Stanford Technology Law Review

NOTE

Access to Bio-Knowledge:

From Gene Patents to Biomedical Materials

LISA LARRIMORE OUELLETTE*

CITE AS: 2010 STAN. TECH. L. REV. N1
http://stlr.stanford.edu/pdf/ouellette-access-to-bio-knowledge.pdf

ABSTRACT

Patents claiming DNA sequences have been subject to extensive public and scholarly criticism due to their potential to impede innovation and to restrict access to affordable healthcare. Recent empirical studies, however, indicate that access to materials is a much more serious problem than patents are for basic biomedical researchers, and access to materials is also a critical problem for producers of biomedical end products like biopharmaceuticals. This Note argues that these physical research tools should be included in a more expansive concept of "bio-knowledge," and that solving the access to materials problem is critical for increasing biomedical innovation. This problem has been caused in part by changing norms among basic researchers, but fully undoing the commercialization of university research is neither possible nor desirable. Instead, partial solutions may be found within the patent system, both through reducing the transaction costs associated with material transfers and through increased use of official material depositories by both basic and industrial researchers.

* © 2010, Lisa Larrimore Ouellette, Yale Law School, J.D. expected 2011; Cornell University, Physics Ph.D. 2008; Swarthmore College, B.A. 2002. I am grateful to Lea Shaver, Laura DeNardis, and my classmates in Yale Law School's Spring 2009 Access to Knowledge Practicum who provided useful feedback on drafts of this Note.

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INTRODUCTION

¶1 Nearly twenty percent of all human genes were claimed in U.S. patents by 2005[1] and thousands more patents on DNA are issued each year.[2] In a *New York Times* opinion, science-fiction author Michael Crichton warned, "You, or someone you love, may die because of a gene patent that should never have been granted in the first place."[3] Myriad Genetics' aggressive enforcement of patents on genes linked to breast cancer has sparked international criticism and a recent ACLU lawsuit.[4] DNA patents have also been subject to extensive scholarly criticism for being legally unsound, impeding innovation, restricting health care, and violating individual rights.[5] In response to these concerns, Congressmen Xavier Becerra (D-CA) and David Weldon (R-FL) introduced the Genomic Research and Accessibility Act in 2007 "to prohibit the patenting of human genetic material."[6]

¶2 Recent evidence, however, suggests that concerns about gene patents may be exaggerated.[7] Surveys show that patents rarely directly impede basic research because scientists simply ignore the patents.[8] DNA patents can have more effect on access to end products like genetic tests[9] and biopharmaceuticals,[10] but such problems are not particular to DNA patents. Banning DNA patenting altogether without providing an alternative incentive for drug development would likely result in fewer new biopharmaceuticals.[11] Furthermore, recent judicial trends that limit the patentability of genetic sequences will likely mitigate the problems that do exist.[12]

¶3 Recent empirical studies show that a bigger impediment to basic biomedical innovation than DNA patents is practical access to materials.[13] For example, one survey of academic biomedical researchers found that while 75% of them had requested a material—such as a cell line, gene, or organism—in the past two years, 18% of such requests to academics and 33% to industry were denied.[14] Access to materials is also a critical issue for biomedical end products, particularly for the biopharmaceutical industry.[15] While some access problems stem from the effects of patenting on academic norms, any policy changes should focus on these practical barriers to access, rather than on the patents themselves.

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[1] Kyle Jensen & Fiona Murray, *Intellectual Property Landscape of the Human Genome*, 310 SCI. 239, 239 (2005).

[2] *See infra* Part I.A.2.

[3] Michael Crichton, Op-Ed., *Patenting Life*, N.Y. TIMES, Feb. 13, 2007, at A23, *available at* http://www.nytimes.com/2007/02/13/opinion/13crichton.html.

[4] *See* Timothy Caulfield, Tania Bubela & C.J. Murdoch, *Myriad and the Mass Media: The Covering of a Gene Patent Controversy*, 9 GENETICS IN MED. 850, 850 (2007); Press Release, ACLU, ACLU Challenges Patents on Breast Cancer Genes (May 12, 2009), *available at* http://www.aclu.org/freespeech/gen/39572prs20090512.html.

[5] *See, e.g.*, Lori B. Andrews & Jordan Paradise, *Gene Patents: The Need for Bioethics Scrutiny and Legal Change*, 5 YALE J. HEALTH POL'Y L. & ETHICS 403, 405-11 (2005); Linda J. Demaine & Aaron Xavier Fellmeth, *Reinventing the Double Helix: A Novel and Nonobvious Reconceptualization of the Biotechnology Patent*, 55 STAN. L. REV. 303, 310-11 (2002); Michael A. Heller and Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698, 699 (1998).

[6] Genomic Research and Accessibility Act, H.R. 977, 110th Cong. § 2(a) (2007).

[7] *See, e.g.*, Editorial, *Property Rights*, 458 NATURE 386, 386 (2009).

[8] *See, e.g.*, Zhen Lei, Rakhi Juneja & Brian D. Wright, *Patents Versus Patenting: Implications of Intellectual Property Protection for Biological Research*, 27 NATURE BIOTECHNOLOGY 36, 37 (2009). *See generally* Rebecca S. Eisenberg, *Noncompliance, Nonenforcement, Nonproblem? Rethinking the Anticommons in Biomedical Research*, 45 HOUS. L. REV. 1059, 1063-75 (2008) (summarizing several other surveys of research scientists).

[9] *See, e.g.*, Roger D. Klein, *Gene Patents and Genetic Testing in the United States*, 25 NATURE BIOTECHNOLOGY 989, 990 (2007).

[10] *See* Amy Kapczynski et al., *Addressing Global Health Inequities: An Open Licensing Approach for University Innovations*, 20 BERKELEY TECH. L.J. 1031, 1034, 1095 (2005).

[11] *See, e.g.*, Gregory C. Ellis, *Emerging Biotechnologies Demand Defeat of Proposed Legislation That Attempts to Ban Gene Patents*, 15 RICH. J.L. & TECH. 1, ¶¶ 45-55 (2008), http://law.richmond.edu/jolt/v15i1/article1.pdf.

[12] *See* discussion *infra* Part I.A.3.

[13] *See* Eisenberg, *supra* note 8, at 1063-75; Lei et al., *supra* note 8, at 37-39.

[14] John P. Walsh, Wesley M. Cohen & Charlene Cho, *Where Excludability Matters: Material Versus Intellectual Property in Academic Biomedical Research*, 36 RES. POL'Y 1184, 1191 (2007).

[15] *See, e.g.*, S.D. Roger & D. Goldsmith, *Biosimilars: It's not as Simple as Cost Alone*, 33 J. CLINICAL PHARMACY & THERAPEUTICS 459, 461 (2008).

¶4 This Note proceeds in three Parts. Part I critically examines the gene patent controversy. The historical development of patenting DNA sequences is briefly summarized, along with questions about the validity of many of these patents. I then discuss the normative concerns about whether DNA *should* be patented. Most "moral concerns" arise from a misunderstanding of patents, but there are legitimate policy concerns. DNA patents on "upstream" basic research have the potential to create an "anticommons," in which too many rights to exclude lead to underuse of a resource.[16] This concern is reevaluated in light of recent empirical evidence that patents rarely hinder basic biomedical research directly.

¶5 DNA patents can also limit access to "downstream" healthcare end products, including genetic diagnostic testing and biopharmaceuticals. A recent study indicates that relatively few DNA patents have been asserted through litigation,[17] suggesting that the problem is less dire than predicted. DNA patents, however, still prevent competition from driving down prices for medically essential products. These problems, however, simply reflect the tradeoff in the patent system between providing incentives for new research and promoting access to current products. Broader patent reform may be needed to address these problems, but there is no reason to target DNA patents in particular.

¶6 Part II seeks to expand the current understanding of intellectual property protection for biomedical knowledge. The controversy surrounding gene patents has focused on *information*—the genetic sequence for a piece of DNA—and whether use of that information can be restricted through patents. Raw information, however, is not the only type of knowledge necessary for innovation and production of biomedical goods: information-embedded research tools, such as cell lines, are also critically important.[18] A more expansive concept of "bio-knowledge" must be incorporated into the consideration of intellectual property protection in biomedical research and development. Many types of bio-knowledge are protected through means other than patents, and these alternate forms of protection have received far less scrutiny.

¶7 Accessing forms of bio-knowledge other than patented information is a significant problem for both academics and industrial researchers, and I examine the problems in both contexts. Restrictions on material transfers imposed by patent-conscious universities often make it difficult for upstream academic researchers to obtain necessary bio-materials from other labs. Patents are indirectly part of the problem, as they have changed traditional scientific sharing norms. It is not clear, however, that an experimental use exemption from patent infringement would reverse trends toward withholding and secrecy. Access to materials is also a critical problem for companies that want to make generic versions of biopharmaceuticals because the necessary cell lines are often fiercely guarded trade secrets of brand-name companies.

¶8 Based on these observations, Part III examines two ways to increase access to biomedical knowledge. First, academics should embrace initiatives to increase openness among researchers by reducing the transaction costs associated with material transfers. Second, both basic and industrial researchers should make greater use of official material depositories to facilitate these transfers. For academics, these depositories may serve as a market-based solution to the access to materials problem. For industrial researchers, use of depositories should be enforced to satisfy the enablement and best mode requirements for patent protection, which will increase access to biomedical end products.

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[16] *See* Heller & Eisenberg, *supra* note 5, at 698-99.

[17] Christopher M. Holman, *The Impact of Human Gene Patents on Innovation and Access: A Survey of Human Gene Patent Litigation*, 76 UMKC L. REV. 295, 323-51 (2007) [hereinafter Holman, *Survey*]; Christopher M. Holman, *Trends in Human Gene Patent Litigation* 322 SCI. 198, 198-99 (2008).

[18] This classification of knowledge is based on Yochai Benkler's four-part framework. *See* YOCHAI BENKLER, THE WEALTH OF NETWORKS: HOW SOCIAL PRODUCTION TRANSFORMS MARKETS AND FREEDOM 311-15 (2006), *available at* http://cyber.law.harvard.edu/wealth_of_networks/.

I. EVALUATING THE CONCERNS ABOUT DNA PATENTS

¶9 Concerns about patenting DNA and human genes can be broadly divided into legal, moral, and policy issues. This Part summarizes the legal basis for patenting DNA and the doctrinal concerns that have been raised about these patents. I then turn to the normative debate over whether DNA patents *should* be allowed. Much of the public debate focuses on moral qualms about "owning" part of a human being, but these concerns often stem from a misunderstanding of patents. Instead, greater focus should be placed on the policy questions of the degree to which DNA patents hinder basic research and restrict access to healthcare.

A. The Legal Basis for Patenting DNA

1. Statutory and Doctrinal Foundations

¶10 Under § 101 of the Patent Act of 1952, a patent may be granted for a "process, machine, manufacture, or composition of matter, or any new and useful improvement thereof."[19] Additionally, the patented subject matter must be useful, novel, and nonobvious.[20] The U.S. Patent and Trademark Office (PTO) has been granting patents on DNA sequences for nearly three decades, but the boundaries of biotechnological patentability remain unclear.[21]

¶11 Plants,[22] single-celled organisms,[23] and complex organisms[24] have all been patented under § 101.[25] Although products of nature are not patentable, the Supreme Court held in *Diamond v. Chakrabarty* that a genetically modified organism is "a nonnaturally occurring manufacture or composition of matter—a product of human ingenuity"—and is thus patentable subject matter.[26]

¶12 Soon after *Chakrabarty* was decided in 1980, the PTO began granting patents for human genes.[27] Under the "product of nature" doctrine, a patent cannot be issued for DNA in its naturally occurring form (i.e., in a living organism).[28] Patents have instead claimed "isolated and purified" DNA or recombinant DNA—products that do not exist in nature.[29]

¶13 The patentability of purified versions of naturally occurring biological compounds dates back to Judge Learned Hand's 1912 upholding of a patent on extracted, purified adrenaline because its removal from the adrenal gland made it "for every practical purpose a new thing commercially and therapeutically."[30] Although the Supreme Court held in the nineteenth century that mere purification

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[19] 35 U.S.C. § 101 (2006).

[20] 35 U.S.C. §§ 101-103 (2006).

[21] Rebecca S. Eisenberg, *Re-Examining the Role of Patents in Appropriating the Value of DNA Sequences*, 49 EMORY L.J. 783, 784 (2000).

[22] Plants were initially patented under the Plant Patent Act, ch. 312, § 1, 46 Stat. 376 (1930) (codified as amended at 35 U.S.C. §§ 161-64 (2006)) and the Plant Variety Protection Act, Pub. L. No. 91-577, 84 Stat. 1542 (1970) (codified as amended at 7 U.S.C. §§ 2321-2583 (2006)). The Supreme Court later held that plants can also be patented under § 101 in *J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred International, Inc.*, 534 U.S. 124 (2001).

[23] *See* Diamond v. Chakrabarty, 447 U.S. 303 (1980); *see also* U.S. Patent No. 141,072 (filed May 9, 1873) (patent granted to Louis Pasteur for purified yeast).

[24] *See Ex parte* Allen, 2 U.S.P.Q.2d (BNA) 1425 (B.P.A.I. 1987) (holding that a genetically modified oyster is patentable subject matter but rejecting the patent on obviousness grounds), *aff'd*, *In re* Allen, 846 F.2d 77 (Fed. Cir. 1988); U.S. Patent No. 4,736,866 (filed June 22, 1984) (issued Apr. 12, 1988) (patent for Harvard's cancer-prone OncoMouse).

[25] For a thorough review of the history of patenting plants, animals, and naturally occurring compounds, see Demaine & Fellmeth, *supra* note 5, at 312-60.

[26] Diamond v. Chakrabarty, 447 U.S. at 309-10.

[27] *See*, *e.g.*, U.S. Patent No. 4,517,294 (filed Jul. 30, 1982) (issued May 14, 1985) (claiming a DNA sequence encoding human antithrombin III); U.S. Patent No. 4,363,877 (filed Apr. 19, 1978) (issued Dec. 14, 1982) (claiming DNA vectors for human somatomammotropin and for human growth hormone).

[28] *See* Eisenberg, *supra* note 21, at 785-86; *see also* Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127 (1948) (invalidating a patent for a combination of preexisting soil bacteria as a phenomenon of nature, rather than a man-made invention).

[29] Eisenberg, *supra* note 21, at 786. Recombinant DNA is formed by combining DNA from two or more sources. DAVID L. NELSON & MICHAEL M. COX, LEHNINGER PRINCIPLES OF BIOCHEMISTRY 307 (4th ed. 2005).

[30] Parke-Davis & Co. v. H. K. Mulford Co., 189 F. 95, 103 (C.C.S.D.N.Y. 1911), *aff'd*, 196 F. 496 (2d Cir. 1912).

of a product of nature is insufficient for patentability,[31] other courts later followed Judge Hand's reasoning.[32]

¶14 In 1991, the Federal Circuit stated that a "purified and isolated DNA sequence" is patentable subject matter in *Amgen, Inc. v. Chugai Pharmaceutical Co.*[33] This holding has been criticized as conflicting with Supreme Court precedent and with recent congressional intent,[34] but the Federal Circuit has consistently upheld the patentability of DNA.[35] In 1998, the PTO Director of Biotechnology Examination stated that patents on DNA sequences could be granted if the application "state[s] that the invention has been purified or isolated or is part of a recombinant molecule or is now part of a vector."[36]

2. The Rise of DNA Patents and the EST Controversy

¶15 Following *Amgen*, the number of DNA patent applications skyrocketed.[37] In 1991 and 1992, after the publicly funded Human Genome Project was launched, the National Institutes of Health (NIH) sought patents on over six thousand fragments of DNA of unknown function, known as expressed sequence tags[38] (ESTs).[39] The resulting backlash caused the NIH to withdraw its applications in 1994, but the PTO maintained that ESTs were patentable due to their utility as probes and issued the first EST patent in 1998.[40] This decision "incited the equivalent of an academic four alarm fire,"[41] which continued until the PTO decided that ESTs did not meet the utility requirement for patentability.[42]

¶16 Opponents of DNA patents won the battle over ESTs, but thousands of new DNA patents are still issued each year. Jensen and Murray's oft-cited 2005 study found that nearly twenty percent of human genes are claimed in U.S. patents.[43] As of February 2, 2010, the DNA Patent Database maintained at Georgetown University contained 52,716 issued patents and 77,410 published patent applications that have not yet issued.[44] Several sources have claimed that the number of DNA patents per year has fallen off since the human genome was published in 2001;[45] my patent search, however, found that this trend reversed after 2005, as shown in fig.1.

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[31] *See* Cochrane v. Badische Anilin & Soda Fabrik, 111 U.S. 293, 311-12 (1884) (holding that a purer version of a dye that already existed in nature is unpatentable); American Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. (23 Wall.) 566, 593-94 (1874) (holding that purified cellulose is a mere "extract" that "cannot be called a new manufacture").

[32] *See, e.g.*, *In re* Bergstrom, 427 F.2d 1394, 1401 (C.C.P.A. 1970) (holding that while a compound "merely discovered from nature is not patentable," hormones isolated from animal prostate glands "do not exist in nature in pure form" and thus meet the novelty requirement of patentability).

[33] 927 F.2d 1200, 1206-07 (Fed. Cir. 1991).

[34] *See* Demaine & Fellmeth, *supra* note 5, at 331-61; *see also* Allen K. Yu, *Why It Might Be Time To Eliminate Genomic Patents, Together with the* Natural Extracts Doctrine *Supporting Such Patents*, 47 IDEA 659, 754 (2007) ("[T]he [natural extracts] doctrine has been expanded to apply to contexts far beyond what was originally envisioned, in the process misconstruing broad areas of science . . . .").

[35] *See, e.g.*, *In re* Deuel, 51 F.3d 1552 (Fed. Cir. 1995); *In re* Bell, 991 F.2d 781 (Fed. Cir. 1993).

[36] John J. Doll, *The Patenting of DNA*, 280 SCIENCE 689, 689-90 (1998), *available at* http://www.sciencemag.org/cgi/content/full/280/5364/689.

[37] *See* Demaine & Fellmeth, *supra* note 5, at 359.

[38] ESTs mark expressed genes (i.e., the DNA that is transcribed into RNA) and were used to help sequence the human genome. NELSON & COX, *supra* note 29, at 318.

[39] Demaine & Fellmeth, *supra* note 5, at 323.

[40] *Id.* at 324-26.

[41] *Id.* at 326.

[42] The PTO issued these new guidelines for public comment in 1999, Revised Utility Examination Guidelines; Request for Comments, 64 Fed. Reg. 71,440 (Dec. 21, 1999), and a final version issued in 2001, Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001). The Federal Circuit endorsed these guidelines by upholding an EST patent rejection in *In re Fisher*. 421 F.3d 1365 (Fed. Cir. 2005).

[43] Jensen & Murray, *supra* note 1.

[44] DNA Patent Database, http://dnapatents.georgetown.edu/ (last visited Feb. 5, 2010). This is "the most extensive database of U.S. 'gene' patents." NATIONAL RESEARCH COUNCIL OF THE NATIONAL ACADEMIES, REAPING THE BENEFITS OF GENOMIC AND PROTEOMIC RESEARCH: INTELLECTUAL PROPERTY RIGHTS, INNOVATION, AND PUBLIC HEALTH 101 (Stephen A. Merrill & Anne-Marie Mazza eds., 2006), *available at* http://www.nap.edu/catalog/11487.html. However, the database's "highly inclusive nature" means that many of these patents "only tangentially involve DNA" and "are not what one would normally consider gene patents." Holman, *Survey*, *supra* note 17, at 318.

[45] *See* Michael M. Hopkins et al., *DNA Patenting: The End of an Era?*, 25 NATURE BIOTECHNOLOGY 185, 185-87 (2007); Lori

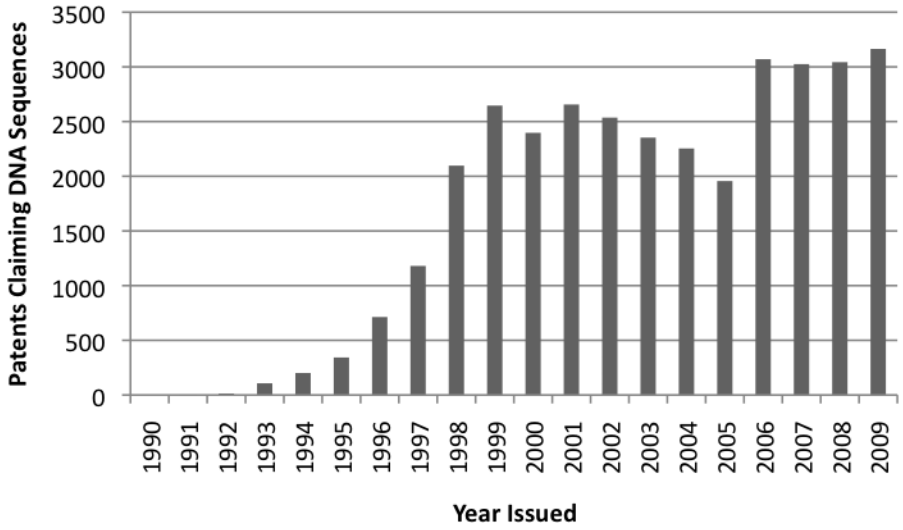

Figure 1. Patents claiming DNA sequences using "SEQ ID NO." [46]

¶17 Although DNA patents are ubiquitous, stating that twenty percent of human genes are "owned" is misleading, since most patents cover only a narrow use of a DNA sequence. Indeed, Jensen and Murray's study found that some genes are claimed in up to twenty different patents.[47] Patented applications of DNA fall into four general categories: genetic diagnostic testing, research tools, gene therapy, and the recombinant production of therapeutic proteins to be used as medicines.[48] Grouping all of these patents together may be simpler for courts and commentators, but the science behind each application is very different, and each type of DNA patent has different policy implications.[49]

3. Questions about Patentability and Recent Judicial Trends

¶18 The doctrinal soundness of many DNA and biotechnology patents continues to be debated. Scholars have argued that DNA patents often do not meet "invention,"[50] "alternativeness,"[51] or "originality"[52] requirements; that the PTO misapplies case law on the utility standard;[53] that DNA patents violate the "products of nature" doctrine because courts misunderstand the science of

Pressman et al., *The Licensing of DNA Patents by US Academic Institutions: An Empirical Survey*, 24 NATURE BIOTECHNOLOGY 31, 35 (2006).

[46] The PTO has required patents claiming DNA sequences to use "SEQ ID NO" to internally refer to these sequences since 1990. 37 C.F.R. § 1.821 (2005). I searched the PTO database for patents claiming "SEQ ID NO" or "[SEQ ID NO" in a given year. PTO Patent Full-Text and Image Database, http://patft.uspto.gov/netahtml/PTO/search-adv.htm (last visited Feb. 5, 2010). Note that this method retrieves all patents with a DNA sequence in their claims, including synthetic and non-human DNA, but not patents claiming a gene without reciting its sequence. For a discussion of the difficulty of counting gene patents, see Holman, *Survey*, *supra* note 17, at 307-19.

[47] Jensen & Murray, *supra* note 1.

[48] *See* NUFFIELD COUNCIL ON BIOETHICS, THE ETHICS OF PATENTING DNA: A DISCUSSION PAPER 47-48 (2002), *available at* http://www.nuffieldbioethics.org/go/ourwork/patentingdna/introduction; Holman, *Survey*, *supra* note 17, at 323; *see also* Jorge A. Goldstein & Elina Golod, *Human Gene Patents*, 77 ACAD. MED. 1315, 1316-17 (2002) (providing specific examples of the kinds of gene patents the PTO has issued).

[49] *See* NUFFIELD COUNCIL ON BIOETHICS, *supra* note 48, at 48-66 (making separate policy recommendations for each category of DNA patents); Holman, *Survey*, *supra* note 17, at 359 (arguing that reforms should distinguish between naturally and non-naturally occurring nucleotide sequences, and between genetic and non-genetic uses of DNA).

[50] Demaine & Fellmeth, *supra* note 5, at 461.

[51] Nuno Pires de Carvalho, *The Problem of Gene Patents*, 3 WASH. U. GLOBAL STUD. L. REV. 701, 701 (2004).

[52] Oskar Liivak, *Maintaining Competition in Copying: Narrowing the Scope of Gene Patents*, 41 U.C. DAVIS L. REV. 177, 183-84 (2007).

[53] Timothy A. Worrall, *The 2001 PTO Utility Examination Guidelines and DNA Patents*, 16 BERKELEY TECH. L.J. 123 (2001).

DNA;[54] and that many DNA patents are unconstitutional because they do not "promote the Progress of Science."[55]

¶19 When the Supreme Court granted certiorari in 2005 on the question of whether a patent can "claim a monopoly over a basic scientific relationship" in *LabCorp v. Metabolite Laboratories*,[56] it raised hopes that it would clarify patent eligibility for biotechnology.[57] Unfortunately, the case was dismissed as improvidently granted,[58] but the Court may narrow the scope of patentable subject matter if it takes up the issue again.[59]

¶20 The latest Supreme Court decision that may prove significant for biomedical patenting is *KSR International Co. v. Teleflex Inc.*,[60] which revised the interpretation of the obviousness standard for patents.[61] Although this case was not directly related to biotechnology (the Court invalidated a patent for a car pedal assembly), the Pharmaceutical Research and Manufacturers of America (PhRMA) submitted an amicus brief expressing concerns about the potential impact on pharmaceutical patents.[62] Despite PhRMA's concerns, the Court "reject[ed] the rigid approach of the Court of Appeals" in favor of its own "expansive and flexible approach" to invalidating patents for obviousness.[63]

¶21 Post-*KSR*, many DNA patents may be found invalid for obviousness if challenged.[64] In a recent case, *In re Kubin*, the Federal Circuit concluded that "the Supreme Court in *KSR* unambiguously discredited" the Federal Circuit's earlier assessment of the obviousness of biotechnological inventions, and the court held that the human gene patent at issue was invalid for obviousness.[65] Although claims that this decision "[s]ounds the [d]eath [k]nell for [g]ene [p]atents"[66] probably overstate its importance, *Kubin* seems to be part of a trend toward raising the patentability requirements for DNA claims.

¶22 In summary, patents involving DNA are ubiquitous, but the validity of some DNA patents has been questioned by commentators and by courts. As more DNA patents are struck down for obviousness or lack of novelty, those concerned about the policy implications of intellectual property for biomedical research will have even more incentive to focus on the problems of access to materials discussed in Part II.

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[54] *See* Eileen M. Kane, *Splitting the Gene: DNA Patents and the Genetic Code*, 71 TENN. L. REV. 707 (2004).

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

[56] Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc., 548 U.S. 124, 125 (2006) (dismissing certiorari as improvidently granted) (Breyer, J., dissenting).

[57] *See, e.g.*, Rebecca S. Eisenberg, *Biotech Patents: Looking Backward While Moving Forward*, 24 NATURE BIOTECHNOLOGY 317 (2006).

[58] *Lab. Corp.*, 548 U.S. at 124.

[59] Justice Breyer, joined by Justices Stevens and Souter, issued a strong dissent in *LabCorp*, arguing that the patent at issue was invalid as a natural phenomenon, and that the Court should have reversed. *Id.* at 135 (Breyer, J., dissenting). This dissent, along with Justice Scalia's comments during oral arguments, "offer hope that the Court will provide sensible, appropriate, and essential guidance in this area." Roger D. Klein & Maurice J. Mahoney, LabCorp v. Metabolite Laboratories*: The Supreme Court Listens, but Declines to Speak*, 36 J.L. MED. & ETHICS 141, 148 (2008).

[60] 550 U.S. 398 (2007).

[61] 35 U.S.C. § 103 (2006).

[62] Brief of Amicus Curiae Pharmaceutical Research and Manufacturers of America in Support of Respondents, KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398 (2007) (No. 04-1350), 2006 WL 2967758.

[63] *KSR Int'l Co.*, 550 U.S. at 415.

[64] *See* Rebecca S. Eisenberg, *Pharma's Nonobvious Problem*, 12 LEWIS & CLARK L. REV. 375, 375 (2008) (noting that many pharmaceutical patents are invalid for obviousness and that *KSR* may make it easier for the PTO to reject patent applications on obviousness grounds); Anna Bartow Laakmann, *Restoring the Genetic Commons: A "Common Sense" Approach to Biotechnology Patents in the Wake of* KSR v. Teleflex, 14 MICH. TELECOMM. & TECH. L. REV. 43, 72 (2007) ("Gene patents may not be able to withstand an obviousness inquiry that incorporates the concepts articulated by the Supreme Court in *KSR v. Teleflex*.").

[65] 561 F.3d 1351, 1358-61 (Fed. Cir. 2009).

[66] Posting of Joshua D. Sarnoff to On the Edges of Science and Law, *In re* Kubin*: Federal Circuit's Decision Sounds the Death Knell for Gene Patents*, http://blogs.kentlaw.edu/islat/2009/04/in-re-kubin-federal-circuits-decision-sounds-the-death-knell-for-gene-patents.html (Apr. 28, 2009, 11:22 EST).

B. Moral and Ethical Concerns

¶23 Although tens of thousands of issued patents claim DNA sequences, many members of the public still consider DNA patenting "troubling and counterintuitive."[67] Scholars have argued that DNA patents degrade moral values and threaten human dignity by treating humans as commodities.[68] The public discourse on gene patents reflects these concerns. When introducing the Genomic Research and Accessibility Act, Rep. Becerra said that one-fifth of our genes are "owned by someone else. And we have absolutely no say in what those patent holders do with our genes."[69] Similarly, in his *New York Times* opinion, Michael Crichton said that a "gene may exist in your body, but it's now private property."[70]

¶24 Courts have not been receptive to concerns about the morality of patenting life.[71] Those raising concerns often misunderstand the difference between owning a gene patent and owning a gene.[72] The "product of nature" doctrine prevents a gene in a human body from being patented. Gene patents convey only a limited right to exclude others from the subject matter defined in the claims, which is often a very narrow use of that gene.[73]

¶25 Indeed, the Nuffield Council on Bioethics rejected the argument that gene patents violate an "inalienable right to self-ownership," noting that "[t]he problem with this argument is that patents with claims to DNA sequences do not entail ownership of genes as they occur in our bodies—they relate instead to the isolated versions of such sequences which are held to be patentable."[74] Instead, the Nuffield Council's ethical concerns focused the consequences of DNA patents on healthcare and basic research,[75] which I discuss in the remainder of this Part.

C. The Tragedy of the Anticommons and Biomedical Innovation

¶26 The problem of an "anticommons" in biomedical research was first proposed by Michael Heller and Rebecca Eisenberg in 1998.[76] Their concern was that "[a] proliferation of intellectual property rights upstream may be stifling life-saving innovations further downstream in the course of research and product development."[77] If biotechnology companies need to negotiate with multiple rightsholders, the high transaction costs of negotiating licenses will result in fewer and more costly end products.

¶27 Although the "tragedy of the anticommons" originally referred to the breakdown of negotiations when there are too many upstream rightsholders, the "phrase . . . has since become a buzzword for a broader range of potential detrimental effects of intellectual property."[78] Even a single rightsholder can impede innovation and product development when technology is cumulative.[79] This Part focuses

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[67] Rebecca S. Eisenberg, *How Can You Patent Genes?*, 2 AM. J. BIOETHICS 3, 3 (2002).

[68] David B. Resnik, *DNA Patents and Human Dignity*, 29 J.L. MED. & ETHICS 152, 152-53 (2001) (arguing that DNA patents may threaten human dignity by "taking us further down the path of human commodification"); *see* Brian Gargano, *The Quagmire of DNA Patents: Are DNA Sequences More Than Chemical Compositions of Matter?*, 2005 SYRACUSE SCI. & TECH. L. REP. 3, 16-21, http://justice.syr.edu/sstlr/wp-content/uploads/the-quagmire-of-dna-patents-are-dna-sequences-more-than-chem.pdf (discussing and rejecting arguments that DNA patents treat humans as commodities).

[69] 153 CONG. REC. E315, E316 (daily ed. Feb. 9, 2007) (statement of Rep. Becerra).

[70] Crichton, *supra* note 3.

[71] ROBERT P. MERGES, PETER S. MENELL & MARK A. LEMLEY, INTELLECTUAL PROPERTY IN THE NEW TECHNOLOGICAL AGE 138 (rev. 4th ed. 2007).

[72] Holman, *Survey*, *supra* note 17, at 301.

[73] *See id.* at 302-03. See *infra* Part I.D.1 for a discussion of Berlex Laboratory's narrow patent on the human interferon-β gene.

[74] NUFFIELD COUNCIL ON BIOETHICS, *supra* note 48, at 22.

[75] *Id.* at 47-66.

[76] Heller & Eisenberg, *supra* note 5.

[77] *Id.* at 698.

[78] Eisenberg, *supra* note 8, at 1060-61.

[79] *See* Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839 (1990); Suzanne Scotchmer, *Standing on the Shoulders of Giants: Cumulative Research and the Patent Law*, 5 J. ECON. PERSP. 29 (1991).

on the problems biomedical patents raise, either individually or through "patent thickets," for basic researchers.

1. Calls for an Experimental Use Exemption

¶28 Heller and Eisenberg theorized that a patent anticommons would also affect basic researchers "when too many owners hold rights in previous discoveries that constitute obstacles to future research."[80] Since Heller and Eisenberg's seminal paper, many others have echoed these concerns about the negative impact of patents on basic science.[81] It is not clear, however, that patents are actually hindering basic researchers in the United States.

¶29 Many other countries have experimental use exemptions from patent infringement to prevent patents from impeding basic research. Germany, the United Kingdom, and most other European nations, as well as Japan and Korea, have legislatively enacted experimental use exemptions; Canada has a judicially created exemption.[82] These exemptions prevent those who use patents only for basic research from being sued for infringement.

¶30 No such exemption exists in the United States. Although one court suggested that such a defense exists as early as 1813,[83] it has rarely succeeded in practice.[84] In 1984, the Federal Circuit characterized the experimental use exemption as "truly narrow."[85] Then, in the 2002 case *Madey v. Duke University*, the Federal Circuit made clear that university research is not exempt from patent infringement:

> [R]esearch universities . . . often sanction and fund research projects with arguably no commercial application whatsoever. However, these projects unmistakably further the institution's legitimate business objectives, including educating and enlightening students and faculty participating in these projects. These projects also serve, for example, to increase the status of the institution and lure lucrative research grants, students and faculty.
>
> . . . [S]o long as the act is in furtherance of the alleged infringer's legitimate business and is not solely for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry, the act does not qualify for the very narrow and strictly limited experimental use defense.[86]

¶31 This decision has been sharply criticized,[87] and many commentators have urged Congress to enact an experimental use exemption similar to the exemptions in other countries.[88] The worry is that basic research will be delayed or stopped completely while scientists determine whether their work is infringing and while they negotiate the necessary patent rights.[89] International comparative studies are

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[80] Heller & Eisenberg, *supra* note 5, at 698.

[81] *See, e.g.*, Lori Andrews et al., *When Patents Threaten Science*, 314 SCI. 1395 (2006); Donald Kennedy, *Enclosing the Research Commons*, 294 SCI. 2249 (2001).

[82] John F. Duffy, *Rethinking the Prospect Theory of Patents*, 71 U. CHI. L. REV. 439, 457 n.68 (2004).

[83] Whittemore v. Cutter, 29 F. Cas. 1120, 1121 (C.C.D. Mass. 1813) ("[I]t could never have been the intention of the legislature to punish a man, who constructed such a [patented] machine merely for philosophical experiments, or for the purpose of ascertaining the sufficiency of the machine to produce its described effects.").

[84] Rebecca S. Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use*, 56 U. CHI. L. REV. 1017, 1023 (1989).

[85] Roche Prods., Inc. v. Bolar Pharm. Co., 733 F.2d 858, 863 (Fed. Cir. 1984).

[86] Madey v. Duke Univ., 307 F.3d 1351, 1362 (Fed. Cir. 2002).

[87] *See, e.g.*, Andrew J. Caruso, *The Experimental Use Exception: An Experimentalist's View*, 14 ALB. L.J. SCI. & TECH. 215, 218 (2003); David G. Sewell, *Rescuing Science From the Courts: An Appeal for Amending the Patent Code to Protect Academic Research in the Wake of* Madey v. Duke University, 93 GEO. L.J. 759, 760 (2005); Katherine J. Strandburg, *What Does the Public Get? Experimental Use and the Patent Bargain*, 2004 WIS. L. REV. 81, 85. *But see* Elizabeth A. Rowe, *The Experimental Use Exception to Patent Infringement: Do Universities Deserve Special Treatment?*, 59 ME. L. REV. 283, 285 (2007) (arguing that although "[v]irtually all commentators since *Madey* have criticized the ruling," "a narrow experimental use exception is . . . sound public policy, and appropriate for the current nature of university research").

[88] *See, e.g.*, Rebecca S. Eisenberg, *Patenting the Human Genome*, 39 EMORY L.J. 721, 743 (1990) (recommending an experimental use exemption to address "the conflict between patent law and scientific norms"); Gargano, *supra* note 68, at 37; Donna M. Gitter, *International Conflicts Over Patenting Human DNA Sequences in the United States and the European Union: An Argument for Compulsory Licensing and a Fair-Use Exception*, 76 N.Y.U. L. REV. 1623, 1679-90 (2001).

[89] *See, e.g.*, Caruso, *supra* note 87, at 220 ("[U]nnecessary restriction of the experimental use exception squanders time . . . as researchers . . . grapple with complex legal issues (such as the metes and bounds of a patent claim) before carrying out even a

difficult because of the many variables involved, but there is no evidence that experimental use exemptions have a significant effect on a country's research output.[90] As described in the following Part, however, recent empirical results in the United States indicate that patents seldom impede basic researchers.

2. Empirical Results: Patents Rarely Impede Basic Science

¶32 Researchers are generally aware that they could be liable for patent infringement: in 2005, Lei, Juneja, and Wright found that over 80% of eighty-five U.S. agricultural biology faculty disagreed with a statement that academic researchers have a research exemption.[91] Fewer than 10% of these same respondents, however, had checked whether a research tool they needed in the past five years was patented.[92] Based on follow-up interviews, the authors attribute this result to the scientists' belief that they will not be sued even if they are infringing.[93]

¶33 Walsh, Cohen, and Cho conducted a survey of 414 genomics and proteomics academic researchers in the United States in 2004, 10% of whom were engaged in drug development or related downstream work.[94] They similarly found that only 5% regularly check for patents on their research tools, only 1% had to delay or modify their research due to third-party patents, and none had to abandon a project altogether.[95] The limited effect of patents on research is attributed to lack of awareness of relevant patents[96] and to the difficulty of detecting infringement or enforcing patents in academic settings.[97]

¶34 This survey of biomedical researchers also addressed the concern that patents are influencing the initial decision to pursue a research project. When asked how important different factors are in choosing a project, only 7% attributed high importance to patentability of results and lack of patents on research inputs; scientific importance (97%), interest (95%), feasibility (88%), and funding (80%) were much more important.[98] When asked about the importance of factors in *not* pursuing a project, only 3% gave high importance to patents covering research inputs.[99]

¶35 In a follow-up survey of ninety-three academics studying heavily patented signaling proteins (conditions under which access problems due to patents should be most prevalent), fewer than 15% reported adverse effects from patents, and only 3% reported abandoning a project.[100] Patents impeded basic research more than in the random sample, but still infrequently.

¶36 These survey data support the anecdotal findings of earlier interviews by Walsh, Arora, and Cohen with people involved in various aspects of biomedical research and drug development in the United States.[101] The interviewers summarized their findings: "We . . . find little evidence that

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simple experiment.").

[90] *See* Kevin Iles, *A Comparative Analysis of the Impact of Experimental Use Exemptions in Patent Law on Incentives to Innovate*, 4 NW. J. TECH. & INTELL. PROP. 61, ¶¶ 63-72 (2005), http://www.law.northwestern.edu/journals/njtip/v4/n1/3/Iles.pdf.

[91] Lei et al., *supra* note 8, at 37. While agricultural faculty rarely deal with *human* gene patents, much of this research involves patented DNA.

[92] *Id.*

[93] *Id.* ("One respondent declared . . . "[E]ven if I broke the law, nothing would happen to me. I am just doing research for the public.").

[94]John P. Walsh, Charlene Cho & Wesley M. Cohen, *View from the Bench: Patents and Material Transfers*, 309 SCI. 2002, 2002 (2005) [hereinafter Walsh et al., *View from the Bench*]; Walsh et al., *supra* note 14, at 1185-86.

[95] Walsh et al., *View from the Bench*, *supra* note 94, at 2002; Walsh et al., *supra* note 14, at 1189-90.

[96] Walsh et al., *supra* note 14, at 1191.

[97] Wesley M. Cohen & John P. Walsh, *Real Impediments to Academic Biomedical Research*, 8 INNOVATION POL'Y & ECON. 1, 12-13 (2008).

[98] Walsh et al., *supra* note 14, at 1188.

[99] *Id.* at 1189.

[100] *Id.* at 1199.

[101] *See* John P. Walsh, Ashish Arora & Wesley M. Cohen, *Effects of Research Tool Patents and Licensing on Biomedical Innovation*, *in* PATENTS IN THE KNOWLEDGE-BASED ECONOMY 285 (Wesley M. Cohen & Stephen A. Merrill eds., 2003) [hereinafter Walsh et al., *Effects of Research Tool Patents*], *available at* http://www.nap.edu/catalog/10770.html; John P. Walsh, Ashish Arora & Wesley M. Cohen, *Working Through the Patent Problem*, 299 SCI. 1021 (2003).

university research has been impeded by concerns about patents on [biomedical] research tools."[102] (Their one exception is the case of genetic diagnostics,[103] which I discuss in Part I.D.2.) Their explanation was that researchers develop "working solutions" such as a "'research exemption' that is broader than the existing legal exemption and that is supported by norms of trust and exchange in the research community."[104]

¶37 All nine university or government-lab interview respondents (as well as a third of the industrial respondents) admitted occasional patent infringement and said that infringement of research-tool patents was widespread.[105] Interviewees from both academia and industry noted that suing universities for this infringement would be counterproductive, in that damages would be insignificant, opportunities for development of technology would be limited, and there would be a loss of goodwill in the biomedical community. As one university technology transfer officer said, "You will become an instant pariah if you sue a university."[106]

¶38 These studies have failed to substantiate concerns about biomedical patents impeding academic research. In fact, Eisenberg, one of the authors of the original anticommons hypothesis, has recently reevaluated the hypothesis in light of some of this empirical evidence.[107] She notes that "in both [commercial and academic] settings it is rare for an ongoing project to be stopped because of patents" and that academic scientists "generally ignore patents and rarely face patent enforcement," which she attributes to either "the continuing vitality of sharing norms in academic science" or the fact that "patent owners conclude that enforcement of patents against academic researchers is not worth the cost."[108] Eisenberg does note, however, that scientists "report more problems in gaining access to 'practically excludable' resources such as tangible materials and data,"[109] which I discuss in Part II.

¶39 Even though these empirical studies indicate that DNA patents themselves rarely impede basic biomedical research, they do not suggest that there would be any *negative* effect from an experimental use exemption; they simply show that researchers have been able to work around the increasing number of patents, so the need for an experimental use exemption is not as pressing as some have suggested. Future problems could still arise, however, if university research continues to become more commercial and if universities begin to litigate their own growing patent portfolios aggressively.

¶40 These empirical studies have focused on the impact of patents on innovation in upstream academic settings; there is less evidence as to whether DNA patents restrict downstream industrial innovation, which was the focus of the original anticommons hypothesis. The industry responses in the 2003 interviews indicated that the patent landscape has become more complex and more costly to navigate, but that industry has also developed "working solutions" to prevent patents from stopping projects.[110] Eisenberg suggests that these interviews, along with others from Australia, "offer qualified support for the anticommons hypothesis," although she notes "the risk of an anticommons [is] perhaps smaller than might have been feared a decade ago."[111]

¶41 In summary, empirical studies have shown that biomedical patents themselves are rarely a problem for upstream academic research because scientists typically ignore patents and are rarely

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[102] Walsh et al., *Effects of Research Tool Patents*, *supra* note 101, at 285; *see also infra* Part III.A.1 (discussing sharing norms among basic researchers).

[103] *Id.* at 285-286.

[104] *Id.* at 334.

[105] *Id.* at 327.

[106] *Id.* at 325.

[107] Eisenberg, *supra* note 8.

[108] *Id.* at 1098.

[109] *Id.*

[110] Walsh et al., *Effects of Research Tool Patents*, *supra* note 101, at 331.

[111] Eisenberg, *supra* note 8, at 1079-80. A different study that focused on the lag between the date of cited prior art and the date of the new patent application also concluded that "university patenting may indeed be hindering or at least slowing industrial innovation." Kira R. Fabrizio, *University Patenting and the Pace of Industrial Innovation*, 16 INDUS. & CORP. CHANGE 505, 505-06 (2007).

sued, so enacting an experimental use exemption would likely have little effect at present. The growing patent landscape creates more problems for downstream industrial research, although these researchers also develop "working solutions" to prevent patents from derailing projects.

D. Reduced Access to Healthcare and Biomedical End Products

¶42 The other major policy concern that has been raised regarding DNA patents is their potentially negative impact on biomedical end products. The two most common end products that are protected by DNA patents are genetic diagnostic tests and biopharmaceuticals. Offering exclusive patent rights for these downstream innovations can lead to an effective monopoly for the duration of the patent, raising the prices for consumers and reducing access to essential medical treatments.

¶43 Part I.D.1 describes how patents do increase prices on biopharmaceuticals, but the problem is not limited to DNA patents—it is equally a problem for patents on non-genetic small-molecule drugs. For all of these drugs, *some* incentive is needed for drug innovation to balance the high cost of bringing products to market. Legislation banning DNA patents altogether is both too narrow (in ignoring patent problems for small-molecule drugs) and too sweeping (in eliminating the current incentive for drug development without providing an alternative).

¶44 While biopharmaceuticals are often ignored in the gene patent debate, the genetic diagnostic tests discussed in Part I.D.2 are at its center. Empirical studies indicate that the access problems caused by patent rights to these tests are much smaller than the public discourse suggests. But even if patents on genetic tests have not greatly hurt the public, neither have they helped—the low cost of bringing these tests to market means that the patent incentive is not very important for their development. Furthermore, patent problems will likely become larger as genome sequencing becomes easier and cheaper. A narrow legislative exemption to infringement, such as has already been enacted for surgical procedures, therefore makes good policy sense.

1. Biopharmaceuticals

¶45 Biopharmaceuticals are defined as "protein or nucleic acid based pharmaceutical substances used for therapeutic or *in vivo* diagnostic purposes, which are produced by means other than direct extraction from natural (non-engineered) biological sources."[112] Although many biopharmaceuticals are proteins, not DNA sequences, they are often produced by recombinant expression of a human gene and are thus protected by gene patents.[113] As of 2006, 165 biopharmaceuticals had gained regulatory approval in the United States or European Union, and their worldwide market was projected to reach $70 billion by the end of this decade.[114] This use of gene patents is often ignored by gene-patent critics.[115]

¶46 The first biopharmaceutical produced by genetic engineering was erythropoietin, a protein used to treat anemia.[116] The erythropoietin drug Epogen®, approved by the FDA in 1989,[117] was developed by Amgen, Inc., one of the world's largest biotechnology companies.[118] The first claim in Amgen's patent for the erythropoietin gene reads: "A purified and isolated DNA sequence encoding erythropoietin, said DNA sequence selected from the group consisting of: (a) the DNA sequences

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[112] GARY WALSH, BIOPHARMACEUTICALS: BIOCHEMISTRY AND BIOTECHNOLOGY 2 (2d. ed. 2003). "Biopharmaceutical" is often used interchangeably with "biologic" in legal scholarship to refer to any drug created from living cells or DNA technology; *see, e.g.*, Ellis, *supra* note 11, ¶ 51; Kapczynski, *supra* note 10, at 1095 n.287. Their technical definitions, however, are distinct. WALSH, *supra*, at 1-2 ("While it might be assumed that 'biologic' refers to any pharmaceutical product produced by biotechnological endeavor, its definition is more limited. In pharmaceutical circles, 'biologic' generally refers to medicinal products derived from blood, as well as vaccines, toxins and allergen products.").

[113] Holman, *Survey*, *supra* note 17, at 324.

[114] Gary Walsh, *Biopharmaceutical Benchmarks 2006*, 24 NATURE BIOTECHNOLOGY 769, 769 (2006).

[115] *See, e.g.*, Andrews & Paradise, *supra* note 5, at 406 (arguing that "[t]he discovery of genes does not require the same commercial incentives as drug development" and ignoring the drug-development uses of gene patents).

[116] WALSH, *supra* note 112, at 268.

[117] Walsh, *supra* note 114, at 777 tbl.1.

[118] WALSH, *supra* note 112, at 10.

set out [in the figures] or their complementary strands; and (b) DNA sequences which hybridize under stringent conditions to the DNA sequences defined in (a)."[119]

¶47 This "unusually broad" patent has been vigorously defended by Amgen through the courts.[120] This litigation pattern is also unusual: a survey of gene-patent litigation found that cases involving Epogen "provide the only examples of final, unappealable judicial determinations . . . where a human gene patent has been found infringed and not invalid."[121] Because Epogen was the first product in this class, litigation to define the scope of its patent might have been expected. Under the quid pro quo theory of patent law,[122] one could argue that Amgen deserves broad patent protection for this groundbreaking innovation.

¶48 Another biopharmaceutical that has been subject to litigation is the multiple sclerosis drug Betaseron, produced by Berlex Laboratories, Inc., and approved by the FDA in 1993.[123] Betaseron is produced from the human interferon-β gene, which had already been claimed in a patent filed in 1987.[124] Berlex's patents were therefore only able to make narrower claims to methods of producing interferon-β. The first claim of its first interferon patent reads:

> A DNA construct for expression in a Chinese hamster ovary cell comprising a human interferon gene and a dihydrofolate reductase gene, said construct being effective for transcription and translation of said interferon gene in a Chinese hamster ovary cell into which it has been introduced or in progeny cells thereof.[125]

¶49 In 1996, the FDA approved Biogen's competing interferon-β drug, Avonex.[126] Berlex had sued the FDA to prevent the approval, and Biogen then sought a declaratory judgment that it did not infringe Berlex's patent.[127] The district court granted summary judgment for Biogen, and the Federal Circuit affirmed that Biogen did not literally infringe Berlex's patent.[128] While the case was on appeal, however, the parties reached a settlement where Biogen paid $75 million to Berlex.[129]

¶50 Christopher Holman's extensive search for human gene patent litigation found that the majority of these actions involve biopharmaceuticals,[130] probably due to the money at stake. He also found that the overall rate of litigation (relative to the total number of patents) is smaller than the rate of patent litigation in general: only 0.4% of the patents in Jensen and Murray's study have been litigated, and half of these patents were invoked in a single retaliatory lawsuit that quickly settled with a non-exclusive license to the patents.[131] Pharmaceutical litigation costs are still substantial,[132] but this is endemic to the pharmaceutical industry in general, not DNA patents in particular.

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[119] U.S. Patent No. 4,703,008 col.39 l.62-68 (filed Nov. 30, 1984).

[120] Holman, *Survey*, *supra* note 17, at 325-31 (describing suits by Amgen against four different pharmaceutical companies).

[121] *Id.* at 331.

[122] *See* Pfaff v. Wells Elecs., Inc., 525 U.S. 55, 63 (1998) ("[T]he patent system represents a carefully crafted bargain that encourages both the creation and the public disclosure of new and useful advances in technology, in return for an exclusive monopoly for a limited period of time." (citing Bonito Boats, Inc. v. Thunder Craft Boats, Inc., 489 U.S. 141 (1989))).

[123] Walsh, *supra* note 114, at 777 tbl.1.

[124] U.S. Patent No. 4,738,931 (filed July 6, 1987). Claim one: "A DNA consisting essentially of a DNA containing a human interferon β gene and a human interferon-β gene control DNA responsible for controlling the transcription of said human interferon-β gene which has a nucleotide sequence, as follows: [DNA sequence]." *Id.* col.7 l.52-56.

[125] U.S. Patent No. 5,376,567 col.27 l.22-27 (filed Jan. 9, 1992). Berlex later filed a continuation patent. U.S. Patent No. 5,795,779 (filed Aug. 12 1994).

[126] Walsh, *supra* note 114, at 777 tbl.1.

[127] Complaint, Biogen, Inc. v. Berlex Labs., Inc., 113 F. Supp. 2d 77 (D. Mass. 2000) (No. 96-10916).

[128] Biogen, Inc. v. Berlex Labs., Inc., 318 F.3d 1132 (Fed. Cir. 2003) (remanding for consideration under the doctrine of equivalents).

[129] Holman, *Survey*, *supra* note 17, at 334-35.

[130] *Id.* at 324.

[131] *Id.* at 354-55.

[132] James E. Bessen & Michael J. Meurer, *The Private Costs of Patent Litigation* 25, 36 tbl.7 (Boston Univ. Sch. of Law Working Paper Series, Law & Econ., Working Paper No. 07-08, 2008), *available at* http://papers.ssrn.com/abstract=983736 (estimating that litigation costs are 14.1% of research and development costs for pharmaceutical companies).

¶51 The pharmaceutical industry is often used as a poster child for the patent system, since the patent right provides an incentive to undertake the financially risky research and development needed to bring a new drug to market.[133] PhRMA justifies high drug prices by the high development costs of new drugs: $1.3 billion in 2006 for small-molecule drugs, up from $802 million in 2001, and $1.2 billion in 2006 for biologic drugs.[134] These figures, however, come from PhRMA-funded studies that examine only a subset of new drugs—the actual average development cost may be under $100 million.[135]

¶52 Although the magnitude of the cost of drug development is disputed, some incentive is needed to encourage new drug innovation. The patent system is one such mechanism, but it may not be the most efficient.[136] A number of recent proposals advocate separating research and development costs from manufacturing costs by rewarding innovation with prizes based on the product's health impact.[137] Until some such system is implemented, however, banning DNA patents would reduce incentives for development of a large class of medicines.

¶53 Furthermore, for those who are worried about the role of patents in reducing access to medicines, invalidating existing drug patents would accomplish far less to reduce biopharmaceutical prices than it would to reduce small-molecule drug prices due to biopharmaceuticals' greater complexity. Part II.C describes how access to materials such as cell lines is just as critical to generic biopharmaceutical production as access to intellectual property.

2. Genetic Diagnostics

¶54 Most public concerns over gene patents have focused on a different type of biomedical end product: genetic tests. The proposed Genomic Research and Diagnostic Accessibility Act of 2002 would have created an exception to patent infringement for "the performance of a genetic diagnostic, prognostic, or predictive test."[138] The Genomic Research and Accessibility Act of 2007 was also introduced largely out of concerns over genetic diagnostics.[139]

¶55 The most frequently cited gene-patent controversy is Myriad Genetics' enforcement of its patents on breast cancer genes.[140] Myriad Genetics owns patents on the BRCA1[141] and BRCA2[142] genes, which are important in 5-10% of breast cancer cases among white women in the United States.[143] Myriad has enforced these patents in court twice, against OncorMed and the University of Pennsylvania for providing commercial testing services, although both cases settled before a court

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[133] *See* Rebecca S. Eisenberg, *Patents, Product Exclusivity, and Information Dissemination: How Law Directs Biopharmaceutical Research and Development*, 72 FORDHAM L. REV. 477, 479-80 (2003).

[134] *See* PHARMACEUTICAL RESEARCH & MANUFACTURERS OF AMERICA, PROFILE 2008: PHARMACEUTICAL INDUSTRY 57 (2008), *available at* http://www.phrma.org/files/2008%20Profile.pdf.

[135] MARCIA ANGELL, THE TRUTH ABOUT THE DRUG COMPANIES: HOW THEY DECEIVE US AND WHAT TO DO ABOUT IT 37-46 (2004).

[136] Kapczynski, *supra* note 10, at 1045.

[137] Medical Innovation Prize Act of 2007, S. 2210, 110th Cong. (2007); AIDAN HOLLIS & THOMAS POGGE, THE HEALTH IMPACT FUND: MAKING NEW MEDICINES ACCESSIBLE FOR ALL (2008), *available at* http://www.yale.edu/macmillan/igh/; Proposal by Barbados, Bolivia, Suriname and Bangladesh: A Prize Fund to Support Innovation and Access for Donor Supported Markets (Apr. 15, 2009), *available at* http://www.who.int/phi/Bangladesh_Barbados_Bolivia_Suriname_DonorPrize.pdf.

[138] H.R. 3967, 107th Cong. (2002). The bill would also have enacted an experimental research exemption.

[139] *See* 153 Cong. Rec. E315, E316 (daily ed. Feb. 9, 2007) (statement of Rep. Becerra).

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

[141] U.S. Patent No. 5,747,282 (filed June 7, 1995) (claiming "[a]n isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO: 2"); U.S. Patent No. 5,710,001 (filed June 7, 1995) (claiming methods of screening for the BRCA1 gene); U.S. Patent No. 5,693,473 (filed June 7, 1995) (claiming mutations of the BRCA1 gene).

[142] U.S. Patent No. 6,033,857 (filed Mar. 20, 1998) (claiming methods of screening for the BRCA2 gene); U.S. Patent No. 5,837,492 (filed Apr. 29, 1996) (claiming the isolated BRCA2 gene).

[143] Tom Walsh et al., *Spectrum of Mutations in BRCA1, BRCA2, CHEK2, and TP53 in Families at High Risk of Breast Cancer*, 295 JAMA 1379, 1379 (2006).

could rule on patent validity or infringement.[144] Letters from Myriad also led other commercial testing centers to exit the market rather than face potential litigation.[145]

¶56 Although Holman only found seven specific instances of patent infringement litigation related to genetic testing,[146] a 2001 survey of genetic testing laboratory directors provides more evidence of the chilling effect of patents in the field of genetic diagnostics.[147] Of 122 respondents, 75% held licenses of at least one patent, 65% had been contacted by a patent holder about possible infringement, 25% had stopped offering a test after being contacted by a patent holder, and 53% had decided not to develop or perform a test because of a patent.[148] These results suggest that DNA patents are limiting both the availability of testing and the development of new genetic tests.

¶57 Lori Andrews has raised other policy concerns about patents on genetic testing.[149] No FDA-approval is needed for genetic tests, and patent owners lack incentives to confirm that the test is actually a good predictor of future disease.[150] For example, a 2006 study found that the commercial BRCA1 and BRCA2 screening by Myriad Genetics missed 12% of relevant mutations in these genes.[151] Andrews also points out that some companies might patent a test so that it is never developed: "GlaxoSmithKline, Plc, has filed for a patent on a genetic test to determine the effectiveness of one of its drugs, but will not develop the test, or let anyone else develop it, possibly because such a test would cause the company to lose customers."[152]

¶58 A committee formed by the Department of Health and Human Services recently released a draft report on the impact of gene patents on genetic diagnostic testing.[153] In contrast with pharmaceutical pricing, it found that diagnostic tests offered by US companies with exclusive licensing rights are often priced comparably to those without exclusive licensing.[154] In particular, it did not find evidence that Myriad's exclusive patents increased the price of its BRCA testing.[155] The committee also concluded that "patents covering genetic tests . . . do not appear to be causing wide or lasting barriers to patient or clinical access."[156] In response to concerns about the quality of patented genetic tests, such as the 2006 critique of Myriad's test, they note that Myriad began more extensive testing that same year, and that tests with non-exclusive licenses have had similar delays in detecting additional mutations.[157]

¶59 The committee did not, however, advocate for the status quo. Several of the report's authors summarized their conclusion: "Despite the fears, patents have not caused irreparable harm in genetic diagnostics, but neither have they proven greatly advantageous."[158] Because genetic tests do not have the high development costs of drugs requiring FDA-approval, companies do not need patent rights

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144 Holman, *Survey*, *supra* note 17, at 347.

145 *See* Mildred K. Cho et al., *Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services*, 5 J. MOLECULAR DIAGNOSTICS 3, 6 tbl.2 (2003) (reporting that nine survey respondents stopped performing BRCA1/BRCA2 testing because of Myriad's enforcement).

146 Holman, *Survey*, *supra* note 17, at 346.

147 Cho et al., *supra* note 145.

148 *Id.* at 4-5.

149 *See* Lori B. Andrews, *Genes and Patent Policy: Rethinking Intellectual Property Rights*, 3 NATURE REVIEWS GENETICS 803 (2002).

150 *Id.* at 804-05.

151 Walsh et al., *supra* note 143, at 1386.

152 Andrews, *supra* note 149, at 804.

153 SECRETARY'S ADVISORY COMMITTEE ON GENETICS, HEALTH, AND SOCIETY, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, PUBLIC CONSULTATION DRAFT REPORT ON GENE PATENTS AND LICENSING PRACTICES AND THEIR IMPACT ON PATIENT ACCESS TO GENETIC TESTS (2009), *available at* http://oba.od.nih.gov/SACGHS/sacghs_documents.html (follow "Download Public Consultation Draft Report" hyperlink) [hereinafter SACGHS REPORT]; *see also* Robert Cook-Deegan, Subhashini Chandrasekharan & Misha Angrist, Commentary, *The Dangers of Diagnostic Monopolies*, 458 NATURE 405 (2009) (summarizing the committee's findings).

154 SACGHS REPORT, *supra* note 153, at 108.

155 *Id.* at 72.

156 *Id.* at 109.

157 *Id.* at 74.

158 Cook-Deegan et al., *supra* note 153, at 405.

to bring a new test to market. The committee found that "patents offer minor if any stimulus to the development of genetic diagnostics," since academic scientists are motivated to research new genetic tests for non-monetary incentives, and many unpatented discoveries have been developed into tests.[159]

¶60 Given the limited utility of DNA patents for encouraging innovation in genetic diagnostics and the potential drawbacks of exclusive providers for public health, it seems that the quid pro quo of patent law is not functioning in this context: the public is receiving little benefit in exchange for the patent right it gives. This problem will only increase as sequencing becomes more inexpensive and full-genome sequencing becomes feasible:[160] the need to collect all the patent rights needed to sequence entire genomes for clinical use could lead to a huge anticommons problem.

¶61 For these reasons, a legislative exemption to infringement for research and diagnostic testing uses of human DNA, such as that proposed in the Genomic Research and Diagnostic Accessibility Act of 2002, seems to make good policy sense. Congress has already carved out an exception to infringement for public health reasons: in 1996, after one eye surgeon sued another for using his patented technique,[161] Congress enacted an exemption for licensed doctors who perform surgical procedures.[162] A number of scholars have called for a similar exception for genetic testing.[163]

¶62 While a legislative solution would be the best response to this issue, other actors could ameliorate the problem. In light of the Supreme Court's admonition in *eBay Inc. v. MercExchange, L.L.C.* that injunctive relief is not automatic for patent infringement,[164] courts could conclude that the adequacy of monetary damages to compensate patent holders and the strong public interest involved indicate that most genetic diagnostic patent infringement should be protected by a liability rule, not a property rule.

¶63 Private organizations could also form patent pools, perhaps facilitated by genetic diagnostic standards from international or nonprofit institutions.[165] Universities are "major players in the patenting and licensing of DNA-based inventions"[166] and can therefore also make a significant difference through their licensing strategies. The National Institutes of Health and the Association of University Technology Managers have strongly encouraged universities to negotiate nonexclusive licenses for genomic inventions and to provide research exemptions for nonprofit institutions.[167] Individual academic researchers and patient advocacy groups should encourage universities to follow these practices,[168] or simply to leave these genetic sequences in the public domain.

II. THE PROBLEM OF ACCESS TO BIOMEDICAL MATERIALS

¶64 The gene patent controversy has focused on access to information—what is the sequence for a given gene, and who can use that information. But publishable data is only one type of biological knowledge, and patents are only one type of intellectual property protection. This Part discusses the

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[159] SACGHS REPORT, *supra* note 153, at 111.

[160] *See* Robert Koenig, *Genome Scans: Impatient for the Payoff*, 324 SCI. 448 (2009) (discussing the growing use of genome-wide scans to link gene variants and diseases).

[161] Todd Martin, *Patentability of Methods of Medical Treatment: A Comparative Study*, 82 J. PAT & TRADEMARK OFF. SOC'Y 381, 401-02 (2000) (citing Pallin v. Singer, 36 U.S.P.Q.2d (BNA) 1050 (D. Vt. 1995)).

[162] Omnibus Consolidated Appropriations Act, Pub. L. No. 104-208, § 616, 110 Stat. 3009, 3009-67 to -68 (1996) (codified at 35 U.S.C. § 287(c) (2006)).

[163] *See, e.g.*, Sherizaan Minwalla, *A Modest Proposal to Amend the Patent Code 35 U.S.C. § 287(c) to Allow Health Care Providers to Examine their Patients' DNA*, 26 S. ILL. U. L.J. 471, 473 (2002); Michele Westhoff, *Gene Patents: Ethical Dilemmas and Possible Solutions*, 20 HEALTH LAW., Apr. 2008, at 1, 9-10.

[164] 547 U.S. 388 (2006).

[165] *See* Ted J. Ebersole, Marvin C. Guthrie & Jorge A. Goldstein, *Patent Pools and Standard Setting in Diagnostic Genetics*, 23 NATURE BIOTECHNOLOGY 937 (2005).

[166] Pressman, *supra* note 45, at 33.

[167] David H. Ledbetter, Commentary, *Gene Patenting and Licensing: The Role of Academic Researchers and Advocacy Groups*, 10 GENETICS IN MED. 314, 316, 318 (2008) (citing Best Practices for the Licensing of Genomic Inventions: Final Notice, 70 Fed. Reg. 18,413 (Apr. 11, 2005)).

[168] *Id.* at 318.

different types of "bio-knowledge" and how that knowledge is protected as intellectual property through patents, copyrights, and trade secrets doctrines.[169] Empirical evidence demonstrates that access to other forms of bio-knowledge, particularly tangible materials, is an important problem in both basic research and for production of some end products like biopharmaceuticals.

A. Expanding the Definition of Biological Knowledge

¶65 Applying Yochai Benkler's framework for knowledge classification, information-based advantages can be categorized as information, human knowledge, information-embedded tools, or information-embedded goods.[170] Each of these categories raises different issues of intellectual property law.

¶66 *Information* refers to raw data that can be transferred through publication.[171] In the biomedical context, it includes gene sequences, information about what a gene encodes, protein structures, research papers, and clinical trial results for pharmaceuticals. The Supreme Court has made clear that "facts are not copyrightable,"[172] and "[t]he laws of nature, physical phenomena, and abstract ideas have been held not patentable."[173] Many types of biomedical information, however, can be protected with patents, copyrights,[174] and trade secrets. Also, in the case of clinical trial results used for FDA approval, drug companies receive sui generis intellectual property protection known as data exclusivity.[175]

¶67 *Human Knowledge* refers to know-how that is transferred through hands-on experience or formal education.[176] By definition, human knowledge cannot be "taught" through publication, whether through the "written description" requirement of a patent[177] or through "original works of authorship" that could receive copyright protection.[178] Instead, know-how is typically protected through secrecy. Industrial researchers protect their know-how with state trade secret law, and academics protect their know-how by simply limiting the number of people they share it with.

¶68 *Information-embedded tools* are the physical tools needed to innovate.[179] These include cell lines, reagents, gene sequencing tools, microscopes, genetic analysis programs, and other physical equipment or materials that would be found in a biomedical research laboratory. Access to these tools can be restricted with patents, but it is often more effective to protect them by restricting physical access and keeping them as trade secrets.

¶69 *Information-embedded goods* are end products "that are not themselves information, but that are better, more plentiful, or cheaper because of some technological advance embedded in them or associated with their production."[180] Biopharmaceuticals are the most relevant example of goods that embed genetic information. These consumption goods often have layers of intellectual property protection, both for the goods themselves and for the information embedded in them.

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[169] The fourth subfield of intellectual property law, trademarks, is important for designating the source of biomedical products, but is less relevant for protecting biological knowledge as described here. *See* M. Scott McBride, *Bioinformatics and Intellectual Property Protection*, 17 BERKELEY TECH. L.J. 1331, 1334 n.14 (2002).

[170] BENKLER, *supra* note 18, at 311-15; *see also* Posting of Jack Balkin to Balkinization, http://www.balkin.blogspot.com/2006/04/what-is-access-to-knowledge.html (Apr. 21 2006).

[171] BENKLER, *supra* note 18, at 313.

[172] Feist Publ'ns, Inc. v. Rural Tel. Serv. Co., 499 U.S. 340, 344 (1991).

[173] Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980).

[174] Copyright protection restricts access to publications, but it has not been used to protect DNA sequences themselves. *See* Stephen R. Wilson, *Copyright Protection for DNA Sequences: Can the Biotech Industry Harmonize Science with Song?*, 44 JURIMETRICS J. 409, 457 (2004).

[175] *See* Henry Grabowski, *Follow-On Biologics: Data Exclusivity and the Balance Between Innovation and Competition*, 7 NATURE REVIEWS DRUG DISCOVERY 479, 479 (2008) (noting that competitors are excluded from using the data on a new drug's safety and efficacy for five years after the drug's approval).

[176] BENKLER, *supra* note 18, at 314-15.

[177] *See* 35 U.S.C. § 112 (2006).

[178] *See* 17 U.S.C. § 102 (2006).

[179] BENKLER, *supra* note 18, at 312.

[180] *Id.* at 311.

¶70 Although lack of access to patented information is rarely a problem for basic researchers,[181] Part II.B describes evidence that lack of access to human knowledge and information-embedded tools causes significant delays in academic research programs, and seeks to understand this access problem in terms of changing scientific norms. Part II.C describes how access to these types of bio-knowledge is also an important problem for producers of end products.

B. Access to Bio-Materials in Basic Research

1. Empirical Results: Access to Materials is a Critical Problem

¶71 In Part I.C.1, I demonstrated that the information protected through patents, such as the sequence and function of a given gene, rarely limits the ability of basic researchers to access and use this information. Basic researchers are encountering much higher barriers to access, however, for other forms of bio-knowledge or non-patented information. The biggest difficulty is often acquiring information-embedded tools.

¶72 The Lei, Juneja & Wright 2005 survey of ninety-three US agricultural biology faculty members revealed that the majority believed that intellectual property was having a negative impact on research in their area, even though most did not worry about patent infringement.[182] The problems they reported were not with patents themselves, but with the material transfer agreements (MTAs) that universities require to protect intellectual property. Most respondents agreed that "[g]etting access to proprietary research tools often involves contractual restrictions on publication that cause significant constraints on academic freedom" and that "getting access to others' proprietary research tools has become more difficult over the past five years."[183] Only 6% agree that scientific competition has increased in the past five years, whereas 45% agree that MTA use has increased.[184] The average transfer time for material covered by an MTA was four months from an academic provider and six months from industry.[185]

¶73 These delays in acquiring information-embedded tools negatively affected the professors' research. Thirty-four faculty (42%) experienced a total of ninety-seven delays in research, with an average delay of 8.7 months.[186] Most of these delays were due to difficulty acquiring information-embedded tools like vectors and cell lines; a smaller number were due to difficulty acquiring information like gene sequences.[187] In fourteen cases, access problems prevented projects from being initiated; in another five, projects had to be abandoned.[188]

¶74 The Walsh, Cohen & Cho 2004 survey of 414 genomics and proteomics academics found similar results. About 75% had made at least one request for materials or data in the past two years, but 18% of requests to academics and 33% of requests to industry went unfulfilled.[189] An earlier survey of genomics researchers found that about 10% of materials or data requests were denied from 1997-1999;[190] Walsh et al. conclude that non-compliance with requests has grown over time.[191] Based on a regression analysis, they also determined that commercial incentives, the effort involved in compliance, and scientific competition were all independently related to non-compliance.[192]

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[181] *See supra* Part I.C.

[182] Lei et al., *supra* note 8, at 38.

[183] *Id.*

[184] *Id.*; *see also* Philip Mirowski, *Livin' with the MTA*, 46 MINERVA 317, 317 (2008) (arguing that the recent "tidal wave of MTAs" has "harmed the research process").

[185] Lei et al., *supra* note 8, at 38.

[186] *Id.*

[187] *Id.*

[188] *Id.* at 39.

[189] Walsh et al., *supra* note 14, at 1191.

[190] Eric G. Campbell et al., *Data Withholding in Academic Genetics: Evidence from a National Survey*, 287 JAMA 473, 477 (2002).

[191] Walsh et al., *supra* note 14, at 1191-92.

[192] *Id.* at 1196-97.

¶75 MTAs were demanded after 42% of requests, and 8% of those who requested inputs reported research delays of over one month while negotiating MTA terms.[193] Typically requested research inputs were information-embedded goods or tools, including genes, plasmids, cell lines, proteins, and drugs; unpublished information, data, and software represented about 15% of requests.[194] With the exception of drugs, these materials were requested because of the difficulty or expense of making them in-house, and not because the materials were patented.[195]

¶76 In a survey of American Association for the Advancement of Science (AAAS) members, of whom about 25% were academics in the biological, medical, or agricultural sciences, 33% reported difficulties acquiring patent-protected materials for their work.[196] Of respondents who had difficulties, 45% had problems obtaining MTAs, 37% had to delay their research projects, and 11% had to cancel a project altogether.[197]

¶77 The Walsh, Arora, and Cohen interviews with people involved in different aspects of biomedical research support all these survey results. One academic researcher expressed his frustration with MTAs:

> Things are becoming more bureaucratic. MTAs, they are crazy. Before, whenever someone wanted a plasmid from my lab, I would just send it. Now, the university says they own it and I have to go through the IP office. . . . [I]t takes a long time. . . . Basic science is now becoming interested in 'value.'[198]

Nearly all respondents who addressed MTAs agreed that delays involving MTAs "could be substantial."[199]

2. Understanding the Problem through Changing Norms

¶78 These empirical results show that access to materials is becoming an increasingly critical problem for academics. These sharing behaviors of basic researchers are regulated not through formal intellectual property rights, but through informal academic norms.

¶79 Since the mid-1990s, there has been an explosion of scholarly interest in the regulation of behavior through social norms.[200] Robert Ellickson has suggested that small communities develop efficient, utilitarian social norms to govern their interactions.[201] Law and norms both influence each other, and in some cases, norms may do better than laws at regulating behavior, and the introduction of laws can reduce compliance with norms.[202]

¶80 Empirical sociological studies of traditional scientific norms found that "scientists work in communities, where sharing information, theories, and even materials fundamentally facilitates basic research."[203] As discussed in Part II.B.1, however, current studies of basic biomedical researchers show that they often do not follow these traditional sharing norms, and that non-compliance has been growing over time.[204]

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[193] *Id.* at 1192-93.

[194] *Id.* at 1192.

[195] *Id.*

[196] STEPHEN A. HANSEN, MICHAEL R. KISIELEWSKI & JANA L. ASHER, AM. ASS'N FOR THE ADVANCEMENT OF SCI., INTELLECTUAL PROPERTY EXPERIENCES IN THE UNITED STATES SCIENTIFIC COMMUNITY 24, 78 (2007), *available at* http://sippi.aaas.org/Pubs/SIPPI_US_IP_Survey.pdf.

[197] *Id.* at 24-25.

[198] Walsh et al., *Effects of Research Tool Patents*, *supra* note 101, at 319.

[199] *Id.*

[200] Robert C. Ellickson, *Law and Economics Discovers Social Norms*, 27 J. LEGAL STUD. 537, 543 (1998).

[201] *See, e.g.*, ROBERT C. ELLICKSON, ORDER WITHOUT LAW: HOW NEIGHBORS SETTLE DISPUTES (1991).

[202] RICHARD A. EPSTEIN, PRINCIPLES FOR A FREE SOCIETY: RECONCILING INDIVIDUAL LIBERTY WITH THE COMMON GOOD 60-66 (2002).

[203] Peter Lee, Note, *Patents, Paradigm Shifts, and Progress in Biomedical Science*, 114 YALE L.J. 659, 671 (2004) (describing the work of sociologist Robert Merton).

[204] *See also* Jeremy M. Grushcow, *Measuring Secrecy: A Cost of the Patent System Revealed*, 33 J. LEGAL STUD. 59, 60 (2004) (finding increased secrecy among cancer researchers from 1980 to 1990 due to a "widespread change in norms"); Wei Hong & John P.

¶81 Even though patents themselves have little direct impact on biomedical research, the effect of the culture of patenting on these scientific norms is significant. The Bayh-Dole Act of 1980[205] gave recipients of federal research funds the right to patent and license their results. Arti Rai described the impact of this change on academic culture:

> [T]he post-1980 move towards greater intellectual property rights has clearly had a significant impact on the traditional norms of research science. Perhaps most obviously, the communalism norm has been undermined by the dramatic increases in patenting activity. In addition, both communalism and norms against secrecy have been eroded by delays in publication and restrictions on the sharing of research materials and tools caused by concerns about intellectual property rights.[206]

¶82 Similarly, Robert Merges has argued that "[n]othing could be further from the aspirational norm of openness" than "the now widespread practice of seeking *formal* property rights—in the form of patents—over research results."[207] He noted that "patents have affected the way science is done," but also that these formal rights are rarely asserted.[208] Instead, "the arguments are over another issue: the dissemination of assays, reagents, and other research tools of the trade, which have come to be known generically as *biological materials*."[209]

¶83 The increased commercialization of universities has had a negative impact on open dissemination of bio-knowledge among academics, but it is not clear that this in the scientists' best interest. Merges described the situation as a prisoner's dilemma, in which scientists who "defect" by refusing to share materials receive higher payoffs than those who "cooperate."[210] It is not obvious, however, that non-cooperative behavior really yields higher payoffs, at least for scientists who most value prestige among their peers.

¶84 There is some evidence of the value of openness for academics. When scientists allow free online access to their publications, they are more frequently cited.[211] Another study found that if the results described in a published paper are later patented, the average rate of citation rate to the paper declines by approximately ten to twenty percent.[212] More empirical research should be done to examine the effects of other forms of openness on academic prestige. But even if the potential payoffs create a prisoner's dilemma, scientists are better off if everyone cooperates than if no one does. They should therefore embrace efforts to return to a more open research culture.

¶85 Many legal academics have argued for a broader interpretation of the experimental use exemption to ensure patent law reflects traditional sharing norms.[213] Such an exemption may be helpful, but the extent to which it would actually influence norms is unclear. Walsh, Arora, and Cohen have noted this problem: "It is not easy to discern when research is commercial or noncommercial . . . . Thus it is not apparent that society would benefit from a policy response as opposed to continued reliance on current ad hoc practices of *de facto* infringement . . . ."[214]

Walsh, *For Money or Glory? Commercialization, Competition, and Secrecy in the Entrepreneurial University*, 50 SOC. Q. 145, 145 (2009) ("[W]e test whether scientists have become more competitive and more secretive over the last 30 years. . . . We find that secrecy has increased, and has increased particularly for experimental biologists.").

[205] Pub. L. No. 96-517, § 6(a), 94 Stat. 3015, 3019-28 (1980) (codified as amended at 35 U.S.C. §§ 200-212 (2006)).

[206] Arti Kaur Rai, *Regulating Scientific Research: Intellectual Property Rights and the Norms of Science*, 94 NW. U. L. REV. 77, 115 (1999).

[207] Robert P. Merges, *Property Rights Theory and the Commons: The Case of Scientific Research*, *in* SCIENTIFIC INNOVATION, PHILOSOPHY, AND PUBLIC POLICY 145, 149-50 (Ellen Frankel Paul et al. eds., 1996).

[208] *Id.* at 150.

[209] *Id.* at 151.

[210] *Id.* at 157-58.

[211] James A. Evans & Jacob Reimer, *Open Access and Global Participation in Science*, 323 SCI. 1025 (2009).

[212] Fiona Murray & Scott Stern, *Do Formal Intellectual Property Rights Hinder the Free Flow of Scientific Knowledge? An Empirical Test of the Anti-Commons Hypothesis*, 63, J. ECON. BEHAV. & ORG. 648 (2007).

[213] *See, e.g.*, Rebecca S. Eisenberg, *Proprietary Rights and the Norms of Science in Biotechnology Research*, 97 YALE L.J. 177, 224-26 (1987); Lee, *supra* note 203, at 691-92; Merges, *supra* note 207, at 164-65; Rai, *supra* note 206, at 139.

[214] Walsh et al., *Effects of Research Tool Patents*, *supra* note 101, at 335.

¶86 Since the main problem of access to bio-knowledge is not caused by patents themselves, but rather by the effect of the culture of patenting on scientific norms, it is not clear that giving scientists permission to use patented information will improve the situation. Technology transfer offices will continue to seek patents on university research and to require basic researchers to use MTAs when sharing materials. The continued commercialization of universities will likely continue unless Bayh-Dole is repealed entirely, which is neither likely nor necessarily desirable—for some classes of university discoveries, the patent incentive is important for public dissemination.

¶87 To address the access to bio-knowledge problem in basic research, it is therefore necessary to work within the current framework imposed by the patent system. I discuss some possible solutions in Part III, but first I briefly describe why access to materials is a problem not only for basic researchers, but also for producers of biomedical end products.

C. Commercial Innovation and Biopharmaceuticals

¶88 Access to bio-knowledge, in this broader meaning of the term, is not only a problem for basic researchers who have trouble obtaining materials from other academics. Access is also a critical problem in industry. The problem is most relevant for companies wishing to produce generic versions of biopharmaceuticals.

¶89 In industry, information-embedded tools and goods and human knowledge (know-how) are generally protected as trade secrets. Pharmaceutical companies always patent some aspects of biopharmaceuticals, but "the master cell lines and details of manufacturing processes . . . are fiercely guarded corporate secrets and are not part of the patent . . . . In fact, not patenting the process makes it unavailable for straightforward replication."[215] These other forms of bio-knowledge cannot be reverse engineered, so companies receive stronger, and potentially indefinite, protection by keeping them as trade secrets.

¶90 For companies that wish to produce generic versions of biopharmaceuticals (known as biosimilars or follow-on biologics), it is therefore not enough to wait for the pioneer pharmaceutical company's patents to expire—they also require access to the other forms of bio-knowledge that are involved in producing these drugs. In fact, it has been suggested that "[t]he production process is 90 percent of the intellectual property related to the product."[216]

¶91 For traditional small-molecule pharmaceuticals, under the Hatch-Waxman Act,[217] generic manufacturers can receive FDA approval simply by showing that their drug is "bioequivalent" to a drug that is already on the market.[218] Because biopharmaceuticals are significantly more complicated than small-molecule drugs, however, the Hatch-Waxman pathways for FDA approval of generics are unlikely to apply.[219]

¶92 A number of bills have been introduced in Congress to provide expedited FDA approval for biosimilars; the two competing bills in the 111th Congress are the Promoting Innovation and Access to Life-Saving Medicine Act,[220] which is favored by the generics industry, and the Pathway for Biosimilars Act,[221] which is preferred by the biotechnology industry. Neither bill, however, contains provisions allowing access to the materials and know-how that are needed to produce biosimilars, and as a result, neither would be effective in promoting generic competition.[222]

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[215] Roger & Goldsmith, *supra* note 15, at 461.

[216] WENDY H. SCHACHT & JOHN R. THOMAS, CONG. RESEARCH SERV., RL33901, FOLLOW-ON BIOLOGICS: INTELLECTUAL PROPERTY AND INNOVATION ISSUES 7 (2009) (quoting Debra Weintraub, *Next Generation of Biopharmaceuticals*, 9 J. MANAGED CARE MED. 35, 38-39 (2006)), *available at* http://opencrs.com/document/RL33901.

[217] Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended at 21 U.S.C. § 355 and 35 U.S.C. § 271(e) (2006)).

[218] SCHACHT & THOMAS, *supra* note 216, at 5-6.

[219] *Id.* at 3.

[220] S. 726 111th Cong (2009); H.R. 1427, 111th Cong. (2009).

[221] H.R. 1548, 111th Cong. (2009).

[222] Sarah Sorscher & Sara Crager, *Digest Comment - Newly Abbreviated Approval Pathway Will Not Solve the Biologics Problem*, HARV.

¶93 Until generic companies have access to all the forms of bio-knowledge that biopharmaceutical production requires, brand-name companies "will be able to maintain their monopolies—and resulting high prices—even after the new legislation takes effect."[223]

III. IMPROVING ACCESS TO MATERIALS WITHIN THE PATENT SYSTEM

¶94 The previous Parts have demonstrated that the main problem with DNA patents for basic researchers is not the patents themselves, but how the culture of patenting has changed norms in basic research, leading to increased secrecy and less sharing. Although the information in the patents is freely used, access to other forms of bio-knowledge remains a significant problem, both for basic researchers and for producers of end products like biopharmaceuticals.

¶95 As discussed in Part II.B.2, part of the problem basic researchers face results from changing academic norms, and it is unclear to what extent an experimental use exemption would actually improve the situation. The commercialization of university research is unlikely to be reversed, but partial solutions to the access problems may be found within the current patent system.

¶96 Transaction costs are a significant cause of the withholding of data and materials.[224] These costs may be reduced through initiatives to streamline contracts covering these transfers and through increased use of material depositories. These depositories can also help solve the access to materials problem for industrial manufacturers, since stringent enforcement of the enablement and best mode requirements for patent protection would require more companies to place critical manufacturing materials like cell lines in these depositories for public access.

A. Reducing Transaction Costs of Material Transfers

¶97 The first attempt to standardize material transfer agreements was the 1995 Uniform Biological Materials Transfer Agreement (UBMTA).[225] In 1999, the NIH urged recipients of NIH funding to "take every reasonable step to streamline the process of transferring their own research tools freely to other academic research institutions using either no formal agreement, a cover letter, [a simpler 1-page version of the UBMTA], or the UBMTA itself."[226]

¶98 Over 100 universities signed the UBMTA, but its success has been limited because many of these universities substitute their own MTA, which increases administrative overhead and may be more restrictive.[227] A second problem is that the UBMTA is also only for use among academic researchers, making collaboration with for-profit researchers challenging.[228]

¶99 One recent initiative, the Science Commons Biological Materials Transfer Project, builds off the success of Creative Commons and its limited number of standard copyright licenses.[229] This project promotes use of the UBMTA for transfers among academics by "provid[ing] tools and infrastructure to facilitate listing, searching, contracting, and tracking downstream impact" using "an extension of the same meta-data framework that has made content under the Creative Commons licenses widely

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J.L. & TECH. DIG., Mar. 19, 2009, http://jolt.law.harvard.edu/digest/patent/digest-comment-newly-abbreviated-approval-pathway-will-not-solve-the-biologics-problem.

[223] *Id.*

[224] *See* Campbell et al., *supra* note 190, at 478 (finding that the number one reason for withholding among geneticists is the effort required to produce the materials or information, which was cited by eighty percent of geneticists who had intentionally refused requests to share); Walsh et al., *supra* note 14, at 1196-97 (performing a regression analysis to find that "the effort involved is also an important reason why labs may not respond to requests for research inputs," along with commercial incentives and scientific competition).

[225] Mirowski, *supra* note 184, at 327.

[226] 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, 72,093 (Dec. 23, 1999).

[227] Arti K. Rai & Rebecca S. Eisenberg, *Bayh-Dole Reform and the Progress of Biomedicine*, LAW & CONTEMP. PROBS., Winter/Spring 2003, at 289, 305-06.

[228] Thinh Nguyen, *Science Commons: Material Transfer Agreement Project*, INNOVATIONS, Summer 2007, at 137, 140.

[229] Science Commons Biological Materials Transfer Project, http://sciencecommons.org/projects/licensing/ (last visited Feb. 21, 2010).

available for Web-based sharing."[230] Science Commons also created a new set of MTAs for transfers between academia and industry.[231] This attempt to remove legal barriers and reduce transaction costs will hopefully improve the access to materials problem for both basic and industrial researchers.[232]

B. Increasing Access Through Bio-Material Depositories

¶100 Another way to reduce the transaction costs associated with sharing materials is through increased use of material depositories. These depositories may also help solve the material access problems for generic companies who want to produce biopharmaceuticals.

1. The Development of Material Depositories

¶101 In addition to the requirements of novelty, utility, and nonobviousness described in Part I.A.1, patents must also meet the disclosure requirements of § 112: there must be (1) "a *written description* of the invention" that (2) "*enable[s]* any person skilled in the art to which it pertains . . . to make and use [the invention]" and (3) "set[s] forth the *best mode* contemplated by the inventor of carrying out his invention."[233] These three requirements are known as the written description requirement, the enablement requirement, and the best mode requirement. The disclosure requirements can be difficult to meet for many biotechnological patents, since a purely written description may be insufficient to enable others to practice the invention.

¶102 Since 1970, courts have found that the disclosure requirements can be met by putting necessary microorganisms in a public depository.[234] The Federal Circuit summarized this practice in *In re Wands*:

> Where an invention depends on the use of living materials such as microorganisms or cultured cells, it may be impossible to enable the public to make the invention (i.e., to obtain these living materials) solely by means of a written disclosure. One means that has been developed for complying with the enablement requirement is to deposit the living materials in cell depositories which will distribute samples to the public who wish to practice the invention after the patent issues. . . . A deposit has been held necessary for enablement where the starting materials (i.e., the living cells used to practice the invention, or cells from which the required cells can be produced) are not readily available to the public. Even when starting materials are available, a deposit has been necessary where it would require undue experimentation to make the cells of the invention from the starting materials.[235]

¶103 The PTO has adopted administrative rules governing the use of deposits.[236] The requirements for internationally recognized depositories are set by the Budapest Treaty of 1977.[237] There are two such depositories in the United States: the Agricultural Research Service Culture Collection (also known as the NRRL Collection) in Illinois and the American Type Culture Collection in Virginia.[238] Using these depositories is not prohibitively expensive: they charge $500 and $2500 to maintain a sample and $20 and $107-$640 to furnish a sample, respectively.[239] The deposited materials must be

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[230] Nguyen, *supra* note 228, at 141.

[231] *Id.*

[232] *But see* Mirowski, *supra* note 184, at 329.

[233] 35 U.S.C. § 112 ¶ 1 (2006) (emphasis added).

[234] *See In re* Argoudelis, 434 F.2d 1390 (C.C.P.A. 1970).

[235] *In re* Wands, 858 F.2d 731, 735 (Fed. Cir. 1988) (footnotes omitted).

[236] 37 C.F.R. §§ 1.801-.809 (2008).

[237] Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure, Apr. 28, 1977, 32 U.S.T. 1241, T.I.A.S. No. 9768.

[238] *See* World Intellectual Property Organization, Depositary Institutions Having Acquired the Status of International Depositary Authority Under the Budapest Treaty, http://www.wipo.int/export/sites/www/treaties/en/registration/budapest/pdf/ida.pdf (last visited Feb. 21, 2010).

[239] *Id.*

available to the public once the patent issues,[240] and the patentee may pay an additional fee to be informed of those who receive materials.

2. Depository Use for Basic Researchers

¶104 Material depositories may help improve access to information-embedded goods and tools for basic biomedical researchers. Walsh, Arora, and Cohen made the following observation from their interviews with people from diverse sectors of biomedical research:

> [T]he availability of supply houses to provide licensed copies of patented research materials did facilitate access and distribution according to some respondents. Our interviews also point to an intriguing possibility: This commercialization of research materials may actually increase access by creating market-based institutions for distributing them rather than relying on gift exchange among researchers. Several university scientists noted that the demand for important reagents can easily become overwhelming, and licensing these to a commercial firm was seen as a way of increasing, rather than limiting, access for the research community.[241]

¶105 Materials deposited for patent requirements are available at little cost to academics, although an experimental use exemption may be useful to ensure that these researchers are not sued. Academics could also be encouraged by the NIH and other grant agencies to place materials in depositories even when they are not seeking patents. This increased use of depositories may help reduce the transaction costs that often burden sharing among basic researchers.

3. Biopharmaceuticals and Enablement

¶106 These material depositories could also help improve access to bio-knowledge for downstream industrial scientists who wish to produce biosimilars (generic versions of biopharmaceuticals). As discussed in Part II.C, producing biosimilars requires access not only to the information protected by patents, but also to the materials and know-how involved in the manufacturing process, such as proprietary cell lines.

¶107 During the debate over creating a pathway to FDA approval of biosimilars, brand-name pharmaceutical companies have argued that bioequivalence cannot be established for biopharmaceuticals. They suggest that these drugs are so complex that versions produced by generic companies may not have the same safety and efficacy.[242]

¶108 Gregory Mandel has noted that the brand-name companies are thus admitting that their patents fail the enablement requirement, and that they are "caught in a Catch-22: either they must concede that generic manufacturers can produce equivalents of pioneer biologics, or pioneer biologic patents are not enabled."[243] He also suggests that many of these patents *could* be enabled:

> [P]ioneer firms contend that they can reproduce manufacturing facilities and processes so precisely that they can ensure production of equivalent biologics at alternate facilities and using alternate processes. Where this is the case, if correct, it means that enablement can be accomplished in these instances. The firms have simply chosen not to include enough manufacturing information in their patents to provide for reproduction.[244]

¶109 Mandel admits that biologic patents are partially enabled, in that "persons having ordinary skill in the art can make some form of the biologic that is claimed."[245] Brand-name companies would probably argue that this is sufficient, and that they have the right to use trade secrets, rather than patents, to protect the additional materials and know-how needed to make their particular form of

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[240] 37 C.F.R. § 1.809 (2008).

[241] Walsh et al., *Effects of Research Tool Patents*, *supra* note 101, at 321-22.

[242] Gregory N. Mandel, *The Generic Biologics Debate: Industry's Unintended Admission that Biotech Patents Fail Enablement*, 11 VA. J.L. & TECH. 8, ¶ 9 (2006), http://www.vjolt.net/vol11/issue4/v11i4_a8-Mandel.pdf.

[243] *Id.* ¶¶ 10, 71.

[244] *Id.* ¶ 77.

[245] *Id.* ¶ 71.

the drug. But the Federal Circuit has repeatedly held that the specification "must describe the manner and process of making and using the invention so as to enable a person of skill in the art to make and use *the full scope of the invention* without undue experimentation."[246]

¶110 If brand-name companies want their particular drugs to fall within the scope of their patent claims, then their patents must enable generic companies to produce those same products without undue experimentation.

¶111 Alternatively, one could argue that even if the patent enables some form of the claimed biopharmaceutical, it fails to meet the best mode requirement unless the cell lines and materials needed to make the commercial product are disclosed through depositories. In *Amgen v. Chugai*, the Federal Circuit held that "exact duplication" of the cells needed for patentee's best mode was unnecessary,[247] although this decision received a scathing critique from Lawrence Tribe:

> The fundamental premise of American patent law has been that one cannot both have the 17-year monopoly represented by a patent and conceal the best mode of implementing one's invention that one contemplates at the time one sought the patent. One has to give up the benefits of trade secrecy under American patent law in order to enjoy the benefits of patent monopoly. That fundamental quid pro quo is radically destroyed by the Federal Circuit decision, which enables one, as long as one sets forth instructions that might permit someone to get close to one's invention but only by having to in effect reinvent the wheel, to retain trade secrecy.[248]

¶112 Even if the Federal Circuit or the Supreme Court do not choose to reexamine *Amgen*'s holding, a narrow reading of the decision may still invalidate some biopharmaceutical patents. The court noted that a patentee may not disclose only the second-best embodiment or conceal the best mode, and it found that Amgen's patent was sufficient because even if others could not produce Amgen's exact cells, they could produce cells with similar production levels of the biopharmaceutical.[249] In cases where those skilled in the art cannot produce a commercially viable version of the patented product, the best mode requirement is not met.

¶113 Allowing a company to obtain patent protection for a product and to protect that same product with potentially infinite trade secret protection seems to violate both the letter and the spirit of the Patent Act, as well as raising questions of preemption.[250] The PTO and the courts should make sure that patents satisfy the disclosure requirements. Companies should be required to deposit any cell lines or other materials that are needed to produce the end-product biopharmaceuticals in an official depository, and other details of the manufacturing process should be disclosed in the patent application. Any legislation that creates a pathway for FDA approval of biosimilars should recognize the importance of access to these other forms of bio-knowledge, and should make sure that generic companies have some way of receiving relevant materials and know-how.[251]

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[246] LizardTech, Inc. v. Earth Res. Mapping, Inc., 424 F.3d 1336, 1344-45 (Fed. Cir. 2005) (emphasis added); *see also* Invitrogen Corp. v. Clontech Labs., Inc., 429 F.3d 1052, 1070 (Fed. Cir. 2005).

[247] Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1212 (Fed. Cir. 1991).

[248] The Bureau of Nat'l Affairs, Inc., *Interview with Laurence Tribe on Supreme Court Review of* Amgen Inc. v. Chugai Pharmaceutical Co., 42 PAT. TRADEMARK & COPYRIGHT J. (BNA) 466, 468 (1991).

[249] *Amgen*, 927 F.2d at 1211-12.

[250] In *Kewanee Oil Co. v. Bicron Corp.*, the Supreme Court held that state trade secret law is not preempted by federal patent law because trade secret protection is weaker: "The possibility that an inventor who believes his invention meets the standards of patentability will sit back, rely on trade secret, and after one year of use forfeit any right to patent protection is remote indeed." 416 U.S. 470, 490-91 (1974). However, this assumption that patents will always be chosen over trade secrets is simply wrong: many industrialists choose trade secret protection because it has the potential to last forever, it is significantly cheaper to obtain, and it does not have the enforcement problems that patents do when infringement is difficult to detect, such as for manufacturing processes. Daniel C. Munson, *The Patent-Trade Secret Decision: An Industrial Perspective*, 78 J. PAT. & TRADEMARK OFF. SOC'Y 689, 708 (1996).

[251] *See* Sorscher & Crager, *supra* note 222.

CONCLUSION

¶114 This Note has argued that concerns about access in biomedical research must be framed in terms of a comprehensive understanding of bio-knowledge and its protection as intellectual property. Although much of the work in this field has focused on the patent protection of genetic sequences, the protection of materials through secrecy is often a more serious problem for researchers. This problem is related to the commercialization of university research, which has increased the transaction costs associated with sharing materials. One effort that may reduce these costs is the Science Commons Material Transfer Project, which attempts to streamline the legal barriers to transfers. Another way to reduce the effort involved in transfers may be increased use of material depositories. More stringent enforcement of the patent disclosure requirement of placing necessary materials in these depositories would help to solve the access to materials problem for both basic and industrial researchers.