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Are patents beneficial to patient care? There is ample evidence that patents with an "I"—where the "I" indicates investors—benefit patients by making diagnostic assays and therapeutic products available to the public through commercialization. In particular, since the landmark U.S. Supreme Court decision that opened the portals to the wonders of biotechnology,[1] and the passage of the Bayh-Dole Act enacted on December 12, 1980, which allowed commercialization by the private sector of patented inventions arising from federally funded research, biotechnology patents have been the foundation of hundreds new therapeutic products, vaccines and diagnostic assays.[2] Living testimonials to the success of modern medicine are cancer survivors, notably those cured of childhood leukemia, transplant recipients, and those at cardiovascular risk who are populating the streets instead of graveyards.

The correlation between beneficial scientific advances and development of patent systems is demonstrated internationally. The Bayh-Dole Act has

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1. Diamond v. Chakrabarty, 447 U.S. 303, 318 (1980).

2. *Stifling or Stimulating – The Role of Gene Patents in Research and Genetic Testing: Hearing Before the Subcomm. on Courts, the Internet, and Intellectual Property of the H. Comm. on the Judiciary*, 110th Cong. 60-65 (2007) [hereinafter Statement of Jeffrey P. Kushan] (prepared statement of Jeffrey P. Kushan, on behalf of the Biotechnology Industry).

been a template for countries (for example, India and China) that adopt patent systems as they develop indigenous drugs and products, and move enthusiastically toward more robust patent systems as technology develops.[3]

Despite demonstrated successes of biotechnology, opponents of biotechnological patenting continue to argue that the present patenting system stifles innovation and blocks the public's access to beneficial inventions. This position is partly responsible for aborted attempts by the U.S. Patent and Trademark Office (USPTO) to change its rules,[4] and for Congress' consideration of patent reform.[5]

Most of these arguments fail to acknowledge that patents are difficult to obtain and limited in what they exclude. Patents only give rights to exclude others from practicing the invention *as claimed*, without approval of the patent owner.[6] During patent prosecution, patent claims may be narrowed to escape prior art barriers to patentability so much as to be of no practical value.[7]

It is difficult to invent a composition of matter, method or apparatus that is patentable. There are formidable obstacles in moving from a laboratory bench to issued patents, even more obstacles in successful commercialization, including expensive or lengthy obstacles clearing regulatory hurdles and enforcing patents. These long delays limit the time period over which patent rights can be enforced—from a routine maximum of twenty years after filing the patent application, to sometimes only one to two years after a patent issues.[8] Consequently, assuming that "profit" is a selfish goal ignores the practical necessity of covering research, development, and patenting costs.

Basic research may be too early to be patentable, since utility is one

3. *The Bayh-Dole Act (P.L. 96-517, Amendments to the Patent and Trademark Act of 1980) – The Next 25 Years: Hearing Before the Subcomm. on Technology and Innovation of the H. Comm. on Science and Technology*, 110th Cong. 148 (2007) (written statement of the Biotechnology Industry Organization).

4. *See, e.g.*, Tafas v. Doll, 559 F.3d 1345, 1349-51 (Fed. Cir. 2009).

5. Patent Reform Act of 2009, H.R. 1260, 111th Cong. § 1 (2009); *Patent Reform Act of 2009: Hearing on H.R. 1260 Before the H. Comm. on the Judiciary*, 111th Cong. (2009) (written testimony of the Biotechnology Industry Organization) (official transcript not available), *available at* http://bio.org/letters/20090430.pdf.

6. 35 U.S.C. §§ 103, 271 (2006).

7. *See* U.S. PATENT & TRADEMARK OFFICE, MANUAL OF PATENT EXAMINING PROCEDURE ch. 700 (8th ed., rev. 7, 2008) [hereinafter MPEP], *available at* http://www.uspto.gov/web/offices/pac/mpep/mpep_e8r6_0700.pdf.

8. 35 U.S.C. § 154(a) (2006) ("[S]uch grant shall be for a term beginning on the date which the patent issues and ending 20 years from the date on which the application . . . was filed, or if the application contains a specific reference to an ealier filed application . . . from the date on which the earliest such application was filed."); *see also* MPEP, *supra* note 7, at ch. 2700.

criteria applied by the USPTO.[9] Broad patents on early stages of research may be thrown out by the USPTO or the courts, if no actual use is proved. On the other hand, later stages of research may not be patentable if early stage inventions are patented or otherwise published, serving as the basis for finding that the later work is obvious.

If a patent issues, this does not necessarily remove the patented invention from free use by others. Some options to get around patent infringement are "designing around" the invention; that is, making or doing something that does not fall within the scope of the issued patents, going offshore to produce or sell a product in a country where there is no patent protection, challenging the validity of the patent, ignoring it, or having the government step in to exercise its rights if the research resulting in a patented invention was funded by a government agency.[10] There are non-patenting options to protect innovation.

Some argue that patenting restricts academic freedom,[11] but publication delays are not a necessary consequence of the patenting system. Patent applications can be prepared in one day if necessary to beat a bar date, for example, the date of publication.[12]

The patent system is far from perfect and is not fair to all, but alternatives for stimulating and commercializing inventions are not demonstrably better. If the patent system becomes untenable, inventors may resort to trade secrets. However, the Founding Fathers of the United States specifically empowered Congress to institute a patent system to promote science.[13] Would a world without patents, or only with narrow or late-stage patents, be more beneficial to society than the present system?

I. THE "I" IN PATIENT: HOW TO GET FROM BENCH TO BEDSIDE

Those who argue that patents do not serve the common good, and that some sort of "open source" sharing would be a better method to bring medical and agricultural innovations to the public, ignore the realities of bringing life science innovations to the bedside. Opponents of the patent system fail to demonstrate how to fund innovation from bench to bedside in

9. *See* 35 U.S.C. § 101 (2006) (requiring an invention or discovery to be "new and useful" in order to be patentable).

10. *See* 35 U.S.C. §§ 200-212 (2006); 37 C.F.R. § 401 (2008).

11. *E.g.*, Zhen Lei et al., *Patents Versus Patenting: Implications of Intellectual Property Protection for Biological Research*, 27 NATURE BIOTECHNOLOGY 36, 37-38 (2009) (concluding, based on a survey of academic researchers, that the proliferation of intellectual property protection has a negative effect on research).

12. MPEP, *supra* note 7, § 706.02(a); *see also* 35 U.S.C. § 102(a), (b), (e).

13. U.S. CONST. art. I, § 8, cl. 8 ("To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries").

the absence of patent-protected investors. The government does not do it. Taxpayer funding through, e.g., the National Institutes of Health (NIH), supports "bench" work, mostly basic research and pre-clinical work, but generally does not fund either drug development or regulatory costs (for example, Federal Drug Administration (FDA) costs). Before the Bayh-Dole Act, few drugs emerged from government funding. [14]

Yes, there are a few examples of philanthropic associations, such as the Gates Foundation, funding research and distributing the resulting products and methods at reduced costs to those in need, who are usually unable to pay the price of medicine. Such plans may not involve patenting. However, these routes are exceptional and would not suffice to serve the needs of the world. More pragmatic plans are needed overall:

> The key to success of the biotechnology industry—across of all [sic] its sectors—is a business model that is based on taking significant risks to develop products based on innovation. Specifically, the biotechnology business model is based on making significant investments (often hundreds of millions of dollars) in early stage research and development with the hope that some of these investments and efforts will yield a commercial product. This model has worked despite the fact that it is lengthy (often taking more than a decade) and that most biotechnology R&D investments and efforts do not result in a commercial product reaching the market. It is only by pushing boundaries of science and taking these risks that breakthrough inventions are discovered and converted into commercially viable products and services.[15]

Some form of protection of innovation is required by investors. In order to pursue drug development, investors including stockholders, must be assured their investment will be protected:

> The biotechnology business model requires an environment that, as much as possible, eliminates unpredictability in the commercial sector. One important factor in this environment is the guarantee of patent exclusivity. Specifically, by ensuring that the products or services that may eventually be marketed can be protected from unauthorized copying and use, companies can justify taking risks and making significant R&D investments. Introducing unpredictability by changing the availability of patent rights, or the conditions in which patent rights can be asserted, will

14. *Cf. University and Small Business Patent Procedures Act: Hearing on S.414 Before the S. Comm. on the Judiciary*, 96th Cong. 7-9, 14 (1979) (statement of Elmer B. Staats, Comptroller General of the United States) (noting the Pharmaceutical Manufacturers Association's position that "exclusive interest is essential if Government-financed new drug compounds are to enter clinical programs funded by the private sector. . . . patent policy should not be structured so as to 'restrain or regulate' the availability of inventions resulting from HEW research").

15. Statement of Jeffrey P. Kushan, *supra* note 2, at 62.

> adversely affect business environment that is so crucial to supporting innovation in the biotechnology sector.[16]

> Patents in the life sciences sector protect the type of products and processes that are integral to companies doing business in the biotech sector. By enabling these companies to prevent the unauthorized use of the patented technology, companies can justify pursuing their research and development efforts. Indeed, it is the guarantee of securing and using rights in the future that companies rely to justify making investments in R&D today.[17]

Although exclusivity is one of the primary justifications for innovation resulting in therapeutic drugs, non-patent exclusivity is also available. Because altruistic development of therapeutics is almost non-existent, except for the contributions of a few well-funded donors, companies are often reluctant to invest a substantial amount of time and money in developing products that either do not have patent protection or for which the target market is too small for commercial viability. Recognizing this need, the U.S. government has implemented a variety of measures that afford exclusivity regardless of patent protection. In some cases, the exclusivity is added on to existing patent protection.

There are at least five types of non-patent exclusivity in the U.S. These include: (i) new chemical entity (NCE) exclusivity (five years); new clinical study exclusivity (three years); orphan drug exclusivity (seven years); pediatric exclusivity (six months); and generic drug exclusivity (180 days).

The new chemical entity exclusivity of up to five years is granted to a drug that contains no active moiety that has been approved by FDA in any other application submitted under section 505(b) of the Act.[18] The new clinical study exclusivity of up to three years is granted to submissions of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant for a new use of a previously approved drug.[19] The NCE and the new clinical study exclusivity are also known as Hatch-Waxman exclusivity.[20]

Orphan drug exclusivity of up to seven years is awarded to drugs intended for treatment of a "rare disease or condition."[21] The term "rare

16. *Id.*

17. *Id.* at 63.

18. 21 U.S.C. § 355(c)(3)(E)(ii) (2006); 21 U.S.C. § 355(j)(5)(F)(ii) (2006); 21 C.F.R. § 314.108(b)(2) (2008).

19. 21 C.F.R. § 314.108(b)(4)(iv) (2008).

20. 21 U.S.C. § 355(b)(2) (2006); *e.g.*, FDA.gov, Frequently Asked Questions for New Drug Product Exclusivity, http://www.fda.gov/cder/about/smallbiz/exclusivity.htm (last visited May 10, 2009).

21. 21 U.S.C. § 360cc(a) (2006); 21 C.F.R. § 316.31(a) (2008).

disease or condition" means:

> [A]ny disease or condition which (A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug.[22]

The pediatric exclusivity of up to six months is granted to applicants who conduct clinical trials of a drug in a population of pediatric age and obtain FDA approval.[23] The 180-day generic exclusivity is granted to the first successful abbreviated new drug applicant who files paragraph IV certifications challenging patents that may be invalid, not infringed by the product that is the subject of the application, or unenforceable.[24]

Therefore, apart from patent exclusivity, the government provides various incentives to promote drug development (e.g., orphan drug or pediatric formulations) and also to challenge patented drugs (e.g., generic exclusivity for paragraph IV certification). For example, since the Orphan Drug Act was established in 1983, about 1,950 drugs have received orphan drug exclusivity and 300 new treatments have been established, compared to only a handful prior to the Act.[25] Exclusivity, whether patent-based or otherwise, promotes the progress of research and development and leads to new drug approvals; therefore, it benefits patients in the long run.[26]

It is difficult to obtain research funding, and there is generally no incentive to invest, if the resulting commercialization is available to all. Besides patent protection, other protections include keeping innovations as trade secrets, but that approach poses the risk of losing one's rights once the "cat is out of the bag."

A difficult issue is whether research tools should be available non-exclusively. Research tools include those methods and compositions that

22. 21 U.S.C. § 360bb(a)(2) (2006).

23. 21 U.S.C. § 355a(b) (2006); *see also* CTR. FOR DRUG EVALUATION & RESEARCH, GUIDANCE FOR INDUSTRY: QUALIFYING FOR PEDIATRIC EXCLUSIVITY UNDER SECTION 505A OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT (1999) *available at* http://www.fda.gov/downloads/Drugs/GuidanceCompliance RegulatoryInformation/Guidances/UCM080558.pdf (providing guidance on pediatric exclusivity applications).

24. 21 U.S.C. § 355(j)(5)(B)(iv) (2006).

25. OFFICE OF INSPECTOR GEN., DEP'T OF HEALTH & HUMAN SERVS., THE ORPHAN DRUG ACT: IMPLEMENTATION AND IMPACT 7 (2001), *available at* www.oig.hhs.gov/oei/reports/oei-09-00-00380.pdf; U.S. Food and Drug Administration, List of Orphan Designations and Approvals, http://www.fda.gov/orphan/designat/list.htm (last visited Apr. 11, 2009).

26. Gregory J. Glover, *The Influence of Market Exclusivity on Drug Availability and Medical Innovations*, 9 AAPS J. E312, E315 (2007), *available at* http://www.aapsj.org/articles/aapsj0903/aapsj0903034/aapsj0903034.pdf.

are used in the pathway from bench to bedside, but are not directly used in patient care, and generally are not subject to regulatory approval.[27] These are hard to patent for several reasons, including the utility requirements of patent law, but they can be sold to the research community for a profit. Research tools also benefit academic programs and some company programs.

II. THERE IS A CORRELATION BETWEEN STIMULATING INNOVATION, PATENTING, AND MEDICAL ADVANCES

As countries embrace modern technology as a means to improve their citizens' health and stimulate their national economies, they follow the path that led the United States to leadership in biotechnology. Countries such as China, India, and South Africa realize that offering intellectual property rights (IPRs) for life sciences innovation attracts investment capital. Homere notes, "[m]odern economists have been increasingly inclined to recognize IPRs as a tool capable of stimulating economic growth when tailored to the particular needs of a country."[28]

Homere summarizes how IPRs have promoted economic growth, education, quality of life, research and development in developed and developing countries.[29] The author postulates that although developing countries should and can implement the intellectual property protection systems mandated by the Trade-Related Aspects of Intellectual Property Rights (TRIPS),[30] implementation will only benefit the least-developed countries if it protects "traditional knowledge."[31] The results contrasted between countries such as Singapore, Malaysia, and Indonesia, which implemented more stringent intellectual property protection systems to prevent trade sanctions and to encourage foreign investment, and countries such as Vietnam and Thailand, which did not emulate Western patent policies: piracy flourished in the latter group of countries, while it was virtually eliminated in the former group.[32]

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27. *See* William L. Warren, *Safe Harbor Provisions for Preclinical Research: Supreme Court Seeks a New Definition*, GENETIC ENGINEERING NEWS, Aug. 1, 2005, *available at* http://www.sutherland.com/files/Publication/cadcc0b0-7339-46fe-9179-eae3d1d692c7/Presentation/PublicationAttachment/fa5a8bc9-12db-4088-ab5c-0cf69f8e65fe/bill%20warren.pdf.

28. Jean Raymond Homere, *Intellectual Property Rights Can Help Stimulate the Economic Development of Least Developed Countries*, 27 COLUM. J.L. & ARTS 277, 277 (2004) (citation omitted).

29. *Id.* at 278.

30. Agreement on Trade-Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, Legal Instruments—Results of the Uruguay Round, 33 I.L.M. 1197 (1994).

31. Homere, *supra* note 28, at 291-98.

32. Homere, *supra* note 28, at 284.

Also, the patent-favorable countries experienced a rising influx of foreign direct investment in the 1990s, while Vietnam and Thailand did not attract similar economic opportunities:[33]

> [T]he implementation of a stronger IPR system in Singapore permitted joint ventures with computer companies who refused to do business there before these stricter laws were enforced. Similarly, in the early 1990s, Poland experienced a forty-fold increase in inward [foreign direct investment] FDI following its rapid liberalization and deregulation program. After showing a willingness to strengthen its IPRs, China experienced a ten-fold increase in FDI between 1990-1995, receiving nearly $36 billion in 1995. Additionally, Mexico experienced a sharp increase in FDI following the passage of NAFTA, as did Chile.[34]

> According to an empirical economic study conducted by Edwin Mansfield, who surveyed both executives of major U.S. corporations and patent attorneys, increased foreign direct investments are positively correlated with higher levels of intellectual property protection. Foreign investments in the electrical, chemical and pharmaceutical sectors increased particularly with higher levels of protection. Another economic study ranking the IPRs of eighteen developing countries reveals that research and development of new technology bears higher financial risks than any other commercial activities and that stronger protection can help reduce that risk and stimulate higher levels of investments in developing countries.[35]

Prior to implementing the TRIPS treaty, India's patent law in the pharmaceutical area, like that of other developing countries, only covered methods of making drugs, not the drugs themselves.[36] That situation allowed Indian generic pharmaceutical companies to "reverse engineer" and manufacture pharmaceutical products patented outside India, sell the drugs and medicines at lower costs than their patented counterparts in India and other developing countries, and yet escape infringement lawsuits in India.[37]

As India expanded innovation within the country, the balance shifted towards creating incentives for innovation while still attempting to protect

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33. *Id.*

34. *Id.* at 287 (citations omitted).

35. *Id.* (citations omitted).

36. Linda L. Lee, Note, *Trials and TRIPS-ulations: Indian Patent Law and Novartis AG v. Union of India*, 23 BERKELEY TECH. L.J. 281, 282 (2008).

37. Aparna Meduri, Product Patent Protection – India's Interest (Dec. 2005) (presented at the National Seminar on IPR: Its Impact on Trade and Services, Hindu College, Guntur, India, Dec. 2005), *available at* http://works.bepress.com/cgi/viewcontent.cgi?article=1001&context=aparna_meduri.

consumers' access to medicines.[38] India had to compete with other countries for foreign investors who prefer stringent patent rights.[39] As India became a science and technology innovator, patent laws evolved accordingly.[40]

A controversial provision of the new Indian patent laws is that patents for "new uses for known molecules," known active ingredients are difficult to obtain as Novartis found out when the company could not patent Gleevec®, a drug for leukemia.[41]

New uses of known drugs face difficulties in other countries,[42] but European countries have resolved this issue in various ways.[43]

In China, as in many other countries, the evolution of intellectual property rights, economic development, and international trade correlate with each other. Modern patent and trademark laws were enacted in China in 1984.[44] Copyright law was enacted in 1990.[45] However, coverage for,

38. Lee, *supra* note 36, at 285.

39. *Id.* at 297.

40. *Compare* The Patents Act, No. 39 of 1970 India Code (1999), § 5 (Inventions "claiming substances for intended use . . . as medicine or drug . . . or relating to substances prepared or produced by chemical processes" are not patentable, "but claims for the methods or processes of manufacture shall be patentable.") *with* The Patents (Amendment) Act, 2005, No. 15, Acts of Parliament, 2005 (omitting Section 5 of the 1970 Act, making pharmaceutical products patentable inventions).

41. Novartis AG v. Union of India, Writ Petition Nos. 24759 & 24760 of 2006, 4 Madras L.J. 1153 (2007), *available at* http://judis.nic.in; *see also* Novartis, History of Glivec in India, http://www.novartis.com/downloads/about-novartis/glivec-history-india.pdf (last visited Apr. 11, 2009).

42. *See* Schering Corp. v. Geneva Pharm., Inc., 339 F.3d 1373 (Fed. Cir. 2003) (holding that patents on derivatives of known substances are invalid, and double patenting is not allowed).

43. *See* Lee, *supra* note 36, at 308.

> In Europe, a new use can either be a product claim or a process claim, depending on whether the product had previous pharmaceutical use. A new therapeutic use of a known product having no previous pharmaceutical use, known as a "first indication" or "first medical use," can be protected by a product patent. This specialized form of product patent claim is known as "purpose-limited-product" claim, which limits the scope of the patent protection to the particular purpose or use of the product. However, a new use for a product that already has an existing pharmaceutical use, known as a "second indication" or "second medical use," is protected by a process patent. The claim format is known as a "Swiss claim" and is merely limited to the new use of the known compound or composition. *Id.* (citations omitted).

44. Kong Qingjiang, *The Political Economy of the Intellectual Property Regime-Building in China: Evidence From the Evolution of the Chinese Patent Regime*, 21 PAC. MCGEORGE GLOBAL BUS. & DEV. L.J. 111, 116 (2008).

45. Copyright Law (Promulgated by the Standing Comm. Nat'l People's Cong., Sept. 7, 1990, effective June 1, 1991, revised Oct. 27, 2001) (P.R.C.), *translated by* State Intellectual Property Office, *available at* http://www.sipo.gov.cn/sipo_English/laws/relatedlaws/200804/t20080416_380362.html.

e.g., pharmaceuticals was only provided in 1992.[46] China has been pressured by other countries, notably the United States, to provide and enforce laws protecting intellectual property. Enforcement of intellectual property rights poses a particular problem in China.

When China was mostly importing foreign goods, the laws did not favor protection of foreign inventors. As China evolved into both an importer and exporter, and into both a recipient and a source of foreign investment, reciprocal patent protection became the goal.

In South Africa, a 2008 Act presents goals similar to the U.S. Bayh-Dole Act: to seek protection of intellectual property produced with the assistance of public funding, to stimulate economic development of the country through commercialization of intellectual property, and to promote public health.[47]

An empirical analysis of the effect of a system to protect intellectual property on economic development led to the conclusion that "[o]verall there is a positive impact on growth, but this impact depends on the competitive nature of the economy."[48]

In the absence of a patent system, competitors could appropriate innovation, and therefore investors would stay away.[49] A primary goal of the patent system is to encourage innovation.[50]

Economic theory demonstrates that the patent system could play either a positive or negative role in fostering growth and development. One opinion is that modern systems are not sufficient by themselves to encourage effective technology transition, but must be part of complementary policies that maximize the potential for IPRs to raise dynamic competition. Such policies include strengthening human capital and skill acquisition, promoting flexibility in enterprise organization, ensuring a strong degree of competition on domestic markets, and developing a transparent, nondiscriminatory, and effective competition regime.

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46. Susan B. Fentress, *Biopharmaceutical IP Protection in China Lessons to Be Learned from the Dispute over Chinese Patent Related to Viagra*, 27 GENETIC ENGINEERING & BIOTECHNOLOGY NEWS, Sept. 1, 2007, *available at* http://www.genengnews.com/articles/chitem.aspx?aid=2194&chid=0.

47. Intellectual Property Rights from Publicly Financed Research and Development Act 51 of 2008 (S. Afr.).

48. Keith E. Maskus, *Intellectual Property Rights and Economic Development*, 32 CASE W. RES. J. INT'L L. 471, 472 (2000).

49. *Id.* at 473 ("Absent such rights, economically valuable information could be appropriated without compensation by competitive rivals. Firms would be less willing to incur the costs of investing in research and commercialization activities.").

50. *Id.* at 476 ("Indeed, that governments strengthen their IPRs systems as their economies become wealthier and attain a deeper basis of technological sophistication is well established. The claim that strong IPRs promote technical change and development is more debatable.").

III. TESTIMONIALS TO THE SUCCESS OF INNOVATIONS IN MEDICINE ARE IN OUR HOMES AND WORKPLACES—THEY ARE OUR LEADERS, OUR EDUCATORS, OUR ENTERTAINERS, OUR FAMILIES

Who has not been touched by the miracles of modern medicine? At the annual BIO (Biotechnology Industry Organization) convention, personal, heartwarming, and encouraging stories are presented of successful treatment of conditions and diseases that would have been debilitating or lethal in the past. In these true stores, specific medications, diagnostic assays, and procedures are identified that helped the affected persons have fulfilling lives.

Examples from the 2008 BIO Convention in San Diego demonstrate the miracle of medications that make it possible for a young girl with cystic fibrosis, a genetic disease, to live a full life; a young man with a genetic disorder (phenylketonuria) diagnosed shortly after birth to use a special diet, and now breakthrough drug therapies to live an active life; and an adult with Alpha-1 antitrypsin deficiency to alleviate symptoms through drug therapy. The following are excerpts from materials provided by BIO:

> There are approximately 30,000 people with Cystic Fibrosis and as many as 30,000 people with ALS in the United States alone.
>
> . . . .
>
> [A young girl, Hillary, is aided by an] inhalation medication regime [that] includes Pulmozyme by Genetech, Tobi by Novartis, Hypotonic Saline by Pari, Colistimethate by X-Gen, Advair by Glaxo Smith Kline and a pancreatic enzyme, Ultrase MT20, made by Axcan Scandipharm.
>
> . . . .
>
> After nine months of chronic lung infections, acid reflux and failure to thrive, Hillary was diagnosed with Cystic Fibrosis, a genetic, life threatening disease which affects the digestive system and the lungs. Although they had no family history of the disease, Hillary carries two defective genes for CF including the most common, F508.
>
> Despite suffering from chronic lung infections and digestive problems, Hillary is very active in school and at home. Although her illness causes her to miss more school than most children her age, Hillary is on the Honor and Effort Roll at her school. She is an active member of her church, plays modified school volleyball, and enjoys jazz dancing, scrap booking, rubber stamping and cooking. She recently began babysitting and baby sits regularly for a toddler with Downs Syndrome. Hillary is an active fundraiser for both the Cystic Fibrosis Foundation and the ALS

Association.

Effects of another genetic disorder, phenylketonuria, are alleviated by modern medicine after detection at birth by diagnostic assays, as a result of universal newborn screening for early detection of rare, inherited conditions which can be life or brain-threatening, causing irreversible harm before signs or symptoms are noticeable:[51]

> John, 21, . . . is keenly interested in sports and weightlifting, plays hockey and basketball and works part-time for . . . [a] TV program.
>
> . . . .
>
> John has managed, sometimes with difficulty, a highly restrictive diet (more restrictive than vegan) which eliminates almost all forms of protein and requires daily intake of a vile-tasting medical food, a synthetic substitute for amino acids.[52]
>
> John is doing well on a breakthrough drug therapy for PKU, called Kuvan, an orphan drug approved for sale in the United States by the FDA in December, 2007. John volunteered for an FDA-approved study and began taking this drug in early October, 2007 via Dr. Barbara Burton's PKU clinic at Children's Memorial Hospital in Chicago, [Illinois]. Dr. Burton was the Principal Investigator of the pivotal clinic trials of this drug.
>
> . . . .
>
> [John's] motivation to try the drug was to help meet a fitness goal of increasing overall muscle mass. Despite strenuous workouts and nutritional supplements over 18 months, he could not fully achieve his goal without change to his low-protein diet.
>
> In his case, the drug lowered the level of the problem amino acid by 75% in just one day. The drug enabled the defective enzyme to work

51. PKU was the original reason to start screening newborns in the 1960s and is found in about one birth in 15,000 in the USA and Canada. The best estimate is that there are about 15,000 people with PKU in the USA. In PKU, one enzyme in the liver is not working properly and so the body cannot process an essential amino acid (phenylalanine) present in most protein foods. Levels of this amino acid can build up in the blood then cross the blood-brain barrier where excess amounts are toxic to the central nervous system. *Id.*

52. Most persons with PKU lose diet control as older children, teens, or young adults. There has been growing evidence of subtle nutritional insufficiencies with the PKU diet despite improvements over the years. For example, John is being tracked for loss of bone density, whose evidence began years ago. *Id.*

better. . . . His body has continued to adapt to the use of the drug and on medical advice he has been able to gradually liberalize his diet. Today he can eat regular protein foods such as meat, fish and chicken and has stopped taking the synthetic formula. After taking this orphan drug for most of a school year, his marks improved.

John is fortunate to be a super-responder to this first-ever PKU drug as its clinical trials showed that many people with PKU do not respond or to his extent. He looks forward to the results of clinical trials, the first just begun, for a second PKU drug, PEG-PAL, which it is hoped will work for almost all persons born with PKU. This investigational drug is also designated an orphan product by the FDA.

Patients afflicted with another orphan disease, Alpha-1 Antitrypsin Deficiency, have benefited from medications such as Prolastin, manufactured by Talecris Biotherapeutics, Advair by GlaxoSmithKline and Spiriva by Boehringer Ingelheim and Pfizer:

[John Walsh's] introduction to orphan diseases began in childhood when his mother . . . died at age 46 of lung disease from a then-unknown cause, leaving her husband Jack and four children in their teens or younger.

Walsh, who never smoked, was symptomatic at age 35 and misdiagnosed with allergy-induced asthma. He was finally diagnosed correctly at age 40, with his twin brother Fred, with the genetic disorder Alpha-1 Antitrypsin Deficiency (Alpha-1), in 1989. The brothers joined the National Institutes of Health's seven-year study of Alpha-1 and were involved in the NIH study that resulted in the FDA approval of Prolastin as an orphan drug in the 1990s.

Walsh became an activist for awareness and detection of Alpha-1, co-founding the Alpha-1 Foundation in Miami, FL, with two other Alpha-1 patients in 1995. The same year the trio also founded AlphaNet, a not-for-profit health management company which created a unique distribution and service partnership with Bayer (now Talecris Biotherapeutics), in the distribution of Prolastin. AlphaNet, with the slogan "Alphas Serving Alphas," hired patients to provide patient service to their fellow Alpha-1 community members.

. . . .

Due to the infrastructure and support provided by the Foundation and AlphaNet, several companies have drugs in development for the

treatment of Alpha-1. . . .[53]

But one does not need to attend the BIO convention for such examples; one need only look around in daily life. Anyone reading this paper undoubtedly either knows similar stories personally or within a circle of friends, family or acquaintances. How many of these medical advances would have been available without the patent system?

IV. EVIDENCE DOES NOT WARRANT DISMANTLING THE PATENT SYSTEM

Caulfield and his co-authors make a good point: "[w]hen it comes to gene patenting, policy makers may be responding more to high-profile media controversies than to systematic data about the issues."[54] It is fascinating that so much controversy has been generated, in particular, by the issue of patenting genes.

Antagonism towards patenting has been obvious for many years, despite empirical data that fails to show any adverse effect on patient care or further innovation.[55] Based on his investigation, and actual litigation to enforce patents on genes, Holman concluded that "for the most part, fears expressed concerning human gene patents have not been manifested overtly in patent litigation."[56] Interestingly, Holman discounted the concerns raised in a 2004 report by Jensen and Murray, by finding that one of the 4,270 patents in their litigation data set resulted in a decision favoring a patent holder. In contrast, substantial data exists showing that medicines developed through biotechnology have had substantial benefits in alleviating mankind's medical problems.

As Caulfield summarizes, "policy activity has been largely stimulated by a convergence of a general social unease, the emergence of preliminary data and literature on the possible adverse practical ramifications of gene patents, and several high-profile patent protection controversies."[57] Some of the events that have prompted adverse reactions to patenting include the Myriad Genetics' enforcement of patents over gene mutations associated with breast cancer risks, diagnosis of Canavan disease where family members were upset that their biological samples were used to develop

53. Press Conference on the Orphan Drug Act: 25 Years of Innovation, June 18, 2008. Excerpts from materials provided at the 2008 BIO International Convention (San Diego, Cal., June 17-20, 2008) (on file with the Biotechnology Industry Organization).

54 Timothy Caulfield et al., *Evidence and Anecdotes: An Analysis of Human Gene Patenting Controversies*, 24 NATURE BIOTECHNOLOGY 1091, 1091-94 (2006).

55. Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698, 698 (1998).

56. Christopher M. Holman, *Trends in Human Gene Patent Litigation*, 322 SCI. 198, 199 (2008).

57. Caulfield, *supra* note 54, at 1091.

diagnostic assays without direct benefit to the donor's families, and the National Institute of Health's (NIH) attempts to patent express sequence tags (ESTs). Other noteworthy controversies include patenting of genetically modified seeds companies such as Monsanto, whose lack of public relations caused problems in trying to sell these seeds in Europe and other countries. For many of these controversies, the actual problems lie not in the existence of the patents themselves, but in the enforcement procedures, which in some cases are not tempered by public policy concerns or social amenities.

A particularly venomous theoretical concern is called the "tragedy of the anticommons" advanced by Heller and Eisenberg.[58] This catchy phrase has led to numerous misconceptions that a perceived public service concerning the wisdom of suppressing patents, particularly on early stage inventions or genes. According to Heller and Eisenberg, the basic concept behind the "tragedy of the anticommons" was that large numbers of patents owned by diverse owners would inhibit access to all rights needed to make further innovations: "people underuse scarce resources because too many owners can block each other," and that "[a] proliferation of intellectual property rights upstream may be stifling life-saving innovations . . . ."[59] Despite all of these prophecies of doom, no one has produced evidence that these situations have inhibited further research or kept medicines from the public; nor has anyone proposed alternatives that would attract investors, promote research and development, and provide life-saving innovations without protecting intellectual property.

Various empirical studies fail to demonstrate any effects that were predicted by the "anticommons" hypothesis.[60] In the United States, only one percent of academic biomedical researchers reported having to delay a project, and none reported abandoning a project as a result of other patents: this suggests that neither "anticommons" nor restrictions on activity seriously limit academic research.[61] This may be because, with rare exceptions, patent holders are leery of suing or threatening to sue university-based researchers, unless the researchers are developing commercially-infringing products, or using methods for commercial purposes.[62]

There are several potential solutions to concerns about patent monopolies

58. Heller & Eisenberg, *supra* note 55, at 698.

59. *Id.*

60. Holman, *supra* note 56, at 198-199.

61. John P. Walsh, Charlene Cho, & Wesley M. Cohen, *View from the Bench: Patents and Material Transfer*, 309 SCI. 2002, 2002 (2005).

62. *Cf.* Caulfield, *supra* note 54, at 1092 ("Such unlicensed lab testing, from the perspective of the patent owner, competes with its commercial activity, and hence it is not surprising to find owners asserting their rights.").

blocking patient access to resulting products. Compulsory licensing has been incorporated into some countries' patent laws;[63] strengthening research exemptions to allow scientists to work with patented material has been proposed, and cross-licensing is another option.

One area that has generated public concern is diagnostic testing for genetic disorders and other health problems. In these situations, the public policy appears to suggest that the testing fees are too high or should be non-existent, at least for those patients who helped develop the diagnostic assay, therapy, or cell line that was patented.[64] There is, according to Caulfield, "substantial empirical evidence that university researchers are becoming more secretive and less willing to share research results or materials."[65] However, the causes for this are unclear, and the effect is minimal. The Myriad Genetics controversy, over testing for genes which increase the risk for developing breast cancer, was a focus and a stimulus for calls to limit enforcement of diagnostic patents.[66] Unfortunately, the Patent Office approaches patent applications in the biotechnology area by raising barrier after barrier—which discourages research that could potentially lead to patents; this, in turn, discourages funders from investing in research, and inhibits innovation. This is the opposite outcome of the one predicted by patent-squelching advocates.[67]

Adelman and DeAnglis conducted an empirical study of biotechnology patents to determine whether or not "biotechnology patenting has reached unsustainable levels."[68] They concluded there was "little evidence that the rise in biotechnology patenting is adversely affecting innovation."[69] However, they cautioned that empirical methods may be inadequate to answer the question, due to complexities in the patenting-innovation system.[70]

V. THE REALITIES OF OBTAINING PATENTS

The obstacles toward getting a patent issued have been reinforced over time, in part by the Supreme Court's reduction of the power and rights of

63. Patents Act, 1990, c. 12 § 133 (Austl.); Patent Act, Act No. 121 of 1959, art. 93 (Japan).

64. *Cf.* Caulfield, *supra* note 54, at 1091 (noting that researchers sometimes claim that patent owners assert license terms or exclusivity that is "widely viewed as inappropriate").

65. *Id.* at 1092.

66. *Id.* at 1093.

67. *Id.*

68. David E. Adelman & Kathryn L. DeAnglis, *Patent Metrics: The Mismeasure of Innovation in the Biotech Patent Debate*, 85 TEX. L. REV. 1677, 1678 (2007).

69. *Id.*

70. *Id.* at 1730.

patent owners over the past several years.[71]

FIG. 1 illustrates the steps in obtaining a patent. The USPTO policies affect the length of transit time from a patent application to an issued patent. The USPTO policies also dictate when a patent will issue, and if it does, the scope of its claims. The USPTO has increasingly erected barriers that have caused the number of patent applications filed,[72] and new patents issued,[73] to decline. It has increased the time until a patent issues, and has limited claim scope. The present goal is, in practice, to reduce the number of issued patents by attrition, and to discourage filing patent applications by prolonging prosecution so that applicants' money and/or patience runs out.[74] The remaining enforcement time (until the patent term ends) is, with some exceptions, twenty years from its priority date, so if a patent issues ten years after filing, only ten years remain. There are extensions available, however, owing to USPTO delays or submissions to regulatory agencies (e.g. FDA), but they are usually, at most, five years—not enough time to adequately compensate for the delay.[75]

Patent examiners make many types of rejections, and there are popular trends at any point in time. Also, trends occur where it appears that, at times, certain rejections seem to be popular due to concurrent case law, such as the *KSR* case on obviousness.[76] Also, the perceived public policy that methods which (1) are not tied to a particular machine or apparatus, or (2) do not transform a particular article into "a different state or thing" are non-patentable subject matter.[77]

In 1995, and again in 2001, the USPTO issued guidelines relating to the "utility" standard of 35 U.S.C. § 101.[78] Under these guidelines, applicants must identify a specific, substantial, and credible utility for their inventions.[79] The USPTO has supplemented these guidelines with training

71. Donald J. Curry, *Will the Supreme Court Push Back Again on the Patent Pendulum?*, INTELL. PROP. TODAY, Feb. 2009, at 28, *available at* http://www.fitzpatrickcella.com/images/pub_attachment/attachment519.pdf.

72. Posting of Dennis Crouch to Patently-O Blog, http://www.patentlyo.com/patent/2009/04/economic-downturn-downturn-in-patent-filings.html (Apr. 12, 2009, 5:48 PM).

73. Posting of Posting of Gene Quinn to IPWatchdog, , *PTO Hiring Freeze and Budget Problems*, IPWATCHDOG http://www.ipwatchdog.com/2009/03/02/pto-hiring-freeze-and-budget-problems/id=2009/ (Mar. 2, 2009) ("[A]llowance rates have dropped to 42% for the first quarter of 2009.").

74. Professional observation of the co-authors.

75. 35 U.S.C. § 154 (2006); 25 U.S.C. § 155 (2006).

76. KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398 (2007) (motivation to combine publications need not be explicit).

77. In re Bilski, 545 F.3d. 943 (Fed. Cir. 2008).

78. *See, e.g.*, Utility Examination Guidelines, 66 Fed. Reg. 1,092 (Jan. 5, 2001).

79. In re Fisher, 421 F.3d 1365 (Fed. Cir. 2005) (finding potential use of expressed sequence tags, ESTs, which are short nucleic acids and used to locate coding genes, not sufficient to satisfy utility criteria).

materials that illustrate how to apply the standards properly.[80]

In 2001, the USPTO issued guidelines on the "written description" requirement of the first paragraph of 35 U.S.C. § 112.[81] This is currently a popular basis for examiners' rejections, or is at least used to narrow claims. The inventor must show "possession." In practice, the examiners try to limit claim scope to the actual embodiments (examples) described.

The enablement is a criterion according to the "Wands Factors."[82] Recently, the USPTO has shifted its focus to rejections based on indefiniteness.[83]

"Inherency" was a popular rejection a few years ago, when the necessary basis to support an anticipation rejection, express support for an element of an invention, could not be found in the art. Examiners would invoke "inherency" without due regard for the legal criteria required to support it.[84]

Before analyzing a patent application on the merits, an examiner often sets forth a restriction requirement stating that more than one invention is claimed, and forces the applicant to elect one for initial prosecution.[85] Typically, claims to compounds, methods, and apparatuses are separated, justified on the grounds that they require separate searches for art. Although other initially non-elected groups can be prosecuted as separate applications, a separate filing fee is required for each group. For two to three groups this may not be prohibitive, but as restriction groups become numerous, costs become prohibitive; for example, if ten types of vectors are listed to transport a gene into a patient for gene therapy, there the USPTO may label them as ten groups including ten separate inventions. This policy, though not necessarily the patent applicant's plans, may lead to a proliferation of patents and assumes the applicant can afford multiple filing and prosecution costs. In addition, species election is generally requested, which narrows claims dramatically, and leads to proliferation of patents.

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80. *See* U.S. PATENT & TRADEMARK OFFICE, EXAMINATION GUIDELINES; PUBLIC COMMENTS ON GUIDELINES; EXAMINER TRAINING MATERIALS, http://www.uspto.gov/web/offices/pac/dapp/mpep_examguide.html (last visited Apr. 28, 2009).

81. Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, P1, "Written Description" Requirement, 66 Fed. Reg. 1,099 (Jan. 5, 2001); U.S. PATENT & TRADEMARK OFFICE, WRITTEN DESCRIPTION TRAINING MATERIALS (2008). Written Description, Learning Materials, March 25, 2008, www.uspto.gov/web/menu/written.pdf.

82. In re Wands, 858 F.2d 731 (Fed. Cir. 1988) (setting forth "factors" for fulfillment of the "enablement" requirement of 35 U.S.C. § 112, first paragraph). In order to anticipate a claimed invention, a prior art reference must enable one of ordinary skill in the art to make the invention without undue experimentation. FinisarCorp. v. DirecTV Group, Inc., 52 F.3d 1323, 1336 (Fed. Cir. 2008) (citing In re Omeprazole Patent Litig., 483 F.3d 1364, 1379 (Fed. Cir. 2007)). In other words, the prior art must enable the claimed invention. Minn. Mining & Mfg. Co. v. Chemque, Inc., 303 F.3d 1294, 1301 (Fed. Cir. 2002).

83. 35 U.S.C. § 112 (2006).

84. Personal experience of the co-authors.

85. 35 U.S.C. § 121 (2006).

These practices contradict the stated USPTO goal of reducing the number of issued patents.

VI. CONCLUSION AND SUMMARY

Patents with an "I" do equal patients, more accurately patient care, when investors (including the government) commercialize what is patented and obtain any necessary regulatory approvals. In the absence of means to protect innovations, they are likely to languish in laboratories or on the printed page.

There is plenty of living evidence of the value of patented medications, procedures, and apparatuses. In contrast, there is, at best, mostly speculation about a deleterious effect of the patent system on patients. Correlations exist in many countries between increased innovation, improved patent systems, and improved health care.

The authors conclude that no suggestions to replace or improve the patent system have produced the same beneficial effects. In fact, obstructions by the USPTO to patent procurement, coupled with a failing economy, jeopardize further advances in health care.

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FIG. 1 - THE TORTUOUS ROUTE OF INVENTIONS: FROM BENCH TO PATENT