scientifically meaningful way, inventors are awarded a finite period of exclusive rights in the invention that is patented.

Over the patent 20 years, the Congress, the Patent and Trademark Office (PTO) and the courts have been ensuring that this bargain is a good one for the American public. For example, in 1995, Congress changed the term of patents to run 20 years from the date patents are filed, rather than 17 years from the date patents are granted. As a consequence, the fixed period of exclusive rights is now more certain, and in many cases, is shorter, than it had been before 1995. Then, in 1999, the Congress enacted changes to the patent system that require publication of patent applications 18 months after they have been filed. This means that the public gets their part of the bargain – a meaningful public disclosure of the invention – regardless of whether the patent applicant emerges with any rights.

The PTO, almost from the dawn of the biotechnology industry, has been focused on granting high quality patent grants. In 1988, barely years after the first wave of biotechnology applications had been filed, the PTO formed a special new group to focus on examination of biotechnology applications, aggressively devoting resources to accurate examination of biotechnology applications. This group has since grown to more than 485 examiners today, more than 80% of which have advanced degrees, including more than 385 examiners with Ph.D's. This is by far the most technologically advanced and competent group of patent examiners in the PTO today.

A critical threshold for any invention to be patented is that it is new. In the field of biotechnology, this raises two issues. First, to be eligible to be patented, the invention must be claimed in a form that distinguishes it from the form it is found in nature. A nucleic acid patent, thus, cannot be issued with claims that define nucleotide sequences that are indistinguishable from the form in which the nucleic acid exist in nature (e.g., in a human chromosome). A nucleic acid patent, thus, must be limited to a specific nucleotide sequence that does not occur in that form in nature. Second, there is extensive information that has been published regarding genetic sequences. To be patentable, the claim must be distinct from any nucleotide sequence that has been reported in the literature. If the claim covers nucleic acid sequences that are already known from earlier experimental work, the patent should not issue, or if it is, will likely be held invalid.

Other patentability criteria operate to limit the scope of patent rights in the field of nucleic acids. The PTO has aggressively applied these patentability criteria in examining biotechnology applications for more than 25 years. In fact, the PTO has promulgated several sets of guidelines that set forth aggressive examination standards aimed specifically at biotechnology patent applications, such as those claiming nucleic acid inventions.

In 1995, and again in 2001, the PTO issued guidelines relating to the "utility" standard of 35 U.S.C. §101. See, e.g., *Utility Examination Guidelines*, 66 Fed.Reg. 1092 (Jan. 5, 2001). Under these guidelines, the PTO has demanded applicants identify a specific, substantial and credible utility for their inventions. This

disclosure must appear in the patent application, which is filed shortly after an invention is made. The guidelines do not permit an applicant to simply guess about what a nucleic acid might be useful for – they require the disclosure to be supported by a scientifically credible basis of support. The PTO has supplemented these guidelines with training materials that illustrate how to apply the standards properly. See, **http://www.uspto.gov/web/offices/pac/dapp/mpep_examguide.html**.

In 2001, the PTO issued guidelines on application of the "written description" requirement of 35 U.S.C. §112, first paragraph. See, *Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, P1, "Written Description" Requirement*, 66 Fed. Reg. 1099 (2001). As applied by the PTO, the guidelines require applicants to provide a comprehensive written description of what they perceive their invention to be as of the filing date of the patent. The guidelines, in particular, direct examiners to conduct a critical review of whether broad claims, such claims to broad class of related nucleic acids, are adequately supported by the patent disclosure. For example, the guidelines direct examiners to question whether a representative number of nucleic acids covered by a broad "genus" claim are described in the patent application, or whether the applicant has shown that there is a common structural relationship between the sequences and a function shared by all the nucleic acids in the genus. *Id* at 1106. Again, the PTO followed the guidelines with training materials that provide examples of commonly encountered scenarios, with clear guidance on when to impose rejections. See, **http://www.uspto.gov/web/offices/pac/dapp/mpep_examguide.html**.

These PTO efforts have been aided by a series of decisions of the Supreme Court and the Federal Circuit over the past two decades.

As noted above, the principles of broad eligibility for patents on living organisms and materials derived from them has been affirmed by the Supreme Court in *Chakrabarty*, and was again confirmed in 2001 by the Supreme Court in *J.E.M. Ag. Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc.*, 534 U.S. 124 (2001) (holding non-naturally occurring plants eligible to be patented under utility patents).

A series of decisions of the Court of Appeals for the Federal Circuit have both laid the foundation for the PTO guidelines, and affirmed the legitimacy of these guidelines.

- In *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988) the Federal Circuit set forth a practical guide for applying the "enablement" requirement of 35 U.S.C. §112, first paragraph. This requirement demands that an applicant provide a disclosure that enables a person skilled in the field of the invention to practice the full scope of the claimed invention. As the court explained, unpredictability in the field of the invention, which is common in the field of biotechnology, often demands a more comprehensive disclosure. The so-called "Wands factors" are a central focus of the PTO examination process in the biotechnology area. See, e.g., MPEP 2164.01(a).

- The principles in the PTO utility guidelines were affirmed by the Federal Circuit in 2005 in the case of *In re Fisher*, 421 F.3d 1365 (Fed. Cir. 2005). *Fisher* specifically addressed the patentability of expressed sequence tags, which are short nucleic acids produced incidental to the

expression of a gene in a cell. EST sequences correspond to at least part of a gene that encodes a protein, and thus have some value in conducting research to discover a gene or a protein encoded by the gene. The Federal Circuit, largely affirming the rationale of the PTO which had rejected claims under §101 in the case, held that this mere potential for use in discovering a gene was not sufficient to satisfy the specific and substantial utility requirements of §101, which were the focus of the PTO guidelines. In particular, the court observed that labeling the invention as a "research" tool or not was not helpful to the analysis, stating:

> [a]n assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the invention is in fact "useful" in a patent sense. [The PTO] must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted utility requires further research to identify or reasonably confirm.

Fisher at 1372. Instead, the court emphasized that the patent applicant must identify in the patent application a utility that (i) is specific to the claimed invention, rather than being generally applicable to all molecules in the class of the invention, and (ii) must be substantial, in that it provides "real world value" (i.e., that "one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public."). The court then held that claims based on the EST sequences described in the application were not sufficient under §101. The Federal Circuit specifically observed that the "...PTO's standards for assessing whether a claimed invention has a specific and substantial utility comport with this court's interpretation of the utility requirement of § 101." *Id.*

- The Federal Circuit has also found the PTO's guidelines concerning the written description requirement to be consistent with the requirements of this section of the patent law. See, Enzo Biochem v. Gen-Probe, 323 F.3d 956, 964 (Fed. Cir. 2002) ("We are persuaded by the Guidelines on this point and adopt the PTO's applicable standard for determining compliance with the written description requirement"); see also, *University of Rochester v. Pharmacia*, 375 F.3d 1303 (Fed. Cir. 2004).

The efforts of the PTO, and the decisions of the Federal Courts, have ensured that patents on nucleic acids that are issued or asserted today are valid, reflect a true inventive contribution, and provide a balanced set of rights for innovators relative to the public at large. In simple terms, given the rigor of examination of patent applications in this sector and the stringent legal standards governing patent eligibility and claim scope, there is no basis for any criticism of the quality of patents issuing that claim nucleic acids or other biotechnology inventions.

Nucleic Acid Patents Are Used In Different Ways by the Biotechnology Industry

Some have identified concerns with "gene patents" and offered solutions that would, as a practical matter, eliminate the possibility of obtaining patents on nucleic acids. Before addressing the merits of those concerns, it is important to appreciate the far-ranging impact such a proposal would have on the biotechnology industry.

Patents on a specified nucleotide sequence give rights to prevent the unauthorized making or use of the nucleotide sequence. This right can be applied

in a variety of commercial settings. One use is to incorporate the sequence into a host cell, and use it to produce a protein encoded by that sequence. Another application is to use the sequence to screen samples from patients to detect the presence in the sample of the sequence, which might indicate that the person being tested has a condition that justifies further investigation or treatment. Other uses of the sequence can be envisioned, each having some distinct final outcome (e.g., a product that incorporates the sequence, a product made via use of the sequence, information that provides clinical diagnostic value, a therapy based on interfering with expression of a gene). The same type of patent rights are implicated in each application – patent rights in a discrete nucleotide sequence.

As such, a patent on a nucleic acid has significant commercial value because the single patent can support a variety of distinct commercial applications ranging from producing a new drug product to a new diagnostic agent. Consider the case of a company that has developed a protein that is useful for treating a disorder. This company will use the nucleic acid patent to control which companies, if any, may be authorized to manufacture the protein. If the protein is identical to a protein that occurs in nature, patent rights in the protein may be limited or non-existent. The nucleic acid rights, by contrast, provide practical value by enabling the innovator to control the commercial production of the protein. Without protection for the nucleic acid embodiment of the invention, there may be no exclusivity available that could justify investment in developing the therapeutic product.

Legislation Altering Patent Rights in Nucleic Acid Inventions Would Harm the Biotechnology Industry and Be Inconsistent With WTO Standards

Prohibiting the issuance of patents on nucleic acids would fundamentally disrupt expectations that were set for the industry nearly 30 years ago in *Chakrabarty*. The capacity of a biotechnology company to secure comprehensive commercial protection against free-riding on its investments and efforts has been a crucial factor contributing to the success of the biotechnology industry. Biotechnology companies for nearly three decades have used patents to secure this commercial protection, and count on it in a critical fashion to guide their business development and investment decisions. In a setting where hundreds of millions of dollars of investment must precede the commercial launch of a product, eliminating or even limiting patent protection for a commercially important aspect of the product (i.e., nucleic acids) would be severely disruptive and harm long-settled expectations.

Legislation prohibiting the issuance of nucleic acid patent claims, or limiting use of patents on nucleic acids, also would place the United States out of compliance with its international obligations. For example, under the World Trade Organization Agreement on Trade Related Aspects of Intellectual Property Rights (WTO TRIPS Agreement), WTO members may not exclude protection for specific categories of inventions, such as nucleic acids, or limit their "enjoyment" (i.e., the ability of the owners of those patents to use them). Doing so would run counter to obligations of the United States under Article 27.1, which prohibits discrimination

in the availability or enjoyment (i.e., use) of patents and patent rights, based on the field of technology of the invention.

Legislation is Unnecessary

Three different types of concerns have been raised regarding gene patents. None of these concerns merits legislative action, in the view of BIO.

One concern that has been voiced is that the existence of patents on nucleic acids is preventing academic research from being conducted. This perspective is inconsistent with the experiences of BIO and its members. An important historical aspect of the biotechnology industry is its close affiliation with the academic scientific community – particularly professors in universities and in other public research institutions. This relationship is built upon shared principles, such as a desire to advance scientific understanding through both basic and applied research, publication of scientific advances and sharing of information regarding research results.

This concern is based, in part, on fears of an increased frequency of patent infringement assertions by biotechnology companies against universities and other public research institutions following the decision in *Madey v. Duke University*, 307 F.3d 1351 (Fed. Cir. 2002). Most working in this field recognize that unique circumstances were presented by the *Madey* case, in which patent rights in a machine were entangled in a broader dispute between Duke University and an ex-employee. These circumstances are unlikely to be viewed as a harbinger of a new

wave of patent litigation by biotechnology companies against universities. And, since 2002, there has not been a significant increase in patent infringement actions against university researchers. Certainly, if a university researcher is being supported by a commercial competitor of a patent owner to develop a competing product that infringes a patent, that researcher may become part of a broader landscape of commercial disputes between the companies. But, concerns that basic research will face significant new obstacles from patent litigation patent are unfounded and not borne out by experience, either from before or after the *Madey* decision.

A similar theoretical concern has been expressed that the number of patents issued in the field of biotechnology will create an overall impediment to the performance of research or in the development of products. The so-called "anticommons" effect, as hypothesized by Drs. Heller and Eisenberg, *Science*, vol. 280, (May 1998), was that the "overpatenting" of biotechnology inventions would stifle research and development in the biotechnology sector. Nearly a decade later, the conflicts hypothesized about in the paper have not materialized. Instead, research and development activities, both in the public and private sectors, has continued to enjoy vigorous growth. A summary of the paper and experiences since it was published is provided as Attachment C to this testimony.

Another concern that has been voiced is that gene patents are impeding the delivery of clinical diagnostic services. Examples have been identified of disputes between companies that own patents on nucleic acids and entities attempting to

perform clinical testing for gene-linked diseases. The fact that only one or two disputes of this type have been identified despite the fact that thousands of patents have been issued relating to nucleic acids, in one sense, confirms that the vast majority of gene patents do not create significant impediments to performing clinical diagnostic testing.

Finally, concerns have been expressed that patent rights in nucleic acids will confer rights to control use of genetic information, including by individuals. Patents give rights only in the making, using, selling, offering for sale or importation into the United States of what is patented. In the case of a patent on a nucleic acid, this means that the patent can be used vis-à-vis entities that make or use the nucleic acid that has been patented. Dissemination and use of information about the nucleic acid is part of the bargain of the patent system -- patent rights in a nucleic acid cannot be used to stop use of the dissemination or use of information *per se*.

The granting of valid patent rights, in response to investments and innovative activity, gives the innovator a certain degree of discretion to pursue and exploit the patent rights. To the extent that the business model pursued by a company is impractical, the market should and will respond to address the shortcomings of that business model. It should also be kept in mind that patent rights are inherently limited; they give the owner of the patent the right to prevent others from using the patented invention without authorization. Patents do not convey positive rights to perform diagnostic testing, impose impractical or unlawful conditions (through contract or otherwise), or to waive compliance with laws

governing competition or the regulation of human diagnostic products. Patents only provide the right to prevent others from using the patented invention.

From a broader perspective, BIO submits that granting patents in exchange for public disclosure of inventions – including for nucleic acid inventions that are new, useful, non-obvious and adequately disclosed – reflects sound public policy. The benefits after nearly 30 years of experience cannot be contested – more than a thousand companies, employing more than a million highly skilled people, and producing hundreds of life-saving and life-changing products and services. Indeed, the biotechnology industry is proof that the patent system is working as it should – promoting billions of dollars of investments in crucially important research and development, generating millions of jobs, and delivering new hope to patients and consumers.

Conclusion

The U.S. patent system allows for broad subject matter eligibility. This system has served this country well over the past thirty years. Everyday, new innovative products enter the market place, and every day, a new discovery is made in biotechnology. The House Subcommittee is to be commended for undertaking this examination of the role of gene, nucleic acid based system. In BIO's view, altering the legal standards of eligibility for gene based inventions, or limiting the ability of innovators to use gene patents, would seriously harm the biotechnology industry. BIO appreciates the opportunity to provide insight into the role of gene based

patents in the growth of the biotech industry and to describe the nature of the industry and its contributions to the improvement of the human condition.

Attachments

A. Biotechnology Industry Facts

B. Ted Buckley, *The Myth of the Anticommons* (May 31, 2007)

C. BIO Position on Research use Exemption

D. BIO FAQ on Gene Patents

Biotechnology Industry Organization
1201 Maryland Avenue, SW
Suite 900
Washington, DC 20024-2149

Close Window

Biotechnology Industry Facts

- The biotechnology industry originated in the 1970s, based largely on a new recombinant DNA technique whose details were published in 1973 by Stanley Cohen of Stanford University and Herbert Boyer of the University of California, San Francisco. Recombinant DNA is a method of making proteins-such as human insulin and other therapies-in cultured cells under controlled manufacturing conditions. Boyer went on to co-found Genentech, which today is biotechnology's largest company by market capitalization.

- Biotechnology has created more than 200 new therapies and vaccines, including products to treat cancer, diabetes, HIV/AIDS and autoimmune disorders.

- There are more than 400 biotech drug products and vaccines currently in clinical trials targeting more than 200 diseases, including various cancers, Alzheimer's disease, heart disease, diabetes, multiple sclerosis, AIDS and arthritis.

- Biotechnology is responsible for hundreds of medical diagnostic tests that keep the blood supply safe from the AIDS virus and detect other conditions early enough to be successfully treated. Home pregnancy tests are also biotechnology diagnostic products.

- Consumers are enjoying biotechnology foods such as papaya, soybeans and corn. Biopesticides and other agricultural products also are being used to improve our food supply and to reduce our dependence on conventional chemical pesticides.

- Environmental biotechnology products make it possible to clean up hazardous waste more efficiently by harnessing pollution-eating microbes without the use of caustic chemicals.

- Industrial biotechnology applications have led to cleaner processes that produce less waste and use less energy and water in such industrial sectors as chemicals, pulp and paper, textiles, food, energy, and metals and minerals. For example, most laundry detergents produced in the United States contain biotechnology-based enzymes.

- DNA fingerprinting, a biotech process, has dramatically improved criminal investigation and forensic medicine, as well as afforded significant advances in anthropology and wildlife management.

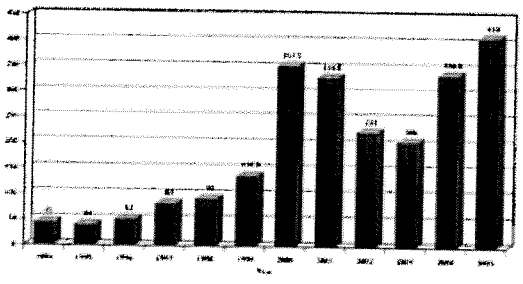
- The biotech industry is regulated by the U.S. Food and Drug Administration (FDA), the Environmental Protection Agency (EPA) and the Department of Agriculture (USDA).

- As of Dec. 31, 2005, there were 1,415 biotechnology companies in the United States, of which 329 were publicly held.

- Market capitalization, the total value of publicly traded biotech companies (U.S.) at market prices, was $410 billion as of Dec. 31, 2005.

- The biotechnology industry has mushroomed since 1992, with U.S. health-care biotech revenues increasing from $8 billion in 1992 to $50.7 billion in 2005.
- Biotechnology is one of the most research-intensive industries in the world. The U.S. biotech industry spent $19.8 billion on research and development in 2005.
- The top five biotech companies invested an average of $130,000 per employee in R&D in 2005.
- In 1982, recombinant human insulin became the first biotech therapy to earn FDA approval. The product was developed by Genentech and Eli Lilly and Co.
- Corporate partnering has been critical to biotech success. In 2005, biotech companies signed 564 new agreements with pharmaceutical firms and 354 with fellow biotechs, according to BioWorld.
- Most biotechnology companies are young companies developing their first products and depend on investor capital for survival. Biotechnology attracted more than $20 billion in financing in 2005 and has raised more than $150 billion since 2000.
- The biosciences including not just biotechnology but all life sciences activities employed 1.2 million people in the United States in 2004 and generated an additional 5.8 million related jobs.
- The average annual wage of U.S. bioscience workers was $65,775 in 2004, more than $26,000 greater than the average private sector annual wage.
- Bioethanol made from crop wastes using biotech enzymes could meet a quarter of U.S. energy needs by 2025.
- The Biotechnology Industry Organization (BIO) was founded in 1993 to represent biotechnology companies at the local, state, federal and international levels. As of December 2006, BIO's membership consisted of more than 1,100 biotechnology companies, academic centers, state and local associations and related enterprises.

Market Capitalization, 1994-2005*



* Amounts are in U.S. dollars in billions.
Sources:

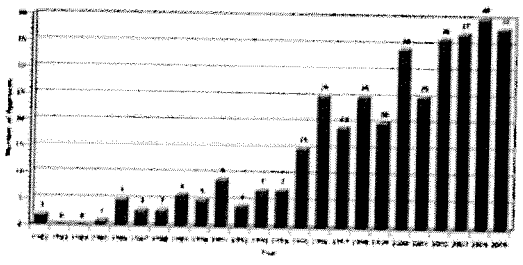
Ernst & Young LLP
BioWorld

U.S. Biotech Industry Statistics: 1994-2005*

Year	2005	2004	2003	2002	2001	2000	1999	1998	1997	1996	1995	1994
Sales	52.1	48.1	49.4	44.3	41.4	39.3	28.1	24.5	19	19.8	9.9	7.7
Revenues	80.7	73.8	73.2	69.8	69.6	68.1	52.3	50.2	47.4	44.6	42.5	41.2
R&D Expense	19.8	18.6	17.8	20.5	15.7	14.2	10.7	10.6	9.8	7.9	7.7	7.5
Net Loss	4.1	6.8	5.4	9.4	4.6	5.4	4.4	4.1	4.7	4.6	4.1	3.6
No. of Public Companies	329	331	314	318	342	336	300	316	317	294	266	261
No. of Companies	1,415	1,346	1,473	1,466	1,457	1,379	1,273	1,311	1,274	1,287	1,308	1,311

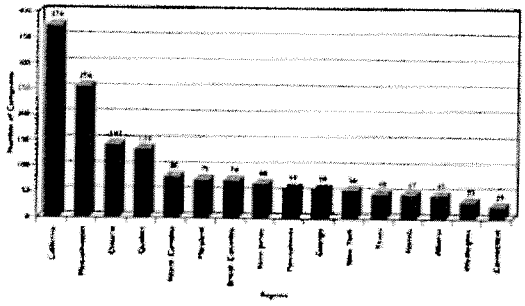
*Amounts are U.S. dollars in billions.
Source:
Ernst & Young LLP, annual biotechnology industry reports, 1995-2006. Financial data based primarily on fiscal-year financial statements of publicly traded companies.

New Biotech Drug and Vaccine Approvals: New Indication Approvals by Year



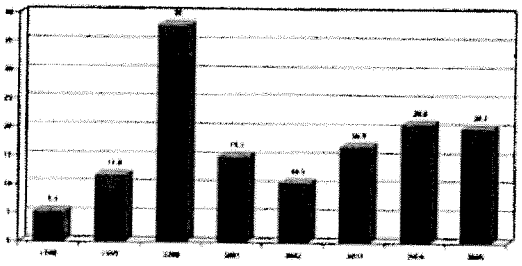
Source:
BIO

North American Biotech Companies by State and Province



Source:
Ernst & Young LLP

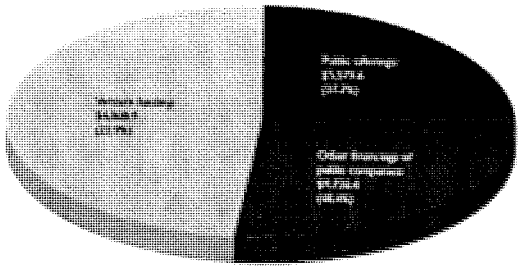
Total Financing, 1998-2005 (in billions of U.S. dollars)



Source:
Biomarket

Biotech Industry Financing, 2005

Total: $20,114.9 Million
(all figures in millions)



Source:
bioWorks

Bio
BIOTECHNOLOGY

The Myth of the Anticommons

Ted Buckley, Ph.D.
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May 31, 2007

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Executive Summary:

The theory called the *tragedy of the anticommons* was put forth in 1998 and claimed that over-patenting of research in the field of biotechnology was hindering research and development of new innovative treatments. Although no empirical evidence was cited, the theory quickly gained traction.

This paper examines the theory from both a theoretical *and* empirical basis. From a theoretical perspective, we find that the geographical interpretation that has been implied is too limited.

On the empirical side, rather than finding an industry unable to continue to find innovative therapies due to a patent thicket, we find an industry that is actively engaged in discovering and inventing innovative therapies. Specifically, we find that:

1. Since 1998 R&D of publicly traded biotech companies has increased over 60%.
2. From 1995 – 2005 the amount of venture capital funding for biotechnology companies has increase 300%.
3. Employment has increased by 21% since 1998.
4. Annual original INDs received by the FDA, while steady for a number of years, has shown a sharp increase in 2004 and 2005.
5. The number of biological compounds entering preclinical trials in 2005 was 37% higher than the number entering trials in 1998.
6. None of the academics surveyed reported abandoning a line of research due to patents on knowledge inputs.

Thus, we conclude that there is neither theoretical support nor empirical evidence to support the idea of the *tragedy of the anticommons*.

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Myth of the Anticommons:

I. Introduction:

In 1998 Heller and Eisenberg put forth an idea in a paper that suggested that over-patenting was threatening innovation in the biotechnology industry.[1] The idea was called the *tragedy of the anticommons*. The theory posited that, because of the excess number of patents in the biotechnology arena, innovation would be stifled due to an inability to conduct research without patent infringement. Although no empirical evidence was cited, the idea quickly gained a good deal of attention and traction.

This paper examines the theory of the anticommons from both a theoretical and empirical perspective. The paper finds that the theoretical construct, upon which the theory of anticommons is based, is too simplistic to adequately characterize the biotechnology world. Further, though a number of metrics are examined, none of the metrics empirically support the idea that there is over-patenting in the biotechnology industry.

The paper is arranged as follows. Section one contains a brief overview of the economics of patents. Section two provides an overview of the theory of the *tragedy of the anticommons*. Section three discusses the theoretical shortcomings of the theoretical construct. Section four examines the empirical evidence. A brief conclusion follows.

II. Overview of the Economics of Patents:[2]

The idea underpinning the US Patent system is the balance between giving incentives to inventors and giving society broad access to innovation. Abraham Lincoln may have put it best when he said, "The Patent System added the fuel of interest to the fire of genius." On one hand inventors need to be rewarded for the time and effort that they have put into their inventions. Thus, society grants patents to inventors which bestow a property right to the individual inventor. The invention belongs to the inventor and can not be copied or used without the permission of the inventor. The result of this exclusive ownership is that the price of the invention that is able to be charged is higher than it would be in a competitive market, and therefore, the inventor makes a higher profit for the invention that has been patented.

The ability to charge the higher price for their innovative products provides the innovators with an incentive to develop innovative products. Without the incentive

[1] Heller, M.A. and Eisenberg, R.S. "Can Patents Deter Innovation? The Anticommons in Biomedical Research." Science Vol 280. 1 May 1998.

[2] The discussion presented in the paper is a simplified overview of the patent system in order to facilitate an examination of whether there is evidence of the *tragedy of the anticommons*. Please refer to http://www.bio.org/privacy/patent.asp for a fuller discussion of the U.S. patent system.

provided by the patent, the pace of innovation would slow because inventors would not be rewarded as much for the time, effort and risk that it took to develop the innovation. Indeed, intellectual property protection has been found to be a significant determinant of economic growth.[3]

The patent system is especially important to the biotechnology industry.[4] Each biopharmaceutical that is brought to market requires on average $1.2 billion in research and development. The cost is high for a number of reasons. The reasons include the number of failures that occur along the way. For every biopharmaceutical that is brought to market, there are approximately 10,000 failed attempts. In addition, the time to go through clinical development and regulatory approval to market for the biopharmaceutical is 97.7 months on average.[5][6] Finally, the cost of the clinical trials is quite high and has risen substantially in the past decade. On average the cost of research and development rose 7.5% above the annual rate of inflation during the 1990s, the latest years for which figures are available.[7] Patents granted on a biotechnological innovation allow the inventors to recoup the research and development costs which have been invested.

III. Overview of the Anticommons Argument:

As has been discussed, patents are central to the development of innovative therapies in the biotechnology industry. However, in 1998 an idea was put forth that suggested that patents, instead of encouraging innovation, had the potential to actually stifle innovation in the biotechnology industry. This stifling of innovation was called the *tragedy of the anticommons*.[8] The authors posit that innovation may be stifled if there are too many owners who may exclude others from a scarce resource. Specifically, if there are too many patent holders of upstream technology, they may inhibit downstream innovation because of transaction costs and strategic behaviors. Imagine that a biotechnology

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[3] Grosld, D. M. and Graben W. C. "The role of intellectual property rights in economic growth." *Journal of Development Economics* Vol 48 (1996) 323 – 150.

[4] See for example, Cohen, W. M., Nelson R. R. and Walsh, J. P. "Protecting their Intellectual Assets: Appropriability Conditions and Why U.S. Manufacturing Firms Patent (Or Not)." NBER Working Paper 7552. February 2000.

[5] DiMasi, Joseph A. and Henry G. Grabowski. "The Cost of Biopharmaceutical R&D: Is Biotech Different?" *Managerial and Decision Economics*. Forthcoming.

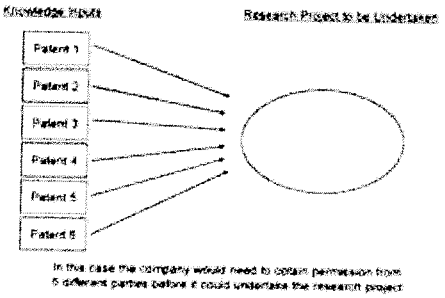
[6] Note: This does not include pre-clinical time of development.

[7] DiMasi, J. A., Hansen, R. W. and Grabowski, H. G. "The price of innovation: new estimates of drug development costs." *Journal of Health Economics* 22 (2003).

[8] Heller, M. A. and Eisenberg, R. S. "Can Patents Deter Innovation? The Anticommons in Biomedical Research." *Science* Vol 280 1 May 1998.

company seeks to do research in a particular area to bring an innovative therapy to market and that in order to do research in this area the company must use a set of knowledge inputs. Further, suppose that each of the knowledge inputs has been patented by a different company. In order for the biotechnology company to proceed with the research, it must first receive permission from each of the patent holders to use the patent holder's knowledge input for its research.

Figure 1:



Getting permission may take considerable time and may require considerable money. Thus, the research to bring an innovative therapy to market may be delayed, may cost more or may not take place if the company can not obtain permission from all of the upstream patent holders. In this scenario one patent holder in the set of knowledge inputs could suppress the research by not granting permission for the biotechnology company to use its patented input.

IV. Theoretical Shortcomings of the Anticommons:

The theory outlined above is appealing for its simple elegance. However, the simplicity of the argument is one of its short comings. An implicit part of the argument is that there is a scarcity to the biological commons akin to a geographical scarcity. Indeed, in responding to Heller's and Eisnberg's call for a formal economic model to be developed,

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Buchanan and Yoon developed an economic model and illustrated it geometrically.[9] Further, in another paper that discusses the *tragedy of the anticommons* Scherer states, "The problem is analogous to conditions on the Rhine River during the 18th Century. Over the 85-kilometer stretch between Mainz and Koblenz in 1780, there were nine toll stations . . ."[10] The result of the excessive number of tolls was a significantly lower amount of traffic on the river.

The geographic analogy is appealing but is flawed when applied to the biotechnology industry. In the examples above, there is a single starting point and a single ending point. In addition in the Rhine River analogy there is only one route from the starting point to the ending point. However, the "geography" in the biopharmaceutical world is much more complex than geography that is described in the world of the anticommons. In biotechnology world there are many starting points and many routes that will lead to the desired ending point, which in this case is an innovative therapy. In applying the "geography" of the biopharmaceutical world to the Rhine River analogy, imagine that a shipper wants to transport good from Mainz to Koblenz but is faced with having to go through nine toll stations on the river. Whereas in the 18th century, the shipper had no other option but to traverse the river, in the 21st century biotechnology world, the shipper has alternative routes, such as roads, rail or air. Thus, the shipper can reach the desired ending point by going around the river tolls.[11]

The idea of going around a toll is well known in the biopharmaceutical industry, as well as other industries, and is called inventing around a patent. An illustrative example is the class of pharmaceuticals called statins, which are medicines designed to lower blood cholesterol levels. In this case, the desired endpoint is a lower blood cholesterol level. According to the geographical example above, there is only one route to the desired endpoint and thus, one would expect only one statin to be on the market. However, there are more than five statin products on the market presently. The statins are but one class among many therapeutic classes of pharmaceuticals in which there are two or more products. There are multiple products in clinical testing for the treatment of breast cancer that utilize a variety of mechanisms of action. Some of these products' mechanisms of action overlap with the mechanisms of action utilized by other products.[12] Likewise, there are multiple products being developed for the treatment of chronic myeloid

[9] Buchanan, J. M. and Yoon, Y. J. "Symmetric Tragedies: Commons and Anticommons." *Journal of Law and Economics* Vol. 43, No. 1 (April 2000).

[10] Scherer, F. M. "The Economics of Human Gene Patents." *Academic Medicine* Vol. 77, No. 12 (December 2002) Part 2, p. 1363.

[11] Epstein, R. A. and Kuhlik, H. N. "Is there a Biomedical Anticommons?" *Regulation* Summer 2004.

[12] Waltz, Emily. "GlaxoSmithKline Cancer Drug Threatens Herceptin Market." Nature Biotechnology Vol. 23, No. 12 December 2005.

leukemia.[11] Therefore, one can conclude that the geography of the biopharmaceutical world is much richer and more complex than the geography posited by the world of the anticommons.

V. Empirical and Experiential Evidence and the Anticommons:

While the discussion above showed that the geographical assumption of the anticommons theory is too limited, that does not demonstrate that the *tragedy of the anticommons* is not occurring. We can not categorically prove that there is no *tragedy of the anticommons*. To do so would require an examination of a world without patents that does not exist. However, we are able to examine the world as it is and determine what evidence, if any, exists for over-patenting. If over-patenting were occurring in the biotechnology industry, one would expect that fewer innovative therapies would be brought to market. However, given that the timeline to bring a product to market is approximately 12 years from time of patent, it is likely too soon to examine number of innovative therapies for evidence of the anticommons. Therefore, we examine the inputs that produce the innovative therapies. That is, we examine the amount of research and development that is occurring, the result of that research and development and the experience of companies and researchers in the industry. If the *tragedy of the anticommons* is occurring, one would expect the following:

1. The amount of research and development would decline
2. *Ceteris paribus* fewer potential innovative therapies would be tested
3. Companies and researchers would clamor for a public policy remedy

We examine each of these in turn:

1. The amount of research and development would decline

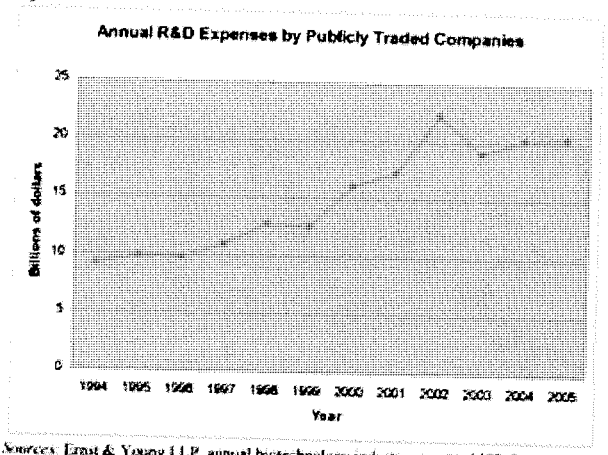
Recent R&D History

Companies will spend research and development dollars until the point at which it is no longer profitable for them to do so. From a more formal economic stand point, companies will spend until the expected marginal benefit of the research and development (e.g., the expected revenue derived from the research and development) equals the expected marginal cost of the research and development. The idea of the anticommons is that upstream knowledge inputs, which would be used in developing innovative therapies, have been "over-patented" and thus research in these areas is difficult, if not impossible, to do without engaging in patent infringement. The practical effect of this over-patenting is to make research and development more difficult (e.g., costly) to undertake. Thus, one would expect that because the research has become more costly, the amount of research and development undertaken by biotechnology firms

[11] Hampton, Tracy. "Looking Beyond Imatinib." JAMA. Vol. 295, No. 4. January 25, 2006.

would decrease. However, if one examines the amount spent on biotechnology research and development, the evidence does not indicate that *tragedy of the anticommons* is occurring.

Figure 2:



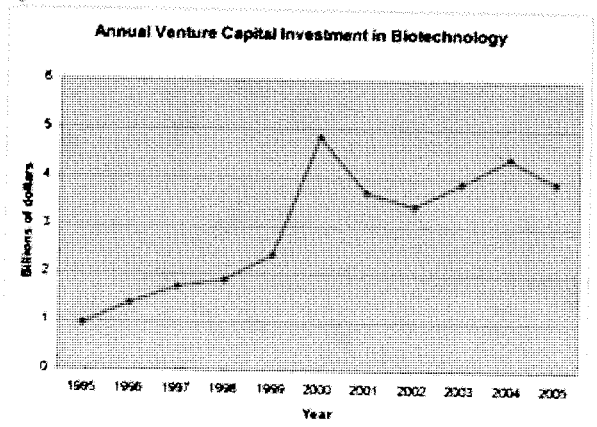
Sources: Ernst & Young LLP, annual biotechnology industry reports, 1993–2006. Financial data based primarily on fiscal-year financial statements of publicly traded companies, constant 2005 dollars.

Figure 2 indicates that the amount of research and development by publicly traded companies in the biotechnology arena has grown substantially over the past decade. Indeed, since 1998 when the *tragedy of the anticommons* was posited, R&D has increased by over 60%.[14]

[14] However, one could argue that perhaps the cost of doing research and development has actually decreased during the time period. If the costs decreased at a faster rate than the cost increase associated with the *tragedy of the anticommons*, one could argue that the investment in research and development would therefore increase. However, according to DiMasi, the cost of research and development of innovative therapies has increased at a rate of 7.4% over and above the cost of inflation during the 1990s. DiMasi J. A., Hansen R. W. and Grabowski H. G. "The price of innovation: new estimates of drug development costs." *Journal of Health Economics* 22 (2003).

While figure 1 focuses on publicly traded companies, privately held biotechnology companies play a pivotal role in the biotechnology industry.[4] Much of the funding for these companies comes from the venture capital (VC) community. If companies were unable to perform research and development due to the presence of the anticommons, one would expect the VC investment in biotechnology to dry up.

Figure 3:



Source: National Venture Capital Association, constant 2005 dollars

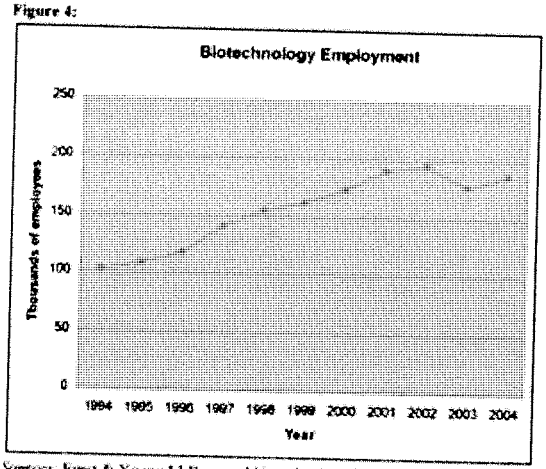
Figure 3 shows that the amount of VC has increased substantially in the past decade. In 2005 the amount of VC funding was almost $4 billion, up 300% from 1995.

Another aspect of research is the number of personnel. If the industry were experiencing a significant slow down due to the *tragedy of the anticommons* and the inability to pursue research on innovative therapies, one would expect that the difficulties of the industry

[4] Indeed, according to figures in Ernst and Young's Beyond Borders 2006, three quarters of the U.S. biotechnology companies in 2005 were privately held

would be reflected in a decrease in the number of industry employees. However, biotechnology employment has risen over the past decade

Figure 4:



Sources: Ernst & Young LLP, annual biotechnology industry reports, 1993–2005

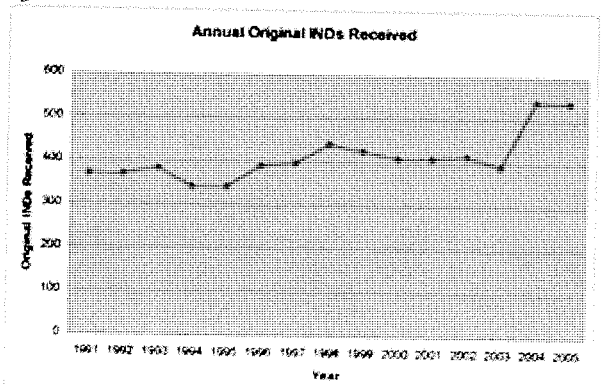
Since 1998, the number of employees has increased by 21%. Thus, instead of seeing what one would expect if an industry were experiencing the *tragedy of the anticommons* – lower research and development and with it falling employment – one observes an industry which is increasing research and development levels and increasing employment

2. *Ceteris paribus* fewer potential innovative therapies would be tested

If the *tragedy of the anticommons* were occurring one would expect that the R&D that was being undertaken would be less efficient. That is, because so many of the knowledge inputs had patents that needed to be licensed or invented around, the research projects would take longer or the research projects would be abandoned altogether. As a result of the increased difficulty of doing research, the number of innovative therapies would decrease. However, given the long lead time that it takes to research and develop an innovative therapy and bring it to market, approximately 12 years, it may be too early to see evidence of the *tragedy of the anticommons*. Therefore, we examine the number of

annual Investigational New Drug (IND) submissions, which would be affected in a similar way. Because of the shorter timeframe, if the *tragedy of the anticommons* were occurring, one would expect the number to have decreased.[9]

Figure 5:



Source: FDA, Pricevel's Bio Pharmaceutical R&D Statistical Sourcebook 2006/2007

One would expect the number of INDs to drop if the *tragedy of the anticommons* were occurring. One finds a relatively stable number of INDs being originated annually from 1991 – 1998, the seven year time period before the *tragedy of the anticommons* was posited, and a relatively stable number of INDs being originated from 1998 – 2003. However, there is a sharp increase in the number of original INDs received in 2004 and 2005. These years are precisely the time period when one would expect a decrease if over-patenting were starting to occur in 1998. One would expect a decrease in INDs approximately six to seven years after the phenomenon began to occur because pre-clinical testing (that is the time from a drug being patented until it reaches the IND stage) takes on average between 3 – 6 years. If there were an anticommons problem, it would take 3 – 6 years to manifest.

[9] Because biotechnological inputs are used for the development of both small molecule therapies and therapeutic biologics, we examine both in turn.

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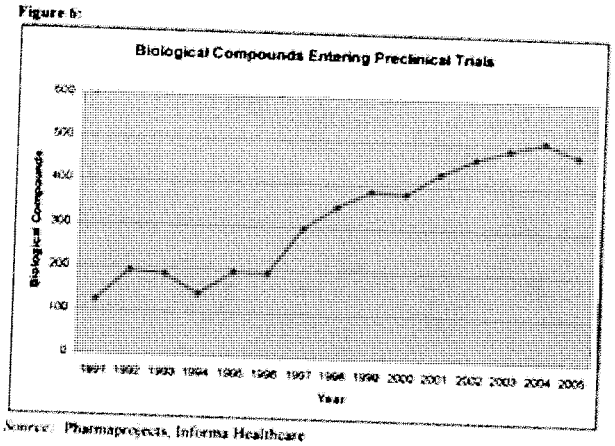
Next, we examine the number of biological compounds that enter preclinical testing on an annual basis.

Figure 6:



Source: Pharmaprojects, Informa Healthcare

Rather than finding a decrease in the number of biological compounds entering preclinical trials, we find there has been a substantial increase in the number of biological compounds entering preclinical trials both before and after 1998. While the percentage growth has dropped from the 1991 – 1998 to the 1998 – 2005 time periods, in 2005 there were still more than 37% more compounds entering preclinical trials every year than were entering in 1998. This finding is inconsistent with research being stifled or hampered as one would expect to find if the *tragedy of the anticommons* were occurring.

3. Companies and researchers would clamor for a public policy remedy.

A substantial number of members of the Biotechnology Industry Organization (BIO), the trade association for the biotechnology industry, are companies who depend on the ability to research and develop innovative therapies. Thus, if there were a *tragedy of the anticommons*, one would expect that BIO would be clamoring for a public policy remedy especially patent reform. However, rather than implying that there is a *tragedy of the anticommons* which is impeding research, BIO's position implies that the patent system encourages innovation. That is, the patent system is not hindering innovation, but rather,

the patent system is allowing companies to engage in research and development of innovative therapies.[17]

The *tragedy of the anticommons* focuses specifically on the patenting of upstream research. However, BIO's position specifically supports the patenting of "novel and useful nucleotide sequences..." BIO also supports patenting research tools which, like nucleotide sequences, are akin to the knowledge inputs that the *tragedy of the anticommons* discusses. Further, BIO's position fundamentally opposes the notion that patents on this broad array of biotechnology inventions are hindering innovation. BIO says unequivocally that it supports patenting of these types of inventions. In addition, it affirms that intellectual property rights are a prerequisite for the commercial success of these companies and for future innovation in these knowledge inputs.

While the discussion above focuses on companies and shows no evidence of the anticommons, one may argue that perhaps the *tragedy of the anticommons* is affecting academic researchers rather than companies. The National Academy of Sciences commissioned a study to examine the issue.[18] Walsh *et al* surveyed 414 academic researchers from universities, non-profits and government labs to examine whether their research had been impacted by patents. The authors found that only 3% of the academic respondents stated that they had experienced delays on their projects of more than a month due to patents on knowledge inputs. None of the academics reported abandoning a line of research due to patents on knowledge inputs.

Thus, neither biotechnology companies nor academic researchers are claiming to be adversely affecting by the patenting that is occurring in the biotechnology arena. Indeed, none of the academic researchers surveyed have abandoned research because of patent issues. Further, biotechnology companies have stated not only are patents not hurting them, but on the contrary the ability to patent is a prerequisite for commercial success.

We find no evidence of a *tragedy of the anticommons* either among companies or among the researchers who work in academic, non-profit or governmental settings.

VI. Conclusion:

The *tragedy of the anticommons* is an elegant and compelling theory. The theory claims, that instead of encouraging innovation as patents have been found to do in the biopharmaceutical industry, the patenting that has been occurring in the 1980s has the potential to hinder innovation. However, as has been discussed, the theoretical construct of the anticommons world is too simplistic to describe the world of biotechnology. We

[17] BIO's Principles for Patent Reform Approved March 29, 2004 Board of Standing Committee.

[18] Walsh, J. P., Cho, C. and Cohen, W. M. "View from the Bench: Patents and Material Transfers." *Science* Vol 309. 23 September 2005.

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acknowledge that we can not categorically state that there is no *tragedy of the anticommons*. To do so would require an examination of a world without patents that does not exist. However, we are able to examine the world as it is and determine what evidence there exists for over-patenting. Indeed, if over-patenting were occurring, the outcome of this over-patenting would be "fewer useful products for improving human health."[1] Because of the long development time of innovative therapeutic products, we inspect the inputs of those products. The first input is R&D. If there were a *tragedy of the anticommons*, one would expect that the amount of R&D would decline because of the increased difficulty of undertaking research. Yet, we find the exact opposite. R&D in both the publicly traded and privately held biotechnology companies is increasing. Further, we find that the number of people employed in the industry is increasing over time. Next, we inspect the pipelines of biopharmaceutical industry. If the research were becoming more difficult, one would expect that the number of innovative therapies in testing would be decreasing. Rather, we find the opposite. We find that the pipeline of both chemically and biologically based innovative therapies is expanding. Thus, the information that we examine paints a picture of an industry that is growing in terms of research and development with an increasing number of products in the pipeline. The argument could be made that perhaps researchers – either those in industry or in academia - are encountering problems that are not reflected in the R&D figures or in the numbers associated with the product development pipeline. However, the biotechnology industry is strongly supportive of the patent system and contends that it encourages innovation. Thus, industry is not supportive of the idea that over-patenting is occurring and hindering its ability to bring innovative therapies to the marketplace. Further, none of the academic researchers surveyed by Walsh *et al* abandoned their line of research due to patents on knowledge inputs. Therefore, we conclude, based on both empirical and experiential evidence, that there is no support for the idea that a *tragedy of the anticommons* is occurring in the biotechnology industry.

[1] Heller, M. A. and Eisenberg, R. S. "Can Patents Deter Innovation? The Anticommons in Biomedical Research." *Science* Vol 280. 1 May 1998.

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Biotechnology Industry Organization
On Research Use Exemptions
July 28, 2005

Overview

In exchange for complete disclosure of an invention, a patent grants the right to exclude others from using the invention for a limited time. This time-tested contract is the cornerstone of technological progress in a free economy, as it provides incentive to research and invent while society gains access to the eventual products and knowledge. Nowhere is this more evident than in the biotechnology industry. Biotechnology offers enormous hope for curing intractable diseases and meeting many of the world's environmental and agricultural challenges, thereby improving the health and well being of people today and for generations to come.

The current intellectual property system in the United States has been instrumental in creating the biotechnology industry and sustaining biotechnology companies. By protecting inventions that are essential to the development of biotechnological products, the patent system's time-limited protection spurs investment into the research and development of technological products, particularly biotechnology products. It is common for a biotechnology company to expend hundreds of millions of dollars and work for more than a decade before it reaps its first dollar of product revenue. The risks are great, and few companies actually succeed in their quest to get products approved by regulatory authorities. Without strong, predictable, comprehensive and enforceable patent protection, it is unlikely that investors would risk their capital or resources to fund biotechnology endeavors. Through patent protection for the molecules that serve as modern biotechnology's foundation (proteins and nucleic acids) the biotech community can invest in the R&D needed to bring these important and innovative healthcare products to market.

BIO members are dedicated to translating cutting-edge technologies into products for use in healthcare, agriculture and the environment to benefit humanity. BIO recognizes the importance of the tools being used in modern biotechnological research, including those used in the private and public sector to decipher the human genome and other genomes. BIO supports the ability of developers of innovative research tools to obtain patents on their discoveries. BIO also supports the rights of developers to use intellectual property

rights to succeed commercially so that investment in needed innovation will continue and society will reap the benefits.

Through their close relationship with the research and academic communities, both public and private, BIO members are dedicated to promoting the larger objectives of scientific progress against disease and famine.

Research Use Exemptions

Exemptions from patent enforcement are rare in U.S. patent law. However, there are two types of existing exemptions that are of importance to BIO members.

One exemption is the judicially created research-use exemption. This narrow exemption permits making and using a patented invention to better understand **that** invention. It provides that it is not an act of infringement to make and use a patented invention if the use is limited to research or experimentation and the user does not obtain any commercial advantage or benefit.

The courts have interpreted this exemption narrowly. In *Madey v. Duke*[1], the Court of Appeals for the Federal Circuit held that activities that could be construed to have a business-related objective (e.g., publishable research to further a university's prestige, image, & ability to bring in grant money) are considered to be outside the scope of a research use exemption. Thus, academic researchers may be outside the scope of exemption if their activities further the interests of their institutions, such as attracting researchers or securing research grants. As a practical matter however, a patent owner will generally not enforce his patent against a researcher if the research activities in question do not damage the patent owner's commercial interests.

A second type of research exemption is included in the Hatch-Waxman Act of 1984[2]. This exemption allows making and using a patented pharmaceutical compound or device to collect data for submission to a U.S. Government regulatory agency (typically for a generic drug manufacturer to submit to the FDA). This "safe harbor" is intended for individuals or entities making and using patented materials for uses "reasonably related" to the development and submission of information to the government. In *Merck v. Integra*[3], the Supreme Court held that a certain amount of experimentation using a patented invention falls within the "safe harbor" provision of the Hatch-Waxman Act as long as the experimentation is reasonably related to the development and submission of data for the government regulatory agency. At the same time the Court held that not all experimentation falls within the safe harbor.

BIO believes that taken together, existing practice[4] and law[5] [6]pertaining to research use of patented inventions is appropriate and provides the appropriate balance between product development and research.

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[1] John M.J. Madey, Plaintiff-Appellant, v. Duke University, Defendant-Appellee., 307 F.3d 1351; 2002 U.S. App. LEXIS 20823; 64 U.S.P.Q.2D (BNA) 1737

[2] PL 98-417

[3]Integra Lifesciences I, Ltd. and The Burnham Institute, Plaintiffs-Cross Appellants, and Telios Pharmaceuticals, Inc., Plaintiff-Appellee, v. Merck KGaA, Defendant-Appellant, and The Scripps Research Institute and Dr. David A. Cheresh, Defendants. 331 F.3d 860; 2003 U.S. App. LEXIS 11335; 66 U.S.P.Q.2D (BNA) 1865

[4] Existing material transfer and licensing practices.

[5] *Merck v. Integra*

[6] *Madey v. Duke*

Gene Patenting FAQ's

What is a patent?

A patent is an agreement between the government and an inventor whereby, in exchange for the inventor's complete disclosure of the invention, the government gives the inventor the right to exclude others from using the invention in certain ways. The property right granted is quite different from what we typically think of when we own land or other real property. A patent does not provide the right to make, use, offer for sale, sell or import, but the right to stop others from making, using, offering for sale, selling or importing the invention.

Can living things be patented?

Some, but not all, living things. The United States Patent and Trademark Office, PTO (the agency charged with granting patents) enforces strict standards, set by Congress, on what can be patented. Like any invention or discovery, a living thing must be "new", non-obvious, and useful in order to be patented. More importantly, living organisms under consideration for patenting cannot be those that occur or exist in nature "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." 35 USC 101. One cannot obtain a patent on just any living creature, such as a mouse, because mice have been around for a long time. If, through manipulation of genes, someone makes a kind of mouse that never existed before, however, then that kind of mouse might be patentable.

For example:

- **Microbes**

  As long ago as 1873, Louis Pasteur received a US patent for yeast "free from organic germs or disease." With the growth of genetic engineering in the late 1970's, the patentability of living organisms was re-examined, and confirmed. A landmark case involved Ananda Chakrabarty's invention of a new bacterium genetically engineered to degrade crude oil. In 1980, the US Supreme Court clearly stated that new microorganisms not found in nature, such as Chakrabarty's bacterium, were patentable. Chakrabarty received a patent in 1981 (US Pat. No. 4,259,444). In its Chakrabarty decision, the US Supreme Court stated that "anything under the sun that is made by the hand of man" is patentable subject matter. Therefore, if a product of nature is new, useful and nonobvious, it can be patented if it has been fashioned by humans.

- **Plants**

In 1930, the US Congress (Congress) passed the Plant Patent Act, which specifically provides patent protection for newly invented plants that are asexually reproduced. In 1970, Congress provided similar protection for newly invented sexually reproduced plants.

- **Animals**

In the 1980s, the question of whether multicellular animals could be patented was examined. The key case involved a new kind of "polyploid" oyster that had an extra set of chromosomes. This new, sterile oyster was edible all year round because it did not devote body weight to reproduction during the breeding season. The PTO found that such organisms were in fact new but this particular type of oyster was determined to be obvious, and thus into patent was allowed. Nonetheless, the polyploid oyster paved the way for the patenting of other nonnaturally occurring animals. In 1988, Philip Leder and Timothy Stewart were granted a patent on transgenic nonhuman mammals (U.S. Pat. No. 4,736,866) that covered the so-called Harvard mouse, which was genetically engineered to be a model for the study of cancer. The PTO does not allow anyone to patent a human being under any circumstances. A 1987 PTO memo issued by Donald J. Quigg, Assistant Secretary of Commerce and Commissioner of Patents and Trademarks, states, "A claim directed to or including within its scope a human being will not be considered to be patentable subject matter." Accordingly, since 1987, the PTO has rejected any application that encompasses a human being.

- **Natural Compounds**

Natural compounds, such as a human protein or the chemical that gives strawberries their distinctive flavor, are not themselves "living," but do occur in nature. Thus, they are new, and can be patented, only if, they are somehow removed from the setting in which they naturally occur (*isolated*). Therefore, a compound that is *purified* away from a strawberry, or a protein that is *purified* away from the human body can be patented *in its purified state* (provided that, the purified, e.g., protein or compound, also meet the other requirements for patentability, as well). Such a patent would not cover the chemical while in the strawberry or the protein while in the person. Such a patent would not cover the strawberry or the person. The USPTO does not allow anyone to patent a human.

What is a gene?

A gene is the fundamental physical and functional unit of heredity. It is made up of tightly coiled threads or polymers of deoxyribonucleic acid (DNA). DNA is an informational molecule and is made up of four distinct nucleotides: deoxyadenosine (A), deoxyguanosine (G), deoxythymidine (T), and deoxycytidine (C). It is the nonrandom order of these individual "bases" that results in DNA being an

informational molecule. However, in and of itself, DNA has no functional property. It is a chemical that, when placed in an appropriate environment, will direct the synthesis of particular and specific proteins, which make up the structural components of cells, tissues and enzymes (molecules that are essential for biochemical reactions). Organisms, from single-celled protozoans to far more complex human beings, are made up of cells containing DNA and associated protein molecules. The DNA is organized into structures called chromosomes, which encode all the information necessary for building and maintaining the organism. A DNA molecule may contain one or more genes, each of which is a specific sequence of nucleotide bases. It is the specific sequence of these bases that provides the exact genetic instructions that give an organism its unique traits.

Can genes be patented?

Isolated and *purified* genes are patentable inventions if they meet the patentability requirements of Title 35 (including being novel, nonobvious, adequately described and useful). It is difficult to identify genes and even after we recognize them, it is very difficult to isolate them and put this information to use.

Gene and nucleic acid-based patents have helped attract the biotechnology and pharmaceutical industry's interest in the development of gene-based therapeutics, diagnostics and processes. For example, the isolated and characterized gene associated with a certain type of breast cancer, Her-2, was patented after years and millions of dollars spent in its identification, isolation and characterization. This discovery and the patents protecting its various aspects, enabled companies to develop therapeutics and diagnostics for breast cancer.

Are patents granted on an individual's genes?

No. Patents do not provide any rights to a person or to the genes in his or her body. Instead, patents are granted on *isolated* genes and gene products that have real-world applicability. That is, the patents cover genes and gene products that could be obtained from any person, for example, from a blood sample. Genes are not unique to an individual. Two unrelated people with brown hair may have the same gene that causes their respective locks to be brown. Or two women may have the same mutant gene that makes them susceptible to breast cancer. In that sense, a gene is generic and could be obtained from any number of people who posses that gene. (What makes an individual unique is the collection of genes that make up their DNA). As previously mentioned, patents may also cover genes of microbes as well as genes from animals and plants.

When considering the patentability of nucleic acids, which are the building blocks of genes, one must take into account the nature of the object for which protection is being sought. A nucleic acid, regardless of its source, is chemically indistinguishable from any other nucleic acid. While its sequence of bases may change, there is no *a priori* means of

establishing its source. Human DNA is no different, at least chemically, from that of a bacterium.

If one were presented with a nucleic acid, its sequence could be chemically characterized, and any protein that it might encode could be determined. However, it would not be possible to ascertain what species the DNA came from. In fact, DNA as an isolated molecule does not exist within living cells. It is always associated with various other molecules, such as proteins, sugars and fats. It is well established that subject matter that is a product of nature is not eligible for patent protection. However, isolated nucleic acids do not exist in nature.

How will the patents on DNAs, RNAs, and their correlates help society?

Gene and nucleic acid-based patents have helped attract the biotechnology industry's interest (and the pharmaceutical industry's interest) in the development of gene-based therapeutics, diagnostics and processes. Many, if not most, human diseases have their roots in our genes. More than 4,000 diseases are suspected to stem from mutated genes inherited from one or both parents. As of April 2000, 1,792 individual genes had been linked to disease, including common disorders such as heart disease and many cancers. In addition, discovery of new genes holds promise for new treatments, diagnostics, predictive tests, and agricultural and environmental innovations. However, in most cases, these discoveries will not be further developed if they are not patent protected.

Without patents, these discoveries will remain just that, discoveries sitting on laboratory shelves, and society will miss out on the public benefit that could have come from such discoveries. Without the ability to protect core biotech inventions such as DNAs, RNAs (ribose in place of deoxyribose, uracil (U) in place of thymine (T)) and their correlates, the prospect of investing in biotech is so risky that investors will choose other industries and technologies in which to invest. The road to putting a biotech product on the market is long (10 to 14 years) and expensive (hundreds of millions of dollars) and, that, only a small percentage (one out of 1,000) of biotech products ever make it to clinical trials and, of those, an even smaller number (one in five) ever make it to the market. These odds are astronomical, and patents provide the investor with an assurance that if anyone benefits from the research, it will be the party that took the risk to invest in that research. Without patents on biotech inventions, investing in biotech would be akin to a donation rather than an investment and investors will choose other industries and technologies in which to invest. The lack of availability of patents for biotech inventions will be detrimental, not just to the growth of, but also to the survival of, the biotechnology industry.

Mr. BERMAN. Well, thank you all very much.

I will recognize myself for 5 minutes to begin the questioning process.

Dr. Sung, you proposed in your written testimony a very specific legislative proposal that creates a research use exception. One problem I have heard often in designing a research use exception is being able to draw a bright line between commercial use and a research use of an invention. How did your proposal deal with that issue?

Mr. SUNG. Well, Congressman, I should say that the research use proposal that I laid out in my written submission was used as a piece for further discussion points about that very aspect of it. I do not think that it has been traditionally very easy to make that delineation between commercial and noncommercial use. In fact, a focus of the Federal Circuit opinion in *Madey v. Duke* related to that difficulty.

That being said, the proposal, therefore, takes it and makes it a selective opt-in process whereby it is a self-identification issue on the part of entities interested in engaging in that type of "academic" research use, and to the extent they are willing to self-identify, there would need to be some transparency and accountability for what they plan on doing through the submission of a detailed research plan.

This is not meant to put both the academics and the private industry at odds, but, hopefully, to help foster a more open working relationship between the two for that purpose.

Mr. BERMAN. So the researcher opts in and then has some kind of transparent process submitted to, what, the PTO or another authority?

Mr. SUNG. Actually, it could be a notice directly to the patent owner for that purpose and, again, to facilitate the dialogue. Now some may say that it is problematic because oftentimes researchers would not know about a patent in existence, much less the patent owner, and the reason this is drafted as an opt-in procedure is you could certainly rely on status quo and conduct your affairs accordingly.

Mr. BERMAN. Mr. Kushan, you say that any change to the law regarding gene patents would negatively affect expectations by investors in biotechnology companies. You also indicate that the biotechnology industry has had a long tradition of refraining from asserting their patents against universities, and you point to data that supports this.

Since the biotechnology industry does not sue universities that are making research use of their gene patents, would legislating a clear research use exception upset investor expectations? Wouldn't an explicit research use exception for gene patents just codify an already existing practice and, therefore, be of no real importance to investors?

Mr. KUSHAN. Well, as your past 3 years of effort in carefully drafting patent reform has shown, the words you choose to articulate that line will be very difficult to write down and to make sure they do not have an overbroad or underbroad or unintended consequences.

Mr. BERMAN. We will not use a second window. [Laughter.]

Mr. KUSHAN. I think it is fair to say that this has been kind of an academic question that we have seen for the past 15 years, whether it is necessary to create this kind of statutory bright line to shield purely academic research. One of the challenges we see, is that we very infrequently see purely academic research.

I think one concern that can immediately come up is if you have an academic researcher who is sponsored by your biggest competitor running programs intending to make an infringing product, we would not want to see a statutory research exemption somehow shield that person from the commercial liability they are going to create, and I think as you go through some of these types of scenarios——

Mr. BERMAN. Why would it? Take Dr. Sung's formulation. The researcher opts in and then tells the patent holder, even though he is being asked to do this by the potential competitor, exactly what he is doing, and the patent holder is sitting there watching to see the day it goes from research into commercial development and whacks him not only for infringement, but for breach of contract or whatever.

Mr. KUSHAN. Well, I will go back to kind of whether that would ever happen. First, there are two scenarios that are out there on this example.

One is that a researcher who is doing purely academic research is going to be concerned about a patent and liability from that, and I do not think there are many researchers who do purely academic research that believe that they are at risk.

The second scenario is if there is really a commercial motivation driving that researcher, putting yourself squarely in the headlights of a patent owner would not be recommended by most attorneys representing the company that is sponsoring that research because it will create unnecessary risks.

I think as a practical matter, we see very few instances of patent owners going after purely academic research, both because there are very limited damages at the outset. You know, the work that is being done does not reflect the kind of scale——

Mr. BERMAN. Well, my time has expired, but——

Mr. KUSHAN. Yes, I am sorry.

Mr. BERMAN. You say they very rarely go after purely academic research, and then you say but they really do not do purely academic research.

Mr. KUSHAN. Well, that is part of the challenge of drawing that line you are trying to draw. I think if it is truly academic research, there is nothing they should be concerned with. If it is something that is not—if it is a sheep in wolf's clothing or a wolf in sheep's clothing—then you should not really be shielding that activity under a research exemption because it is not appropriate to do that. That is actually commercially competitive types of scenarios.

Mr. BERMAN. Thank you.

Mr. Coble?

Mr. COBLE. Thank you, Mr. Chairman.

Let me direct this question to all the witnesses.

Are most of the complaints about gene patents based on isolated incidents or anecdotal evidence? The appendices of Dr. Grodman's testimony cite some disturbing cases, and I am wondering is there

a systematic problem with the exclusive licensing of genetic associations.

Mr. Grodman, why don't I start with you?

Dr. GRODMAN. Thanks.

In the testimony, we both have in there, both peer-reviewed articles. There is one article, that from JAMA, that talks about breast cancer specifically and talked about in those areas where there were two genes that were found out that scientific research said that there were other areas, other insertions, genetic arrangements and mutations that, in fact, that 17 percent of the cases in which it seemed to be negative were, in fact, positive under the light of new studies. But in the cases of the one laboratory doing the test, it was not the same incentive or urge to be able to go up and update the test, as if there was another laboratory that was keeping it up to date.

There also were in there specific cases when results come back in an indeterminate manner, which is something that no degree of regulation could attach, could be able to deal with, that in those cases, it is up to between the referring geneticist and the doctor in the laboratory to come up with a satisfactory result, and in that case, that geneticist who referred the test had nowhere else to go for the test.

So the concern is that exclusive licenses in diagnostic gene testing, we believe, does lead to a situation of where there is no proper competition or urge to produce a better service.

Mr. COBLE. Mr. Kushan, let me ask you this. What would happen to the biotechnology industry if the Federal Government exercised march-in rights on a regular basis, A, and should the standards of section 203 of the Patent Act be amended to encourage greater use of march-in rights?

Mr. KUSHAN. Those are two difficult questions, and I will do what I can to respond to that.

Mr. COBLE. Well, you are a Carolina man. That is why I put it to you.

Mr. KUSHAN. Thank you. Notice my Carolina blue tie.

I think the first question of the use of the march-in authority would have a fairly significant chilling effect on the biotech industry, in part because the political decisions that might drive use of that authority are very scary to companies that have invested money in developing a product. The idea that you are going to do all this work, spend all this money, finally reach the market, and then at the back end of your business model, an uncertainty that you could not have imagined will pop up and deprive you of the patent exclusivity is going to have an impact on use of those funds.

The second part of this is that we have seen the NIH takes steps in the past decade to use their influence without the march-in authority. To set standards of conduct, for example, they developed guidelines relating to use of materials and sharing of research tools when there had been Federal funding involved in that, and that is kind of a better model, essentially putting on the table that before you take funding, you know that there will be conditions attached to it.

I think when you look at the march-in experience, the fact that they have never been used, and that there is so much reticence

about going to that as a mechanism, has created a fairly significant set of expectations in the industry that they will not be used at the back end in the commercial setting.

Mr. COBLE. Thank you.

Before my time expires, let me go to Dr. Sung and-or Dr. Soderstrom.

We have compulsory licenses in the Copyright Act. Why shouldn't we have compulsory licenses for patented pharmaceuticals and biologics, either of you two?

Mr. SODERSTROM. I would simply echo many of the comments that Mr. Kushan just made in that when we are negotiating licenses, particularly to start-up companies or biotech companies, this issue comes up all the time. What are the Government reserved rights? What are march-in rights? How often are they used?

It is something that for investors is of extreme concern because of the reasons he pointed out. If they are going to put a significant amount of money at risk over a long period of time in a fairly high-risk technology development exercise, they need some assurance that that investment, if they are successful, would be protected.

Mr. SUNG. I would have little to add to those particular comments, just to say that I think the standard recourse for purposes of saying compulsory licensing is bad defeats investment-backed expectations at the front end.

Mr. COBLE. Quickly, Dr. Grodman. The red light is about to illuminate.

Dr. GRODMAN. It is already on there.

Mr. COBLE. It has illuminated.

Dr. GRODMAN. One point about it: As you mentioned in your opening comments, the cost of getting a new drug to market may well be a billion dollars. What we are talking about, what I am really addressing are diagnostic genetic tests, the cost of which could take from the association between the clinical rendition of this sequence that is done in the university and then licensed out. To have a laboratory to bring up that test, that might be anywhere from $25,000 to $50,000 to, at most with new technologies, may be a quarter of a million dollars. It is not the same investment that we are talking about with therapeutics. It is very, very different.

Mr. COBLE. I yield back, Mr. Chairman. Thank you.

Mr. BERMAN. Thank you.

We will have a chance to explore that specific subject you are raising later in the third and fifth rounds of questioning.

Mr. Issa?

Mr. ISSA. Thank you.

The fifth round is where I get my really tough questions in.

You know, I looked for something that was akin to this subject. You know, when did we discover something and grant it a patent? And, oddly enough, I found something that was a little bit close, and that was when the product now known as Botox took something that was commonly understood and said, "But you can do it for this. Do what it does, and you can do it for this reason," and it was granted a patent and continues to be an ever more broadly successful product, including for people with migraine headaches now. I think Congress should figure out that Botox is the antidote for what we do.

So, I mean, I see the importance of it, and I guess I will ask two major questions.

Dr. Grodman, this is Coca-Cola. It is a secret. Nobody knows what it is. And I understand that you support the patents, but just because you support it and yet have a problem with the exclusion, if we were to not grant patents in this area, would it be a little bit like this, except we would not see it in the marketplace?

People would discover and then continue to keep it a secret so that they could do the follow-on work. Isn't that a risk we take when we do not patent something which we want discovered, but it could be discovered and kept a secret and, for example, diagnostic centers could preclude you from knowing what you need to know while they know what they need to know and say, "Just send it to us, and we will tell you whether you have this fatal disease."

Dr. GRODMAN. Well, I would probably be scarcely the last one on this panel who would be championing patents. I think that in the medical arena, we do know what the formula, if you will, of Coca-Cola is. It has been well researched and referenced in medical journals. The question is whether or not we are able to go in and have access to that different information.

So I am by no means, for my purpose today, supporting or not supporting patents. What I am supporting is the fact that there needs to be competition that when we have certain information about diagnostics that people can compete over producing a better test.

My own preference is that the information is open and that people do benefit. In a system of what I am addressing, that license for Coke is the best one there is and everyone knows what it is, I am saying, fine, but pay them a license if you want to be able to do it, but be able to allow everyone to be able to enjoy Coke no matter what the outside——

Mr. ISSA. So, essentially, you have to make the argument for a patent. Otherwise, there would be nothing to license. It would just be a secret.

Dr. GRODMAN. I am not making the case for or against patents. My concern is the ultimate amount of patient care and creating the competition for the exclusionary idea that people cannot perform a test.

Mr. ISSA. Mr. Sung, I guess I will switch to you just to see if I can get a dissenting opinion.

If we, in fact, deny patents in this field, don't we induce universities, perhaps the private sector because universities might choose to publish regardless, don't we induce people to cloak discoveries in a way that allow them to further their business practices without ever releasing them? Couldn't you end up with five or ten or 20 different research facilities discovering the same thing, but keeping it to themselves because if they cannot enjoy a period of patent protection, they might as well enjoy a period of exclusivity through nondisclosure?

Mr. SUNG. No, I agree with those comments. I think that what you are risking if you were to deny patent exclusivity in a particular area is to risk that, without that encouragement for disclosure, that there may be, I guess, more of a motivation, if you will, toward keeping something secret for a business purpose, but that

would depend in a particular industry on the various market and business approaches. But I do agree that you would be removing the encouragement for disclosure that the patent system was designed to protect.

Mr. ISSA. And, Dr. Grodman, I will go back to you. I will get off Coca-Cola for a moment.

I was an electronics manufacturer with now hundreds, but in those days 37 of my own patents, and I made it a practice not to license anybody. I made it a practice to produce my own products and to provide a superior product based on my patent.

Why is it, you think, that a medical diagnostic company, whether or not they invented it or they licensed it, should not have that same ability to do it, and why do you think that it, per se, causes them not to want innovation? Isn't their clock ticking, and that if there is not an encouragement by the licensee to get the inventor to invent more and to continue, if that encouragement is not there by the large dollars and the ticking clock on the patent, why wouldn't that, in fact, induce good development and good products?

Dr. GRODMAN. I would argue that that is not necessarily the case when it comes to medical diagnostic and genetic diagnostics, that when you go in and have an area which has a clinical association, what you are really doing is not having a product or something that you are going to sell. You are patenting an association, whether it be for a type of arrhythmia in three or four different genes, and if you go in and you will do that test, if you do it without competition, you will perform that test, and if people have that, they will have nowhere else to go for that answer.

Let us say someone else goes in and says, "You know what? There are three or four other genes that we can discover that will make the answer clearer, better for those who are at risk, maybe with medicines they need to be on or not. There is no possible way that a test could be done on those without getting the permission or a license on the original genes. As a result, innovation in that case, gets to be stifled and patient care is affected.

If the second group of people had a license to perform those tests, they can go in and make the ultimate test better. That would be lost if only one person had the innovation.

The example in the testimony that we gave about where there were certain genes about breast cancer that were done, it took 10 years of time for the one company that had the exclusive license to include those other genes to help make the test clearer for risk of breast disease. In a competitive framework, that would not be the case.

I would argue that the genes on products or patents on products or drugs is different than in this case of the diagnostic association between a clinical condition and a sequence. There are fundamental differences which makes it important for multiple people to do the test.

Mr. ISSA. Thank you. I yield back.

Mr. BERMAN. I think we will do a second round.

I have a couple of questions, but let me just make sure I understand. You are not arguing to nullify gene patents? Is there something different between a patent on a gene segment and a patent on a genetic diagnostic test? Are those two different?

Dr. Soderstrom?

Mr. SODERSTROM. No, sir. They are essentially the same. In fact, were we as universities to have that competition on the front end where there are multiple companies that are interested in commercializing these products, that would be a great thing. That is not often the case. In fact, it is seldom the case with universities, and this is another misconception.

We often think of it as there is a patent, and there is a product, and, as you know from your experience, those two things are not necessarily equal and, in fact, oftentimes, we are in the business of aggregating technology so that we can create the product, and that is one of the misconceptions.

So, while I admit that there have been some examples where we probably as universities could have done licenses differently in hindsight, oftentimes we are not in that admirable position. We are looking toward trying to induce somebody to invest in the technology and trying to bring it into a product form as quickly as possible.

So we do take a nuanced view. We do not necessarily always grant across-the-board licenses. We divide it up into fields of use, for example.

Mr. BERMAN. For me, I want to really get it down to something so simple that I can pretend to understand it. I think of a medicine, and biotechnology produces medicines, and then I think of tests, which determine whether or not you have something, or you have a predisposition to something or a genetic makeup that might mean a higher likelihood of getting something. Should I be thinking about patents in the context of these different things, or does it all blur into one?

Mr. SODERSTROM. Ultimately, they are the same. They are products that embody claims to a patented invention, and to the extent that you deliver that in a pill bottle or to the extent that you deliver that in a set of reagents that are going to be mixed with a patient's blood and then spotted on a slide, they are no different.

Mr. BERMAN. In other words, they may have different goals, treating versus diagnosing, but——

Mr. SODERSTROM. When we are presented with a discovery of a new gene that affects a disease category, there are usually four different sets of claims that you write for it. One is the use of the protein that is expressed as a therapeutic, the gene itself as a potential diagnostic, the gene potentially as an antigen that would be used in a vaccine or other prophylactic, and then the third is as a research reagent for the discovery of other things. Those are the four major claims that are on all DNA-based sequences that we typically use. How they——

Mr. BERMAN. You mean it is sort of boilerplate?

Mr. SODERSTROM. It is pretty close nowadays, yes. It is fairly routine. It is still expensive, but it has become much more routine.

Mr. BERMAN. All right. Then I will ask at least one other question that I wanted to ask before I went down this road.

Mr. Kushan, why wouldn't BIO support the use of march-in rights in the kind of case that Dr. Grodman is talking about, where the need to have others provide genetic tests is great? Again, I

guess some of that depends on how I understand the questions I was asking you.

Can you have march-in rights for this? I guess march-in rights exist. They are just never utilized. But can we encourage the use of march-in rights in this sort of subset of an area where the investment is not billions, it is thousands, tens of thousands, hundreds of thousands to achieve the kinds of purposes that Dr. Grodman was talking about?

Mr. KUSHAN. Well, I think your earlier question is getting to the challenge that is at the root of this problem. The patents that issue are going to have claims on nucleic acids corresponding to a gene that, you know, you discovered. That single patent is going to protect many different potential applications.

One might be development of a method of making the protein which then becomes a drug. Another might be using this clinical diagnostic setting where you are going to be screening and trying to determine if that gene is present in a sample. I do not know what another application might be, but for the purposes of this process, you are talking about the single patent.

Putting a condition through march-in rights on limiting the use of that patent right is the thing that cause concern within the biotech sector. The idea that at the back end of the process, once you have reached the market, there is going to be a Government-mediated decision to limit those patent rights, that is, I think, the chilling effect that I was trying to describe before.

Mr. BERMAN. My——

Mr. KUSHAN. I think——

Mr. BERMAN. I am sorry.

Mr. KUSHAN. No, I think one of the other questions that I wanted to address is just can you address the concerns that have been raised in these settings of clinical diagnostic use versus patent rights and product development. I do not think you can do that cleanly through the patent system or by limiting patent rights.

One of the things we always like to point out is that the patent rights are rights over the invention, and if there is conduct or other types of conditions that are seen in the market regarding the behavior of these companies, there are other ways of addressing that, other than through the patent system, and I guess that is one question to tackle, is whether that is something that is worth looking into.

Mr. BERMAN. Mr. Coble?

Mr. COBLE. Thank you, Mr. Chairman.

Because this issue is firing away, I will come back at you with a two-part question. What is your opinion of the biotech examiners at PTO, A, and, B, are they approving overly broad biotech patents similar to what occurred with business method patents in the late 1990's?

Mr. KUSHAN. Well, I was at one point in my life a biotech examiner, and I think for that sector of the Patent Office, I feel like those patent examiners probably are on the higher end of the scale of experience and training of most patent examiners. Many of them have Ph.D.s. They are probably the best of the group over at the Patent Office based on their training, experience, et cetera.

I think the Patent Office is doing the best job I have seen of really tying down our patent claims. I think anybody that works in the area of getting patents out of that group can share my pain of saying that the claims that you emerge with are often viewed to be exceedingly narrow, driven by both the strictness of the examiner's perspective and how the Patent Office uses these significant cases that have come down.

That goes to one of my comments in my testimony. This is one area where you are not talking about a patent that should not have issued. These are patents that are meritorious. They are narrow. They match the contribution in the patent application, and so that is why we are looking at these rights with great interest. They are very strong patent rights that should be respected.

Mr. COBLE. Thank you, sir.

To either of the other three witnesses, gentleman, to what extent are patent pools used today and should the Congress do anything to encourage their use?

Mr. SODERSTROM. Congressman, the use of pooling of patents has become much more routine on universities' parts, but probably the most impressive one is the pharmaceutical industry's patent pooling on snips, the small repeated segments, unique segments in genes that we find.

It has become a reality for most of us in licensing technologies that we only own a small part, in part because of what Mr. Kushan just said, which is our claims have become significantly narrowed, and that is a significant reality in the last 6 or 7 years, that it has become much more difficult to get broad claims in the Patent Office.

In my case at my university, it is very frequent, probably 10 to 20 percent of the time, we are putting together intellectual property, not just from Yale, but from other university colleagues to try to put together a package which then could be licensed.

It is not difficult to do. It has become relatively routine, and I do not see it as being a significant barrier to entry for a product.

Mr. COBLE. Yes, sir?

Dr. GRODMAN. I cannot comment on what it is like in the academic environment. In the commercial environment, you know, it is a noble attempt to be able to overcome a problem, but it is something which has not taken hold. I mean, there are many cases in which we can talk about where some genes will diagnose a condition and three other genes may diagnose it better or differently, and in those cases, there is very little camaraderie or ability to be able to share information, often, when that happens, causing conflict. It is a noble attempt, but it has not helped the diagnostic arena in a commercial environment.

Mr. COBLE. Dr. Sung, do you want to weigh in before my time expires?

Mr. SUNG. Only to say that what we have here as a result for looking at patent pools is that DNA is a de facto industry standard for biological sciences. You cannot wake up tomorrow and say, "I will not use DNA for these purposes," and so for that reason, the ability to design around in this field is very different than you might see in other mechanic or electrical technologies where patent

pools first grew up. So I think there is a need for this in many instances that are more heavily——

Mr. COBLE. Thank you.

Thank you, gentlemen.

I yield back, Mr. Chairman.

Mr. BERMAN. Mr. Issa, here is my problem.

Mr. ISSA. Yes, sir.

Mr. BERMAN. I have to go to the DOD Authorization Conference Committee to push language that the Foreign Affairs and Judiciary Committees are both recommending on the issue of Iraqi refugees. They want me there now for this Conference Committee. My inclination would be to give either of you the gavel to let you keep going, but I am told I am not allowed to do that.

Mr. ISSA. Yes, the Senate has gotten in trouble for doing that, too.

Mr. BERMAN. To give it to a Republican?

Mr. ISSA. Giving it to me. [Laughter.]

Mr. ISSA. And I did not even abuse it. Okay. You want me to wrap up?

Mr. BERMAN. So, I mean, the fact is I have five or eight more questions I want to ask all of you, but I am not going to be able to do it during this process. I would hope you would allow us to be in touch with you to pursue some of these things because we have in some cases just touched the surface, and we intend no commercial use of our research. [Laughter.]

Mr. ISSA. Thank you, Mr. Chairman. I will be quick.

Dr. Soderstrom, there was an earlier statement that somehow patents were barring people from doing follow-on research to discover new genes. In your experience, is that incorrect?

Mr. SODERSTROM. That is incorrect.

Mr. ISSA. Okay. So Yale University does not feel that even if somebody over here has an exclusive license, that you read the patent, that it allows you to take what they have done and look at it for your follow-on work. You just cannot incorporate it in your later release. Would that be fair?

Mr. SODERSTROM. Two points: One, is there is no tendency to look at patents prior to conducting research. At Yale, university faculty members are free to pick any area of inquiry. Second, in terms of the discovery that they ultimately make, we do do novelty searches to see if there is other intellectual property——

Mr. ISSA. Sure.

Mr. SODERSTROM [continuing]. And in those cases, we may choose not to patent simply because we do not see the point, and we would just encourage publication as soon as possible. If we do think that it would be a significant improvement, we usually would approach whoever has the exclusive rights.

Mr. ISSA. Okay. Now this is an academic question, but, for me, it was not academic. My experience has been that exclusivity, being excluded from somebody's invention, caused me to, in fact, figure out a way to skin the cat differently.

I am not in your industry. I am not in your academic endeavors, but isn't it somewhat true in all areas of endeavor that what you do not have access to—and, Dr. Sung, Larry, I saw you perk up on this, so you get first thing—isn't it true that in a sense there is a

benefit to exclusivity which is it causes people to go elsewhere and discover other things or around it? Isn't that an experience that even in medicine goes on?

Mr. SUNG. Well, I do think as a generality the patent system is designed to encourage design-around efforts and forward progress as a result of those efforts. I do think that in certain instances, again, because we are talking about genomic information here, the ability to do so may be somewhat stricter and harder to do. So I think there are instances where there may be blocking patents that might issue to this that are impossible as a technological matter to design around.

Mr. ISSA. Okay.

Mr. SUNG. But I think your general proposition is correct.

Mr. ISSA. And isn't the pooling that has gone on, to a certain extent, the result of those blocks causing people to go to other areas, create, if you will, block backs that then lead to the pooling being a necessity so that you have an ability to invent in an area in which very little is known?

Doctor?

Mr. SODERSTROM. That has certainly been our experience. That is what we have recognized, because people see it as a utility, as an opportunity to get around some of the things that are blocking them.

Mr. ISSA. Same? Same?

Dr. GRODMAN. No, I would disagree with that.

Mr. ISSA. So we only have three out of four. Okay. Well, you know that we can get a suspension pass with that here. Time is limited for the Chairman, too, so I appreciate that we sort of have a disagreement, but at least we got that out, as to what the value of exclusivity is potentially.

Thank you, Mr. Chairman.

Mr. BERMAN. All right.

With great regret, I have to adjourn because of the way this place works, but I do appreciate you coming, all your efforts, particularly the effort some of you made coming a ways to testify, and we will be following up individually and perhaps with questions.

Thank you very much.

[Whereupon, at 3:28 p.m., the Subcommittee was adjourned.]

APPENDIX

MATERIAL SUBMITTED FOR THE PRINTED HEARING RECORD

THE NATIONAL ACADEMIES

REPORT IN BRIEF

Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health

The molecular era in biology in the 1940s and 1950s and the development of recombinant DNA tools in the mid-1970s made it possible for scientists to isolate individual genes and determine their chemical composition, and ultimately to sequence entire genomes. The sequencing of the human genome with the Human Genome Project, nearly completed in 2003, has provided arguably the most powerful dataset in biomedical research. These milestones have explained how genes are assembled into genomes, answered questions regarding evolution, increased knowledge about genetics, and led to the development of new treatments for diseases.

The potential benefits of these discoveries require careful scrutiny when protecting intellectual property (IP) in the fields of genomics, the study of an organism's genome and the functions of genes, and proteomics, the large-scale study of protein structures and functions. Patents are sought by scientists in all sectors for research in these areas. The freedom of others to conduct research on a gene or protein and their ability to use them in healthcare could be constrained by the existence of a patent.

In recent years, the U.S. Patent and Trademark Office (USPTO) has been inundated with requests for patents on genes, gene fragments, proteins, and methods to study or produce them. Because thousands of genes or proteins can now be examined simultaneously, there is the possibility that a number of restrictions could impede scientific progress by blocking access to previous findings. In light of this changing environment, the National Institutes of Health (NIH) asked the National Research Council (NRC) to study the granting and licensing of IP rights on discoveries relating to genomics and proteomics, and the effects of these practices on research and innovation.

The patent landscape could become considerably more complex and burdensome over time. Several steps may be taken to anticipate and prevent problems for research in genomics and proteomics in the near future. As more knowledge is created, more patent applications are filed, and more restrictions are placed on access to information and resources. The nation's policy-makers, courts, and health and patent officials should take the steps outlined below to prevent the increasingly complex web of IP protections from getting in the way of potential breakthroughs in genomic and proteomic research.

THE NATIONAL ACADEMIES

National Academy of Sciences • National Academy of Engineering • Institute of Medicine • National Research Council

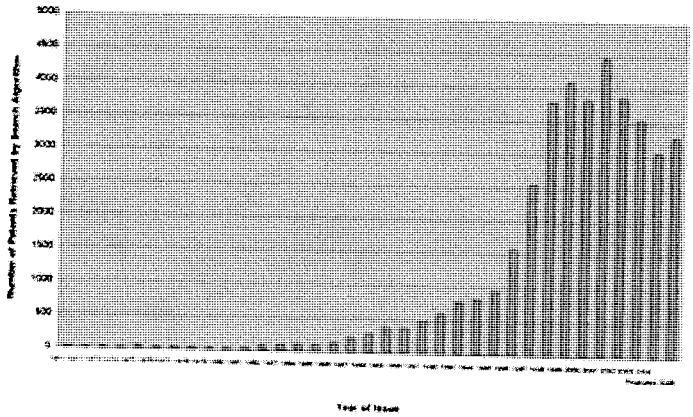

Figure 4-1 Number of DNA-based U.S. Patents (as of June 30, 2005) 2005 Projection is based on mid-year total.
Source: Georgetown University Database

BEST PRACTICES

Many of the potential problems for genomics, proteomics, and IP can be avoided if scientists and institutions follow the best practices already outlined by NIH, NRC, and others to facilitate the free exchange of materials and data.

Foster Free Exchange of Data, Information, and Materials

NIH should continue to encourage the free exchange of material and data among its grantees and contractors. Additionally, NIH should require these individuals to comply with the agency's guidelines for obtaining and disseminating biomedical research resources and for licensing genomic inventions. Industries and nonprofit institutions should standardize and streamline their processes for exchanging biological material or data.

NIH also should adapt and extend the "Bermuda Rules," which were created in 1996 by scientists involved in the publicly funded Human Genome Project. The rules instruct genomics researchers to share their data in a free public database called GenBank. They should be extended to include protein-structure data that NIH-funded centers generate for large projects in genomics. Researchers in both the public and private sectors should make this information freely available in the Worldwide Protein Data Bank, a project overseen by a consortium of international research groups.

Foster Responsible Patenting and Licensing Strategies

NIH has issued two publications, *Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources* and *Best Practices for the Licensing of Genomic Inventions* that provide guidance to NIH-funded institutions on balancing the need to protect IP rights with the need to broadly disseminate new discoveries and to maximize the public benefit whenever technologies owned or funded by the Public Health Service are transferred to the

commercial sector. NIH should require recipients of all research grants and awards, cooperative agreements, contracts, and intramural research studies to follow these guidance documents. Other funding organizations (such as other federal agencies, nonprofit and for-profit sponsors) should adopt similar guidelines.

In addition, patent recipients should analyze whether further research, development, and private investment are needed to realize the usefulness of their research results and that proprietary or exclusive means of dissemination should only be pursued when there is a compelling need. Also, whenever possible, licenses should be limited to relatively narrow and specific commercial application rather than as blanket exclusive licenses for uses that cannot be anticipated at the moment.

ADAPTING THE PATENT SYSTEM TO GENOMICS AND PROTEOMICS

Some of this research has the potential to blur the boundaries between abstract ideas and applications. USPTO should create a formal mechanism, such as an advisory board of leading scholars in these fields, to inform examiners of new developments and research directions and to improve the understanding of complex and rapidly evolving technologies.

Nonobviousness

To qualify for a patent, an invention must be useful and represent a creative leap; it cannot be obvious to a person of ordinary skill in a given area. When applying the "nonobviousness" standard to genomic and proteomic inventions, USPTO and the courts should consider whether a scientist of ordinary skill would have been able to create a given invention with reasonable expectations of success at the time the invention was made.

Utility Standard

The Supreme Court established a standard in its 1966 decision in *Brenner v. Manson* requiring that a patent applicant show that an invention has "specific benefit in its current form." However, this standard has not been applied in a consistent manner. Investigators and their institutions should avoid seeking patents for genes or proteins whose functions are unknown. These include proteins that are useful for research but do not have therapeutic or diagnostic functions.

FACILITATE RESEARCH ACCESS THROUGH LICENSING AND SHIELDING FROM LIABILITY FOR INFRINGEMENT

Experimental Use Exemption

A federal appellate court recently rejected the claim that the so-called "experimental use" legal defense shields academic research from patent infringement liability. In the future, academic and other nonprofit research institutions may feel compelled to protect themselves from liability by trying to regulate investigators' behavior. This may hinder research and fail to prevent legal problems because researchers are often unable to determine how existing patents apply to their work. It is also possible that patent holders, knowing that universities do not currently have legal protection from such liability, could increase demands for patent-licensing fees or dictate other terms that would burden the research enterprise. The situation could worsen over time as licensing restrictions imposed by patent holders increase. Congress should consider legislation that would allow scientists to conduct research on patented inventions in order to discover novel uses or improvements without fear of liability for patent infringement.

Patent Pooling

A patent pool is an agreement between two or more patent owners to license one or more of their patents to one another or third parties. Patent pooling is an approach that might address some issues of access to patented upstream technology and its possible applications to biomedical research and development. One

issue that may be important in the health field is the willingness of academic scientists to have their inventions pooled if that would reduce their share of royalties provided by universities. Therefore, NIH should study potential university, government, and industry arrangements for the pooling and cross-licensing of genomic and proteomic patents, as well as research tools.

Ensuring the Public's Health

A few cases of refusals to license practices by some companies have generated controversy because of the potential adverse effects on public health. In the United States, courts have denied injunctive relief in cases where health and safety are an issue. Should the rare case arise in which restricted access works against the interests of public health, courts should follow legal precedents and allow the provision of products or services that the public needs, while awarding compensation to particular inventors for the use of patented material.

Gene-Based Diagnostic Testing

There is concern about independent validation of genomic- or proteomic-based test results. Patent owners may control access to genomic- or proteomic-based diagnostic tests and then prevent others from using the patented technologies to validate the results of clinical tests. This may cause problems and encourage patent owners to enter into licenses that will permit others to use patented technologies for the purpose of independently confirming the results of a diagnostic test. Owners of patents that control access to diagnostic tests should establish procedures that provide for independent verification of test results. Congress should consider whether it is in the interest of the public's health to create an exemption to patent infringement liability to deal with situations where patent owners prevent independent verification of their tests.

COMMITTEE ON INTELLECTUAL PROPERTY RIGHTS IN GENOMIC AND PROTEIN RESEARCH AND INNOVATION

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For More Information

Copies of Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health are available from the National Academy Press (NAP); call (800) 624-6242 or (202) 334-3313 (in the Washington metropolitan area), or visit the NAP website at www.nap.edu.

Advancing Excellence

College of American Pathologists

Statement to the
U.S. House of Representatives Subcommittee on Courts,
the Internet and Intellectual Property

Hearing on "Stifling or Stimulating—The Role of Gene Patents
In Research and Genetic Testing"

October 30, 2007

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THE COLLEGE OF AMERICAN PATHOLOGISTS

The College of American Pathologists, representing more than 16,000 physicians who practice clinical and/or anatomic pathology appreciates the opportunity to submit comments to the House Judiciary Subcommittee on Courts, the Internet, and Intellectual Property regarding an issue of critical importance to pathologists and the patients they serve—access to genetic testing.

Our member pathologists practice in community hospitals, independent clinical laboratories, academic medical centers and federal and state health facilities.

Pathologists play an integral role in health care as physicians who obtain and interpret data as the result of examination of tissues, blood, and other body fluids for diagnosis and patient care. The mission of the College is to represent the interests of patients, the public, and pathologists by fostering excellence in the practice of pathology and laboratory medicine worldwide.

IMPACT OF GENE PATENTS ON MEDICINE AND HEALTH CARE

The current scientific revolution in genetics promises extraordinary advances in clinical medicine. As the medical specialists in the diagnosis of disease, pathologists recognize that genetic testing is an area of growth and change for pathology and medical practice now and in the decades to come. The research, development, and practice of genetic testing in academic and other medical centers is essential to medical progress, the training of physicians, researchers and health-care professionals, and the continued improvement of the quality of medical care. Most discoveries of human or pathogen genes can be effectively translated into gene-based diagnostic test services without the incentives provided by patents or exclusive license agreements. Pathologists therefore have a keen interest in ensuring that gene patents do not restrict the ability of physicians to provide quality diagnostic services to the patients they serve.

Gene patents pose a serious threat to medical advancement, medical education, and patient care. When patents are granted, subsequent exclusive license agreements, excessive licensing fees, and other restrictive licensing conditions prevent physicians and laboratories from providing genetic-based clinical testing services. As a consequence, patient access to care is limited, quality of patient care is jeopardized, clinical observations as the basis for new discoveries are compromised, and training of health care providers is restricted.

Throughout history, medical discoveries have progressed from the discovery of basic anatomy to histology and cytology—none of which are patented—to the more recent discovery of genes. The trend of using patents to monopolize gene-based testing services is a radical departure from historical precedent in clinical laboratories, and it works against the goal of making these procedures widely accessible and affordable for the public. Especially troubling is the fact that under patent protection, the increasing understanding of the utility of the test, as well as the underlying disease processes, also becomes proprietary, thereby imposing a profound change in how the profession and the public acquire knowledge about these rapidly evolving tests, the diseases diagnosed by the tests and their clinical utility.

The patent system in the United States generally encourages entrepreneurs to make new discoveries and to benefit directly from making their efforts broadly accessible. Limitations in how this patent system is applied to patents of genes compromises medical progress and access to new gene-based tests. The patent system should be reexamined to ensure the public interest in improving healthcare decisions based on gene-based tests and access to those tests.

Physicians and scientists can easily and rapidly translate the fundamental genetic information derived from sequencing the human genome into diagnostic genetic tests and use these tests for patient care. Because information about gene sequences is so fundamental to understanding specific diseases, patent holders can essentially gain ownership of diseases through patents. Exclusive or restrictive license agreements on gene-based tests have been used to prevent physicians and clinical laboratories from performing genetic tests as diagnostic medical procedures. Patients suffer because diagnostic test services are less readily and affordably accessible.

Medical education and research related to laboratory testing also are threatened. The National Academy of Sciences Committee on Intellectual Property Rights in Genomic and Protein Research and Innovation last year recommended in a report that policy-makers take appropriate steps to prevent the increasingly complex web of intellectual property protections from impeding potential breakthroughs in genomic and proteomic research. The report suggests several approaches to improving public access to patented inventions. Specifically, it recommends that Congress consider legislation to exempt research on certain aspects of patented technologies or inventions from patent-infringement liability, with the goal of promoting scientific discovery. The report also recommends that owners of the patented technology behind certain gene-based diagnostic tests should establish procedures that allow other clinicians to validate test results. If these patent holders do not take this step voluntarily, the report suggests that Congress consider, in the interest of public health, whether work to validate such results should be shielded from liability. This sole clinically-focused recommendation falls short, however, in recommending specific protections for physicians and other providers of clinical laboratory services against gene patent infringement enforcement. The College has supported policy recommendations and advocated for legislation in Congress that would extend certain protections to laboratory physicians.

In 1996, Congress recognized that medical procedure patents might impede the advancement of medicine, curtail academic access, place unreasonable limits on the research community, and interfere with medical education and the quality of care provided to the patient. As a result, in October 1996, legislation was signed into law (Frist-Ganske Amendment, 35 USC Sec. 287) that permanently precludes the filing of infringement suits against physicians and other medical practitioners for the performance of "medical activities" that would otherwise violate patents on medical or surgical procedures. A "medical activity" is broadly defined to include the performance of a medical or surgical procedure on a human body, organ or cadaver or on an animal used in medical research. However, the Act does not explicitly affect enforcement of biotechnology patents or extend to clinical laboratory services. With the advent of new and innovative approaches to gene based diagnostic testing, and the promise of enhanced and expanded diagnostic testing, laboratory services and clinicians should have the same protection from patent infringement as other medical providers and procedures.

Because of this oversight, medical practitioners who perform tests to diagnose genetic disease have received "cease and desist" notification letters from gene patent holder's indicating that continued patient testing would be a patent infringement. Examples of diseases where testing has been halted due to patent enforcement include breast cancer, Alzheimer disease, Canavan disease, and Charcot-Marie-Tooth disease. To address this issue, the Frist-Ganske law should be amended to protect clinical laboratory medical practitioners from patent infringement – just as other medical providers are protected. This would ensure that gene based diagnostic test services, which are part of medical practice and increasingly important, can be performed without fear of reprisal for the benefit of patient care, medical training, and medical research. Additionally, the College supports H.R. 977, the *Genomic Research and Accessibility Act,* introduced by Congressman Xavier Becerra (D-CA) and Congressman Dave Weldon (R-FL) that would prohibit patents from being obtained for a nucleotide sequence, or its functions or correlations, or the naturally occurring products it specifies.

In summary, we are facing the unprecedented situation in which a single patent owner can prevent physicians throughout the country from performing diagnostic procedures that use certain gene-based tests. This sets an extraordinary and dangerous precedent for patients and all of medicine, and strays from the constitutional and social purpose of the patent system to promote progress. Therefore, the College believes that current practices in the patenting and licensing of genetic sequences must be reexamined to ensure that gene based diagnostic tests are widely available and affordable for the greatest public benefit.