OYSTERS & OLIGONUCLEOTIDES: CONCERNS AND PROPOSALS FOR PATENTING RESEARCH TOOLS

I. INTRODUCTION

Research tools pose unique issues for the patent system. Unlike more traditional inventions, the purpose of a research tool is not only to create a product or accomplish a task, but also to further scientific discovery. The problem, simply stated, is that exclusive control over a research tool could prevent further scientific discovery in the relevant technological field. Even if the patent-holder were willing to license use of the research tool, the terms of the licensing agreement could result in the patent-holder maintaining substantial, even exclusive rights in a subsequent end-product, even if that eventual discovery is many steps removed from the use of the research tool. For example, a researcher who invents a way to identify new cell types may, in some cases, retain exclusivity rights over the newly identified cell types, their use in

experimentation, and even drugs designed to target these types of cells. For many, this is an undesirable scenario that is the result of a patent system ill-equipped to handle the rather unique issues that arise in patenting research tools, especially in the field of molecular biology.

In this Note, Part II defines research tools and provides a brief overview of the science and patentability of these various types of tools. Part III articulates the specific fears and objections that arise in patenting research tools. Part IV poses some potential answers and solutions to the problems raised in Part III.

II. DEFINITION, HISTORY, AND PATENTABILITY OF RESEARCH TOOLS

A. *Defining Research Tools*

"Research tool" is not a term of art in patent law, and designation as such does not carry inherent legal consequences.[1] However, a research tool is unique among inventions because it is a sort of intermediate technology that produces information about a particular sample or aids investigators in discovering or developing new biotechnology products.[2] The NIH specifically defines research tools as:

> the full range of tools that scientists use in the laboratory, including cell lines, monoclonal antibodies, reagents, animal models, growth factors, combinatorial chemistry and DNA libraries, clones and cloning tools (such a PCR), methods, laboratory equipment and machines.[3]

Thus, research tools are usually of greatest value to other researchers in the scientific community, rather than the population at large.

---

[1] Rebecca Eisenberg, *Patenting Research Tools and the Law, in* NATIONAL RESEARCH COUNCIL, INTELLECTUAL PROPERTY RIGHTS AND THE DISSEMINATION OF RESEARCH TOOLS IN MOLECULAR BIOLOGY 6, 6 (1997). "Research tools are not categorically excluded from patent protection . . . nor is the use of patented inventions in research categorically exempted from infringement liability." *Id.*

[2] Heather Hamme Ramirez, *Defending the Privatization of Research Tools: An Examination of the "Tragedy of the AntiCommons" in Biotechnology Research and Development*, 53 EMORY L.J. 359, 360 (2004).

[3] Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources: Final Notice, 64 Fed. Reg. 72,090, 72,092 n.1 (Dec. 23, 1999). Not all agree with such a definition, especially since, depending on one's perspective, an invention could be described as both a research tool and an end product. *See* Report of the National Institutes of Health Working Group on Research Tools (June 4, 1998), *available at* http://www.nih.gov/news/researchtools. The NIH recommends considering three factors in determining whether an invention is properly characterized as a research tool: (1) whether the invention's primary usefulness is as a tool for discovery or as an FDA-approved product or part of such a product; (2) whether the invention is broad and enabling or product-specific; and (3) whether the invention is readily usable or distributable as a tool or requires private sector involvement. Principles and Guidelines, *supra*, at 72,094.

The particular issues posed by the patenting of research tools arise, in part, because the founding fathers could not have contemplated the technological developments of the 20th and 21st centuries as they set forth the patent system.[4] At the time Article I, Section 8 of the U.S. Constitution was penned, inventions and discoveries "were in the nature of bifocals, lightening rods, and other clearly practical articles . . . ."[5] Consequently, some have argued that the patent system is ill-equipped to handle the chemical, biological, and pharmaceutical research tools for which patents are commonly sought today.[6]

The controversy over patenting research tools came to a head after Congress enacted the Bayh-Dole Act in 1980.[7] Prior to 1980, scientific knowledge was generally understood as a shared resource, and many scientists freely exchanged information without formal agreements.[8] Furthermore, federally-funded laboratories typically made the inventions they developed available to the public.[9] In 1980, however, the Bayh-Dole Act encouraged federally-funded labs to pursue patents for their inventions and license their technology to the private sector.[10] As a result, the products of federally-funded research no longer came directly into the public domain, but became the subjects of patents and exclusive licensing arrangements.[11]

Today, the patentability of research tools remains contentious. Although many research tools have already been patented — and more are patented each day — critics predict that such a trend will result in a number of serious problems for the scientific community. This note discusses some of these issues, as well as some potential resolutions.

B. *The History of Research Tool Patents*

Research tools have had mixed success as the subject of patent applications. Unsuccessful patent applications have generally been denied by the Patent and Trademark Office ("PTO") on two grounds: (1) non-patentable subject matter and

---

4 Cathryn Campbell, *Intellectual Property: Divying Up Claims God's Blueprints*, SCIENCE CAREERS, Mar. 5, 1999, http://sciencecareers.sciencemag.org/career_development/previous_issues/articles/0070/intellectual_property_divying_up_claims_to_god_s_blueprints/(parent)/12098.

5 Kate Murashige, *Patents and Research – An Uneasy Alliance*, 77 ACADEMIC MEDICINE 1329, 1329 (2002).

6 *Id.* at 1329-30.

7 Act of Jan. 3, 1980, 94 Stat. 3015, 3019 (1980) (codified at 35 U.S.C. § 200) (amending patent and trademark laws) [hereinafter Act of Jan. 3, 1980].

8 *See* Eisenberg, *supra* note 1, at 7.

9 *Id.* at 8.

10 *See* Act of Jan. 3, 1980, *supra* note 7, at 3019; 35 U.S.C. § 202(a) (2000).

11 *Introduction*, *in* NATIONAL RESEARCH COUNCIL, *supra* note 1, at 1, 3.

(2) insufficient utility. Other research tool applications, however, have met few patent obstacles. In this section, I will outline some of the mixed results with which research tool patent applications have met, including the patent history of some of molecular biology's most famous research tools. Reaching an understanding of the types of research tools that are commonly believed to be patentable, and those that are not, will inform further analysis of research tool patents.

Under the Constitution, Congress has the power "[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."[12] Congress, in turn, enacted the Patent Act, effectively granting inventors a twenty-year term of monopoly in exchange for disclosure of their invention. This "quid pro quo"[13] allows a patent holder to exclude others from using the invention during the length of the patent term in exchange for the public's gain of knowledge of the invention at (or just after) the filing of the patent application.[14] The efficiency of the patent system "inheres in the patent system's maintenance of a rough parity between the social value of an invention disclosure and the private value of the exclusionary rights granted to the inventor who makes the disclosure."[15] Ideally, enforcing the statutory requirements with the appropriate stringency yields a well-balanced and economically-profitable patent system.

One of biology's most important research tools, Polymerase Chain Reaction ("PCR"), was patented rapidly and easily. In 1979, researcher Kary Mullis began work for the biotechnology company Cetus Corporation, where he labored as a DNA chemist.[16] During his years there, Mullis developed a technique commonly known as PCR, which allows the specific and rapid amplification of targeted

---

12 U.S. CONST. art. I, § 8, cl. 8.

13 Brenner v. Manson, 383 U.S. 519, 534 (1965) ("The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility").

14 Andrew Chin, *Research in the Shadow of DNA Patents*, 87 J. PAT. & TRADEMARK OFF. SOC'Y 846, 855 (2005).

15 *Id.* Such a balance is primarily achieved by the statutory conditions for patentability: The utility requirement of § 101 and § 112 provides that only inventions capable of providing some benefit to society are entitled to patent. The novelty requirement of § 102 makes sure that a patent issues only when knowledge of the invention is not already available to the public. The nonobviousness requirement of § 103 further restricts patentability to inventions that represent advances beyond the application of ordinary skill to publicly available knowledge. The written description and enablement requirements of § 112 ensure that knowledge of the patented invention is transmitted in a form that can be used immediately by the public. Finally, the best mode requirement of § 112 compels the public disclosure of the most valuable form of the patented invention known to the inventor as of the application date.
Id. at 856 (footnotes omitted).

16 KARY B. MULLIS, DANCING NAKED IN THE MIND FIELD (1998).

DNA sequences.[17] PCR makes possible the analysis of genes in biological samples, including "assays of gene expression in individual cells, in specimens from ancient organisms, or in minute quantities of blood in forensic analysis."[18] In less than a decade, PCR became a standard technique in essentially every molecular biology lab.[19] Without PCR, a number of molecular biology's greatest feats may not have been possible, such as the Human Genome Project.[20] Mullis himself won the Nobel Prize for his work on PCR a mere eight years after he first published the technique, attesting to PCR's "immediate and widely recognized impact."[21] The USPTO awarded Mullis his PCR patent in July, 1987.[22] At the time, "[t]here was virtually no controversy over whether such an important research tool should be patented "[23]

While PCR served as a model for some later research tool patents, not all research tool patent applications have proceeded with such success. Although "laws of nature, natural phenomena, and abstract ideas"[24] are explicitly ineligible for patent protection, the court has allowed patents when naturally occurring products have been sufficiently manipulated. The threshold for human intervention was initially quite high, however, and in *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, the Court held that mixing naturally occurring bacterial strands together in a commercial fertilizer was insufficient for patent protection.[25] Though it was known that different plants required different strains of nitrogen-fixing bacteria, previous attempts to mix the bacteria were unsuccessful because the different strains could not survive together in the same environment.[26] The patent applicant, however, had discovered a particular blend of bacteria in which each strain could survive.[27] Although commercially valuable, the Supreme Court held that the applicant's invention was not patentable because the bacteria performed only their natural function, not a new or improved function.[28]

---

17 *Id.*

18 SUMMARY OF WORKSHOP AT NATIONAL ACADEMY OF SCIENCES, INTELLECTUAL PROPERTY RIGHTS AND RESEARCH TOOLS IN MOLECULAR BIOLOGY, 43 (Feb. 15-16, 1996) [hereinafter SUMMARY], *available at* http://books.nap.edu/openbook.php?record_id=5758 (last visited Sept. 18, 2007).

19 *Id.*

20 JAMES D. WATSON, DNA: THE SECRET OF LIFE 166-73 (2003).

21 SUMMARY, *supra* note 18, at 43.

22 U.S. Patent No. 4,683,195 (filed Feb. 7, 1986).

23 SUMMARY, *supra* note 18, at 43-44.

24 Diamond v. Diehr, 450 U.S. 175, 185 (1981). *See also* Gottschalk v. Benson, 409 U.S. 63 (1972) (holding mathematical algorithms non-patentable subject matter).

25 333 U.S. 127 (1948).

26 *Id.* at 129-30.

27 *Id.* at 130.

28 *Id.* at 130-31.

In the early 1970s, Stanley Cohen of Stanford University and Herbert Boyer of the University of California at San Francisco discovered a way to combine the DNA of two different organisms, creating recombinant DNA ("rDNA").[29] Generally speaking, the researchers identified, isolated, and amplified a gene from one organism, then inserted it into a cell of another organism.[30] This process allowed the combination of genetic sequences not otherwise found in nature.[31] Cohen and Boyer filed their first rDNA patent application in January, 1979, and the USPTO issued the process patent for making biologically functional molecular chimeras in December, 1980.[32]

More than thirty years after *Funk Bros.*, and following the rDNA explosion of the 1970s, the Supreme Court had the opportunity in *Diamond v. Chakrabarty* to clarify its position on patenting products of nature, and allowed a patent on a genetically modified bacterium created with rDNA technology.[33] The bacterium in question had been genetically altered to contain two exogenous genes that encoded enzymes used in hydrocarbon catabolism.[34] The Court held that, unlike the mixture in *Funk Bros.*, the invention here had characteristics different from those found in nature due to the foreign genes the bacterium now incorporated in its genome.[35] The genetically altered bacterium was not merely "nature's handiwork, but [the inventor's] own; accordingly, it is patentable subject matter under §101."[36] Following *Chakrabarty*, "anything under the sun made by man,"[37] including genetically modified organisms,[38] became patentable subject matter.[39]

---

29 Tim Beardsley, *Big-Time Biology*, SCI. AM., Nov. 1, 1994, at 90.

30 WATSON, *supra* note 20, at 93.

31 *Id.* at 94-104. This technique, some argue, has defined modern molecular biology, and fueled the biotechnology industry. Beardsley, *supra* note 29, at 95-97.

32 U.S. Patent No. 4,237,224 (filed Jan. 4, 1979). Product patents were also issued to these researchers in 1984 and 1988. U.S. Patent No. 4,468,464 (filed Nov. 9, 1978); U.S. Patent No. 4,740,470 (filed Apr. 20, 1984). Over the seventeen year life of the patents, royalties from the patents earned approximately $200 million. Chris Rauber, *$200M Patent Runs Out: UCSF and Stanford Scramble to Replenish Looming Loss of Income*, SAN FRANCISCO BUS. TIMES, Nov. 21, 1997.

33 447 U.S. 303 (1980).

34 *Id.* at 305.

35 *Id.* at 309-10.

36 *Id.* at 310.

37 *Id.* at 309.

38 Some have argued that the "human intervention" doctrine, as embraced by the *Chakrabarty* court, is unjustifiable for genetic patents. *See, e.g.*, Helen M. Berman & Rochelle C. Dreyfuss, *Reflections on the Science and Law of Structural Biology, Genomics, and Drug Development*, 53 UCLA L. REV. 871, 890 (2006). The value in genes lies not in their isolated form, but in their informational content and are, in that way, more analogous to algorithms than other chemical molecules. *Id.*

39 *See, e.g.*, *Ex parte* Hibberd, 227 U.S.P.Q. 443 (B.P.A.I. 1985) (finding plants patentable subject matter); *In re* Bergy, 596 F.2d 952 (C.C.P.A. 1979) (holding both a

Following the patenting of genetically modified organisms, genes themselves came to be patentable subject matter.[40] In distinguishing DNA purified in the laboratory from that found in the body, the PTO stated, "[a] patent on a gene covers the isolated and purified gene but does not cover the gene as it occurs in nature."[41] Moreover, "[d]octrinal support for the patentability of DNA is grounded in the structural and functional distinctions between an isolated, purified[42] DNA molecule and its naturally-occurring, impure counterpart."[43]

---

process for preparing a biologically pure culture of a microorganism and the genetically modified organism itself patentable subject matter); *Ex parte* Allen, 2 U.S.P.Q.2d 1425 (B.P.A.I. 1987) (allowing a patent on a genetically modified oyster). *See also* U.S. Patent No. 4,736,866 (filed June 22, 1984) (covering the genetically modified Harvard oncomouse). *But see* Berman & Dreyfuss, *supra* note 38, at 873 (arguing that the "post-*Chakrabarty* default" allowing patents on most biotechnology developments ought to end and a "systematic reevaluation" of patenting genetic inventions should commence).

40 The first patented gene was the retinoblastoma tumor suppressor gene, and the exclusive rights to commercially develop the gene were assigned to the Massachusetts Eye and Ear Infirmary and the Whitehead Institute. U.S. Patent No. 5,853,988 (filed Oct. 8, 1992); Tom Reynolds, *Pricing Human Genes: The Patent Rush Pushes On*, 92 J. NAT'L CANCER INST. 96, 96 (2000). Note that some controversy arose as to whether a patented DNA sequence rendered the process for cloning that gene obvious. In *Amgen v. Chugai Pharmaceutical Co.*, the Supreme Court established that even when a particular DNA sequence has been patented, the process for cloning that gene is not therefore rendered obvious. Amgen v. Chugai Pharm. Co., 927 F.2d 1200 (Fed. Cir. 1991), *cert. denied*, 502 U.S. 856 (1991). And in *In re Bell*, the Federal Circuit held that prior art disclosing a method for preparation of DNA probes from a known amino acid sequence did not render all probe synthesis obvious, but only synthesis of those probes disclosed in the prior art. *In re* Bell, 991 F.2d 781 (Fed. Cir. 1993). Finally, in *In re Deuel*, a DNA sequence could be successfully claimed although a partial amino acid sequence encoded by the DNA sequence was already known. *In re* Deuel, 51 F.3d 1552 (Fed. Cir. 1995).

41 David Holcberg, *Should Genes Be Patented?*, CAPITALISM MAG., Apr. 13, 2002, *available at* http://www.capmag.com/article.asp?ID=1534 (last visited Sept. 17, 2007). *But see* Berman & Dreyfuss, *supra* note 38, at 891 (arguing that, because a gene patent derives value from the information the gene contains, patented genetic material contains the identical information as that found in nature, and there is no difference despite any human interaction in isolation of the molecule). *Id.*

42 The terms "isolated" and "purified" in the context of DNA patents do not necessarily infer a completely homogenous sample, but more generally suggest a form in which large molecules other than the claimed DNA molecule itself are largely absent. Andrew Chin, *Artful Prior Art and the Quality of DNA Patents*, 57 ALA. L. REV. 975, 986 (2006). In a typical DNA patent, the applicant defines a "purified" DNA molecule as one "present in the substantial absence of other biological [macromolecules]," and "isolated" as "separated not only from other [DNA molecules] that are present in the natural source of the macromolecule but also from other macromolecules . . . ." U.S. Patent No. 5,731,427 (filed May 10, 1995).

43 Chin, *supra* note 14, at 869. Some controversy exists over whether an isolated, purified substance qualifies as a patentable composition of matter. Supporting that proposition, *see, e.g.*, Scripps Clinic & Research Found. v. Genentech Inc., 666 F. Supp. 1379 (N.D. Cal. 1987) (finding that a blood clotting protein, Factor VIII:C, though naturally-occurring, is patentable as a purified and concentrated preparation); *In re* Bergstrom, 427 F.2d 1394 (C.C.P.A. 1970) (holding that two prostaglandins, namely PGE(2) and PGE(3), are "new" compositions of matter and patentable in their pure and isolated form, although they are found in a variety of natural sources). *But see* General Electric Co. v. De Forest Radio Co., 17 F.2d 90 (D. Del. 1927) (holding that a substantially pure sample of tungsten is an unpatentable product of nature); Ned Hettinger, *Patenting Life: Biotechnology, Intellectual Property, and Environmental Ethics*, 22 B.C. ENVTL. AFF. L. REV. 267 (1995) (arguing that isolation of a gene is not equivalent to invention of a gene, and

C. *Utility and Research Tools*

The number of molecular biology research tool patents had exploded. With statutory subject matter relegated to an almost non-existent hurdle for research tool patents, especially following *Diamond v. Chakrabarty* and its progeny cases, research tool patents began to face a new obstacle in the utility requirement.

i. The Early Utility Standard

In order to obtain a patent, federal law requires that the claimed invention must be useful.[44] The utility standard was famously addressed by the court in two 1817 cases, *Bedford v. Hunt*[45] and *Lowell v. Lewis*,[46] both opinions penned by Justice Story. In *Bedford*, the court summarily interpreted "useful" in the then-binding Patent Act of 1793[47] as having "some beneficial use in society" but not requiring "such general utility, as to supercede all other inventions now in practice to accomplish the same purpose."[48] Similarly, in *Lowell*, the defendant to an infringement action argued that the plaintiff's pump invention was not new or useful, and that his invention was not of general utility because it did not "supercede the pump[s] in common use . . . [and is not] for the public, a better pump than the common pump."[49] The court held, however, that this was not the appropriate measure of utility and that, instead, "[a]ll that the law requires is, that the invention should not be frivolous or injurious to the well-being,

should not be patentable); Linda J. Demaine & Aaron Xavier Fellmeth, *Reinventing the Double Helix: A Novel and Nonobvious Reconceptualization of the Biotechnology Patent*, 55 STAN. L. REV. 303 (2002) (suggesting that purification of a substance is not a fundamental change in biological function).

[44] *See* 35 U.S.C. § 101 (2007) ("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 . . . ."). *See also* 1 WILLIAM ROBINSON, TREATISE ON THE LAW OF PATENTS FOR USEFUL INVENTIONS 462-63 (1890) (explaining that a patent not only requires that the inventor bestow the invention upon the public, but also that the public gain some benefit from the invention); Paula Campbell Evans, *Patently More Difficult*, BIO-IT WORLD, Nov., 2002, *available at* http://www.bio-itworld.com/archive/111202/insights_patent.html (last visited Sept. 17, 2007) (stating that the utility requirement is rooted in the patent contract, "in which the inventor receives a limited monopoly on his or her invention in exchange for disclosing a useful invention to the public.").

[45] 3 F. Cas. 37 (C.C.D. Mass. 1817)

[46] 15 F. Cas. 1018 (C.C.D. Mass. 1817).

[47] [W]hen any person or persons . . . shall allege that he or they have invented any new and useful art, machine, manufacture or composition of matter . . . and shall present a petition . . . signifying a desire of obtaining an exclusive property in the same, and praying that a patent may be granted therefore . . . and giving a short description of the said invention or discovery, and thereupon granting to such petitioner, or petitioners . . . the full and exclusive right and liberty of making, constructing, using, and vending to others to be used, the said invention or discovery. . . ."
Patent Act of 1793, Ch. 11, 1 Stat. 318-323 (Feb. 21, 1793).

[48] *Bedford*, 3 F. Cas. at 37.

[49] *Lowell*, 15 F. Cas. at 1019.

good policy, or sound morals of society."[50] The invention specifically need not be more useful than presently existing inventions.[51]

In 1966,[52] the Supreme Court in *Brenner v. Manson* strictly applied the utility standard, and denied a patent for a chemical process[53] with an end product of unknown utility.[54] The Court, in attempting to extrapolate the meaning of "useful" in § 101, found "no specific assistance in the legislative materials underlying § 101."[55] Looking to Justice Story's opinion in *Lowell*, the *Brenner* Court could likewise find no guidance because, "[n]arrowly read, it does no more than to compel us to decide whether the invention in question is 'frivolous and insignificant[;]' . . . [r]ead more broadly, [it] allow[s] the patenting of any invention not positively harmful to society."[56] In chemical process claims, the Court reasoned, a patent should not create a monopoly over a product with unknown utility whose scope cannot be clearly delineated.[57] The compounds produced by the applicant, though related to similar compounds with anti-tumor activity, had no

50 *Id.*

51 *Id. But see In re* Holmes, 63 F.2d 642 (C.C.P.A. 1933) (distinguishing "utility" as the measure of patentability from "useful" for an intended purpose. The court held the pipe in question was not patentable without demonstration of advantage over other available pipes because, although patentability is not concerned with degree of usefulness, there must be "utility in the particular form of the structure which appellant claims is invention"). *Id.* at 643.

52 The courts addressed a number of important utility issues in the intervening years. *See, e.g., In re* Bremner, 182 F.2d 216 (C.C.P.A. 1950) (holding patent application was properly rejected because the chemical invention, though novel, did not have any disclosed utility); *Ex parte* Tolkmith, 102 U.S.P.Q. 464 (Pat.Off. Bd.App. 1954) (affirming rejection of patent for chemical invention that, because of its unpredictable toxicity, had only speculative utility); *In re* Nelson, 280 F.2d 172 (C.C.P.A. 1960) (holding that the invention of steroid intermediates were useful in the creation of other steroid products); *In re* Manson, 333 F.2d 234 (C.C.P.A. 1964) (holding that an applicant for a patent on a new process for producing a known product need not establish utility of the known product). *See also* N. Scott Pierce, In re Dane K. Fisher*: An Exercise in Utility*, 6 J. HIGH TECH. L. 1, 17-31 (2006); *In re* Folkers, 344 F.2d 970 (C.C.P.A. 1965) (holding that description of the claimed compound's physical properties, namely its involvement in electron transport, was sufficient evidence of utility).

53 Establishing utility for mechanical inventions is normally straightforward, and can usually be demonstrated through drawings or diagrams. *See* Georgios Zekos, *Utility and Biotechnology Patenting*, 5 WEB JOURNAL OF CURRENT LEGAL ISSUES, Nov. 24, 2006, http://webjcli.ncl.ac.uk/2006/issue5/zekos5.html. Utility in the chemical and biological arts, however, is more difficult to demonstrate for a number of reasons. First, drawings and diagrams are often insufficient to convey the utility of a chemical or biological agent, and second, chemical and biological inventions tend to have an evolving utility. *Id.* That is, such inventions may be used in basic research, and so are more like building blocks than a finished building. *Id.* Consequently, the utility requirement as applied to chemical and biological inventions has caused more controversy than in other technological arts. Shanshan Zhang, *Proposing Resolutions to the Insufficient Gene Patent System*, 20 SANTA CLARA COMPUTER & HIGH TECH. L.J. 1139, 1150 (2004).

54 Brenner v. Manson, 383 U.S. 519 (1965).

55 *Id.* at 533.

56 *Id.*

57 *Id.* at 534.

known utility themselves.[58] Thus, a patent could not be granted because the utility derived by the invention was not specific and substantial.[59] The Court cautioned against allowing patents on products that were merely useful for further research, noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."[60]

Notwithstanding the *Brenner* decision,[61] the Federal Circuit instead applied the utility standard liberally in the 1995 case, *In re Brana*, holding that tests of a claimed pharmaceutical's efficacy in laboratory animals are sufficient to establish utility even when the compound is claimed for human use.[62] Although the applicant had not demonstrated utility of the compound in humans, the court upheld the patent, reasoning that "[t]he stage at which an invention in this field becomes useful is well before it is ready to be administered to humans."[63] Significantly, utility could be established by demonstrating successful tests in similar compounds such that one skilled in the art would trust the asserted utility.[64]

Brana exemplified just one aspect of a growing trend to promote biotechnology and innovation through patenting. That same year, two additional patenting obstacles were lifted: the PTO granted the biotechnology industry's request by lifting the requirement for "substantial" utility from its Utility Guidelines,[65] and the Federal Circuit in *In re Deuel* held patenting of particular DNA sequences is not obvious despite the existence of known methods of isolating DNA sequences.[66] Consequently, an "avalanche" of DNA, specifically expressed sequence tag ("EST")[67]

---

58 *Id.*

59 *Id.* at 534-35.

60 *Id.* at 536.

61 *Brenner* and *Brana* need not be read as inconsistent. *Brenner's* holding speaks to the minimum utility that an applicant must assert, while *Brana* addresses the standard of proof required to make such an assertion. *See* Chin, *supra* note 42, at 988-89.

62 *In re* Brana, 51 F.3d 1560 (Fed. Cir. 1995).

63 *Id.* at 1568. *See also Ex parte* Aggarwal, 23 U.S.P.Q.2d 1334 (B.P.A.I. 1992) (holding that "substantial utility" for pharmaceutical compounds can be sufficiently established by screening assays, as long as the evidence presented is proportionate to the scope of the claimed utility).

64 *Brana*, 51 F.3d at 1567.

65 *Federal Circuit Holds That Expressed Sequence Tags Lack Substantial and Specific Utility /unless Underlying Gene Function Is Identified*, 119 HARV. L. REV. 2604, 2608 (2006) [hereinfter *Federal Circuit*].

66 *In re* Deuel, 51 F.3d 1552, 1552 (Fed. Cir. 1995).

67 ESTs are short DNA sequences, commonly used in molecular genetics. To understand their value, one must realize that the value inherent in DNA is in understanding the information it contains. For that reason, DNA sequencing, or determining the exact order of nucleotides in a DNA sample, has helped to reveal a great deal about genes, their characteristics, locations, and importance. After sequencing techniques were worked out in the late 1970s, scientists were able to compare sequences from different organisms, pinpointing genes of interest, particularly disease-causing

patent applications, flooded the PTO.[68]

The PTO was soon overwhelmed with enormous genetic sequence (EST) patent applications that disclosed sequence information but contained no evidence of specific utility.[69] A sort of defensive, "arms race patenting" trend began, whereby applicants sought out defensive patents that did not really advance the science, but instead only "create[d] thickets of rights that are ever more costly to negotiate and license."[70] Perhaps most notorious were the actions of the National Institutes of Health who, utilizing new technology,[71] generated numerous random

---

genes. WATSON, *supra* note 20, at 110. One of the first organisms to be sequenced was the SV40 tumor virus; once the cancer-causing genes were identified, scientists could compare them with human cancer cells, proving for the first time that cancer arose from changes at the DNA level and not from nongenetic accidents. *Id.* In 1988, the Human Genome Project was formed to sequence the entire human genome. After many hundreds of millions of dollars, the rough draft of the sequence was released in 2001, and the "essentially complete" sequence published in 2003. *Id.* at 166-193. The sequenced genome represents "a marvelous new weapon in our fight against disease and, even more, a whole new era in our understanding of how organisms are put together and how they operate." *Id.* at 193. As of Jan. 2007, nearly 600 species' genomes have been fully sequenced, and the number continues to grow rapidly. K. Liolios et al., *The Genomes On-Line Database* (GOLD) v.2: A Monitor of Genome Projects Worldwide NAR 34, D332-334, http://www.genomesonline.org/gold_statistics.htm (last visited Sept. 1, 2007).

Although a gene's sequence can reveal some information about that gene, understanding its function is the holy grail of genetics research. Various types of sequences have come to be utilized in molecular genetic research, ESTs, being the most prevalent. ESTs are short DNA sequences, or oligonucleotides, usually 200-500 base pairs in length, which are used to "tag" and seek out particular genes in DNA samples. ESTs Factsheet, NCBI Science Primer, http://www.ncbi.nlm.nih.gov/About/primer/est.html (last visited Sept. 1, 2007). ESTs can be used in a host of applications, from mapping to diagnostic tests. *Id.* For example, ESTs could be generated from disease gene candidates then used to examine the DNA of diseased patients to determine whether the candidate gene is mutated in the ill patient. *Id.* Tests like these have already resulted in isolation of genes involved in colon cancer, Alzheimer's Disease, and others, though many believe these represent only the tip of the iceberg. *Id.*

[68] *Federal Circuit*, *supra* note 65, at 2608. The first EST patent was awarded to Incyte in November, 1998, for human kinase homologues. U.S. Patent No. 5,817,479 (filed Aug. 7, 1996); Reynolds, *supra* note 40, at 96. According to Richard Schwartz, a specialist at the patent office:

> only a handful [of EST patents] have been granted since then, and most of these, including Incyte's, 'squeaked out when they really shouldn't have. We have a blue ribbon panel of examiners who are privy to all the nuances of EST cases,' he said, but the approved applications did not explicitly mention ESTs and were mistakenly reviewed by another section.

Id. Despite this apparent oversight, some have defended the patent, distinguishing these ESTs from those claimed by the NIH, for example, because these ESTs "were identified by their specific similarity to known [genes, and so t]he function of the EST – or at least the function of the genes from which they are derived – is therefore known." Campbell, *supra* note 4, at 4.

[69] Stephen G. Kunin, *Written Description Guidelines and Utility Examination Guidelines*, 66 *Fed. Reg. 1092, 1098 (2001).*

[70] Berman & Dreyfuss, *supra* note 38, at 878. This trend was exacerbated by the automatization of gene discovery, including routine nucleic acid sequencing and computerized gene structure and function models. *Id.* at 881.

[71] The new method was referred to as "shotgun sequencing." *See* WATSON, supra note 20, at 104-10.

ESTs to be used as genetic probes.[72] The NIH sought patents on 337 ESTs in June of 1991, submitting patent applications for 2,750 more by the end of that year and another 4,000 the following year.[73] According to Stephen Krunin, "[m]aterially, ESTs are no different from any other nucleic acid. However, in contrast to nucleic acids isolated and characterized by classical approaches, the function for which the EST fragment codes is not known when the sequence is determined."[74] Yet patents on ESTs and other DNA sequences were routinely granted, because assertions of their utility, though extremely vague, were credible.[75]

ii. The Later Utility Standard

Following the onslaught of DNA patents filed prior to 1995, a contrary trend began to develop as courts and the PTO attempted to slow the rush of biotechnology patents.[76] For example, the Federal Circuit held in *Regents of the University of California v. Eli Lilly* that DNA patents required disclosure of the precise sequence of nucleotides.[77] This had the dual effect of delaying patent filing until sequencing was complete, and restricting the scope of the patent to the exact sequence disclosed.[78] In 2001, the PTO revised its guidelines for examining utility under 35 U.S.C. § 101.[79] Under the new guidelines, patent examiners must determine whether the applicant has established for the invention "specific and substantial utility that is credible."[80] Kunin illustrates the application of the new utility guidelines to ESTs:

---

[72] Demaine & Fellmeth, *supra* note 43, at 323. EST claims written as "comprising" claims (rather than "consisting of" claims) were particularly attractive for patent holders because they were entitled to rights,

> not only over the EST itself and its use as a research tool, but also the full gene sequence, the proteins for which it codes, diagnostic tests, and even gene therapies that may subsequently be developed – despite the fact that neither the full gene sequence nor its function is disclosed.

Dianne Nicol, *On the Legality of Gene Patents*, 29 MELB. U. L. REV. 809, 819 (2005).

[73] *Id.* *See* Christopher Anderson, *US Patent Application Stirs Up Gene Hunters*, 353 NATURE 485, 485 (1991); Leslie Roberts, *Genome Patent Fight Erupts*, 254 SCIENCE 184, 184 (1991); Rebecca S. Eisenberg, *Genes, Patents, and Product Development*, 257 SCIENCE 903, 903 (1992). Eventually, several NIH applications were rejected by the PTO, and the NIH withdrew the remaining applications in 1994. Demaine & Fellmeth, *supra* note 43, at 325.

[74] Kunin, *supra* note 69, at § III.A.

[75] *Id.* at § III.C. Today, over a million sequences have been claimed in patent applications, and approximately 20 percent of human gene sequences are patented, some in up to 20 different patents. *See* Byungwook Lee et al., *A Database Server for Biological Sequence Annotation and Analysis in Issued Patents and Published Patent Applications*, 00 NUCLEIC ACID RESEARCH D1 (2006); Kyle Jensen & Fiona Murray, *Intellectual Property Landscape of the Human Genome*, 310 SCIENCE 239 (2005).

[76] *Federal Circuit*, *supra* note 65, at 2608.

[77] Regents of the Univ. of California v. Eli Lilly, 119 F.3d 1559 (Fed. Cir. 1997).

[78] *Federal Circuit*, *supra* note 65, at 2608.

[79] Kunin, *supra* note 69, at 1092.

[80] *Id.* at 1098.

> Those skilled in the art recognize that ESTs *could potentially* have utility in a variety of credible contexts, e.g., as probes, chromosome markers, diagnostic tools, and forensic tools, and therefore claims directed to ESTs generally should not be rejected as lacking a credible utility. However, whether these utilities are *specific* and *substantial*[81] are the core issues to be addressed. . . . If the asserted utility would apply to any general class of nucleic acids, then the utility would not be considered to be *specific (particular).* For example, if the specification generally states that the EST may be used as a probe, but does not identify what chromosome or other target it would be a probe for, then the utility would not be considered specific. . . . Where the sole *immediate* utility constitutes research on the claimed product itself, there is no apparent *immediate* benefit to the public that the patent system is designed to protect.[82]

Given these new utility standards, and that applicants now had to demonstrate substantial and specific utility, many predicted that patents on genetic sequences would be significantly limited.[83]

In 2005, the Federal Circuit heard *In re Fisher*,[84] and for the first time applied the 2001 PTO's Utility Guidelines. Fisher had purified five ESTs from maize plant DNA and, although the functions of the genes from which the ESTs were isolated were unknown, Fisher listed seven general potential uses for the sequences, basically as probes or a source for primers and for use in the identification of polymorphisms.[85]

---

81 "Substantial" utility is further defined as something other than a "throw away" or boilerplate utility, such as use of an object to fill a landfill or act as a paperweight, or use of a transgenic mouse for snake food. *Id.*; Reynolds, *supra* note 40, at 97. At first, the PTO assessed the utility of ESTs according to a compiled list of acceptable utilities, including probing for known and useful genes, chromosome mapping, and forensic identification. Reynolds, *supra* note 40, at 97. However, the latter two uses could apply to virtually any DNA sequence and, after word began to spread, every DNA patent application began to claim these utilities. *Id.* Such tactics contributed to the modified USPTO guidelines requiring "specific and substantial" utility. *Id.*

82 Kunin, *supra* note 69, at § III.D.

83 The new guidelines were seemingly not meant, however, to prevent patenting of all raw biological material. *See* Berman & Dreyfuss, *supra* note 38, at 893. If the genomic invention is associated with a particular characteristic in the organism in which it exists, such as a gene associated with a particular disease in an organism, it may have sufficient utility because it could be used as a diagnostic tool. *Id.*

84 421 F.3d 1365 (Fed. Cir. 2005).

85 *Id.* at 1368. The seven disclosed uses were the following:

> (1) serving as a molecular marker for mapping the entire maize genome, which consists of ten chromosomes that collectively encompass roughly 50,000 genes; (2) measuring the level of mRNA in a tissue sample via microarray technology to provide information about gene expression; (3) providing a source for primers for use in the polymerase chain reaction ("PCR") process to enable rapid and inexpensive duplication of specific genes; (4) identifying the presence or absence of a polymorphism; (5) isolating promoters via chromosome walking; (6) controlling protein expression; and (7) locating genetic molecules of other plants and organisms.

Id.

The court applied the "specific and substantial" test for utility, as discussed in the PTO's Utility Examination Guidelines,[86] and concluded that Fisher's ESTs met neither branch of the utility test. "Substantial" utility, determined the court, must confer an immediate and presently available benefit to the public, not merely proving useful for further research or discovery.[87] "Specific" utility requires the applicant to provide a well-defined and particular use, rather than one that could be applied to a broad class of inventions or that is "so vague as to be meaningless."[88] The court held that Fisher's ESTs had neither specific nor substantial utility; because the seven utilities proposed by Fisher could apply not only to Fisher's claimed ESTs but to any EST derived from any organism, the "alleged uses are so general as to be meaningless."[89] Moreover, the utilities advanced by Fisher in his application are simply research intermediates, tools for further research and not the final product of any research effort.[90]

Fisher embraced reasoning dating back to *Brenner*,[91] and solidly affirmed previous cases that had rejected patents on mere research intermediates.[92] In *In re Kirk*, for example, applicant's steroid compounds were denied a patent because their asserted utility in "biological activity" was non-specific and nebulous, and their potential use as intermediates in the creation of other, undefined steroid compounds was insufficient.[93] Likewise, in *In re*

---

86 Kunin, *supra* note 69, at 1092. Note that these guidelines "are not binding on [the] court, but may be given judicial notice to the extent they do not conflict with the statute." Enzo Biochem v. Gen-Probe, 323 F.3d 956, 964 (Fed. Cir. 2002) (citing Molins PLC v. Textron, Inc., 48 F.3d 1172, 1180 n.10 (Fed. Cir. 1995) (quoted in *Fisher*, 421 F.3d at 1372)).

87 *Fisher*, 421 F.3d at 1371.

88 *Id.* at 1371-72. "Biological activity," "biological properties," and "useful for technical and pharmaceutical purposes" have all been explicitly rejected as non-specific. *In re* Kirk, 376 F.2d 936, 941 (C.C.P.A. 1967) (quoted in *Fisher*, 421 F.3d at 1371). The PTO Utility Guidelines indicate that a utility as a "gene probe" would be considered specific only if the applicant discloses a specific DNA target. Kunin, *supra* note 69, cmt. 5.

89 *Fisher*, 421 F.3d at 1370.

90 *Id.* at 1370, 1373. The court also notes that, although Fisher suggested a number of potential uses for the claimed ESTs, he failed to proffer any evidence that *these* ESTs were used in any such way. "[D]espite the fact that maize leaves produce over two thousand different proteins during anthesis, Fisher failed to show that one of the claimed ESTs translates into a portion of one of these proteins. Fisher likewise did not provide any evidence showing that the claimed ESTs were used to locate genetic molecules in other plants and organisms . . . [or] that any such generic molecules would themselves have a specific and substantial utility." *Id.* at 1374.

91 Brenner v. Manson, 383 U.S. 519 (holding that an intermediate used to produce of product of unknown utility is not itself useful).

92 *But see* Pierce, *supra* note 52, at 17 (arguing that the *Fisher* decision is based on a misunderstanding of *Brenner*). According to Pierce, *Brenner* narrowly addressed the question of whether an applicant need evidence utility of products produced by a claimed process. "The fact that an invention has its sole use as a tool in research was never mandated by the Court in *Brenner* as a basis for finding a lack of utility under 35 U.S.C. § 101." *Id.* at 78.

93 In re Kirk, 376 F.2d 936, 939-941 (C.C.P.A. 1967).

Joly, the patent applicant claimed his compounds were useful as intermediates in preparation of other steroids of unknown utility, and were chemically similar to steroids of known utility.[94] Again, the court affirmed the PTO's rejection because compounds used solely as intermediates in the identification or production of other compounds with unknown utility is insufficient to comply with § 101.[95] Although these precedents relate to the chemical arts, *Fisher* applied the same reasoning to biotechnology, warning that patents are only to award monopolies to useful inventions, and are not to amount to "hunting licenses."[96] Thus, because Fisher only claimed that his ESTs could be used as research intermediates to gather further information on a DNA sample, but the functions of the underlying genes were not identified, and so the ESTs were deemed not substantially and specifically useful.[97]

III. THE PROBLEMS POSED BY PATENTING RESEARCH TOOLS

Essentially, research tool patents are potentially problematic by many because they have the capacity to monopolize a great deal of further research in the field. This could result in a research tool patent-holder directly benefiting from a product very much removed from the patented research tool, one which the patent-holder herself did not realize, envision, or even participate in inventing. Even more problematic, a research tool patent-holder could use her exclusivity rights to block further research or development in the technological area, effectively halting scientific advancement altogether.

A. *Illustrating the Issues*

Early discoverers of genetic sequences, for example, may be positioned to reap a windfall of intellectual property rights that, at the time of filing, are unknown to everyone.[98] Mattias Luukkonen illustrates this potential with the HDGNR10/CCR5 case.[99] In June, 1995, reserchers filed a patent application for the HDGNR10 gene, and this patent was issued by the PTO in February, 2000.[100]

---

94 In re Joly, 376 F.2d 906 (C.C.P.A. 1967).

95 *Id.* at 908-909. See also *Fisher*, 421 F.3d at 1374-75.

96 *Fisher*, 421 F.3d at 1376. *See also Brenner*, 383 U.S. at 535-36.

97 *Fisher*, 421 F.3d at 1375-76.

98 The rationale for such a policy that is commonly proffered argues that granting broad exclusivity rights is socially desirable because it situates one with proven technical sophistication in a position to drive the scientific field pertaining to the invention. *See* Edmund W. Kitch, *The Nature and Function of the Patent System*, 20 J. L. & ECON. 265 (1977).

99 Mattias Luukkonen, *Gene Patents: How Useful are the New Utility Requirements?*, 23 T. JEFFERSON L. REV. 337 (2001).

100 U.S. Patent No. 6,025,154 (filed Jun. 6, 1995).

In 1996, however, the same gene under another name, CCR5, was discovered to be an essential protein in the Human Immunodeficiency Virus (HIV).[101] At the time HDGNR10's application was filed, an applicant need only disclose one specific use of the gene to meet the utility bar.[102] Consequently, the patent on HDGNR10 also effectively granted exclusive rights to CCR5 and its potential drug discovery applications to the HDGNR10 patent-holder, even though the HDGNR10 application did not make any reference to HIV.[103] Such results have prompted Luukkonen and many others to question such a utility standard in which "organizations submitting gene patent applications based on large scale sequencing efforts will reap significant benefits from the subsequent discoveries of a gene's function or utility . . . [but m]ay provide a disincentive for corporations to conduct basic research, or to provide funding options for academic research institutions."[104]

B. *Overbreadth*

As the CCR5/HDGNR10 anecdote illustrates, patenting of research tools has the potential to result in overly broad patent monopolies. While a few extremely broad patent applications have been rejected by the courts, a number of patents have issued on what many have regarded as broad technologies.[105] Nothing in the language of the patent statute discusses nor prevents issuance of a patent for overbreadth, yet there remain widely-held sentiments that overly-broad patents are "unfair."[106] Furthermore, overbreadth may also yield unpredictability. When competitors confront a patent with a clearly-defined scope, they can design

---

101 See HongKui Deng et al., *Identification of a Major Co-receptor for Primary Isolates of HIV-1*, 381 NATURE 661 (1996).

102 Kunin, *supra* note 69, at 1098.

103 Luukkonen, *supra* note 99, at 338.

104 *Id.* at 338-39. After the sequencing of the Human Genome, it was discovered that:

> there is a finite — and surprisingly small — number of human genes, [and] it was soon recognized that each gene codes for many proteins and takes on different regulatory roles depending on the environment in which it operates. For the law this means . . . that one gene patent could potentially generate a 'molecular portfolio' of rights — rights over all the derivative molecules generated by the gene, as well as their functions.

Berman & Dreyfuss, *supra* note 38, at 875. *See also* Eileen M. Kane, *Splitting the Gene: DNA Patents and the Genetic Code*, 71 TENN. L. REV. 707 (2004).

105 Compare O'Reilly v. Morse, 56 U.S. 62 (1854) (rejecting Samuel Morse's "overly broad" patent claim for all ways of using electromagnetic force to transmit letters or symbols at a distance) with U.S. Patent No. 6,988,138 (filed June 30, 2000) (awarding Blackboard a patent for "technology used for internet-based education support systems and methods).

106 *See* 35 U.S.C. § 100, *et seq*; Susan Kuchinskas, *Patently Unfair?*, INTERNETNEWS, Mar. 16, 2004, *available at* http://www.internetnews.com/bus-news/article.php/3326431 (last visited Sept. 16, 2007).

around the patent's provisions to create a distinct invention.[107] This "makes life more predictable, assuring that innovation does not come to a standstill."[108] However, if the scope of the claim is "unclear or unjustifiably broad," competing invention could be severely restrained.[109]

C. *Prevention of Downstream Research*

In a criticism related to overbreadth, some have argued that research tool patents are problematic because they tend to inappropriately award exclusive rights to immature inventions. Research tools have sometimes been termed "upstream" products, because they are inventions used during the discovery process to develop other end products.[110] These end products, or "downstream" inventions, are thus created through the use of a number of upstream tools. When products too far upstream are patented, there can be significant, and some argue disastrous, effects on downstream innovation.

Those who oppose patenting research tools praised the *Fisher* decision, arguing that the balance between patent holder and inventor that so concerned the court in *Brenner* had been restored.[111] Tashica T. Williams argues that *Fisher*, in delaying patentability on ESTs, ensured that patents were only granted when the invention was ripe for patenting.[112] Williams explains:

> If [patent] rights vest too early, a significant impediment in the progress and development of a field could result. Conversely, if the granting of rights is delayed significantly, patent-sensitive industries, like biotechnology, would lack incentive to engage in costly research because of the potentially poor return on the investment. . . . By demanding evidence demonstrating a nexus between an EST and its target gene, the [*Fisher*] court propelled the inventive process forward. Scientists will not expend time and energy attempting to uncover, sequence, and patent as many ESTs as possible, regardless of their utility. Instead, they will probe deeper into the complexities of understanding the various systems that spring from a particular genetic base in order to identify ESTs with specific and substantial utility.[113]

By forcing EST patent applicants to demonstrate specific and

---

107 Campbell, *supra* note 4, at 1.

108 *Id.*

109 *Id.*

110 Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation?: The Anticommons in Biomedical Research*, 280 SCIENCE 622, 698 (1998).

111 Brenner v. Manson, 383 U.S. 519, 534, 534 (1965).

112 Tashica T. Williams, *In re Fisher: Raising the Utility Hurdle for Express Sequence Tags*, 21 BERKELEY TECH. L.J. 123, 137.

113 *Id.*

substantial utility, *Fisher* effectively prohibited DNA patents in early, unripe stages.[114]

Likewise, others applauded the *Fisher* ruling because it prevented patent holders from "stacking out intellectual property claims that extend beyond their actual achievements to include discoveries yet to be made by others."[115] While ESTs certainly provide valuable research information, they do not guarantee that the unknown gene will be identified, and they play an even smaller role in determining the unknown gene's function.[116] Thus, because the usefulness of ESTs is rather limited,[117] patent holders should also have restricted rights when it comes to downstream discoveries.[118] This would ensure that those who make upstream, routine discoveries are not unfairly rewarded, but also that those who determine biological function or medical application are not unfairly penalized.[119]

D. *Tragedy of the Anticommons*

The tragedy of the anticommons is a phenomenon that some have predicted if research tools continue to be patented. The tragedy of the anticommons is the inverse of the tragedy of the commons: in the tragedy of the commons, a resource is likely to be overused because many have privilege of use and no one has right of exclusion; in the tragedy of the anticommons, a resource is likely to be underused because many have right to exclusion but no one has privilege of use.[120] In the context of molecular

---

114 *Id.* While inventions in the mechanical arts tend to satisfy the utility requirement early in their development, inventions in the biological and chemical arts typically feature creation long before discovery of their utility, and thus do not ripen until much later in the developmental process. *Id.*

115 SUMMARY, *supra* note 18, at 53.

116 *Id.* For example, researchers including Caskey, Warren, and Benustra used ESTs to discover the DNA sequence defect underlying Fragile X Syndrome. However, this sequence information provided no information regarding function, and later researchers like Nussbaum and Dreyfus went on independently to identify the gene's function. *Id.*

117 While proposed uses for ESTs and other gene fragments include

> categorizing, mapping, tissue typing, forensic identification, antibody production, or locating gene regions associated with genetic disease . . . each of those suggested uses may not be carried out without considerable further effort and additional biological information tat is not inherent in the sequence alone.

Id.

118 *Id.*

119 *Id.* at 54.

120 Heller & Eisenberg, *supra* note 110, at 623-624, 698. The tragedy of the commons was first proposed by Garret Hardin in 1968 to explain air pollution, overpopulation, and species extinction. Garret Hardin, *The Tragedy of the Commons*, 162 SCIENCE 1243 (1968). A post-socialist Moscow storefront demonstrates the tragedy of the anticommons. Heller & Eisenberg, *supra* note 110, at 622-23. The storefront stands empty while merchants sell from street kiosks because the government endowed many storefront owners with different rights (the right to sell, the right to receive sales revenue, the right to lease, occupy, or use the property) rather than investing in any single individual a bundle of

biology,[121] anticommons can emerge as a result of increased privatization of upstream research tools.[122] In contrast with a single research tool patent-holder preventing downstream research (as described in Part III.C), an anticommons can result when many upstream patent-holders make downstream research a practical impossibility. If patents continue to issue on upstream technologies, some warn that "a proliferation of intellectual property rights upstream may [stifle] life-saving innovations further downstream in the course of research and product development."[123]

While some have suggested that the forecasted "tragedy" is either unlikely to occur or its effects overstated,[124] many recognize that the fear is "far from a merely academic construct" that "threatens to slow or stop the development of new drugs and devices critical to public health."[125] An anticommons is proposed to take place in one of two ways. First, multiple and concurrent fragments of rights could be created in potential future products.[126] For example, "a commercial end-product may require the use of multiple gene fragments, yet different owners may hold the rights to the individual fragments. A company that seeks to commercialize the end-product will need to obtain licenses from multiple owners before proceeding with product development."[127] Alternatively, an anticommons could be established if research

---

rights comprising full ownership. *Id.* Consequently, the storefront remained empty because each partial owner could block the others from using the property. *Id.*

121 Anticommons is more likely to exist in biotechnology than in other areas of intellectual property because patents are more essential in the biotech and pharmaceutical industries. Heller & Eisenberg, *supra* note 110, at 700. However, the tragedy of the anti-commons affects a number of industries other than molecular biology, and is relevant anywhere complex systems are built from patented components. See SUMMARY, *supra* note 18, at 49. For example:

> it was not until cross-licensing practices became widespread in the early development of radio and television that important advances that enabled broad access to the technology took place. When the intellectual property was sequestered in the hands of a few companies, the entire electronics industry remained sluggish.

Id.

122 Heller & Eisenberg, supra note 110, at 698.

123 *Id.*

124 *See* Response by Thomas G. Field, Jr., to Policy Commentary by J. J. Doll, and Review by M. A. Heller & R. S. Eisenberg, at http://www.sciencemag.org/feature/data/980465/field.shl (last visited Mar. 18, 2007); Ramirez, *supra* note 2, at 362. Ramirez points out that privatization not only provides incentive for biotechnology investment, but has also resulted in the exponential growth of the biotechnology industry. *Id.* Furthermore, many scientists and researchers recognize the benefit of freely sharing research tools, and have endeavored to achieve broad dissemination of such materials whenever possible. *Id.* Consequently, the "tragedy" is a remote possibility, and revamping the patent laws seems unwarranted. *Id.*

125 Janice M. Mueller, *No "Dilettante Affair": Rethinking the Experimental Use Exception to Patent Infringement for Biomedical Research Tools*, 76 WASH. L. REV. 7, 66.

126 Heller & Eisenberg, *supra* note 110, at 701.

127 Ramirez, *supra* note 2, at 369.

tool owners were permitted to impose reach-through[128] obligations on downstream users, which would lead to stacking licenses and "a potential developer would have to bargain with all of the rights-holders before developing an end-product."[129] In either case, "a 'patent thicket' could arise to retard innovation and the subsequent development of publicly beneficial commercial applications."[130]

A recent anticommons anecdote may illustrate further. In 2000, Ingo Potrykus of the Institute of Plant Sciences at the Swiss Federal Institute of Technology and Peter Beyer of the University of Freiburg published their successful transplantation of certain daffodil genes into rice.[131] The resulting Golden Rice was capable of producing the precursor chemical to vitamin A, and thus had the potential to aid millions of people, primarily in Africa and Asia, suffering from a vitamin A deficiency.[132] To create the rice, however, researchers had to use a number of technologies that had been licensed to private biotech companies.[133] Over sixty patents and contractual obligations associated with over thirty separate companies stood in the way of Golden Rice production.[134] These private companies were unwilling to provide licenses to the researchers, nearly causing the scientists to abandon the project altogether.[135] Eventually, the private companies were swayed to transfer the rights to the researchers that would allow them to continue the project, but perhaps only because of the global media attention that the controversy received, and the desire of the private companies to maintain a compassionate public

128 A reach-through license is designed to secure rights of a research tool patent-holder in later discoveries made with use of the tool. Heller & Eisenberg, *supra* note 110, at 701. Reach-through royalties are those paid to the research tool patent-holder from downstream products, even if the products do not incorporate the patented research tool. *Id.*

129 Ramirez, *supra* note 2, at 369; Heller & Eisenberg, *supra* note 110, at 701.

130 Michael S. Mireles, *An Examination of Patents, Licensing, Research Tools, and the Tragedy of the Anticommons in Biotechnology Innovation*, 38 U. MICH. J.L. REFORM 141, 148 (2004). A "patent thicket" refers to a scenario where different patent-holders own multiple patent rights in a technological field, and the many rights that must be acquired for further work in the field are so great as to potentially block further research in the area. *Id.* (quoting Organisation for Economic Co-Operation and Development (OECD), Genetic Invention, Intellectual Property Rights and Licensing Practices ch.1, p. 7 (2002), available at http://www.oecd.org/dataoecd/42/21/2491084.pdf). Note that the problem of this "royalty stacking" poses a problem particularly in gene therapy, where many promising advances occur in relation to rare genetic diseases, thereby presenting a small market and limited profitability. SUMMARY, *supra* note 18, at 48.

131 Xudong Ye et al., *Engineering the Provitamin A (Beta-Carotene) Biosynthetic Pathway Into (Carotenoid-Free) Rice Endosperm*, 287 SCIENCE 303 (2000).

132 Madeline Nash, *Grains of Hope*, TIME, July 31, 2000.

133 Justin Gillis, *Researchers to Keep Some Biotech Rights*, WASH. POST, July 11, 2003, at E5.

134 *Id.*; Richard C. Atkinson et al., *Public Sector Collaboration for Agricultural IP Management*, 301 SCIENCE 174, 174 (July 11, 2003).

135 Gillis, *supra* note 133, at 378.

image.[136]

IV. POTENTIAL SOLUTIONS

A. *Increased Experimental Use Exception*

Congress statutorily enacted an experimental use exception in 1994.[137] A few years earlier, the Federal Circuit had held that a generic pharmaceutical company's use of patented active ingredients for equivalency testing to satisfy federal requirements prior to marketing the generic drug was not exempted from infringement.[138] In response, by enacting the statutory experimental use exception, Congress ensured that, in the future, generic drugs could be brought to the market more expediently.[139] The statutory exception "is limited to pharmaceuticals and medical devices and use of the patented invention while preparing for clinical trials."[140]

The common law experimental use exception, however, has had a much lengthier and fuller history. The exception was first recognized in the 1891 case, *Whittemore v. Cutter*.[141] Through a series of judicial decisions, the narrow exception has been well-defined, recognizing that "an experiment with a patented article for the sole purpose of gratifying a philosophical taste, or curiosity, or for mere amusement, is not an infringement of the rights of the patentee."[142] As Justice Story famously explained, "it could never have been the intention of the legislature to punish a man, who constructed such a machine merely for philosophical experiments, or for the purpose of ascertaining the sufficiency of the machine to produce its described effects."[143]

Recently, the Federal Circuit has further limited the already narrow exception. In *Madley v. Duke University*, the court held that the common law experimental use exception did not apply to use of patented inventions by university researchers if there was even a remote commercial purpose, including furthering of the university's legitimate business purposes.[144] And in *Integra*

---

136 *Id.*

137 35 U.S.C. § 271(e)(1) (1994).

138 Roche Prod. v. Bolar Pharm. Co., 733 F.2d 858 (Fed. Cir. 1984).

139 § 271(e)(1).

140 Mireles, *supra* note 130, at 206.

141 29 F. Cas. 1120, 1121 (C.C.D. Mass. 1813) (concerning U.S. Patent No. 17, 600).

142 Poppenhusen v. Falke, 19 F. Cas. 1048, 1949 (C.C.S.D.N.Y. 1861) (concerning U.S. Patent No. 11,279). *See also* Chesterfield v. U. S., 159 F. Supp. 371, 375 (Cl. Ct. 1958); Ruth v. Stearns-Roger Mfg. Co., 13 F. Supp. 697, 703 (D. Colo. 1935); Sawin v. Guild, 21 F. Cas. 554, 555 (C.C.D. Mass. 1813).

143 *Whittemore*, 29 F. Cas. at 1121.

144 Madley v. Duke Univ., 307 F.3d 1351, 1352 (Fed. Cir. 2002).

Lifesciences I, Ltd. v. Merck KgaA, the court held that the statutory experimental use exception, § 271(e)(1) required a potential infringer to demonstrate that its activities were solely for the purpose of submitting information to the FDA, and that activities that do not directly produce information for the FDA are not exempt.[145]

Despite the Federal Circuit's recent disposition, some have proposed the broadening of the experimental use exception as a way to reduce patents on research tools. Rebecca Eisenberg argues that a balance between free access models typical of basic science and proprietary models common of advanced scientific innovation can be achieved by employing a three-prong analysis.[146] First, the experimental use exception should apply to research of a patented invention in order to determine the adequacy or validity of the written description.[147] Second, the exception should not apply to research use of a patented invention when there is a primary market among researchers.[148] Finally, patent-holders should not be permitted to prevent the use of the patented invention in such a way as to impede subsequent research in the field, which could otherwise lead to improvements in the field or an alternative form of the invention.[149]

Janice Mueller expands on Eisenberg's proposal, suggesting that the experimental use exception should be applied especially when transaction costs are significant (usually due to stacking royalties), even if the non-consensual use is ultimately for commercial purposes.[150] While a patent-holder would not be permitted to prevent use of the research tool by others, she would be entitled to compensation with "an ex post royalty set by the market value of any commercial product developed with the tool."[151] Although the NIH has distinguished between "experimenting on" and "experimenting with" the patented invention for experimental use exception purposes, Mueller argues that the distinction is not justified when transactional costs are so high as to prevent further development in the field.[152]

Opponents caution that allowing non-consensual use of all

145 Integra Lifesciences I, Ltd. v. Merck KgaA, 331 F.3d 860, 865-868 (Fed. Cir. 2003).
146 Eisenberg, *supra* note 73, at 1017.
147 *Id.* at 1078.
148 *Id.*
149 *Id.*
150 Mueller, *supra* note 125, at 57.
151 Mireles, *supra* note 130, at 213 (citing Mueller, *supra* note 125, at 9-10).
152 *See* Mireles, *supra* note 130, at 214. Although Mueller admits that exempting all non-consensual users from infringement liability could work to undermine the patent system incentives, she contends that an after-the-fact royalty payment is sufficient to allay these concerns. *Id.*

research tools, even for commercial purposes, would "effectively destroy the market for these tools, thus removing any incentives to create research tools."[153] Even a less extreme version of the exception could damage the incentives that the patent system was designed to induce, especially in the biotech field that relies so heavily on venture capital funding.[154] Furthermore, because the applicability of the exception to any particular non-consensual use can only be determined after litigation, it would be difficult to predict in advance whether and to what extent the exception should apply, and what royalties, if any, a patent-holder will receive.[155] Finally, a broad experimental use exception could encourage researchers to seek trade secret, rather than patent protection, for their research tools, resulting in less public disclosure and slower development in the field.[156]

The experimental use exception has a long and enduring history in the U.S. patent system. However, the exception has traditionally, and perhaps wisely, remained narrow. While broadening the exception may alleviate some of the risks that research tool patents pose, the consequential effect on the patent system, and its likely overthrowing of the incentive-based patent system, is not justified.

B. *Fair Use Exception*

Alternatively, Professor Maureen O'Rourke argues that a fair use exception, like that in copyright law, should be adopted in patent law "when the costs for any one entity to accumulate all the required licenses to develop a socially beneficial product or service is prohibitive."[157] The fair use exception would correct market failures that sometimes render exclusive rights overly broad, and can prevent efficient and desirable use of the patented material.[158] O'Rourke identifies five factors in determining whether a fair use exception should apply to patent infringement:

> (1) the nature of the advance that the infringement represents; (2) the purpose of the infringing use; (3) the nature and strength of the market failure that prevents a license from being concluded; (4) the impact of the use on the patentee's incentives and overall social welfare; and (5) the nature of the

---

153 Mireles, *supra* note 130, at 214.

154 *Id.* at 214-15; *see also* Jordan P. Karp, *Experimental Use as Patent Infringement: The Impropriety of a Broad Exception*, 100 YALE L.J. 2169, 2179-2181 (1991).

155 Mireles, *supra* note 130, at 215.

156 *Id.* at 216.

157 Mireles, *supra* note 130, at 201.

158 Maureen O'Rourke, *Toward a Doctrine of Fair Use in Patent Law*, 100 COLUM. L. REV. 1177, 1187.

patented work.[159]

O'Rourke recommends judicial balancing of these factors to determine whether the fair use exception should apply.[160] If the use is fair, the court then determines whether the infringer must pay the patent-holder any royalties.[161]

The fair use exception is promising because of its attempt to alleviate anticommons concerns. For example, fair use might be employed in some circumstances where a researcher is attempting to invent around a patented invention, even if the end product is commercially marketed.[162] Fair use could also be utilized where a researcher has acquired almost all licenses necessary to proceed, but because of a single or few hold-out patent-holders, the research cannot proceed.[163] Finally, O'Rourke proposes that merely instituting a fair use exception may incentivize parties to come to agreements without actually invoking the exception in the courts.[164]

Opponents argue that a broad and loosely-defined exception could erode the very incentives that the patent system puts into place, especially in biotechnology, where research is uncertain and complex.[165] Strong patent rights may be necessary for venture capitalist investment in biotech companies.[166] Furthermore, a fair use exception may not be translatable from copyright to patent law.[167] Because of the low threshold for obtaining and securing copyright protection, a broad exception may be justified.[168] Patents, however, are only granted after extensive and often costly PTO review; thus, it seems counter-productive to subject patents to a broad exception.[169]

While these objections are well-reasoned, they do not necessarily require that a fair use exception be abandoned altogether. If the requisite burden of proof is high enough, and courts are willing to invoke the exception only in rare cases, the fair use exception could be a last resort for patent applicants or potential infringers facing the serious problems that patenting research tools may pose.

---

159 Mireles, *supra* note 130, at 202-203 (citing O'Rourke, *supra* note x, at 1205).
160 O'Rourke, *supra* note 158, at 1209.
161 *Id.*
162 *Id.* at 1238.
163 *Id.*
164 *Id.*
165 Mireles, *supra* note 130, at 204.
166 *Id.*
167 *Id.*
168 *Id.*
169 *Id.*

C. *Stricter Utility Requirements*

Although the 2001 Utility Examination Guidelines adopt a more stringent approach to utility than had previously been used, some have proposed increasing the utility standard even further.[170] As biotechnology unveils science at ever more rudimentary levels, yet patents remain broad, fundamental biological building blocks could be removed from the public domain altogether.[171] The Bayh-Dole Act also encourages patenting of upstream research tools and licensing to downstream commercial inventors.[172] Because these forces encourage more patenting of research tools, a narrower utility requirement could help balance this trend.

Others have opposed the tightening of the utility requirement, arguing that early patenting is essential for the continued growth of the biotech industry.[173] Patents "provide biotechnology firms assets, often their only assets, with which to secure venture capital funding. Without a patent, venture capitalists may be unwilling to invest in biotechnology research and development."[174] Furthermore, because the FDA requires thorough clinical testing for pharmaceutical compounds, representing a significant investment for researchers, scientists in this field have a particular incentive to patent early in the developmental process, even before a compound's properties are well-understood.[175]

Narrowing the utility requirement, however, can be a successful strategy if it is narrowed in an effective way. Some have proposed, for example, that gene patent applications must disclose the encoded protein along with the function of the protein.[176] Such requirements, which would prevent many DNA sequence patents, are unnecessary. Rather, I propose that issuing patents will only be enforced to the extent the research tool's utility is disclosed. This would block virtually no otherwise patentable application, and would thus have no effect on the quantity of patents issued, but would prevent a patent-holder from exercising exclusivity rights in products too far downstream of the research tool.[177] For instance, consider again the

170 *See, e.g.*, Teresa M. Summers, *The Scope of Utility in the Twenty-First Century: New Guidelines for Gene-Related Patents*, 91 GEO. L.J. 475, 477-78 (2003).

171 *Id.* at 476.

172 *Id.*

173 *See, e.g.*, Mireles, *supra* note 130, at 199-200.

174 *Id.*

175 *Id.* at 200.

176 Summers, *supra* note 170, at 480-81.

177 Some have contended that restricting the utility requirement in a way that prevents patenting of research tools would have disastrous effects on, inter alia, biotech companies that only create research tools. Mireles, *supra* note 130, at 200. Moreover, prevention of

CCR5/HDGNR10 example. If a patent was issued for HDGNR10, without any reference to its use or involvement with HIV, the patent-holders would be unable to enforce their rights in HIV research, because no utility relating to HIV was disclosed in the HDGNR10 application.

The consequences to such a modification to the patent system could be significant. Researchers would be forced to file "follow-up" applications whenever they discover a new utility for their research tool. Although this would increase filing costs for researchers, the system might be beneficial in that no one can claim exclusivity rights in a utility discovered (and patented) by another. Thus, research tool patents would no longer suffer from frequently unfair overbreadth. Furthermore, patented research tools could only block downstream research insofar as the particular use of the research tool in the development of the downstream end-product was disclosed by the research tool patent-holder in the patent application.

D. *Limited Judicial Remedies*

When it comes to research tools and their potential to interfere with, even prevent, life-saving medical research, perhaps the court's remedies in cases of infringement should be limited to prevent issuance of injunctions, and allow only money damages.[178] Similar reasoning could be adopted here. Described by some as compulsory licensing, a research tool patent-holder would be required in some circumstances to license the tool, allowing the patent-holder to be compensated, "but not at a prohibitive rate."[179] Because so many would potentially be affected, or because the effect would be so devastating, or because such important research should not be stopped altogether, an injunction might be considered an inappropriate remedy for violating certain research tool patents.

V. CONCLUSION

Research tools are unique subjects of patents. Just as research tools play a particular role in the laboratories as research

research tool patents may lead to covert development and use of these tools and, without public disclosure, researchers could waste resources in developing an already-invented tool. *Id.* Amending the utility requirement so as to limit exclusivity rights to the disclosed utilities would allow research tool patents to proceed, but limit their downstream enforceability.

178 *See generally* Grace Wong, *Judge: No Blackberry Shutdown Yet*, CNN MONEY, Feb. 24, 2006, http://money.cnn.com/2006/02/24/technology/blackberry/index.htm (discussing the hesitancy of the court in MercExchange v. eBay, to award an injunction).

179 Murashige, *supra* note 5, at 1335.

intermediaries, or tools that lead scientists to later, downstream end-products, they also pose unique issues in the patent system. Patenting research tools can potentially result in a number of undesirable outcomes, including overbreadth, prevention of downstream innovation, and the tragedy of the anticommons. Most agree that these are consequences to be avoided, and many have proposed a number of potential solutions, including the broadening of the experimental use exception, introducing the fair use exception, narrowing the utility requirement, or restricting judicial remedies. Though each proposition offers a number of risks to the delicate balances at play in the U.S. patent system, adopting modest version of one or more of these proposals may offer a long-sought solution to the serious issues posed by inappropriate research tool patenting.

Cara Koss[*]

[*] Senior Articles Editor, 2008, JD candidate Benjamin N. Cardozo School of law; M.S. in molecular genetics from the University of Virginia.