUTM, 2009).

There is considerable evidence that the most important contribution that universities make to industry is through their outputs of research results and well-trained scientists and engineers, which increase the productivity of industrial R&D (Nelson, 1986; Rosenberg and Nelson, 1994; Klevorick et al., 1995).[3] Industrial scientists rely primarily on the existing stock of knowledge in carrying out their research, so are likely to use existing knowledge at least as much as new knowledge. Sometimes, though, advances in basic science lead fairly quickly to new products and processes, with biotechnology (employing knowledge of the principles of recombinant DNA, for example) an obvious case. Mansfield (1991) surveyed R&D executives from 76 major U.S. firms, asking them to estimate the proportion of new products and processes their firms had produced over a ten-year period that could not have been developed (without substantial

[3] For a concise review of the literature on the contributions of academic research to industrial innovation, see Chapter 8 in National Science Board, *Science and Engineering Indicators 1996*.

delay) without the results of academic research that had been conducted during the previous 15 years. The responses indicated that about 11 percent of new products and 9 percent of new processes could not have been developed without the results of academic research. Using these results together with information on the value of sales of new products and the cost savings associated with use of new processes, Mansfield estimated that the social return to investment in academic research was 28 percent.

There is also evidence that academic research is increasingly important to industry. A survey of 1,478 industry R&D lab managers conducted in 1994 by Carnegie Mellon University researchers found that two-thirds of the industries surveyed showed that university research was at least "moderately important" to their R&D. Also, as we saw in an earlier section of this report, the number of patents granted to universities has increased dramatically over the past several decades, as have start-up companies based in university research. Disclosures filed with university technology management offices grew from 13,700 in 2003 to 15,400 in 2005. Likewise, new U.S. patent applications filed by respondents to annual AUTM surveys also increased, from 7,200 in 2003 to 9,500 in 2004 and 9,300 in 2005. The annual number of startup companies established as a result of university-based inventions rebounded after 2 years of downturns in 2002 and 2003 to more than 400 in both 2004 and 2005, and were reported at 555 in the 2007 AUTM survey (National Science Board, 2008; AUTM, 2007).

There is a substantial literature on the broader economic impact of universities (only some studies consider the impact of research as a separate activity), but it consists largely of studies of the impact that universities have had on their regional economies. National impact studies are rare, and the few that have been done focus on the impact of publicly-funded (usually federal) research on the national economy, and most do not separate out university research impacts. In Appendix A we summarize selected studies to illustrate typical approaches used and results obtained to provide a broader context for the specific impact estimates of university licensing we have developed. We stress that licensing of intellectual property is only a minor portion of the activities engaged in by universities that have economic value, so that the total economic impact of universities greatly exceeds that generated through licensing. Appendix A is not intended to be a full literature review; rather, it illustrates the various types of studies that have been done and helps place this report and its results into context.

Estimating the Economic Impact of University Licensing

The BEA national I-O model and data from AUTM provided the basis for our estimates of the national economic impact of university licensing. Two estimates of impacts are made. One measures the impact of university licensing on gross domestic product (GDP), and the other, its impact on other industries' production (gross output). Our estimates cover a 12-year period, 1996–2007.

The national I-O model allows users to assess the impact of specified events on economic activity. The model shows the relationship between final demand and industry production, and may be used to evaluate the interrelationships among industries and the relationships between industries and the commodities they use and produce. It is used to derive input-output requirement tables. These requirements tables show the level of industry gross output or employment required to produce a specified level of final uses.[4]

Using the I-O Model to Assess the Impact of University Licensing

The I-O model is used to measure two different but equally important impacts of university licensing on the economy: the impact on GDP and the impact on other industries production (gross output).

The first is the direct impact of university-licensed products on GDP. It takes into account both licensing receipts of universities and output resulting from licensing agreements. University licensing receipts are part of the output of universities, and include additional license-related sponsored research. It is assumed that all licensing receipts are spent, for example, on additional research equipment and materials, graduate student support, and faculty salaries. These licensing receipts are added to output resulting from licensing agreements. Firms generate sales of new products – goods and services – based on the licensed technology. The contribution to GDP from the sales of these products is the value added of the industries producing them. This contribution is estimated using the ratio of value added to gross output (or sales) of the products produced under the licensing agreements. These ratios are derived from the input-output tables.

The second impact measures that of university licensing on industry gross output or production. It includes the direct effect of expenditures of university royalty receipts (including additional

[4] A more complete discussion of the Input-Output model can be found in Appendix B.

sponsored research for the university generated by its licenses), and the indirect effect on the output or employment of universities as well as all other industries. These university expenditures require other industries that supply goods and services to the universities to increase their output. Licensing and license-related research income is multiplied by the I-O total requirements multipliers to estimate the gross output of all other industries required to support the additional expenditures resulting from licensing and license-related research income.

Estimating the Total Annual Economic Impact of University-Licensed Products

Figure 5, below, provides a schematic representation of how we calculated annual estimates of the impact of university licensed products on the U.S. GDP. Verbally, it is the sum of the estimated direct impact of university licensed products and the direct impact of university expenditures of their total (gross) licensing income. The direct impact of university licensed products is, in turn, derived from the ratio of university licensing income from "running royalties"[5] to the royalty rates (based on percentage of product sales) charged by universities. This ratio yields an annual estimate of the additional revenues to firms generated from sales of products based on university-licensed intellectual property. The I-O model converts this figure into the changes in income (compensation, indirect business taxes, and gross operating surplus—i.e., profits) of companies operating under sales-based university licensing agreements, which together constitutes the contribution to GNP. Also, university expenditures attributable to licensing income have direct impacts on the economy in two ways: first, via expenditures of gross royalty income (for salaries, equipment, overhead costs, etc.) and second, via expenditures of research income from firms that contract for R&D with the university as a direct consequence of the licensing agreement. This is accounted for by the second term in the model.

[5] AUTM defines running royalties as royalties earned on and tied to the sale of products. Excluded from this number are license issue fees, payments under options, termination payments, and the amount of annual minimums not supported by sales. Also excluded from this amount is cashed-in equity. Many universities take equity positions in start-ups in lieu of royalties. The exclusion of these equity payments in our model adds to the conservative nature of our estimates.

Figure 5: Estimating the Total Annual Economic Impact of University-Licensed Products

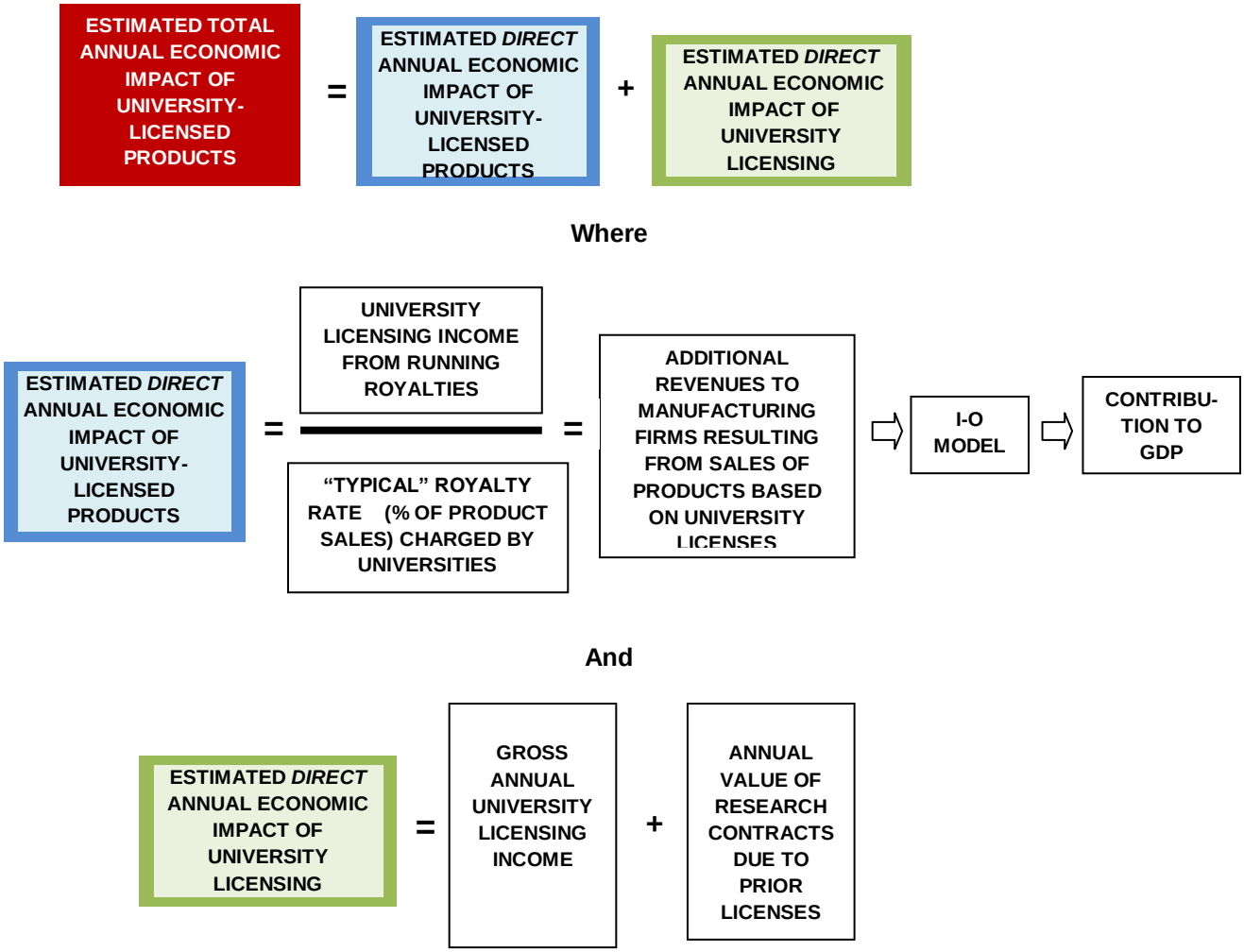
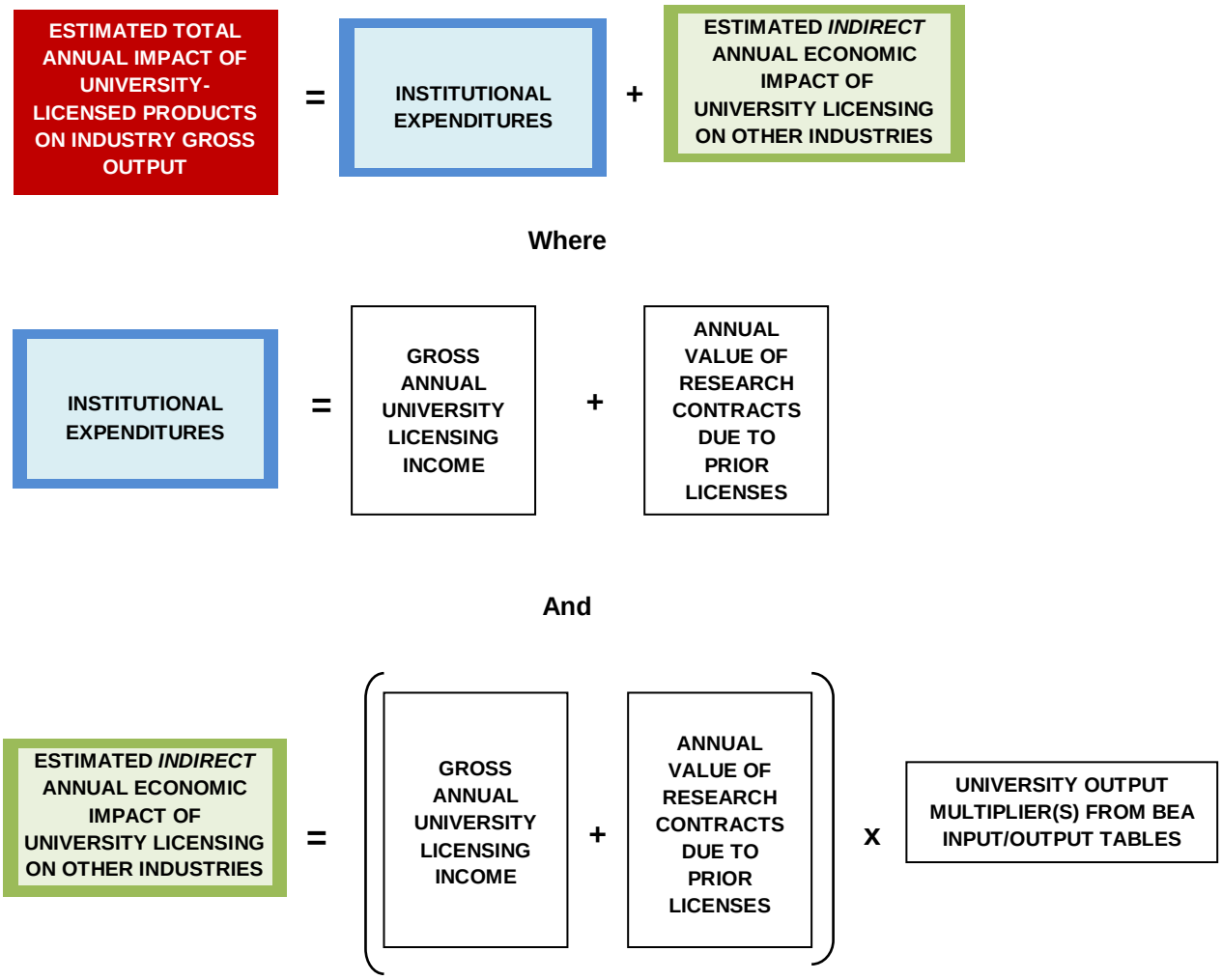


Figure 6 shows how we estimated the change in gross output of all industries due to the university licensing of products. Gross output is a measure of economic activity, but is not GDP. The impact is the sum of sales of companies generated by the licensing agreements plus the change in output at universities (additional income from licensing plus additional research funds attributable to the licensing) plus the changes in gross output of all other industries that directly and indirectly provide inputs to the universities. Note that "institutional expenditures" represent university licensing income that national accountants classify as consumption expenditures.

Figure 6: Estimating the Annual Impact of University-Licensed Products on Industry Gross Outputs



The Data

We used data from AUTM annual surveys to estimate the impact of royalty-related income of universities and sales from products produced from the licensing agreements. AUTM surveys provide information for the years 1996-2007 on:

- Gross royalty income paid to universities from licensing; and
- Running royalties paid to the universities based on product sales.

The royalty-related income paid to universities multiplied by the total requirements multiplier for educational institutions gives the value of gross output in all industries necessary to satisfy the university expenditures of licensing-related income; this is the indirect impact of university

licensing. Employment multipliers can be multiplied times these expenditures to estimate the total impact of royalty income on employment.

A separate, but equally important impact is the contribution of the new products created by the university licensing program to industry value added, or GDP. The value of annual sales of products produced as a result of licensing university technologies is estimated using information on the royalty rates paid to universities based on the annual sales of products, and AUTM survey data on running royalty income received by universities based on product sales. Because of data limitations, a range of sales is estimated, based on information on royalty rates we obtained with the cooperation of AUTM members and staff. Royalty rates based on product sales differ among universities and by industrial sector; also, the derived sales estimates do not take into account the effect that new products have on sales of substitute goods already on the market. Hence, several scenarios are assumed. Royalty rates charged by universities typically range from 2% to 10%, depending on the industry involved and other factors. In principle, product displacement effects could range from 0 percent, when the new product displaces no existing products or services, to 100 percent, when it completely displaces them. These ranges (rather than misleading "typical" or "average" values) provide a way to generate conservative estimates of the increase in GDP due to university licensing of intellectual property, accounting for the wide range of royalty rates charged by universities and for substitution effects when new products are first introduced into the marketplace.

To develop information about "typical" royalty rates charged by universities on which to base our impact estimates, we enlisted the aid of a number of individual university technology transfer officers from various regions of the country and current and former members of the AUTM Public Policy Committee. With their help, we obtained royalty rate information from twelve research universities representing a range of sizes, types (public and private), and geographic locations. The following table (Table 1) summarizes the results of this effort.

Table 1: Royalty Rates Charged by Twelve U.S. Universities for License Fees Based on Product Sales.

University	Life sciences	Software	Other	Overall
A	4-6%	10-20%	0.5-3%	
B	10%+		0.25%	Processes 1-3% composition of matter 4-6%
C				2-3%
D	Devices 5% therapeutics 1-2%			
E	Devices 4-5% therapeutics 1-2%	"higher"		
F				8% (health plus IT)
G	4%			3-4% (mostly medical devices)
H				4-5% (mostly life sciences)
I				1-2%
J				About 5%
K				4.4%
L				5-8%

AUTM and other sources in the literature[6] suggest that about 60-75% of university licensing income is based in the life sciences,[7] another 10-20% in IT/electronics/software, and the remainder in all other fields. This distribution and the results in the table show that it would be difficult and misleading to identify an "average" royalty rate (our respondents strongly resisted this). For these reasons, we decided on a wide range of royalty rates to use in our model: 2%, 5%, and 10%. Note that since royalty rate figures appear in the denominator of the model, the higher royalty rates yield lower estimates of economic impact. Moreover, since they are relative small numbers, the resulting economic impact estimates are highly sensitive to the royalty rates used in the model.[8] One reason for including such a wide range of royalty rates in

[6] Graff, et al. (2002) present data on the average percentage of a university's total licensing revenues by academic field: medicine, 55.2%, engineering and physics 24.1%, agriculture 9.1%, computer science 5.1%, other 6.6%. Mowery, et al. (2001) report field-of-technology patterns in licensing for the University of California, Stanford, and Columbia. 75% of disclosures for Columbia were in biomedicine and most of the rest in software and electronics; at the University of California, about 65% were biomedical; at Stanford just 20% were biomedical and 30% in software.

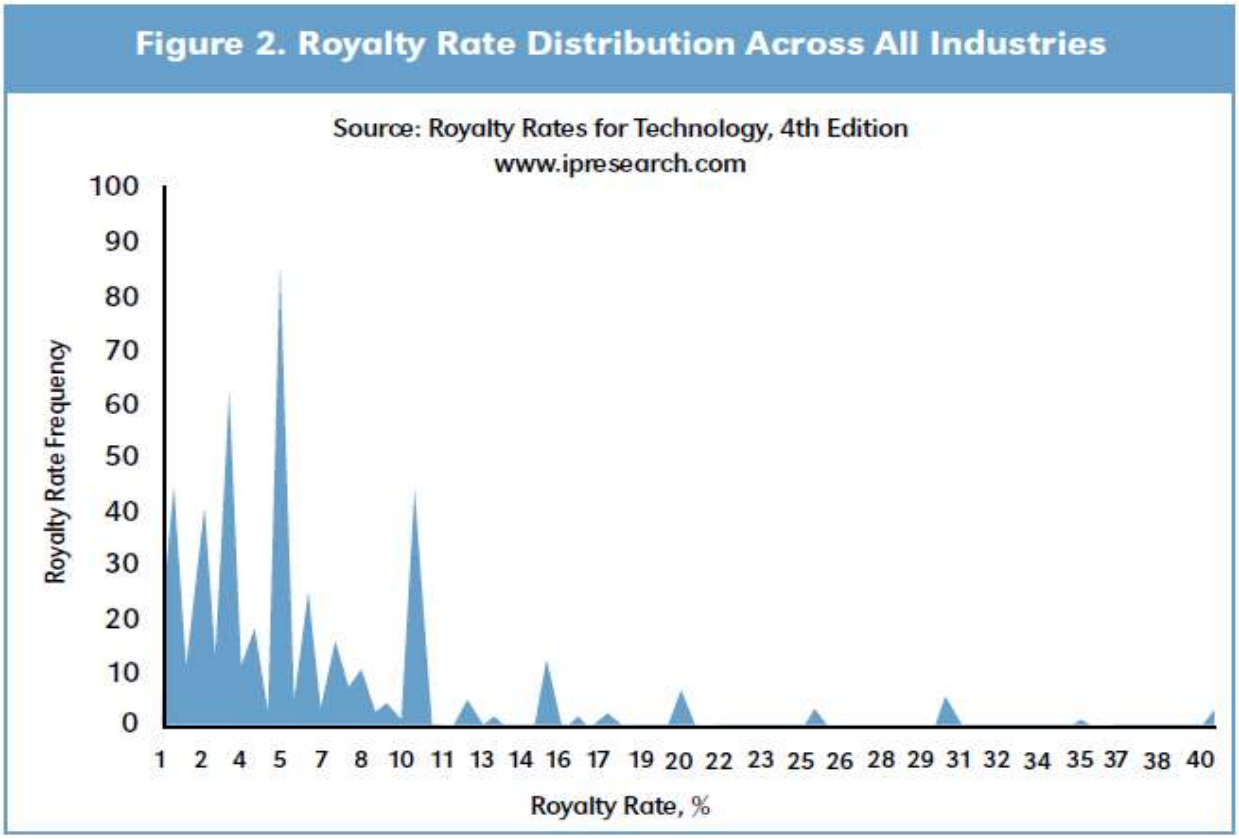
[7] The AUTM Annual Licensing & Activity Survey defines life sciences as all works derived from such disciplines as biology, medicine, chemistry (basic), pharmacy, medical devices, and those involving human physiology and psychology, including discipline-related inventive subject matter such as software and educational material.

[8] Our discussions with experienced university technology transfer officers suggest that this range is itself subject to considerable debate. Royalty rates may be weighted and skewed towards the lower end of the range and actual royalty fees may turn out to be lower than originally reported due to a number of factors; royalties are often offset

our calculations is that users of our model can get a rough feel for the differences in impact that industry sector makes; for example, the data in Table 1 suggest that the 10% rate is appropriate for only very limited industry sectors, sectors that represent only a small proportion of most university licensing portfolios.

Recent data on royalty rates for technology reported in Parr, *Royalty Rates for Technology* (www.ipresearch.com) illustrate the distribution of royalty rates for technology licensing agreements in the U.S. Although the data shown graphically in Figure 7 are for all industries and include both university and private firm licenses, the shape of the distribution, if not the details, shows the inappropriateness of using an average or some other single figure to develop economic impact estimates for university licensing.

Figure 7: Royalty Rate Distribution Chart from Parr (2009).



Source: Parr, 2008, Figure 2, p. 16.

by sublicensing to other firms; "debundling" clauses in which the price of an active ingredient in a pharmaceutical is subtracted out of the royalty base calculation; and companies often return to renegotiate royalty fees. In any case, university licensing portfolios exhibit a range of royalty rates, perhaps 2-10%, with the lower rates typically dominating.

For displacement or substitution effects, there is no standard approach. Under these circumstances, we made what we believe to be a set of reasonable assumptions in order to arrive at a plausible range of product displacement rates:

1. It is highly unlikely that the effect of these new products, when first introduced, will have substantial displacement effects on existing products over the short run. They more frequently are highly innovative products, new to the marketplace, and sometimes result in entirely new industries or changes in behavior rather than merely improvements over or direct substitutes for existing ones, and therefore unlikely to directly displace something in widespread current use. This assumption would lead toward estimates below 50% substitution.

2. A 0% assumption means no market substitution effects whatever on existing products, which also seems unrealistic. Yet small perturbations over a reasonably short period (say 5 years) seem most likely, and this also points to use of substitution rates toward the lower end.

We therefore used substitution rate estimates of 5, 10, and 50 percent in our calculations. Anyone wishing to use alternative assumptions using our base estimates can of course do so easily.

The following two pairs of tables (Tables 2 and 3) and charts (Figures 8 and 9) show the annual AUTM data on running royalties and total royalty income for U.S. universities for the years 1996-2007.[9]

Table 2: Running Royalties for U.S. Universities, 1996-2007, in millions

	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Millions	$282.11	$314.75	$390.33	$475.04	$558.96	$636.56	$786.74	$829.26	$810.15	$855.94	$968.57	$1,806.97
N=	125	122	124	133	138	136	150	158	154	150	153	153

Source: AUTM annual surveys

[9] The increase in royalty income in 2007 is a real increase and is primarily due to the sale by New York University of their worldwide royalty interest in Remicade(R) to Royalty Pharma for $650 million in cash up-front plus additional payments should yearly sales of Remicade(R) exceed certain agreed sales hurdles. NYU retains the portion of the Remicade(R) royalty interest payable to the NYU researchers who are responsible for the development of Remicade(R). So the dramatic increase in 2007 represents royalty income based on estimated future sales that normally would be apportioned in future years, based on the agreed-upon royalty rates. There are likely to be similar agreements with less dramatic effects reflected in the royalty income data for other years and other universities.

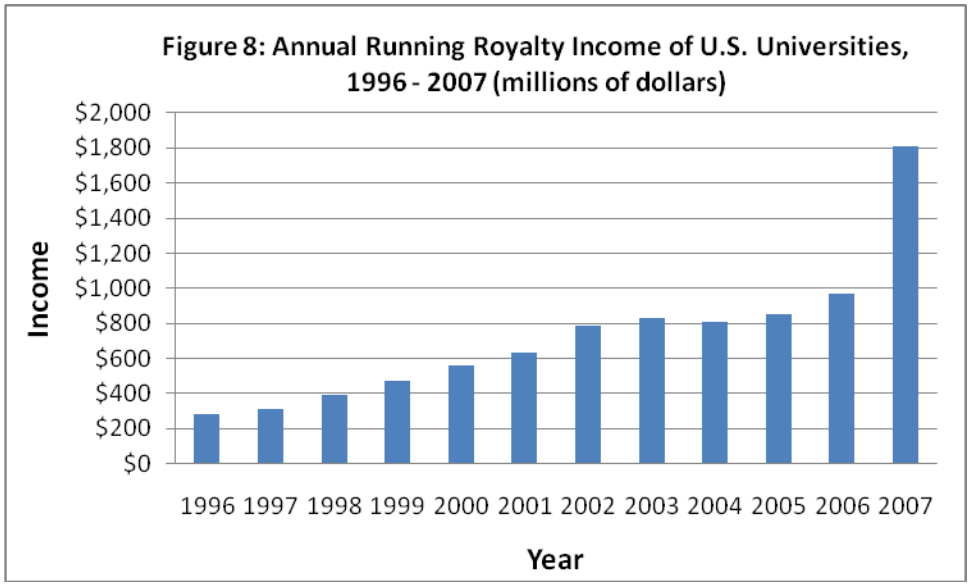
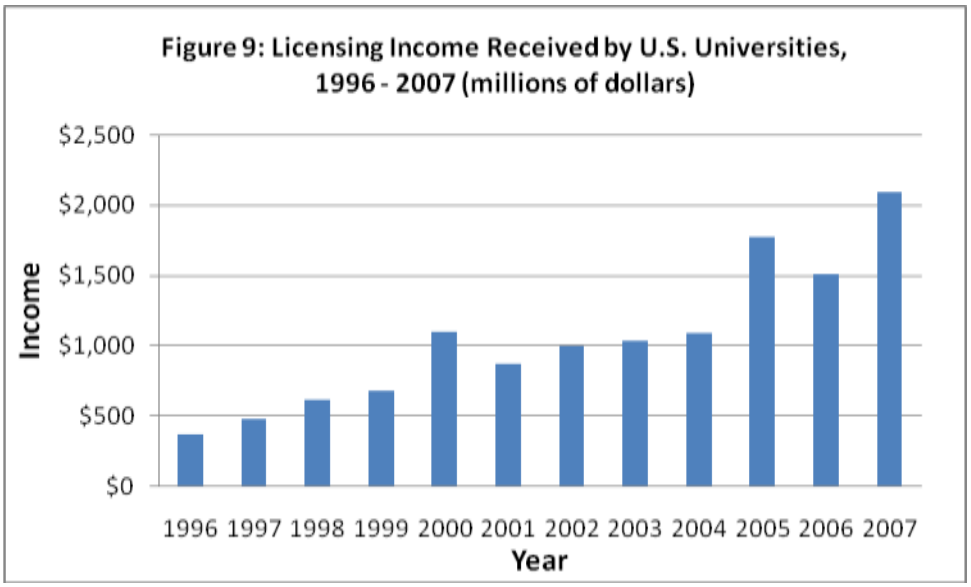


Table 3: Licensing Income Received by U.S. Universities, 1996-2007, millions of dollars

	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Millions	$365.22	$482.79	$613.55	$675.47	$1,099.89	$868.28	$997.83	$1,033.61	$1,088.47	$1,774.97	$1,511.58	$2,098.78
N=	125	122	124	133	138	136	150	158	154	150	153	153

Source: AUTM annual surveys.



Unfortunately, consistent and complete annual data for 1996-2007 are not available from AUTM on the value of research contracts received by universities that were directly related to previous licensing agreements signed between the university and the contracting companies.

Omitting this element in the calculations is another indication that the impact estimates we calculated are on the conservative side.

Results

Impact Estimates, Basic Model

Table 4, below, shows the calculated values resulting from application of the model represented in Figure 5, above. The model generates annual values for sales revenues with a range of assumptions about royalty rates: 2%, 5%, and 10%; outputs from the I-O model under these three assumptions; and estimates of the total change in GDP due to university-licensed product sales under the three royalty rate assumptions. No assumptions are made here about product substitution rates, and the additional impact generated from university income from license-related contract R&D is not included in the calculations. Under a moderately conservative assumption (conservative from the perspective of the magnitude of model's impact estimate), a 5% royalty rate, over the 12-year range of our data university licensing based on product sales contributed $2.6 billion to the U.S. GDP in 1996, and $16.8 billion in 2007. Under a less conservative but realistic assumption (2% royalty rate), the annual contribution to GDP ranged from $5.9 billion in 1996 to more than $38.8 billion in 2007. ***Without accounting for product substitution effects, we estimate that over the period 1996 to 2007, university licensing agreements based on product sales contributed at least $47 billion and as much as $187 billion to the U.S. GDP. A moderately conservative estimate based on 5% royalty rates yields a total contribution to GDP for this period of more than $82 billion.*** The large range of these estimates illustrates clearly the high sensitivity of our results to assumptions about the royalty rates charged by universities on license agreements based on product sales.

Table 4: Annual Change in U.S. GDP due to University-licensed Products, Selected Royalty Rates, 1996-2007

Year	running royalty	sales revenues (2% royalty rate)	sales revenues (5% royalty rate)	sales revenues (10% royalty rate)	Value added ratio from U.S. I-O tables	Income from I-O model (2% royalty rate)	Income from I-O model (5% royalty rate)	Income from I-O model (10 % royalty rate)	total licensing income	total change in GDP (2% royalty rate)	total change in GDP (5% royalty rate)	total change in GDP (10% royalty rate)
	millions	millions	millions	millions		millions	millions	millions	millions	millions	millions	millions
1996	$282.11	$14,106	$5,642	$2,821	0.39	$5,485	$2,194	$1,097	$365.22	$5,851	$2,559	$1,462
1997	$314.75	$15,737	$6,295	$3,147	0.39	$6,120	$2,448	$1,224	$482.79	$6,603	$2,931	$1,707
1998	$390.33	$19,517	$7,807	$3,903	0.40	$7,849	$3,139	$1,570	$613.55	$8,462	$3,753	$2,183
1999	$475.04	$23,752	$9,501	$4,750	0.40	$9,482	$3,793	$1,896	$675.47	$10,158	$4,468	$2,572
2000	$558.96	$27,948	$11,179	$5,590	0.40	$11,159	$4,463	$2,232	$1,099.89	$12,258	$5,563	$3,332
2001	$636.56	$31,828	$12,731	$6,366	0.40	$12,576	$5,030	$2,515	$868.28	$13,444	$5,899	$3,383
2002	$786.74	$39,337	$15,735	$7,867	0.41	$16,123	$6,449	$3,225	$997.83	$17,121	$7,447	$4,223
2003	$829.26	$41,463	$16,585	$8,293	0.40	$16,507	$6,603	$3,301	$1,033.61	$17,541	$7,637	$4,335
2004	$810.15	$40,508	$16,203	$8,102	0.40	$16,371	$6,548	$3,274	$1,088.47	$17,460	$7,637	$4,363
2005	$855.94	$42,797	$17,119	$8,559	0.39	$16,495	$6,598	$3,299	$1,774.97	$18,270	$8,373	$5,074
2006	$968.57	$48,429	$19,371	$9,686	0.40	$19,143	$7,657	$3,829	$1,511.58	$20,654	$9,169	$5,340
2007	$1,806.97	$90,349	$36,139	$18,070	0.41	$36,652	$14,661	$7,330	$2,098.78	$38,750	$16,759	$9,429
Total		**$435,770**	**$174,308**	**$87,154**						**$186,572**	**$82,195**	**$47,403**

Note: Value added ratio = 0.3774 from 2005 I-O table for manufacturing.

Using the model depicted in Figure 6, above, which generates estimates of the contribution to industry gross output due to university-licensed products, we calculated the total output produced annually by university licensing revenues, the direct employment generated by these revenues, and the total change in industry gross outputs due to this licensing activity (Table 5). We again calculated a range of estimates based on the royalty rates charged in sales-based licensing agreements. Under a moderately conservative assumption (5% royalty rates), as a result of university licensing annual industrial output increased by $6.3 billion in 1996 and by $39.7 billion in 2007. Using a less conservative assumption (2% royalty rates), the annual contribution to industry output grew from $14.7 billion in 1996 to nearly $94.9 billion in 2007. ***Summing over the entire 12 years for which we have data, we estimate that the total contribution of university licensing to gross industry output at least $108.5 billion and as much as $457.1 billion (again without accounting for product substitution effects). A moderately conservative estimate based on 5% royalty rates yields an estimated impact of university licensing on total industry output over 1996-2007 of $195.6 billion.***

The I-O model also calculates the number of jobs directly created per million dollars of final purchases and thus provides estimates of the total number of jobs created annually due to university-licensed products. This ranged from about 9,000 jobs in 1996 to 41,000 in 2007. ***We estimate that over the entire 12-year period, university-licensed products created more than 279,000 jobs.***

Table 5: Annual Change in U.S. Industry Output due to University-licensed Products for Selected Royalty Rates, 1996-2007

year	licensing income	output multiplier from U.S. I-O tables	output of other industries	total output	employment multiplier from U.S. IO tables	employ-ment	sales revenues (2% royalty rate)	sales revenues (5% royalty rate)	sales revenues (10% royalty rate)	total change in output (2% royalty rate)	total change in output (5% royalty rate)	total change in output (10% royalty rate)
	millions		millions	millions		thousands	millions	millions	millions	millions	millions	millions
1996	$365.22	0.72	$263	$628	0.026	9	$14,106	$5,642	$2,821	$14,734	$6,270	$3,449
1997	$482.79	0.72	$348	$830	0.026	13	$15,737	$6,295	$3,147	$16,568	$7,125	$3,978
1998	$613.55	0.69	$424	$1,038	0.026	16	$19,517	$7,807	$3,903	$20,554	$8,844	$4,941
1999	$675.47	0.69	$467	$1,142	0.025	17	$23,752	$9,501	$4,750	$24,894	$10,643	$5,892
2000	$1,099.89	0.72	$788	$1,888	0.024	27	$27,948	$11,179	$5,590	$29,836	$13,067	$7,478
2001	$868.28	0.71	$614	$1,482	0.024	21	$31,828	$12,731	$6,366	$33,310	$14,213	$7,848
2002	$997.83	0.68	$678	$1,675	0.023	23	$39,337	$15,735	$7,867	$41,013	$17,410	$9,543
2003	$1,033.61	0.67	$697	$1,731	0.022	23	$41,463	$16,585	$8,293	$43,194	$18,316	$10,023
2004	$1,088.47	0.67	$727	$1,815	0.021	23	$40,508	$16,203	$8,102	$42,323	$18,018	$9,917
2005	$1,774.97	0.69	$1,225	$3,000	0.021	37	$42,797	$17,119	$8,559	$45,797	$20,119	$11,559
2006	$1,511.58	0.69	$1,044	$2,556	0.020	30	$48,429	$19,371	$9,686	$50,984	$21,927	$12,241
2007	$2,098.78	0.69	$1,444	$3,543	0.020	41	$90,349	$36,139	$18,070	$93,891	$39,682	$21,612
Total						**279**				**$457,097**	**$195,636**	**$108,482**

Notes: Output multiplier is millions of dollars of indirect output per million dollars of final purchases of education services. Employment multiplier is the number of jobs (thousands) per million dollars of final purchases. Multipliers are for education. Employment multiplier = 0.021; output multiplier = 0.73.

GDP Impact Estimates, Accounting for Product Substitution Effects

In this section we calculate the effects of product substitution on estimates of GDP impact. As noted in the previous section, we use three "reasonable" assumptions: 5%, 10%, and 50% substitution, with the latter probably excessively conservative. The results are shown below in Tables 6 and 7, with Table 6 calculated with a conservative 5% royalty rate assumed, and Table 7 with a 2% assumption. Under a conservative royalty rate assumption, 5%, the estimated total change in GDP over the 12 year period ranges from $41.1 billion to $78.1 billion, depending upon the substitution rate assumed. Using a 2% royalty rate assumption, the estimated total change in GDP ranges from $93.3 billion to $177.2 billion. We do not show the similar calculations for contribution to changes in total industry output or employment under these different assumptions, but of course the results are proportionately similar.

Table 6: Total Estimated Change in GDP Due to University-Licensed Products, 1996-2009, Basic Model Assuming 5% Royalty Rates and Three Alternative Product Substitution Rates

	total change in GDP (5% royalty rate)	total change in GDP, 5% substitution	total change in GDP, 10% substitution	total change in GDP, 50% substitution
Year		millions		
1996	$2,559	$2,431	$2,303	$1,280
1997	$2,931	$2,784	$2,638	$1,465
1998	$3,753	$3,565	$3,378	$1,877
1999	$4,468	$4,245	$4,022	$2,234
2000	$5,563	$5,285	$5,007	$2,782
2001	$5,899	$5,604	$5,309	$2,949
2002	$7,447	$7,075	$6,702	$3,724
2003	$7,637	$7,255	$6,873	$3,818
2004	$7,637	$7,255	$6,873	$3,818
2005	$8,373	$7,954	$7,536	$4,187
2006	$9,169	$8,710	$8,252	$4,584
2007	$16,759	$15,921	$15,083	$8,380
Total	**$82,195**	**$78,085**	**$73,976**	**$41,098**

Note: 0.3774 value added ratio from 2005 I-O table for manufacturing

Table 7: Total Estimated Change in GDP Due to University-Licensed Products, 1996-2009, Basic Model Assuming 2% Royalty Rates and Three Alternative Product Substitution Rates

Year	total change in GDP (2% royalty rate)	total change in GDP, 5% substitution	total change in GDP, 10% substitution	total change in GDP, 50% substitution
	millions			
1996	$5,851	$5,558	$5,266	$2,925
1997	$6,603	$6,273	$5,942	$3,301
1998	$8,462	$8,039	$7,616	$4,231
1999	$10,158	$9,650	$9,142	$5,079
2000	$12,258	$11,646	$11,033	$6,129
2001	$13,444	$12,772	$12,099	$6,722
2002	$17,121	$16,265	$15,409	$8,561
2003	$17,541	$16,664	$15,787	$8,771
2004	$17,460	$16,587	$15,714	$8,730
2005	$18,270	$17,357	$16,443	$9,135
2006	$20,654	$19,621	$18,589	$10,327
2007	$38,750	$36,813	$34,875	$19,375
Total	**$186,572**	**$177,244**	**$167,915**	**$93,286**

Summary and Discussion

University research and research-related activities contribute in many important ways to the national economy, notably through increased productivity of applied R&D in industry due to university-developed new knowledge and technical know-how, provision of highly valued human capital embodied in faculty and students, development of equipment and instrumentation used by industry in production and research, and creation of concepts and prototypes for new products and processes. These benefits are enabled primarily through publications, conferences, information exchange via consulting and collaborative research, and hiring of trained students. This report documents the economic impact of just one of these research-related activities, licensing of university intellectual property, clearly an impact of major significance for the economy but by no means the largest source of the total impact of university research.

Although some are inclined to consider the "entrepreneurial university" as a relatively sudden, almost discontinuous feature of recent academic life, in fact the economic significance of universities has been recognized since the late 19th century; only the relative importance and sheer size of the various outputs listed above have changed. One especially obvious change is evidenced by the trends in university patenting and licensing of intellectual property, which began in the 1920s but accelerated dramatically in the last twenty-five years. In the 1970s most large, research-intensive universities took steps to manage their intellectual property internally rather than contract it out, so that now university offices of technology transfer are a common feature of university administrative structures. Although there is widespread agreement that university licensing of intellectual property has considerable economic significance, there is very little published, well-documented empirical evidence of its actual impact.

Our review of the literature found few examples of studies that sought to estimate the impact of university research on the U.S. national economy. However, a Canadian study used input-output modeling to estimate that an annual investment (1994-5) of $4.8 billion in university research added $1.5 billion to Canada's GDP and created 13,000 jobs. Accounting for the effects of university research over the long-term using total factor productivity methods yielded a total contribution to GDP of $15.5 billion. Most U.S. studies do not single out the impact of university research, but rather estimate the regional economic impact of all university activities, treating them primarily as sources of additional expenditures in the region. Some studies identify separately the (relatively modest) impact of university-based start-ups on the regional economy and employment. A typical example of the former is a study of the impact of Cornell University on the state of New York for the academic year 2004-5. The results were an

estimated impact of $3.3 billion in additional economic activity in the state, a direct or indirect impact of 36,000 jobs, and $173 million in state and local tax revenues. As an example of the latter, a University of Washington study cited data on the impact of university-related start-ups for 2000; it reported a cumulative figure of 150 start-ups, 7100 jobs created, generation of $1.5 billion in sales revenues, and $25 billion in stock market capitalization.

In one of the rare studies that focused on the economic impact of university licensing, staff of the MIT licensing office surveyed a sample of MIT licensees in 1993 to obtain information on pre-production investment and jobs created. Projecting their results to the entire MIT portfolio, they estimated an induced investment of $922 million and an employment impact of about 2,300 FTEs. They then used AUTM data to project their results to the national level using two methods. One method resulted in a national impact estimate of $2.5 billion in pre-production investment; the second resulted in an estimate of $5 billion. These investment levels were estimated to contribute employment gains of between 20,000 and 40,000.

An AUTM internal study conducted in 1993 used an approach similar to ours in that it resulted in an estimated $17 billion in product sales attributable to university-based licenses, with a related estimate of 137,000 jobs "supported." AUTM used the same approach in 2002 with 2000 data. They assumed a range of 2-4% royalty rates and calculated estimates of sales increases of between $17 billion and 35 billion, 125,000-250,000 jobs supported, and tax payments of $2.5-5 billion. These AUTM calculations did not employ standard measures of economic performance such as value added or GDP (sales revenue estimates alone include purchases of intermediate inputs used to produce the outputs). Nor did they apply I-O employment output multipliers to data on total industry output estimates generated by licensing income, instead apparently estimating employment impact by calculating the number of jobs that could be supported (loaded average salary) by the total sales revenues generated by products based in university licenses.

Our approach to estimating the impact of university licensing employs a number of features that we believe provide considerably more valid and complete estimates of national economic impact, while at the same time incorporating many assumptions that lead to very conservative results. As far as the validity of our estimates is concerned, our approach employs a national input-output model that accounts for the fact that sales revenue estimates do not themselves represent economic impact. As noted above, sales revenue estimates, however generated, include the industry purchases of intermediate inputs; and they do not account for the expenditures of those revenues for multiple purposes before having a final impact on value added or GDP. Furthermore, our approach accounts for the fact that university expenditures of their licensing income has significant direct and induced economic impact and thus should be included in any national (or, for that matter, regional) impact estimates. Finally, although we

were unable to obtain consistent data on university income from license-related R&D contracts, these too add to the total university economic impact of licensing.

We have been very careful to employ conservative assumptions at all points requiring that some judgments be made. First, we used ranges rather than average or median values for key parameters for which there are no reliable data, or for which the distribution of data within the range are unknown but almost certainly skewed. Second, we provided a means for accounting for product substitution effects using a wide range of reasonable rates. Finally, we have made the model and calculations as simple and transparent as possible, so that anyone with a spreadsheet can take our model and the data and enter their own set of assumptions. This seems to be the most appropriate way to generate estimates, since choice of the assumptions should be up to the user.

There are a number of refinements and next steps that would further enhance these estimates. They depend largely on access to data that either do not now exist or are not publicly available. Probably the most important step would be to obtain detailed, representative data on the licensing portfolios of U.S. universities. This would enable more accurate assumptions to be made about the range of royalty rates to enter into the model, thereby reducing the wide range of impact estimates generated. Second, we know that impact estimates will vary by economic sector, so that as sectoral breakdown data become available, even using very broad categories, they can be introduced into the model to generate sector-specific impacts. Ideally, sectoral breakdowns are desirable for ranges of royalty rates charged and for total licensing income and running royalties. Then, I-O output and employment multipliers can be adjusted to reflect more accurately the contribution of industries involved. Third, more complete and internally consistent annual data on the contract R&D income generated by university licenses would be highly desirable and could easily be entered into the calculations called for in our model.

Although somewhat outside the scope of our effort, models similar to ours could be constructed for estimating the national economic impact of pre-production investments in university-licensed technology. This would require sizeable effort and expense, given that the data must be acquired at individual universities, but it may be feasible to develop a representative sample of universities and follow the Pressman, et al. approach, combined with our approach to estimating impact on GDP and employment, to generate national economic impact estimates of pre-production investments. Adding these results to ours would yield even more accurate estimates of university licensing's important contribution to the national economy. Additionally, in the absence of detailed data on which licenses are exclusive vs. nonexclusive, we could not account for the fact that in some cases (e.g. nonexclusive licenses) the university IP may not be fully responsible for the new product and its sales. Of course, additional research on the economic impact of other manifestations of the value of university

IP, notably start-ups and the taking of equity positions, would further expand our knowledge of the economic impact of university research and licensing. Finally, it should be noted that our model can be used to estimate the regional economic impact of single universities by employing a regional input-output model and the university's own data on licensing income and range of royalty rates. Since individual universities have a much better idea of the range of royalty rates they use and the distribution of licenses by industry, they can generate a narrower range of impact estimates than we have been able to do with national data and widely ranging assumptions concerning royalty rates.

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Appendix A

Empirical Evidence of the Economic Impact of University Research and Licensing: an Overview of the Literature

An interesting and, possibly, unique study of the *national* economic impact of university research was done by Canadian researchers and applied to their own country (Martin, 1998; Martin and Trudeau, 1998). Martin and Trudeau first estimated the gross static impact of university research spending using a standard input-output model. The results showed that an annual investment of $4.8 billion in university research (AY 1994-95) "sustained" $5 billion in GDP and supported 81,000 full-time jobs. The authors note that this procedure overestimates the impact because it does not take into account the alternative use of resources. When sources of overestimation were eliminated, the net addition to GDP was $1.5 billion and 13,000 jobs in 1994-95. Martin and Trudeau then point out that input-output models treat all expenditures as having equal impact on the economy—a sports stadium would produce the same static impact as would equal expenditures on genetics or new materials research. But research results--new knowledge--affect industrial productivity over the long term. Accounting for the effects of university research on total factor productivity yielded a total net contribution of university R&D to Canadian GDP of $15.5 billion, corresponding to 150,000 to 200,000 jobs.[10]

Drucker and Goldstein (2007) identify and review four methodological approaches to investigating the impacts of universities on regional economies: single-university impact studies, surveys, knowledge-production functions, and cross-sectional and quasi-experimental designs. They conclude that "the majority of empirical analyses do demonstrate that the impacts of university activities on regional economic development are considerable" (p. 40). A typical example of a single-university impact study is the report on the economic impact of research at the University of Connecticut conducted by the Connecticut Center for Economic Analysis (2005). Using a standard approach to estimating regional impact (input-output modeling and research-related output counts), about $188 million in external funding flowed into UConn programs in FY 2003. Through multiplier effects, expenditure of these funds for salaries and equipment created 5,113 jobs, added $397 million in new Gross State Product, and generated $283 million in new personal income in the long run. In addition, spin-off firms created about 150 new jobs.

[10] Martin and Trudeau simply divided $15.5 billion by a range of average loaded salary figures to obtain these "supported" employment estimates. They do not represent an estimate of actual employment increase.

Using a similar approach, Appleseed, Inc., studied the economic impact of Cornell University on the state of New York (Appleseed, 2007), reporting that the university's direct and indirect expenditures during the academic year 2004-5 generated more than $3.3 billion in economic activity in the state, directly or indirectly accounted for 36,000 jobs, and generated $173 million in state and local tax revenues. In addition, research activity led to creation of 28 spin-off companies. Appleseed (which specializes in these kinds of studies) was commissioned by eight major research universities in the Boston area to estimate their collective impact on the regional economy. Expenditures of $3.9 billion had a collective regional economic impact of more than $7 billion in 2000. The institutions employed nearly 49,000 people, and their spending supported an additional 37,000 jobs. The eight universities assisted in the start-up of 41 new companies and granted 280 licenses to private ventures; licensing of technologies by these eight universities in 2000 generated $44.5 million in income. Focusing on the economic impact of university-related start-up companies alone, a University of Washington report cited data from the year 2000 for a cumulative 150 start-ups: 7100 direct jobs created, $1.5 billion in sales revenues, and $25 billion in stock market capitalization (U. of Washington, nd).

A shortcoming of these kinds of impact studies is that universities are, for impact estimate purposes, treated no differently than any organization that generates expenditures in the regional economy. The unique roles of universities in creating new knowledge and human capital are largely ignored, yet it is just these research-related activities and outputs that are of interest to us in this report. The problem is that converting the value of these outputs into monetized form is difficult, at best. Still, it is essential to acknowledge explicitly the enormous value to the economy of university research and human capital outputs in order to provide the appropriate context for our own impact estimates of university licensing is to be presented. Indeed, the economic impact of all university knowledge and technology transfer activities is considerably larger than the impact of licensed intellectual property alone.

Licensing income to universities based on ownership of intellectual property is, of course, an obvious indicator of the economic value of university research. Patent income to U.S. universities grew from about $200 million in 1991 to over $1.2 billion in 2000 (Graff, et al., 2002). However, it is important to re-emphasize a point made earlier, namely that patenting and licensing is just one channel through which research knowledge is transferred to industry, and likely not among the most important ones. The Carnegie Mellon survey of industrial lab managers referred to above (Cohen, et al., 1998) showed that only 10 percent of those responding said that licensing agreements with universities were "moderately" or "very" important to their R&D activities; more important were publications, informal channels, public meetings and conferences, consulting, and contract research.

In a rare effort to estimate the economic impact of university *licensing*, Pressman and her colleagues (Pressman, et al., 1995) at the MIT Technology Licensing Office surveyed a sample of MIT licensees to obtain information on pre-production investment and jobs created, as a complement to prior estimates of post-production economic impacts by AUTM staff of product sales and jobs created based on 1993 data from the AUTM survey on royalty income.[11] The authors defined pre-production investment as "Money spent developing new products and efficient ways to produce and market these products. It excludes the costs of producing (or investment required to produce) mature products" (p. 30). The information collected from licensees pertained to a sample of MIT's 1993 portfolio of 205 active, exclusive licenses—18 in the physical sciences and 19 in the biotech sample. The total self-reported investment by the sample licensees was $205 million, and the total number of full time equivalents (FTEs) generated was 470. The authors then extrapolated the sample results to the entire portfolio, yielding an induced investment estimate of $922 million and employment estimate of about 2,300 FTEs. The authors then went one step further and extrapolated from the MIT license data to university licenses as a whole, using AUTM data. They used two methods: one based on the MIT results of induced investment per license per year, and a second based on induced investment compared with licensing revenue to the university. This first method yielded an estimate of $2.5 billion for pre-production investment associated with all university licenses per year. The second method yielded an estimate to total induced investment nationally of $5 billion in 1993. These investment levels were, in turn, estimated to contribute 20,000 to 40,000 jobs to the national economy—before sales of licensed products.

In a confirmatory study to the MIT effort published in 1997, counterparts to the MIT TLO staff at the University of Pennsylvania's Center for Technology Transfer used the same approach to estimate the induced investments and jobs produced by exclusive patent licenses. The Penn portfolio consisted of 43 exclusive, active, patent licenses generated $151 million in induced investments and created 242 full-time jobs. Their extrapolation to all universities using 1995 AUTM data yielded a national estimate of induced investments of $4.6 billion and 27,000 jobs created (Kramer, et al., 1997).

The 1993 AUTM estimate of the post-production economic impact of university licensing cited above appears to employ an approach that includes elements of the one we developed for this study. Although details of the method are not published, evidently AUTM used estimates of average royalty rates for 1993 to estimate product sales for that year generated from AUTM data on licensing revenues received by member organizations. To estimate the number of jobs

[11] The post-production study referred to in Pressman, et al., 1995 has not been published. The results yielded estimates of $17 billion in new product sales and 137,000 jobs in 1993. This study used royalty rate data to estimate new product sales attributable to university-based licensing, and in that respect used a portion of the approach we describe in this report.

supported (not created) by these additional sales, they used Census data on total industrial research expenditures and engineers employed doing R&D to obtain an average figure for the loaded cost of an R&D engineer. Then the ratio of sales to average loaded salary of an R&D engineer produced a figure for jobs supported by those sales. In a 2002 presentation made at the annual meeting of the National Association of State Universities and Land Grant Colleges, Lori Pressman (2002) provided more recent estimates using this method for licensing impact "guesstimates" for the year 2000. Using an average royalty rate of 2% yielded pre-production impacts of about $5 billion and product sales of about $35 billion, 250,000 jobs supported, and tax payments of about $5 billion. Use of a 4% average royalty rate yielded impact estimates of about half these amounts.

The National Science Board's *Science and Engineering Indicator* report series has traditionally incorporated indicators of academic outputs and impacts—including numbers of science and engineering (S&E) students graduated at various levels, trends in S&E literature, and patenting and licensing activities of universities. The following Appendix Table A-1 provides some of the patenting and licensing activity data presented in *Science and Engineering Indicators 2008*.

Appendix table A-1

Academic patenting and licensing activities: 1991–2005

Activity indicator	1991 (98)	1992 (98)	1993 (117)	1994 (120)	1995 (127)	1996 (131)	1997 (132)	1998 (132)	1999 (139)	2000 (142)	2001 (139)	2002 (156)	2003 (165)	2004 (164)	2005 (158)
								Millions of dollars							
Net royalties[a]	NA	NA	195.0	217.4	239.1	290.1	391.1	517.3	583.0	1,012.0	753.9	868.9	866.8	924.8	1,588.1
Gross royalties[a]	130.0	172.4	242.3	265.9	299.1	365.2	482.8	613.6	675.5	1,108.9	868.3	997.8	1,033.6	1,088.4	1,775.0
Royalties paid to others	NA	NA	19.5	20.8	25.6	28.6	36.2	36.7	34.5	32.7	41.0	38.8	65.5	54.4	67.8
Unreimbursed legal fees expended	19.3	22.2	27.8	27.7	34.4	46.5	55.5	59.6	58.0	64.2	73.4	90.1	101.3	109.2	119.1
								Number							
Invention disclosures received	4,880	5,700	6,598	6,697	7,427	8,119	9,051	9,555	10,052	10,802	11,259	12,638	13,718	15,002	15,371
New U.S. patent applications filed	1,335	1,608	1,993	2,015	2,373	2,734	3,644	4,140	4,871	5,623	5,784	6,509	7,203	9,462	9,306
U.S. patents granted	NA	NA	1,307	1,596	1,550	1,776	2,239	2,681	3,079	3,272	3,179	3,109	3,450	3,268	2,944
Startup companies formed	NA	NA	NA	175	169	184	258	279	275	368	402	364	348	425	418
Revenue-generating licenses/options	2,210	2,809	3,413	3,560	4,272	4,958	5,659	6,006	6,663	7,562	7,715	8,490	8,976	9,543	10,251
New licenses/options executed[b]	1,079	1,461	1,737	2,049	2,142	2,209	2,707	3,078	3,295	3,569	3,300	3,660	3,855	4,087	4,201
Equity licenses/options	NA	NA	NA	NA	99	113	203	210	181	296	328	373	316	318	278

NA = not available

[a]One-year spikes in royalty data reflect extraordinary one-time payments.

[b]Data prior to 2004 may not be comparable with data for 2004 and beyond due to change in survey wording.

NOTES: Number of institutions reporting given in parentheses. Data from nonuniversity hospitals and medical institutes not included.

SOURCE: Association of University Technology Managers, AUTM Licensing Survey (various years) and *Science and Engineering Indicators 2008*

Appendix B

The Bureau of Economic Analysis National Input-Output Model: a Brief Description

The national I-O model allows users to assess the impact of specified events on economic activity. There are two broad applications of the basic model. The first is the economic accounting model and the other is the analytical model. The accounting model provides a framework for examining the relationship between final purchases (equivalent to gross domestic product, or GDP) and industry gross output. It shows the relationship between the producing sectors, final demand, and income by industry. It also shows industry purchases of goods and services that are used as inputs to produce goods and services commodities. These commodities in turn are inputs for other industries, or are purchases by final users.[12] As employed in this study, the accounting model is used to estimate the impact of university licensing on GDP.

The easiest way to see how the model can be used to analyze this impact is first to look at what national economic accountants call the "Input-Output Table" (Table B-1). The main section of this table, section F, illustrates the commodities (goods and services) that are used by industries in the economy.

Table B-1.—Sample Input-Output Table

	Industries	Final Uses	Total Output
Industries	F	Y	X
Value Added	V		
Total Output	X		

Gross output (sections X), the principal I-O measure of output, includes the value of what is produced and subsequently used by other industries in their production processes (intermediate products or inputs), as well as the value of what is produced and sold to final users (i.e., final products). Gross output is sometimes referred to as "gross duplicated domestic output," because it counts both the industry output that is recorded as final product and the

[12] See Horowitz and Planting, 2006, and www.bea.gov, Industry Accounts.

industry output that is purchased by other industries for use as inputs to their production processes.

Industry "value added" (section V) is defined as the value of an industry's sales to other industries and to final users minus the value of its purchases to produce its output (section F); its purchases from other industries are called intermediate inputs in the accounts. Value added is a non-duplicative measure of production that, when aggregated across all industries, equals the gross domestic product (GDP) for the economy. This measure for industries can be seen in section V of Table B-1. Value added is the sum of: compensation of employees, taxes on production and imports, less subsidies, and gross operating surplus (or more commonly known as profits). Value added or GDP excludes intermediate purchases. Another way to measure GDP is to sum all final uses, represented in section Y of Table B-1. This sum includes: personal consumption expenditures; private fixed investment; changes in inventories; exports of goods and services; imports of goods and services; and government consumption expenditures and gross investment. The sum of the final uses equals the sum of all industries' value added.

The second application of the I-O framework is an analytical model that is derived from the accounting model. It is used to show the relationship between final demand and industry production. Industry production is usually measured in terms of gross output, income, or employment. The model may be used to evaluate the interrelationships among industries and the relationships between industries and the commodities they use and produce. The analytical model is derived from the input-output table, usually referred to as the total requirements tables; a brief description of the calculation of the total requirements is shown in Table B-2. The input-output requirements tables are analytical tables designed to show the level of industry gross output or employment required to produce a specified level of final uses.

Table B-2. Derivation of the Total Requirements Multipliers

Step	
Definitions	• X -- column in I-O matrix representing industry gross output • Y – column in I-O matrix representing final uses of industry output • F – Intermediate portion of the use table (inputs to industries) • A – matrix of industry inputs as a portion of total industry output (direct requirements matrix)
Direct requirements	$A = Fx^{-1}$ where x is a matrix with gross output on the main diagonal of the matrix.
Total requirements	$X – AX = Y$ $(I-A)X = Y$ $X = (I-A)^{-1} Y$

EXHIBIT 6

POLICY FORUM

SCIENCE AND LAW

View from the Bench: Patents and Material Transfers

John P. Walsh,[1,2]* Charlene Cho,[1] Wesley M. Cohen[3]

Scholars have argued that the growing number of patents on research inputs may now impede upstream, noncommercial research by creating an "anticommons" in which rights holders may impose excessive transaction costs or make the acquisition of licenses and other rights too burdensome to permit the pursuit of scientifically and socially worthwhile research (*1*, *2*). Alternatively, owners of the rights over key upstream discoveries may restrict follow-on research through the exercise of exclusivity (*3*, *4*). The prospect of financial gain from upstream research has raised the further concern that academics are becoming more reluctant to share information, findings, or research materials (*5*, *6*). In 2003, a small-sample interview study suggested that, despite numerous patents on upstream discoveries, academic researchers have accessed knowledge without the anticipated frictions (*7*). Receiving material requested from other researchers could, however, prove problematic (*8*, *9*).

The *Madey* v. *Duke* decision of 2002 raised anew the question of the impact of research tool patents on biomedical research by clarifying that there was no general research exemption shielding academic researchers from infringement liability (*10*). This very visible decision and continuing concerns over the impact of research tool patents on academic science prompted our current study.

We report findings from a survey of 414 biomedical researchers in universities, government, and nonprofit institutions (*11*). In this group of academic, biomedical researchers, 19% currently receive industry funding for their research (representing 4% of their research budget); 22% applied for a patent in the past two years, with an average of 0.19 patent applications per year per respondent; 35% have some business activity [i.e., have participated in negotiations over rights to their inventions, have begun developing a business plan, had a startup, had a process or product in the market, or had licensing income].

LOGISTIC REGRESSION PREDICTING RECEIVING REQUESTED MATERIAL

Variable	Estimate
Scientific competition	–0.058 ± 0.029*
Academic supplier	0.007 ± 0.005
MTA	0.012 ± 0.004**
Patented	0.005 ± 0.007
Patent status unknown	–0.004 ± 0.004
Drug	–2.217 ± 0.683**

Values ± SEM. *$P < 0.05$; **$P < 0.01$.

Although common, patents in this field are not typically used to restrict access to the knowledge that biomedical scientists require. To begin with, few academic bench scientists currently pay much attention to others' patents. Only 5% (18 out of 379) regularly check for patents on knowledge inputs related to their research. Only 2% (i.e., 8) have begun checking for patents in the 2 years since *Madey* v. *Duke*, which suggests little impact of the decision. Five percent had been made aware of intellectual property (IP) relevant to their research through a notification letter sent either to them or their institution, which differs little from the 3% who reported having received such notification 5 years ago (prior to the *Madey* v. *Duke* decision). Furthermore, although 22% of respondents report being notified by their institutions to respect patent rights (versus 15%, 5 years ago), such notification did not appreciably affect the likelihood of checking for patents—5.9% of those receiving such instruction checked for patents versus 4.5% of those not receiving instruction.

Only 32 out of 381 respondents (8%) believed they conducted research in the prior 2 years using information or knowledge covered by someone else's patent. However, even for the few who were aware of others' patents, those third-party patents did not have a large impact on their research. Of the 32 respondents who were aware of relevant IP, four reported changing their research approach and five delayed completion of an experiment by more than 1 month. No one reported abandoning a line of research. Thus, of 381 academic scientists, even including the 10% who claimed to be doing drug development or related downstream work, none were stopped by the existence of third-party patents, and even modifications or delays were rare, each affecting around 1% of our sample. In addition, 22 of the 23 respondents to our question about costs reported that there was no fee for the patented technology, and the 23rd respondent said the fee was in the range of $1 to $100. Thus, for the time being, access to patents on knowledge inputs rarely imposes a significant burden on academic biomedical research.

Our research thus suggests that "law on the books" need not be the same as "law in action" if the law on the books contravenes a community's norms and interests (*9*, *12*). Although the new survey did not explicitly ask respondents their opinions about a research exemption, our results suggest that infringement remains of only slight concern. In contrast, research on clinical diagnostic testing (*13*, *14*) suggests that when the research is itself also a commercial activity, patent holders are more likely to assert and clinical researchers more likely to abandon infringing activities.

In addition to examining access to others' intellectual property, we consider the extent to which scientists can access the tangible research materials and data created by other labs, highlighted as another source of friction that may be impeding biomedical innovation (*5*, *8*, *15*). Indeed, concerns about increasing noncompliance with material transfer requests have prompted the National Institutes of Health to issue guidelines designed to encourage the exchange of materials created with federal funding (*16*).

About 75% of our academic respondents made at least one request for a material in the past 2 years. On average, academics made about seven requests for materials to other academics and two requests to industry labs in the past 2 years. However, 19% of our respondents report that their most recent request for a material was denied (*17*). Moreover, noncompliance with such requests appears to be growing (see supporting online text). Campbell and colleagues (*5*) reported that, among genomics researchers, about 10% of requests were denied in the 3 years, 1997–99. For the

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genomics researchers in our sample, the denial rate for 2003–04 was 18% (95% confidence interval, ±3.7%).

Over a 1-year period, an average of one in six respondents reported that delays in receiving materials from other academics caused at least one project they were working on to suffer a greater than 1-month delay, a substantial delay in a fast-moving research field. Noncompliance by other academics with research input requests resulted in about 1 in 14 scientists abandoning at least one of their projects each year.

We conducted two regression analyses to probe the reasons for noncompliance (see supporting online text). The first examined whether the respondent's most recent request was satisfied (see table, p. 2002). Statistically significant predictors of noncompliance included a measure of scientific competition (i.e., the number of competing labs) and whether the requested material was itself a drug. The patent status of the requested material had no significant effect on noncompliance. A second analysis with other variables—particularly characteristics of the prospective supplier—examined predictors of the number of times the respondent failed to comply with requests (see table, this page). Here, the burden of compliance (i.e., number of requests per dollar of funding); scientific competition; and commercial orientation (i.e., whether the respondent has engaged in any of the business activities listed above) increase the likelihood of noncompliance. Finally, the number of respondent publications, indicative of respondent eminence or the opportunity cost of responding, also increases the likelihood of noncompliance.

In addition to these regressions, we also asked respondents directly why they denied requests. The major self-reported reasons for noncompliance included the cost and/or effort involved and protecting the ability to publish, with commercial incentives much less prominent (*5*, *18*). We find, however, the multivariate regression analysis to be more credible than the self-reported relationships for the following reasons: (i) it uses a more objective measure of commercial orientation, while controlling for the effects of other variables and (ii) it is less likely to be influenced by a "socially desirable response bias" that leads academics to subordinate less socially desirable incentives (e.g., commerce) compared with more desirable ones (e.g., intellectual challenge) (*19*).

We also considered costs and burdens associated with material transfer agreements (MTAs). Only 42% of requests required an MTA, and only 11% of requests for research inputs led to an MTA negotiation lasting more than 1 month. Moreover, in almost all cases, there was no immediate fee for the requested material. However, for 8% of research input requests, negotiating the MTA stopped the research for more than 1 month. Although MTAs do not commonly entail delays or impose fees, they frequently come with conditions. MTAs, especially from industry suppliers, often include demands for reach-through rights of some form. Of executed MTAs, 29% had reach-through claims, and 16% provided for royalties. Twenty-six percent of MTAs imposed publication restrictions. Requests for drugs were the most likely to yield such a restriction, with 70% of such agreements including some restriction on publication of the research results using the transferred drug.

As a case study, we also collected data from an additional 93 academic scientists who are conducting research on one of three signaling proteins (CTLA-4, EGF, and NF-κB) that are patent-intensive research areas with enormous commercial interest, involving large pharmaceutical firms, small biotechnology firms, and universities. These are the very conditions where issues of access to IP should be evident. Although the incidence of adverse consequences due to restricted access to IP was more manifest here than in the random sample, it was still infrequent (only 3% of respondents reported stopping a project in the past 2 years because of a patent). On the other hand, access to materials was even more problematic in these areas than in the random sample (*18*). For example, 30% of researchers in these fields did not receive their last requested material.

Our results offer little empirical basis for claims that restricted access to IP is currently impeding biomedical research, but there is evidence that access to material research inputs is restricted more often, and individual research projects can suffer as a consequence. To the extent that any redirection of a scientist's research effort or reallocation across investigators because of denied access impedes scientific progress, this is cause for concern. In contrast, if such redirection reduces duplicative research or increases the variety of projects pursued, social welfare may even increase (*20*, *21*). In addition, it is not clear whether patent policy contributes to restricted access to materials, although the commercial activities fostered by patent policy do seem to restrict sharing, as do the burden of producing the materials and scientific competition.

Scientific progress in biomedicine may be well served by a study of the welfare impacts of restrictions on material transfers, and, if warranted, greater diligence in the monitoring and enforcement of the applicable NIH guidelines.

NEGATIVE BINOMIAL REGRESSION PREDICTING NUMBER OF REFUSALS TO SEND REQUESTED MATERIAL

Variable	Estimate
Commercial orientation	0.010 ± 0.004*
Scientific competition	0.078 ± 0.040*
Publications	0.075 ± 0.037*
Request burden	0.038 ± 0.019*
Budget	0.008 ± 0.042
Industry funding	0.006 ± 0.005
Drug discovery	0.000 ± 0.007
Male	–0.008 ± 0.004†

Values ± SEM. *$P < 0.05$; †$P < 0.10$.

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EXHIBIT 7

BNA's Patent, Trademark & Copyright Journal®

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PATENTS

Contrary to claims by its critics, the Bayh-Dole Act of 1980 continues to provide a superb framework for government-funded research to benefit Americans and improve the lives of citizens worldwide.

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The Bayh-Dole Act and Revisionism Redux

By Howard Bremer, Joseph Allen, and Norman J. Latker

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Summary

It is no secret that the U.S. economy faces serious challenges. However, the United States has tremendous advantages for succeeding in the technology markets creating wealth in the 21st century, if we choose to utilize them.

That choice lies with the policy makers and depends upon their recognizing the inherent strengths of the U.S. innovation system. This paper focuses on a key component of that innovation chain: the combination of our unparalleled research universities and the entrepreneurial spirit which drives the private sector functioning under the auspices of the Bayh-Dole Act of 1980. [1] That partnership has turned the results of publicly funded science into products, jobs, and companies benefiting U.S. taxpayers both economically and through an improved quality of life.

[1] University and Small Business Patent Procedure Act, P.L. 96-517, 1980 (commonly referenced as the Bayh-Dole Act or

While that linkage is generally believed to have been very successful, a persistent school of critics has charged that that is not the case. These advocates have become more vocal in recent years, urging policy makers to make changes in the Bayh-Dole Act to correct what they view as its shortcomings. Their arguments can be summarized as follows:

- The importance and influence of the Bayh-Dole Act is overrated, or at least unproven.
- Key data Congress used to pass the Bayh-Dole Act—the small number of 28,000 government owned patents that were licensed—was misleading.
- Bayh-Dole is not a model that should be adopted by developing countries because of its emphasis on patent ownership. Rather what should be adopted is the pre-Bayh-Dole model of technology dissemination stressing open access to scientific discoveries.

It is unfortunate that some policy makers appear to be accepting the critics' arguments at face value. However, it is important to note that these critics lack the perspective of the pre-Bayh-Dole era, and the difficulties encountered in turning government funded research into tangible commercial and social benefits for the taxpaying public.

Reversing that trend, the Bayh-Dole Act encouraged the private sector to invest billions of dollars to develop inventions made in whole or in part with government-supplied (i.e., taxpayer's) dollars to market-ready products. This partnership between research universities and the private sector created millions of jobs for Americans, significant wealth for the United States, and a higher standard of living, while helping to re-establish the United States as the technology innovation leader in a growing and increasingly competitive global economy.

Because the critics' recommended changes to Bayh-Dole would have a profound—and potentially very harmful—impact on the ability of the United States to respond to renewed international economic competition in the 21st century, any changes must be very carefully considered.

Therefore, it is our purpose to examine the levied charges against Bayh-Dole with the actual facts, and to set the record straight. Thus examined, the authors of this article firmly believe that the common revisionist arguments against Bayh-Dole are unfounded, finding a basis in anecdotal evidence or incorrect interpretations of data, where logical conclusions should have pointed in another direction.

Reams of objective data exist supporting the conclusion that the Bayh-Dole Act greatly improved the commercialization of federally-funded research, that the system is working very well, and that the public sector-private sector partnerships which were generated under the Act are essential both to the well being and the competitive position of the United States.

That these conclusions are correct is strongly reinforced by the fact that our most serious economic rivals have or are now adopting their own versions of Bayh-Dole to enable them to better compete with the United States. Such imitation is the most sincere form of economic flattery.

It would be ironic, indeed, if U.S. policy makers chose this critical moment to weaken the well-established U.S. innovation system which is the envy of the world. That viable and functioning system is needed more than ever at this critical time to maintain a prosperous U.S. economy in an increasingly high technology world. The choice is ours to make.

BACKGROUND

The United States, Europe, and Asia are gearing up for a new round of competition to create wealth from high technology industries driving the international economy. In many ways, this is a replay of the 1970s and 80s when it appeared that Japan and Germany were riding the wave of the future—and many predicted that America's best

days were behind it.

At that time, the United States had lost its lead in traditional fields like automotives, electronics, steel, etc. Many experts confidently predicted that Japan and Germany would soon eclipse the United States in the few remaining markets where it led.

However, these predictions did not come true. Instead, the United States enjoyed a tremendous burst of entrepreneurial activity that restored its competitive advantage and laid the groundwork for decades of economic growth. This turnaround came through the adoption of many new policies that were hotly debated at the time. One of those was the passage of the Bayh-Dole Act of 1980. Here's how the *Economist Technology Quarterly* [2] summarized its impact:

[2] "Innovation's Golden Goose," *The Economist Technology Quarterly* (editorial), Dec. 14, 2002.

> *Remember the technological malaise that befell America in the late 1970's? Japan was busy snuffing out Pittsburgh's steel mills, driving Detroit off the road, and beginning the assault on Silicon Valley. Only a decade later, things were very different. Japanese industry was in retreat. An exhausted Soviet Empire threw in the towel. Europe sat up and started investing heavily in America. Why the sudden reversal of fortunes? Across America, there had been a flowering of innovation unlike anything seen before.*
>
> *Possibly the most inspired piece of legislation to be enacted in America over the past half-century was the Bayh-Dole Act of 1980. Together with amendments in 1984 and augmentations in 1986, this unlocked all the inventions and discoveries that had been made in laboratories throughout the United States with the help of taxpayers' money.*
>
> *More than anything, this single policy helped to reverse America's precipitous slide into industrial irrelevance.*

Further on the article summarized the law:

> *The Bayh Dole Act did two big things at a stroke. It transferred ownership of an invention or discovery from the government agency that had helped to pay for it to the academic institution that had carried out the actual research. And it ensured that the researchers involved got a piece of the action.*
>
> *Overnight, universities across America became hotbeds of innovation, as entrepreneurial professors took their inventions (and graduate students) off campus to set up companies of their own. Since 1980, American universities have witnessed a tenfold increase in the patents they generate, spun off more than 2,200 firms to exploit research done in their labs, created 260,000 jobs in the process, and now contribute $40 billion annually to the U.S. economy. America's trading partners have been quick to follow suit. Odd then, that the Bayh-Dole act should now be under such attack in America.*

Federally Funded Inventions Not Commercialized.

Before examining the specific charges being used to attack the law, it is helpful to examine why Congress enacted the Bayh-Dole Act, and what it does.

Prior to 1980, inventions which resulted from research supported by federal funding were rarely developed into commercial products. Because most government-funded inventions derive from the conduct of basic research, they are at a very early stage in their development. Consequently, it requires substantial time and investment by the private sector to turn them into commercially useful products and processes.

It is frequently estimated that product development requires at least ten development dollars for every dollar spent in conducting the original research. Developing new drugs to market ready condition can cost between $800 million to $1.3 billion and consume more than a decade of time. Even with such a resource commitment, commercial success is far from a sure thing. Many more products fail in the marketplace than succeed. Without an ability to protect

such investments, commercial development is not possible.

Federal policies before 1980 mandated that any invention made with federal funding—whether made by employees, contractors or grantees—would be assigned to the government. They were then generally made available to all applicants through non-exclusive licenses. Thus, a company foolish enough to develop a federally- funded invention could not protect its investment in commercialization since competitors could gain equal access to the technology from the federal government with the additional knowledge that the invention was feasible and there was a market for it.

It became clear that such government policies rarely turned the results of government-funded research into commercially available goods. A series of presidential policy memoranda, dating back to the Kennedy administration, did allow contractors or grantees to petition funding agencies to acquire ownership of government-funded inventions they had made on a case-by-case basis. Decisions on such petitions by the various agencies could take 18 months or more and were generally negative. In the few situations when agencies did grant a petition, they usually also attached many restrictions on the use of the invention.

Not surprisingly, that general policy discouraged innovative small business firms from accepting federal research contracts because the inability to control resulting inventions undercut their capacity to compete in commercial markets. Additionally, federal agencies and their employees could not receive royalties if their discoveries were commercialized.

President Lincoln, himself a patent owner, envisioned the patent system as "adding the fuel of interest to the fires of genius." With regard to federally-funded research, it was evident that those fires were extinguished. This was no small loss because the federal government was funding the majority of basic research—precisely where breakthrough inventions were most likely to occur—and approximately 50 percent of all the research and development in the country at the time.

IPAs Point the Way to Bayh-Dole.

The National Institutes of Health finally recognized that this general policy was not effective in promoting technology transfer. It was apparent that few, if any, NIH funded discoveries were ever commercialized. Consequently, in the 1970s NIH adopted an administrative policy allowing universities with the proven capability to manage inventions, to own inventions made with NIH support. Termed the "Institutional Patent Agreement," this was the precursor to a revolution in federal patent policies. That program proved so successful that it was later adopted by the National Science Foundation.

However, the IPA program was undermined during the Carter administration when the secretary of Health and Human Welfare (now Health and Human Services) attempted to halt the program, and the department later even sought to fire its creator. This reversal prompted several leading universities to approach Sens. Birch Bayh (D-Ind.) and Robert Dole (R-Kan.) requesting that the IPA program be made statutory and binding on all federal agencies, and that it be extended to small business contractors.

One important piece of data examined by the Senate Judiciary Committee as it considered the bill was that the government was licensing less than five percent of the 28,000 patents on inventions that it had amassed. Universities and small companies presented compelling evidence that potentially important discoveries would never be developed as long as the government took them away from their creators. Thus, government policies destroyed the very incentives for development which the patent system was intended to foster. Bayh and Dole stated that such inefficiencies denied U.S. taxpayers the full benefits of their investment in publicly funded research.

Ownership, Licensing: Incentives to Innovation.

Congress agreed with the senators' conclusion and in 1980 overwhelmingly passed the Bayh-Dole Act. The statute encourages the development of inventions made by nonprofit organizations and small business

companies through the use of federal funds by:

- Allowing ownership of such inventions to reside in those entities;
- Providing universities the discretion to license their inventions and discoveries under terms that encourage prompt commercialization through university-industry partnerships;
- Stipulating that a percentage of royalties generated through successful commercialization efforts be shared with inventors. Royalties can also be used to pay for administrative costs associated with technology transfer, with the balance remaining designated to fund additional research, or for educational purposes;
- Providing that preferences be given to licensing small businesses and requiring substantial U.S. manufacturing where an exclusive license is granted for the United States;
- Allowing the government to practice the invention royalty free for governmental and treaty purposes; and
- Allowing the government to "march in" to require additional licensing if legitimate efforts were not being made by a licensee to develop the invention, or in situations where the licensee cannot produce sufficient quantities to meet a pressing national need (an action that has not been necessary in practice).

Congress, subsequent to the passage of the Bayh-Dole Act, created the U.S. Court of Appeals for the Federal Circuit, which has restored faith in that patent system and in the reliability of U.S. patents. Congress also enacted the Small Business Innovation Research Act [3] to bring more technologically cutting-edge companies into government research. The SBIR built upon the assurances of the Bayh-Dole Act that small companies would own inventions they made with federal funding.

[3] Small Business Innovation Development Act of 1982, Pub. L. 97-219, July 22, 1982, 96 Stat. 217.

Bayh-Dole brought into play important factors and resources which other nations simply could not match:

1. The U.S. government funds far more R&D than other national governments, much of which lies in basic research where breakthrough technologies are most likely to occur.
2. This research is largely conducted at universities and other nonprofit institutions that remain world leaders in their respective technological fields.
3. Bayh-Dole permitted translation of this investment in science into practical applications which met important health, safety, environmental, food production, and other critical needs.
4. The United States is the acknowledged leader in entrepreneurship and the forming of small, high-technology companies which take the lead in driving new markets. Many of these companies are spun out of universities because of Bayh-Dole.
5. A key asset of these small companies in attracting venture funding and competing in technology markets against larger companies are the patents they own or license. Those patents not only offer protection for their commercial position, but an opportunity to recoup and reward the business risks that have been assumed.
6. Thus, the U.S. patent system was a significant factor in spurring the revival of American competitiveness.

Skeptics Doubt Success of Reform.

Even though the impact of the Bayh-Dole Act seemed evident as the United States enjoyed the reversal of fortune described in the *Economist Technology Quarterly* editorial, a small group of academics began questioning it.

Their arguments can be summarized as follows:

- Bayh-Dole really wasn't that important. Universities were commercializing inventions anyway.
- Key data Congress used to pass the Bayh-Dole Act—the small number of 28,000 government owned patents that were licensed—was misleading.
- Bayh-Dole is not a model that should be adopted by developing countries because of its emphasis on patent ownership. Rather, what should be adopted is the pre-Bayh-Dole model of technology dissemination stressing open access to scientific discoveries.

In the next section the authors review each of those charges in greater detail and in the light of the admonition of Ralph Waldo Emerson: "Numbers serve to discipline rhetoric. Without them it is too easy to follow flights of fancy, to ignore the world as it is and to remold it nearer the heart's desire."

The Bayh-Dole Act and Revisionist Attacks

The Bayh Dole Act of 1980 is now almost 30 years old. There are not many pieces of legislation that have maintained their viability and significance in a rapidly changing environment for as long. However, it is being subjected to revisionist interpretations of its effects, benefits, and the fundamental needs which caused its inception, passage and implementation.

Representative of these viewpoints is a paper by Bhaven N. Sampat, [4] and later papers by critics such as Arti Rai and Robert Cook-Deegan, [5] as well as the writings of Rebecca Eisenberg. [6]

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[4] "Private Parts: Patents and Academic Research in the Twentieth Century," Bhaven N. Sampat, p. 32, available at http://www.card.iastate.edu/research/stp/papers/SAMPAT-Nov-03.pdf.

[5] *See e.g.*, A. So et al. "*Is Bayh-Dole Good for Developing Countries? Lessons from the Experience,*" PLoS Biology 6(10):e262. Oct. 28, 2008.

[6] Rebecca S. Eisenberg "Public Research and Private Development: Patents and Technology Transfer in Government Sponsored Research," 82 Va. L. Rev. 1663 (1996).

Sampat states:

> The political history of Bayh-Dole in Section 4 revealed that it was passed based on little solid evidence that the status quo ante resulted in low rates of commercialization of university inventions. More remarkably, the hearings completely ignored the possibility of potential negative effects of increased patenting and licensing on open science and on other channels of technology and knowledge transfer.
>
> Nevertheless, the discussion in Section 5 suggests that the net effects of Bayh-Dole (and the rise of university patenting and licensing activity more generally) on innovation, technology transfer, and economic growth remains unclear, and much more research is necessary on that front. As such, while current efforts to emulate Bayh-Dole type policies in other OECD countries (see OECD 2002) are misguided (or at least premature), we also do not have enough evidence to suggest that major changes to the Bayh-Dole act are necessary in the United States.

Tech Transfer Impact Questioned.

Thus, the fundamental premise is that the Bayh-Dole Act was not as influential in promoting the transfer of technology as has been credited to it, and it could be a serious mistake for other countries to emulate it.

The first part of the argument is based on assertions by Rebecca Eisenberg that experts at the time misunderstood why so few of the 28,000 government-managed patents were being utilized before Bayh-Dole. This failure

to commercialize the inventions represented by those patents was a key piece of evidence presented at the hearings on the bill. Supporters of Bayh-Dole said that it showed that the old patent policies (whereby government took inventions away from their creators—the government "title policy") were ineffective and detrimental to achieving subsequent commercialization.

David Mowrey et al. further postulate that: "The theory behind Bayh-Dole was that companies needed exclusive patent rights to develop and commercialize the results of university research." [7]

[7] David C. Mowery, et al. "The Growth of Patent and Licensing by U.S. Universities: An assessment of the Effects of the Bayh-Dole Act of 1980," 30 Res. Pol. 99, 117.

Actually, the driving force and theory behind Bayh-Dole was that the public was not reaping the full potential benefit from the taxpayer's support of basic research, with expenditures for such support amounting to billions of dollars each year. Passage of the Bayh-Dole Act represented the ultimate step in a long term effort toward reshaping government patent policy, and was Congress' response to the paramount question:

> In whose hands—the federal government or the inventing organization—is the ownership and management of federally-funded inventions best placed to promote the prompt development of important discoveries for the benefit of the U.S. taxpayer?

It is not denied that at about the same time the Bayh-Dole Act was passed, there was a confluence of forces which had an effect upon universities' technology-transfer efforts. However, we find the proposition advanced by the critics to be a flawed conclusion. The congressional intent for enacting the law is made abundantly clear in the provisions Bayh and Dole wrote in the legislation as the Policy and Objectives of the Act in 1980 (35 U.S.C. §200):

> *It is the policy and objective of the Congress to use the patent system to promote the utilization of inventions arising from federally supported research or development; to encourage maximum participation of small business firms in federally supported research and development efforts; to promote collaboration between commercial concerns and nonprofit organizations, including universities; to ensure that inventions made by nonprofit organizations and small business firms are used in a manner to promote free competition and enterprise, to promote the commercialization and public availability of inventions made in the United States by United States industry and labor; to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions; and to minimize the costs of administering policies in this area.*

That the effect of the act was so profound, beneficial, and far-reaching is because of several primary factors:

1. It established a uniform patent policy for all agencies of the federal government.

2. It changed the presumption of title to inventions made in whole or in part with federal monies from the government to universities, other nonprofit institutions and small business.

3. It established a certainty of title in such inventions which encouraged the private sector to engage in relationships with university and nonprofit research organizations leading to the development and commercial use of many inventions for the public benefit.

4. The protection offered by the chosen vehicle for technology-transfer—the U.S. patent system—provides needed incentives for the private sector to undertake the considerable risk and expense necessary to take early stage university discoveries from the laboratory to the marketplace. Strong patent protection is also vital to small businesses, which have obtained the vast majority of licenses from universities, so they can engage the venture capital community for needed funding—and for protection against the incursion of dominant companies in their markets.

Experience in the period before enactment of the Bayh-Dole Act clearly established that ownership and management by universities of their inventions was clearly a superior policy than what had preceded it. For example, there had been an utter failure to commercialize university inventions when the National Institutes of Health had retained all rights to inventions made in whole or in part with federal money and adopted a non-exclusive licensing stance for those inventions. As the Comptroller General of the United States later testified: [8]

[8] Testimony of Elmer B. Staats, Comptroller General of the United States, before the Senate Judiciary Committee on S. 414, the University and Small Business Patent Procedures Act, May 16, 1979, Report No. 96-11, p. 37.

> [*W]e reported that HEW was taking title for the Government to inventions resulting from research in medicinal chemistry. This was blocking development of these inventions and impeding cooperative efforts between universities and the commercial sector.*
>
> *We found that hundreds of new compounds developed at university laboratories had not been tested and screened by the pharmaceutical industry because manufacturers were unwilling to undertake the expense without some possibility of obtaining exclusive rights to further development of a promising product.*

IPAs Launched, Then Stalled.

Therefore, a revolutionary approach was announced. NIH established and adopted its IPA program allowing universities with established technology-transfer offices to own and manage inventions made with NIH funding. The program began at NIH in 1968 and was so successful that the National Science Foundation adopted it in 1973.

Here's how the Senate Judiciary Committee summarized the impact of the IPA program:

"Since instituting the I.P.A. program a number of potentially important new drugs initially funded under HEW research have been delivered to the public through the involvement of private industry in developing, testing, and marketing these discoveries. Prior to the I.P.A. program, however, *not one drug* had been developed and marketed from HEW research because of a lack of incentives to the private sector to commit the time and money needed to commercialize these discoveries." [9]

[9] University and Small Business Patent Procedures Act, Report of the Committee on the Judiciary, U.S. Senate, on S. 414, Dec. 12, 1979, Rep. No. 96-480, p. 21.

The program continued in achieving success, but during the Carter administration efforts were made to end it because of the personal philosophy of the new secretary of Health, Education and Welfare (the agency is now Health and Human Services). That philosophy, much like those of many of the current critics of the Bayh-Dole Act, called for a return to case-by-case determination by NIH of whether university inventions made with its funding should be retained by NIH, or the ownership transferred to the universities for management. The Comptroller General testified that such determinations were taking "from 8 to 15 months to complete." [10]

[10] Id. at 37.

It was this movement to end the most successful patent policy in any federal agency that led universities to approach Bayh and Dole, arguing that effective patent policies must have a legislative mandate so they could not be changed at the whim of a political appointee.

The potential to arbitrarily make changes in patent policies at the agency level, and the adherence to a non-exclusive licensing mandate established a lack of predictability unnerving and unacceptable to potential industrial partners. Companies simply would not expend the sizeable amounts of private sector time and money

needed to turn patented university based early-stage technologies into marketable products if the government could change the rules at a whim.

Shortly after introducing their bill, Bayh and Dole held a press conference using examples of potentially important medical discoveries that were being strangled in red tape because of NIH's weakening of the IPA program.

Dole compiled a list of "29 important medical discoveries that had been delayed from 9 months to well over a year before HEW were able to reach a determination whether or not the agency would retain patent rights. Follow-up review has shown no improvement in HEW's performance." [11]

[11] The GAO patent policy study presented to the Senate Judiciary Committee on May 16, 1979 also found that the Department of Energy frequently takes up to 15 month to process these patent ownership requests from its contractors.

As a result, a rapid succession of senators, from across the political spectrum began to sign on as co-sponsors of the proposed Bayh-Dole bill.

While the current critics acknowledge the connection between the IPA programs and the Bayh-Dole Act, the dramatic impact that they collectively had on the commercialization of university inventions tends to be downplayed. For example, Sampat et al. [12] state:

[12] Rep. No. 96-480 at 21.

"Bayh-Dole was passed in the throes of the 'competitiveness crisis' of the 1970's and 1980's in the belief that the requirement to obtain IPAs or waivers and the frequently inconsistent policies of federal funding agencies regarding these agreements (especially regarding exclusive licensing) impeded technology transfer and commercialization of federally funded research results. In particular, the framers of the legislation argued that if universities could not be granted clear title to patents that allowed them to license rights to patented inventions exclusively, firms would lack the incentive to develop and commercialize university inventions."

And then in a footnote, the authors add, "this argument was based on 'evidence' that government-owned patents had lower utilization rates than those held by contractors, evidence that Eisenberg (1996) has shown to be faulty….." [note: the Eisenberg evidence will be addressed later in this paper].

The authors do recognize the existence of the IPA program and some of those same authors in an earlier paper [13] more extensively acknowledge their awareness of that program. However, they tend to minimize the connection between the advent of the IPAs, and increasing university sector patenting and licensing when most of the predominant research universities were operating under such agreements.

[13] "Changes in University Patent Quality after the Bayh-Dole Act: a Re-Examination," Bhaven N. Sampat et al., 21 International Journal of Industrial Organization 1371 (2003).

Statistics Show IPAs Spurred Innovation.

Interestingly, in looking at the actual data, the increase in the filing of patent applications on the results of extramural research sponsored by HEW and NSF directly correlates with the increased participation in their IPA programs. [14] [15]

[14] Mowery, 30 Res. Pol. 99; *see also* S.414 Rep. No. 96-480.

[15] Government Patent Policy: Institutional Patent Agreements, Hearings before the Subcommittee on Monopoly and Anticompetitive Activities of the Select Committee on Small Business, U.S. Senate, 95th Congress, 2nd Session, Part I, May 22-23, June 20, 21, 26, 1978, pp. 147-50.

Here are the numbers for HEW (then the parent agency for NIH):

	1968	1969	1970	1971	1972	1973	1974	1975	1976
[16]IPA participants	17	24	34	39	41	50	57	61	66
[17]Patent applications by HEW contractors			35	51	50	44	76	79	118

[16] Federal Council for Science and Technology Report on Government Patent Policy, Combined Dec. 31, 1973 through Dec. 31, 1976, p. 424.

[17] See Note 14 supra.

Thus, patent applications increased over 300 percent between 1970 and 1976 at HEW as the IPA program expanded.

The numbers are even more striking for the National Science Foundation after it implemented the IPA program in 1973.

	1970	1971	1972	1973	1974	1975	1976
[18]IPA participants	N/A	N/A	N/A	N/A	11	11	13
[19]Patent applications by contractors	6	2	4	8	17	40	67

[18] Note 15, supra.

[19] Note 14, supra.

NSF had an 800 percent increase in patent applications between 1973-1976 as its IPA program kicked in.

These data substantiate a strong correlation between the incentives of patent ownership and management under the IPA program with the subsequent rise in patent applications on university inventions made with federal support. Since the IPA program was essentially later codified by the Bayh-Dole Act, it is only fair to credit these new approaches to federal patent policies with the increases in university patenting.

Yet the critics seem reluctant to clearly acknowledge this connection. Here's how they describe this phenomenon: [20]

[20] University Patents and Patent Policy Debates in the USA, 1925-1980, Industrial and Corporate Change. Vol. 10, Number 3, 2001.

"... Figure 9 shows that institutions with IPAs dominated the growth of university patenting during the 1970's.

Nonetheless, although IPAs may have encouraged entry by lowering the costs of patenting and licensing, fewer than half of entrant institutions had IPAs. Moreover, Figure 10 shows that patenting during the 1970s grew for entrants with IPAs and entrants without IPAs. The diffusion of IPAs alone does not explain entry by universities into patenting.

Analysis of the contributions to entry of these various factors—increased inter-institutional dispersion of federal research funding, the growth of IPAs, the rising costs and inefficiencies in Research Corporation's 'central broker' model, and reduced aversion to university patenting generally and in biomedical technologies in particular—remains an important task for future research. All of these factors appear to have influenced growth in university patenting in the 1970s. Interestingly, only one of these factors (the IPAs) represented a change in federal policy toward the patenting of publicly funded research. It is likely that a similar diverse range of factors, and not the Bayh-Dole Act alone, underpinned the continued growth of U.S. university patenting after 1980."

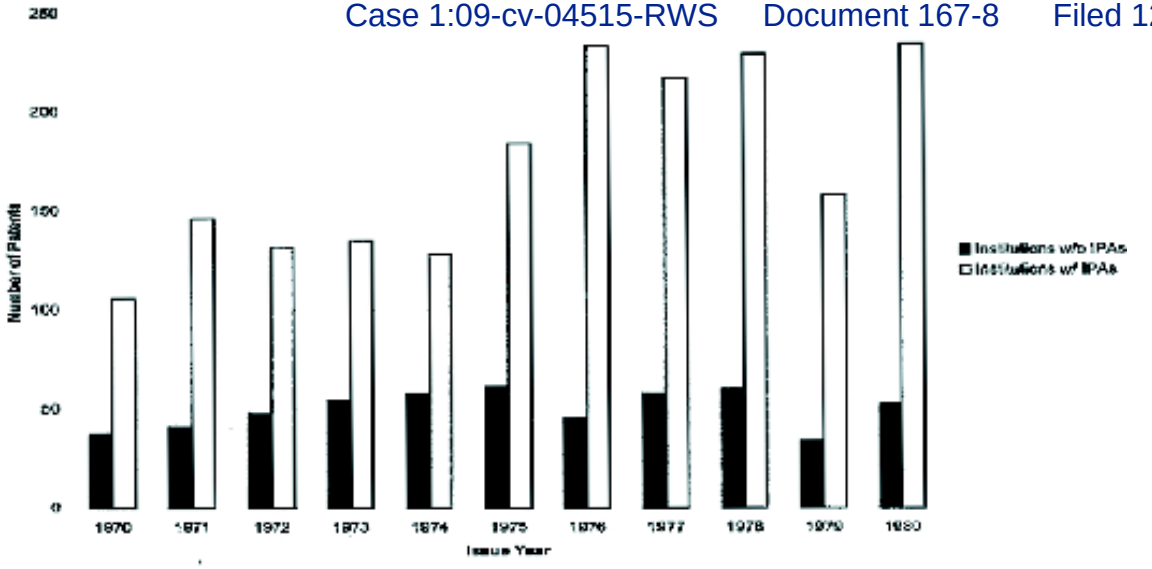

FIGURE 9. Patenting by Carnegie research universities, by IPA status.

What is striking about this conclusion is that their Figure 9 clearly illustrates the impact of IPAs on university patenting. The chart shows that while the IPA program was the only one of the factors cited as "a change in federal policy toward patenting publicly funded research," it clearly made a dramatic and sustained impact that was not occurring without it.

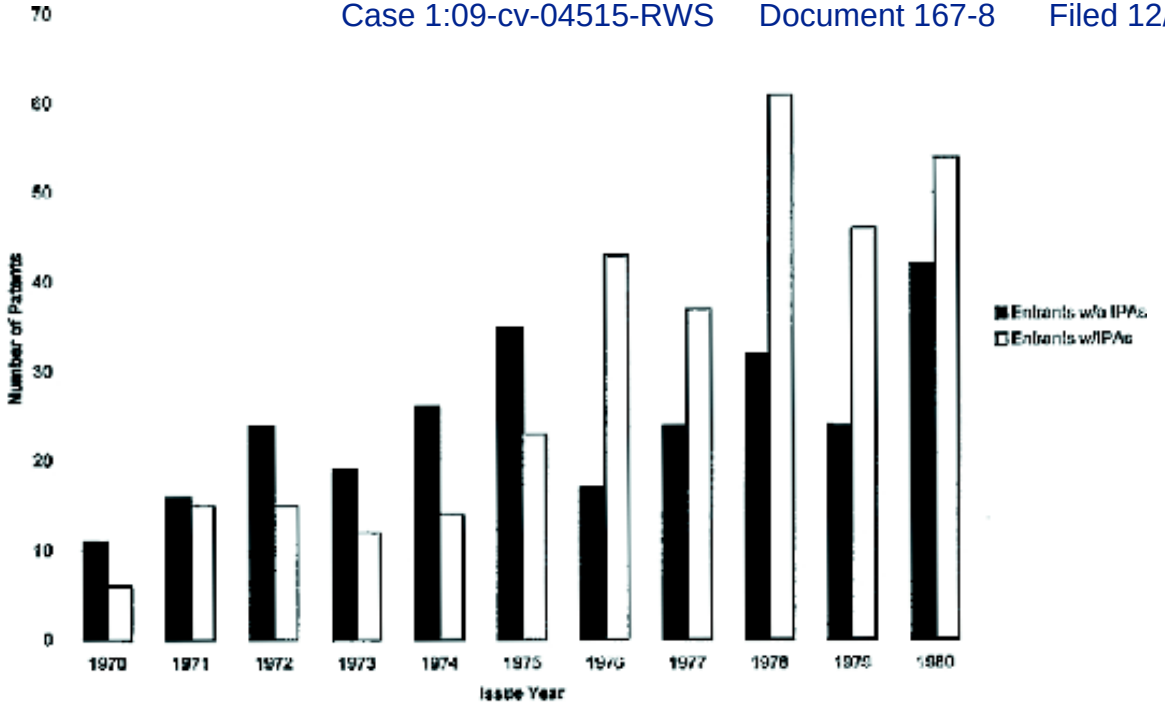

FIGURE 10. Patenting by Carnegie research universities, by IPA status—entrants only.

Even their Figure 10 underscores the importance of the IPA program on university patenting. IPA participants double the number of reported patents between 1973 and 1975. The increase of reported inventions by IPA participants increases almost 400 percent between 1974 and 1976 according to the Figure. Even more striking, as the IPA program starts to grow at the National Science Foundation, and participants increase at NIH as shown in our own chart above, IPA schools permanently pass those not in the program in 1976—and never look back.

MIT: Bayh-Dole Beneficiary.

The impact of Bayh-Dole on individual universities like MIT, which had already been active in technology transfer, is also illustrative. Some might argue that Bayh-Dole did not really impact the legal structure of patent ownership at MIT, because MIT had an existing agreement with the government that generally gave it ownership of its inventions. However, Bayh-Dole did have a major impact because it pushed MIT as well as other universities to recognize that utilizing inventions for the benefit of society could often be best accomplished through commercialization —which required the cooperation and risk taking of the private sector.

For example, a novel and patented chemical entity projected for use as a new pharmaceutical product did not benefit patients unless it was available commercially. Likewise, a newly discovered material or alloy would not make aircraft lighter and stronger unless it could be made commercially.

Within one year of MIT's rethinking its licensing activities as a result of Bayh-Dole, the number of licenses that it issued increased nearly 1000 percent. During the next 20 years, the MIT Technology Licensing Office helped in the formation of nearly 800 new companies. A recent study of MIT spin-off companies shows that if the active companies founded by MIT graduates formed an independent nation, their revenues would make that nation at least the 17th largest economy in the world. [21]

[21] See: http://web.mit.edu/newsoffice/2009/kauffman-study-0217.html?tr=y&auid=4551551]

While MIT clearly was spinning out companies before the passage of Bayh-Dole, the rate of new company formation based upon MIT inventions and discoveries increased almost exponentially after its enactment.

Another point that the critics advance as a basis for the increase of university patenting, making it appear to undercut the influence of Bayh-Dole, was the large subsequent infusion of federal money, primarily through NIH, in the support of life science research. However, the IPA program and later the Bayh-Dole Act were critical incentives for recipient universities to file patent applications to protect important discoveries emanating from research supported by such monies. This would not have happened if NIH had retained its policy to take title to inventions made in whole or in part with NIH funds.

Clearly, it was the incentive of patent ownership and, the certainty of title accompanying ownership upon which the private sector could rely in a licensing arrangement that spurred the increase of university patenting under the IPA program. The patenting activity accelerated even more after Bayh-Dole was enacted because it applied uniformly to all federal funding agencies and all universities in receipt of federal funds in support of research activities could then engage in technology transfer activities.

Thus, there is little doubt that the negotiation, establishment, and existence of the IPAs were of predominant importance in the rapid growth of the university technology transfer function. Moreover, those agreements and the provisions in them were the template for the Bayh-Dole Act. Fundamentally, Bayh-Dole is a codification of terms and provisions of the IPAs. Indeed, when Bayh and Dole first introduced the bill in 1978, they used several inventions whose development was threatened by the Carter administration's undermining of the IPA program as examples of the need for legislation.

Additional data support the proposition that the Bayh-Dole Act, drawing on the preceding IPA program, was a decisive factor in the promotion and growth of the technology transfer profession in the university, nonprofit and small business sectors of the economy. Simple statistical evidence, such as the rapid growth of membership in the Association of University Technology Managers as well as the number of technology transfer offices established within the university community—from about 30 in 1972 to approximately 300 in 2007-08—bear that out.

New Companies, New Products.

Moreover, data presented in the annual AUTM Licensing Survey which show increasing year-to-year activities in invention disclosures, patenting, and licensing are also evidence of the positive effects of the Bayh-Dole Act. The ultimate measure of the wisdom in passage of the Bayh-Dole Act and its success in transferring technology for the public benefit—the Act's primary objective—can be found in a compilation by AUTM titled "The Better World Report." Those reports list and describe some of the university technology-based inventions that have been developed for the market place contributing to the health, safety and welfare of the public—a virtual panoply of inventions in many and diverse scientific disciplines.

Additionally, consider the following evidence of the impact of the law: [22]

- *University technologies helped create 5,724 new companies in the U.S. since the enactment of the Bayh-Dole Act in 1980.* In FY 2006 alone, 553 new companies were spun off based upon campus discoveries and inventions. Astoundingly, that is more than two new companies formed each working day of the year. Formation of new, technology based companies drive state economic development.

- *University research created 4,350 new products from FY1998–2006, with 697 introduced in FY 2006 alone.* This means that 1.32 new products were introduced every day for that period**.** Such success is unique to the U.S.

- *Federally funded research at universities and federal laboratories resulted in 130 new drugs, vaccines, or in vivo diagnostic devices being developed for public use.* Many of these discoveries were treatments for infectious

diseases and new cancer therapies. The majority of licenses initially went to small companies licensed under the provisions of the Bayh-Dole Act. [23]

• *There were almost 5,000 existing active university licenses in FY 2006—each representing a university-industry partnership*. The majority of such licenses were with small businesses and start-up companies. Although the bulk of licensing arrangements were non-exclusive the majority of exclusive licenses issued were to small businesses and start-up companies, which require strong patent protection to succeed in highly competitive markets against larger, established and well financed competitors.

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[22] Association of University Technology Managers (AUTM): U.S. Licensing Activity Survey, 2006.

[23] The Contribution of Public Sector Research to the Discovery of New Drugs. Jonathan J. Jensen, Kathrine Wyller, Eric R. London, Sabami K. Chatterjee, Fiona E. Murray, Mark L. Rohrbaugh and Ashley J. Stevens; poster presented at 2008 AUTM Annual Meeting with updated information.

Important health related and life-saving discoveries commercialized under Bayh-Dole include:

Cisplatin and carboplatin cancer therapeutic —Michigan State University

Hepatitis B vaccine—University of California, University of Washington

Vitamin D metabolites and derivatives —University of Wisconsin-Madison

Human growth hormones—City of Hope Medical Center

Taxol—Florida State University

Citracal® calcium supplement—University of Texas Southwest Medical Center

There was nothing even remotely approximating these successes outside of the IPA program and its subsequent uniform application across all federal agencies caused by the enactment of the Bayh-Dole Act.

The "evidence" [24] disproving the commonly held theory that government-owned inventions had lower utilization rates than those held by contractors (read universities) is based on an article by Rebecca Eisenberg. [25]

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[24] Note 12, supra

[25] Note 7, supra

This same argument is repeated by critics such as Arti Rai and Robert Cook-Deegan in their article "*Is Bayh-Dole Good for Developing Countries? Lessons from the US Experience.*" [26] That paper, intended to warn other countries of the "dangers" in adopting a Bayh-Dole type law, includes the following:

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[26] Note 5, supra

> Nevertheless, many advocates of adopting similar initiatives in other countries overstate the impact of BD in the US... They also cite data (originally used by US proponents of the Act) on the low licensing rates for the 28,000 patents owned by the US government before BD to imply that the pre-BD legal regime was not conductive to commercialization. But as Eisenberg has argued, that figure is misleading because the sample largely comprised patents (funded by the Department of Defense) to which firms had already declined the option of acquiring exclusive title. Moreover, these figures are of questionable relevance to debates about public sector research institutions, because most of the patents in question were based on government-funded research conducted

by firms, not universities or government labs.

As will be shown, this assertion is wrong on both counts.

Value Realized From DOD Innovations.

In her referenced paper, Eisenberg maintains that the primary argument against government ownership was a statistical one based on the testimony of numerous witnesses that only a small percentage of the estimated 28,000-30,000 government patents had been successfully licensed and exploited commercially. She further submits that "the statistical evidence presented was inadequate to document this claim" because it "reflected a huge selection bias; as it consisted largely of inventions made by contractors whose research was sponsored by DOD... that could have retained title to the patents if they had wanted to do so."

On the basis of her analysis, Eisenberg concludes, "It is hardly surprising that few firms were interested in taking licenses from the Government to patents that had already been rejected by contractors that could have been owned by them outright if they had found them at all commercially interesting."

Eisenberg alleged that 17,632 of the 28,021 inventions in the government patent portfolio were made by Department of Defense contractors, waived to the government because they lacked commercial importance.

However, review of the actual data indicates that Eisenberg's conclusion is simply wrong.

The evidence that fewer than 5 percent of government-owned inventions were being successfully licensed came from the 1976 Federal Council for Science and Technology combined report. [27]

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[27] Note 15, supra.

Graphic

In her paper, Eisenberg fails to note that the 1976 report clearly establishes that the 17,632 DOD patents include:

(1) 7,046 U.S. patents granted during the 1970-1976 reporting period to DOD employees obligated to assign their rights to DOD; and

(2) 2,594 U.S. patents based on reported inventions during the 1970-76 reporting period from contractors.

(3) In addition, some portion of these 2,594 contractor generated inventions were taken from universities and other non-profits that, because of the DOD title policy then in place prior to the passage of the Bayh-Dole Act, had no choice but to assign their inventions to the government.

Combining the two categories above totals 9,640 patents accrued to the DOD patent portfolio during the 1970-76 reporting period or about one half of the 17,632 DOD patents identified in the report.

The remaining 7,992 patents (17,632 - 9,640) are unexpired patents granted and assigned to DOD prior to 1970 that remained open for licensing within the 1970-76 reporting period. Since there are no data in the '76 report indicating the source of patents granted before 1970, it is not unreasonable to assume that the ratio of these patents is approximately equal to that of the 1970-76 reporting period. That is, they were about 70 percent government-employee-generated, and about 30 percent contractor-generated (including universities and nonprofit organizations).

Accordingly, of the 7,992 patents granted before 1970, 5,594 would be government-employee-generated patents, and 2,702 would be contractor-generated patents. Thus, the total DOD employee-generated patents would be 12,640 (7,046 plus 5,594) and the total DOD contractor-generated patents would be 4,992 (2594 plus 2398).

Since DOD employee-generated patents came from cutting-edge federal laboratories like the Naval Medical Center at Bethesda, Md., or the Walter Reed hospitals in Washington D.C., they most certainly do not fit Eisenberg's characterization as "rejected" inventions without commercial interest. Nor do they fall within her definition of "contractor" inventions.

The remaining 4,992 patents generated by actual DOD contractors most certainly do not support Eisenberg's allegation that the patents available for licensing "reflected a huge selection bias; (consisting) largely of inventions made by contractors whose research was sponsored by DOD."

The DOD contractor-generated portion of the government patent portfolio amounts to no more than 18 percent (4,992 out of 28,021) rather than the 63 percent (17,632 out of 28,021) erroneously alleged by Eisenberg.

There is also no empirical or documentary evidence advanced that even the 18 percent of the government patent portfolio as identified above are based on inventions "rejected by contractors" as not "at all commercially interesting," as alleged by Eisenberg.

This is because an unidentified number of these 5,296 patents were generated by university and other nonprofit contractors and were simply taken by DOD under its existing patent policies, whether they had commercial potential or not.

It's not even possible to support Eisenberg's contention that there was little commercial value in the unknown subset of patents from for-profit contractors. Most large company contractors of the time kept their government and commercial research operations segregated because of fears that federal agencies would try to assert ownership to important discoveries. In addition, some percentage of this category of inventions was generated by *small business contractors*, who like universities, had no choice but to assign any inventions made to DOD. Thus, Eisenberg's assertion is not even proven in the limited subset of industry contractors.

In summary, the revisionists' theory that the supporters of the Bayh-Dole Act misinterpreted the lack of commercialization of 28,000 government owned inventions does not hold up. The actual data speak for itself and strongly belies that theory.

Model for Developing Countries?

The revisionists are also turning their sights abroad. An article by several critics, "Is Bayh Dole Good for Developing Countries? Lessons from the U.S. Experience," [28] warns of the dangers of following the U.S. model in a series of recitations of virtually every objection the critics have advanced the past 30 years. Building their case, the critics say:

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[28] See Note 5, supra.

> Finally, and most importantly, the narrow focus on licensing of patented inventions ignores the fact that most of the economic contributions of public sector research institutions have historically occurred without patents through dissemination of knowledge, discoveries, and technologies by means of journal publications, presentations at conferences and training of students.

Such arguments present a false dichotomy. Bayh-Dole has not harmed the dissemination of knowledge in the United States, nor has it prevented journal publications, presentations for the training of students, etc. Indeed, it complements the historic mission of university research by making its contribution to social good much more tangible and immediate through the creation of new products directly benefiting the taxpaying public.

More fundamentally, how developing countries in a competitive global economy can hope to prosper by putting their university research freely into the public domain (as the authors advise) is not addressed. The experience in the United States, as previously discussed, certainly does not support this contention.

Unless innovative companies have the incentive of strong intellectual property laws, they cannot undertake the considerable risk and expense of product development. Thus, public sector research lies fallow, despite the claims of the critics. Rather than following the same course that failed in the United States before Bayh-Dole, developing countries would be well advised to heed other advisors.

South American economist Hernando De Soto's groundbreaking book, *The Mystery of Capital,* [29] forcefully demonstrates that the fundamental weakness of perennially underdeveloped countries is the inability of their citizens to establish clear ownership of their property, both physical and intellectual. Without the incentive of ownership, wealth creation is not possible.

[29] Harnando De Soto, *The Mystery of Capital, Why Capitalism Triumphs in the West and Fails Everywhere Else*, Basic Books, 2006.

At its founding the United States was also a "developing country." One of the primary reasons for the American Revolution was an imperial system that doomed its colonies to remain only the providers of raw materials devoid of manufacturing capabilities. It was to reverse this unjust and subservient role and develop a society based on internal innovation that the Founding Fathers placed the intellectual property protection provision in Article I, Section 8 of the Constitution. Their faith in creating such incentives through a strong and viable patent system was well placed.

As President Abraham Lincoln aptly stated, without a patent system "any man might instantly use what another had invented; so that the inventor had no special advantage from his own invention. The patent system changed this; secured to the inventor, for a limited time, the exclusive use of his invention and thereby added the fuel of interest to the fire of genius, in the discovery and production of new and useful things."

Strangely, the modern critics think the way to innovation is by turning Lincoln's dictum on its head. They could not be more wrong.

As inventor Frederick Cottrell said while founding Research Corporation for Science Advancement: "*... a number of meritorious patents given to the public absolutely free have never come upon the market chiefly because what is everybody's business is nobody's business.*"

It was precisely because inventors could secure protection for their discoveries and inventions that in the 20th century a huge era of U.S. innovation resulted. It can be hardly disputed that because of that protection the benefits to humanity have been unprecedented. While the critics bemoan the ability of the patent system to grant such ownership of intellectual property, the only alternatives are open source technology or trade secrets, neither of which provides similar motivation and incentives for innovation. It is truly the protection that the patent system creates that makes the commercial development of ground breaking discoveries possible.

Developing countries would do well to consider these hard-won lessons when urged by external "experts" to freely give the results of their research away. Interestingly, South Africa recently enacted a Bayh-Dole–type law to help integrate its research universities fully into its economy. That a country, which changed so dramatically under leaders like Nelson Mandela, can look past the speculative fears of the critics, and lay the ground work for a confident future should give hope to us all.

Bayh-Dole and Scientific Progress.

Critics have also raised concerns that Bayh-Dole harms the advancement of science. Interestingly, unlike the anecdotes which are the presumed basis for that allegation, data shows that the law has substantially contributed to the U.S. economy, and that U.S. science is actually better because of university-industry research collaborations. Additionally, university researchers are successfully balancing patenting and publishing, and not shifting their focus away from fundamental research.

In 2005, according to the President's Council of Advisors on Science and Technology, [30] fully 29 percent of articles authored worldwide by scientists and engineers were from the U.S.

[30] University-Private Sector Research Partnerships in the Innovation Ecosystem, President's Council of Advisors on Science and Technology, November 2008, p.22

> Publication and citation of scientific results in peer-reviewed journals is one common metric for evaluating research outputs.... The United States remains the world leader in citations of S&E (science and engineering) research articles. The number of U.S. articles with co-authors by sector is a metric that can be used as an indicator of public-private research partnerships. Between 1995 and 2005, co-authorship with academic institutions increased by 10.3 percent, the largest percentage point increase of all cross-sector co-authorships.

This comingling of the best and brightest minds in the public and private sectors in authoring joint scientific publications was fostered by the Bayh-Dole Act. Before passage, industry segregated its most creative researchers from university collaborations because the federal government could assert ownership rights in resulting inventions when federal support of university research was also present.

The health of U.S. scientific publications is also reflected in the findings of the National Science Board's *Science and Engineering Indicators* reports. [31] Traditionally, about three fourths of all U.S. scientific and engineering publications come from academia. In its 2008 report, it found:

[31] Science and Engineering Indicators, National Science Board. 2008, Volume I, p. 5-7, NSB 08-01.

> Although the U.S. share of world article output and article citations has declined, the influence of U.S. research articles has increased, as indicated by the percentage of U.S. articles that are among the most highly cited world-wide. In 1995, authors from U.S. institutions had 73% more articles in the top 1% of cited articles in all S&E fields than would be expected based on U.S. total article output; in 2005, the percentage had grown to 83%.

That the share of U.S. scientific papers has fallen is because of the huge explosion of international publications, particularly from Asia. However, while the percentage of U.S. publications has decreased, their scientific impact has increased.

Scientific papers by U.S. researchers are the most cited across every field of science. [32] The number of citations by other authors is the standard criteria for determining the significance of a scientific publication in its field. The report explains: [33]

[32] *Id.* at 5-41.

[33] *Id.* at 5-49 to 5-50.

> In other words, a country whose research has high influence would have higher shares of its articles in higher citation percentiles.
>
> This is the case in every field for U.S. articles—only U.S. publications display the ideal relationship of consistently higher proportions of articles in the higher percentiles of article citations across the period.
>
> However, when citation rates are normalized by the share of articles during the citation period to produce an index of highly cited articles, the influence of U.S. articles is shown to increase.... In other words, the United States had 83% more articles than expected in the 99th percentile of cited articles in 2005, while the European Union had 16% fewer than expected and the Asia-10 had 59% fewer than expected.

The United States ranked number one in every broad science and engineering field surveyed in the study for 2003. It also held this ranking in 1995.

Another classic argument espoused by the critics is that Bayh-Dole lures academic researchers away from basic research toward applied research in order to attract industry sponsors. Of course, it is precisely because university researchers are doing fundamental research that industry either cannot do, or chooses not to do, that makes academic alliances so attractive. The National Science Foundation looked at that allegation, and here is what it found: [34]

[34] Science and Engineering Indicators, National Science Board. 2006 (two volumes)

Has Academic R&D Shifted Toward More Applied Work?

Emphasis on exploiting the intellectual property that results from the conduct of academic research is growing… Some observers believe that emphasis has been accompanied by a shift away from basic research and toward the pursuit of more utilitarian, problem-oriented questions.

We lack definitive data to address this issue. As indicated earlier in the chapter, it is often difficult to make clear distinctions among basic research, applied research, and development. Sometimes basic and applied research can be complementary to each other and embodied in the same research. Some academic researchers may obtain ideas for basic research from their applied research activities.

Two indicators, however, bear on this issue. One indicator is the share of all academic R&D expenditures directed to basic research. Appendix table 5-1 does not show any decline in the basic research share since the late 1980's. The second indicator is the response to a question S&E (science and engineering) doctorate holders in academia were asked about their primary or secondary work activities, including four R&D functions: basic research, applied research, design and development.

As figure 5-33 (reproduced below) shows, for those employed in academia who reported research as their primary activity, involvement in basic research declined slightly between 1993 and 2003, from 62% to 61% probably not statistically significant. The available data, although limited, provide little evidence to date of a shift toward more applied work. [35]

[35] Science and Engineering Indicators, National Science Board 2006, Volume 1, NSB 06-01, p. 5-36.

Figure 5-33

Graphic

Once again, by examining the data, the critics' charges are unsubstantiated and incorrect.

To reinforce what the Bayh-Dole Act has contributed to the U.S. economy and the worldwide benefit of mankind one need only to look at the inventions listed below, in addition to those listed previously. Of course, these represent only a small sample of commercialized inventions derived from basic research in academia and which were generated in diverse disciplines by different university research institutions. Among such inventions and discoveries are the following:

rDNA technology, central to the biotechnology industry—Stanford University and University of California;

TRUSOPT® (dorzolamide) ophthalmic drop for glaucoma—University of Florida;

Hotbot internet search engine—University of California, Berkeley;

Ultrasonic removal of dental plaque—University of Washington;

Lycos® internet search engine—Carnegie Mellon University;

Mosaic web browser—University of Illinois, Urbana-Champaign;

Yahoo internet search engine—Stanford University; and

Cardiovascular and magnetic resonance imaging techniques—University of Wisconsin, Madison.

Conclusion

The Bayh-Dole Act has clearly exceeded the expectations of its authors and of Congress, and is as viable and needed in today's economic crisis as it was in 1980. Its contributions to the benefit of the United States and its citizens were recognized by a resolution of the U. S. House of Representatives on Dec. 6, 2006 as follows:

> The Bayh-Dole Act (Public Law 96-517) has made substantial contributions to the advancement of scientific and technological knowledge, fostered dramatic improvements in public health and safety, strengthened the higher education system in the United States, served as a catalyst for the development of new domestic industries that have created tens of thousands of new jobs for American citizens, strengthened States and local communities across the country, and benefited the economic and trade policies of the United States.

Moreover, an important factor which is often overlooked is that the success of the Bayh-Dole Act in motivating technology transfer has been accomplished without cost to the taxpayer. In other words, no separate appropriation of government (read taxpayers') funds were needed to establish or manage the effort. Yet, its contributions to the U.S. economy and to its citizens, as well as citizens of the world, has been exemplary. For example, in fiscal year 1999 U.S. economic impact models showed that $40.9 billion could be attributed to academic licensing, and that 270,900 jobs were created. [36]

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[36] AUTM Licensing Survey, FY 1999 pp. 1, 3, 7, 8. Economic numbers derived from Ashley J. Steven's approach entitled "Measuring Economic Impact," AUTM Advanced Licensing Course, Phoenix, Dec. 1994.

Why was the Bayh-Dole Act a determinative factor in the evolution of university technology transfer? There are a number of reasons that the critics conveniently overlook:

1. It produced order out of chaos because it established a uniform government patent policy. Prior to the Bayh-Dole Act, when federal monies were utilized in whole or in part in the making of an invention there were some 20 agency policies depending on where the research was funded. Indeed, there was frequently more than one patent policy in an agency covering different programs. Because universities receive federal funds from a wide number of sources, this made it extremely difficult, if not impossible, to sort out the applicable policies and restrictions on patenting and licensing by the university. The most restrictive of the policies generally controlled, but all funding agency policies applicable had to be considered as did the bureaucratic climate and restrictions within a given agency. Consequently, with the exception of the IPA program—it was seldom that a federally supported university invention found its way into the marketplace.

2. Bayh-Dole was the first statutory authority for government agencies to obtain, hold, and license patents generated within government laboratories. This greatly increased the effective management of important inventions made by federal employees, previously languishing without development.

3. It was the template for the subsequently passed Federal Technology Transfer Act, which promoted technology transfer from federal laboratories and recognized the contributions of federally employed inventors. Indeed, the first version of this legislation by Senator Dole was written as an amendment to Bayh-Dole.

4. It called for the sharing of royalties collected by the contractor with inventors, thus recognizing their

imaginative scientific contributions and supplying them with the incentive to consider the practical applications of the results of their research. It also promoted the contractor's use of the expertise of inventors in the technology transfer function.

5. It promoted collaboration among scientists having diverse funding from different federal sources to explore and embrace interdisciplinary approaches to solving scientific challenges.

6. It promoted the science-innovation interface through the establishment of a new university-industry relationship because of the certainty of title to inventions retained by universities under the provisions of the act. This was, and still is, the critical element for private sector development of inventions for the marketplace.

7. It promoted private sector as well as government investment in university research.

8. It promoted innovation and the attendant creation of jobs through, in part, its mandate to give preference to U. S. industry and small business in technology transfer practices.

9. It protected confidential information in the possession of the contractor and its licenses from undue and untimely disclosure—a prime consideration to the private sector in a globally competitive economy.

10. It preserves certain rights in the government to protect the public against nonuse or unreasonable use of inventions supported in whole or in part with taxpayer's money.

11. It provides the university and nonprofit sectors the possibility for generating income to support research and educational activities through the technology transfer function.

To now suggest that the Bayh-Dole Act was not a critical factor in the development of university technology transfer, and that this evolution would have occurred anyway is simply not a supportable premise.

Prior to the passage of the Bayh-Dole Act, and the predecessor IPAs, the environment in which technology transfer existed was, at best, inhospitable, and at worst, hostile. That environment slowly progressed, through creation of the IPA program, and a succession of unpassed legislation to the enactment of the Bayh-Dole Act–into an environment that actually encouraged technology-transfer.

The result has been of tremendous benefit to the U.S. taxpayer in terms of the availability of important new products —particularly in biomedicine—and improved international competitiveness. Indeed, the U.S. is widely recognized as the most efficient nation on the world in the integration of its research universities into the national economy. The proof is in the number of competing nations seeking to adopt the Bayh-Dole model abroad. This movement is occurring despite the writings and efforts of many critics.

Unfortunately, the Bayh-Dole Act of 1980 has come under relentless scrutiny and attack through the efforts of revisionist historians and their rhetorical pronouncements, with little basis in empirical data. These activities would resurrect the same policies that clearly failed prior to the enactment of the IPAs and the Bayh-Dole Act.

It seems strange that a piece of legislation, which arose out of clearly failed preceding policies almost 30 years ago and which has proven its worth, is now again being decried on many of the same bases as were raised against its initial passage.

Outspoken claims, with little basis in empirical evidence, under the guise of guardianship of the public interest provide a rich field for the cultivation of political power and special interests.

One must recognize that such initiatives are extremely dangerous in an evolving technologically-focused, increasingly fragile, global economy. Intellectual property and its ownership have become the preferred currency for economic growth, where invention and innovation are the hallmarks of not only technological leadership but

of survival.

The authors of this article fully acknowledge that improvement can always be made in the technology-transfer system. It is always possible to find licensing decisions that could be open to criticism or universities that are more difficult to deal with than others. But, it is important to note the difference between poor implementation of Bayh-Dole as opposed to blaming Bayh-Dole for suboptimal practices.

The bottom line is that the Bayh-Dole Act, over its 30 years of implementation, continues to provide a superb framework for government funded research to benefit Americans through job and wealth-creation and to improve the lives of citizens of the worldwide community. This is a lesson it would be well to remember, and perhaps one that the critics could take to heart.

As Nietzsche said: "Convictions are more dangerous foes of the truth than lies."

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