A DEFENSE OF PATENTING HUMAN GENE SEQUENCES UNDER U.S. LAW:

SUPPORT FOR THE PATENTING OF ISOLATED AND PURIFIED SUBSTANCES♦

INTRODUCTION

Everyone is familiar with what happens when you become ill. Robed in a paper gown, you sit down on a cold bench in your doctor's office; he takes your temperature and your blood pressure as you rattle off a list of symptoms. You receive a preliminary diagnosis, and barring any allergies, the doctor prescribes you the drug that has the best success rate for your budget or the drug with which your doctor is most familiar or has had the most success. Instead, imagine now, a trip to your physician begins with your doctor taking a blood sample to sequence your personal genome. With this information, your doctor can tell you detailed informa-

tion about your ancestry, the likelihood you will develop certain diseases, and if you are sick, your doctor can quickly prescribe for you the most effective method of treatment that *your* body will respond to the best.

Technology is not ready for personalized medicine yet, but it is getting closer. In the spring of 2007, Dr. James Watson, one of the men responsible for the discovery of the structure of DNA in the 1950s, publicly announced he had finished deciphering his entire personal genome.[1] The discovery marked the first time a complete diploid genome of a single individual was sequenced.[2] Just days after Watson's announcement, geneticist Dr. J. Craig Venter followed suit, releasing his own individual genome to GenBank, a public DNA database.[3] Both men have since made their diploid genomes available to researchers and the public with the intention that the information will lead to significant advances in genetic research and hopefully allow individuals to learn their entire genetic sequences for prices as low as a few thousand dollars, or even less in the near future.[4]

The Human Genome Project, which began in October 1990 and completed in 2003, was a combined effort of the National Institute of Health ("NIH") and the Department of Energy to determine the sequences of the three billion pairs of chemical bases

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[1] Nicholas Wade, *Genome of DNA Discoverer is Deciphered*, N.Y. TIMES, June 1, 2007, at A19.

[2] *Id.* A diploid genome is the name given to a genome that details all DNA information from the two parent genomes. Emily Singer, *Craig Venter's Genome*, TECH. REV., Sept. 4, 2007, *available at* http://www.technologyreview.com/printer_friendly_article.aspx?id=19328&channel=biotech&section=.

[3] Wade, *supra* note 1. *See also* Amy Harmon, *6 Billion Bits of Data About Me, Me, Me!*, N.Y. TIMES, June 3, 2007, § 4, at 1. The first female genome was sequenced in May 2008 by a team lead by Gert-Jan van Ommen, of Leiden University. John Naish, *X-Rated Sequence*, TIMES (England), May 31, 2008, at 3.

[4] Wade, *supra* note 1. *See also* Singer, *supra* note 2. On November 29, 2007, Knome, a genomics company based in Cambridge, Massachusetts, announced that it would sequence the personal genomes of twenty clients in an attempt to move closer to personalized medicine. Knome, Inc., http://www.knome.com/Recent%20News/tabid/58420/Default.aspx (last visited July 27, 2008). According to their website, Knome offers personal gene sequencing for a cost of $350,000. *Id.*

In November 2007, a Silicon Valley startup company, 23AndMe, launched an internet based service that allowed individuals to request their genome via genotyping. Thomas Goetz, *23AndMe Will Decode your DNA for $1,000, Welcome to the Age of Genomics*, WIRED, Nov. 17, 2007, *available at* http://www.wired.com/print/medtech/genetics/magazine/15-12/ff_genomics. Their service differs from gene sequencing, in that genotyping is the process used to determine which genetic variants an individual possesses, and sequencing determines the exact sequence of all three million base pairs. *See* 23AndMe: Our Service: How the Process Works, https://www.23andme.com/you/faqwin/sequencing (last visited July 27, 2008). Two other companies, deCODE Genetics of Iceland and Navigenics of Redwood, CA, also announced in November 2007 that they will be providing similar, low cost genotyping. Nicholas Wade, *Experts Advise a Grain of Salt With Mail-Order Genomes, at $1,000 a Pop*, N.Y. TIMES, Nov. 17, 2007, at A16.

in human DNA and to identify the human genome.[5] When a final working version of the genome was completed in 2003, the reference sequence was comprised of genes from various anonymous donors.[6] After the project was officially complete, individual researchers like Watson and Venter attempted to use the knowledge gained through the project to sequence individual genomes.[7]

Now that technology has allowed for the sequencing of personal genomes, researchers hope that by studying the genomes of several thousand individuals, they will be able to develop personalized medicine, such as medical treatments tailored to one's genetic profile.[8] The goal is to create a new and improved reference genome that will enable researchers to develop simpler and cheaper methods of obtaining the thousands of personal genomes necessary to conduct the research needed to further the move towards personalized medicine.[9]

Gene sequences, like the ones that make up Watson's and Venter's genomes, and other tools of synthetic biology are treated by the United States Patent and Trademark Office ("USPTO") as naturally occurring substances and chemicals.[10] In order for naturally occurring substances and chemicals to secure patent protection under current United States patent law, they must be extracted, isolated, and purified, and additionally, they must possess differing utility from their natural form.[11] After the Human Genome Project commenced in the 1990s, researchers from the NIH raced to the USPTO attempting to patent thousands of gene sequence fragments.[12] While most of these applications were denied, the project sparked an increase in synthetic biology patent grants, many of which received patent protection. Currently, the USPTO has issued in excess of 6000 patents on gene sequences.[13]

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[5] Human Genome Project, U.S. Human Genome Project Research Goals, http://www.ornl.gov/sci/techresources/Human_Genome/hg5yp/ (last visited July 27, 2008). A rough draft of the genome was released in June 2000, but the final working product was not completed until 2003. *Id.* Celera Genomics was founded in 1998 by Applera Corporation and Dr. J. Craig Venter and was the private sector analog to the Human Genome Project. Celera, Our History, http://www.celera.com/celera/history (last visited July 27, 2008).

[6] Human Genome Project, Facts About Genome Sequencing, http://www.ornl.gov/sci/techresources/Human_Genome/faq/seqfacts.shtml#whose (last visited July 27, 2008).

[7] *See* Wade, *supra* note 1.

[8] Singer, *supra* note 2.

[9] *Id.*

[10] *See* MANUAL OF PATENT EXAMINING PROCEDURE § 2105 (8th ed., 6th rev. 2007), *available at* http://www.uspto.gov/web/offices/pac/mpep/documents/front.htm.

[11] Richard Seth Gipstein, Note, *The Isolation and Purification Exception to the General Unpatentability of Products of Nature*, 4 COLUM. SCI. & TECH. L. REV. 2 (2003).

[12] DAVID B. RESNIK, OWNING THE GENOME: A MORAL ANALYSIS OF DNA PATENTING 1 (2004).

[13] *Gene Patents and Other Genomic Inventions: Hearing Before the Subcomm. on Courts and Intellectual Property of the H. Comm. on the Judiciary*, 106th Cong. 25 (2000) (statement of Todd

It was not long before individuals and organizations alike began to question and protest the patenting of such inventions. The heart of the controversy attacks a question that has been debated and discussed for years: is it appropriate that an isolated and purified substance or thing found in nature be awarded patent protection?[14] Opponents to the patenting of gene sequences and similar biotechnology inventions commonly make three major arguments. First, they argue that gene sequences should not be patentable on the basis of subject matter because they are elements found in nature, and patent protection does not extend to products of nature.[15] Second, they argue that granting biotechnology patents will retard both scientific and economic progress in a very important field because the high cost of licensing will prohibit many from further researching the patented works.[16] Lastly, some opponents assert an ethical argument: by patenting gene sequences, we are essentially granting a monopoly over life, human or otherwise.[17] The last argument is often the most difficult to address, for it hinges upon an individual's understanding of the type of ownership patent protection affords.

Proponents for patenting generally counter the discussed arguments by putting forth two contentions of their own. First, such subject matter has been deemed patentable by the Supreme Court's holding in *Diamond v. Chakrabarty*,[18] and second, the licensing argument has been proven wrong with other biotechnol-

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Dickinson, Under Secretary of Commerce for Intellectual Property and Director of the United States Patent and Trademark Office, Department of Commerce).

[14] The first time that the Supreme Court addressed the issue was in 1874, in *American Wood-Paper Co. v. Fibre Disintegrating Co.*, 90 U.S. 566 (1874). *See also, e.g.*, Gipstein, *supra* note 11 (discussing generally the isolation and purification exception to the general unpatentability of "products of nature"); Christopher D. Hazuka, *Supporting the Work of Lesser Geniuses: An Argument for Removing Obstructions to Human Embryonic Stem Cell Research*, 57 U. MIAMI L. REV 157, 159 (2002).

[15] See RESNIK, *supra* note 12, at 82-92, for a lengthy discussion about the products of nature argument. *See also* Nigel Williams, *New Thinking on Gene Patents*, 12 CURRENT BIOLOGY R577, R577-78 (2002); Stephanie Arcuri, Note, *They Call That Natural? An Analysis of the Term "Naturally Occurring" and the Application of Genes to the Patent Act*, 40 VAL. U. L. REV 743, 743 (2006); Amanda S Pitcher, Comment, *Contrary to First Impression, Genes are Patentable: Should There be Limitations?*, 6 J. HEALTH CARE L. & POL'Y 284, 298 (2003); Press Release, American College of Medical Genetics, Position Statement on Gene Patents and Accessibility of Gene Testing, (Aug. 2, 1999), *available at* http://genetics.faseb.org/genetics/acmg/pol-34.htm.

[16] Lori B. Andrews & Jordan Paradise, *Gene Patents: The Need for Bioethics Scrutiny and Legal Change*, 5 YALE J. HEALTH POL'Y L. & ETHICS 403, 404 (2005). For further discussion, see also Alan R. Williamson, *Gene Patents: Socially Acceptable Monopolies or an Unnecessary Hindrance to Research?*, 17 TRENDS IN GENETICS 670, 670-73 (2001); Tanya Wei, Comment, *Patenting Genomic Technology - 2001 Utility Examination Guidelines: An Incomplete Remedy In Need of Prompt Reform*, 44 SANTA CLARA L. REV. 307, 320 (2003).

[17] RESNIK, *supra* note 12, at 93-131. *See also* Burton T. Ong, *Patenting the Biological Bounty of Nature: Re-Examining the Status of Organic Inventions as Patentable Subject Matter*, 8 MARQ. INTELL. PROP. L. REV. 1, 2 (2004).

[18] Diamond v. Chakrabarty, 447 U.S. 303 (1980). For a discussion using *Chakrabarty* as the support for patenting biotechnology, see, e.g., Andrew Chin, *Artful Prior Art and the Quality of DNA Patents*, 57 ALA. L. REV. 975, 985-86 (2006).

ogy patents that require licensing such as Stanford's Cohen-Boyer gene-splicing patents in the 1980s.[19] Stanley Cohen and Herbert Boyer's patent for cloning recombinant DNA marked the first DNA process patent.[20] What made the patent famous was its unique, low-cost, non-exclusive licensing structure, which not only allowed others to license the patent with a relatively cheap donation to Stanford University, but also made the patent one of the most profitable patents of all time.[21] Considering the explosion of the biotechnology field after the Cohen-Boyer patent, the argument that licensing schemes prohibit innovation is dubious. The debate over the morality of patenting inventions of synthetic biology is a subjective topic resting largely upon how one defines human life.

A thoughtful response to the controversy requires an analysis of all four major doctrines of patent law: novelty, subject matter, utility, and obviousness. Historically, the major bars to patenting isolated and purified substances have been the subject matter and novelty requirements. However, since the late nineties, the most important doctrinal bars to patenting gene sequences and other inventions of synthetic biology have been the utility standard, and now possibly the obviousness standard, as heightened by the recent Supreme Court decision, *KSR v. Teleflex*.[22] The recent changes to the utility and obviousness standards reflect a shift towards a general acceptance of the state of the law in subject matter and novelty. Since 1980, no major changes have been made to the subject matter doctrine.[23] Over twenty-five years have passed since the Supreme Court's decision in *Diamond v. Chakrabarty*, and the courts have resisted any challenges to the state of the law with regard to synthetic biology patents. The heightened utility guidelines for the USPTO, as created in 1999 and finalized in 2001,[24] suggest that the USPTO's response to the growing concern in the 1990s with allowing gene patenting was to reevaluate the current state of the four doctrines in patent law and focus on adjusting

[19] *Gene Patents and Other Genomic Inventions: Hearing Before the Subcomm. on Courts and Intellectual Property of the H. Comm. on the Judiciary*, 106th Cong. 30 (2000) (statement of Todd Dickinson, Under Secretary of Commerce for Intellectual Property and Director of the United States Patent and Trademark Office, Department of Commerce). *See also* U.S. Patent No. 4,237,224 (filed Jan. 4, 1979) and U.S. Patent No. 4,468,464 (filed Nov. 9, 1978).

[20] RESNIK, *supra* note 12, at 52; *see* '224 Patent.

[21] Mark A. Lemley, *Patenting Nanotechnology*, 58 STAN. L. REV. 601, 610 & n.44 (2005) (noting that the Cohen-Boyer patents earned Stanford University over $250 million before they expired in 1997).

[22] KSR Int'l Co. v. Teleflex, Inc., 127 S. Ct. 1727 (2007).

[23] *But see In re* Nuijten, 500 F.3d 1346, 1348 (Fed. Cir. 2007) (holding that signals with embedded digital watermarks encoded in accordance with a specific process were not patentable subject matter under 35 U.S.C. § 101).

[24] Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001).

that which had not been tended to in years: the utility doctrine.[25] The heightened standard for utility established by the 2001 Utility Guidelines was reinforced in the Federal Circuit's 2005 decision, *In re Fisher*, and for now appears to be the most significant bar to the patenting of gene sequences.[26]

The concerns of those opposed to the patenting of gene sequences appear grounded to some extent in misunderstandings and misconceptions. With every new emerging field of technology comes a new breed of concerns over the current state of the law. While the concerns may be silenced with time, the recent advancements in technology, particularly with the recent sequencing of human genomes, render a need to evaluate the current state of patent law and to answer the fundamental underlying question: should the isolation and purification of naturally occurring substances be patentable?

This Note will explore the historical basis for allowing the patenting of human gene sequences and will argue that, despite any moral or ethical concerns one may have, the isolation and purification of naturally occurring substances should be patentable in accordance with the current novelty, obviousness, subject matter, and utility standards. The evolution of United States patent law beginning with the *American Wood-Paper Patent* decision in 1874 and evolving through recent decisions like *In re Fisher* and *KSR v. Teleflex*[27] as well as the text of patent statutes as they stand today[28] provide a substantial basis to support the idea that the isolation and purification of naturally occurring substances should be, and continue to be, patentable, although the requisites under the heightened utility and obviousness standards should make patent protection harder to obtain.

Part I explores the historical justifications for allowing the patentability of isolated and purified substances via the novelty and subject matter doctrines. Part II analyzes the new justifications for allowing the patentability of isolated and purified substances via the recently heightened utility and obviousness doctrines. Part III addresses the criticism of allowing gene sequence patents, focusing on the potentially negative implications of the most recent case law in the biotechnology field responding to the arguments of the opponents to patentability in an attempt to account for the doctrinal shift. Scholars have speculated about the

[25] Since the implementation of the Patent Act in 1952, the courts have only addressed the utility doctrine a handful of times, the most notable being both *Brenner v. Manson*, 383 U.S. 519 (1966), and *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995).
[26] *In re* Fisher, 421 F.3d 1365 (Fed. Cir. 2005).
[27] Am. Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. 566 (1874).
[28] *See, e.g.*, 35 U.S.C. § 101 (2006).

effects of *KSR v. Teleflex* on biotech patents.[29] This Note will argue that despite the heightened utility standard and the decisions following *KSR*, the isolation and purification of naturally occurring substances should continue to be patentable, though practitioners may find patent protection increasingly more difficult to secure.

I. MAJOR HISTORICAL CONCERNS: THE NOVELTY AND SUBJECT MATTER REQUIREMENTS

A. *Patent Law: A Basic Overview*

Article I, § 8, clause 8 of the U.S. Constitution confers upon Congress the power to "promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."[30] Federal copyright and patent law have emerged from this clause.[31] The patent statutes are said to promote such scientific progress by offering inventors exclusive rights for a limited period of time, now twenty years, as an incentive and in exchange for their inventiveness and research efforts.[32] Patent protection is conceptualized as a negative right – a right granting the patent holder the opportunity to exclude others from using, making, selling, offering to sell, or importing any invention for twenty years from the time the application is filed.[33]

Prior to the current patent legislation, the Patent Act of 1952,[34] Congress maintained only two explicit statutory requirements for an invention to receive patent protection: novelty and utility.[35] With the Patent Act of 1952, Congress added a third explicit requirement: obviousness.[36] Patentability now relies upon three major explicit conditions: novelty, utility, and obviousness.[37] A fourth requirement, the subject matter requirement, is implicit in § 101 and requires that the invention be a "process, machine,

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[29] *See, e.g.*, 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 (2007).

[30] U.S. CONST. art. I, § 8, cl. 8.

[31] Andrew Beckerman-Rodau, *Patent Law - Balancing Profit Maximization and Public Access to Technology*, 4 COLUM. SCI. & TECH. L. REV. 1, 1, 2 n.1 (2003).

[32] Diamond v. Chakrabarty, 447 U.S. 303, 307 (1980).

[33] 35 U.S.C. § 251 (2006); David B. Resnik, *DNA Patents and Human Dignity*, 29 J.L. MED. & ETHICS 152, 153 (2001).

[34] Patent Act of 1952, Pub. L. No. 82-593, 66 Stat. 792 (codified as amended in scattered sections of title 35 of the U.S.C.).

[35] Graham v. John Deere Co., 383 U.S. 1, 3 (1966). The subject matter requirement is an implicit requirement and has been written into the legislation since the Patent Act of 1793. *Chakrabarty*, 447 U.S. at 308.

[36] *35 U.S.C. § 103 (1952).*

[37] *Graham*, 383 U.S. at 12.

manufacture, or composition of matter."[38] Thus, for an invention or a discovery to be eligible for patent protection, it must be novel, not obvious, useful, and within one of the statutory categories of permissible subject matter.

Historically, the two major concerns about the patentability of isolated and purified naturally occurring substances have been the subject matter and novelty requirements.[39] These two requisites are often considered in tandem.[40] The subject matter and utility requirements for patentability are both established in 35 U.S.C. § 101, which provides: "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title."[41] The subject matter requirement is derived from the phrase: "process, machine, manufacture, or composition of matter."[42] The utility requirement is derived from the use of the word "useful."[43] The other two requirements, novelty and non-obviousness, are codified in 35 U.S.C. §§ 102 and 103, respectively. When ascertaining whether something can be patented, all four requirements – subject matter, utility, novelty, and non-obviousness – must be satisfied. Since the Supreme Court's 1980 decision in *Diamond v. Chakrabarty*, which helped define the subject matter requirement in the field of synthetic biology, the subject matter doctrine appears to be fairly well-settled. An investigation into the history of both requirements suggests that "isolated and purified" naturally occurring substances have been, and should continue to be, patentable.

B. *The Novelty Requirement*

The novelty-based justification for the patentability of isolated and purified naturally occurring substances has historic roots that can be traced back to the late nineteenth and early twentieth centuries.[44] Several federal courts have considered whether isolated and purified substances were patentable, and the doctrine slowly evolved until it was best expressed in the late 1950s in the Fourth

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[38] 35 U.S.C. § 101 (1952).
[39] *See generally* Gipstein, *supra* note 11 (discussing the major constitutional and statutory concerns of isolated and purified substances).
[40] *See, e.g.*, Merck & Co. v. Olin Mathieson Chem. Corp., 253 F.2d 156 (4th Cir. 1958).
[41] 35 U.S.C. § 101 (2006).
[42] Chakrabarty, 447 U.S. at 307 (citing 35 U.S.C. § 101 (1976)).
[43] Tashica T. Williams, Note, In re Fisher*: Raising the Utility Hurdle for Express Sequence Tags*, 21 BERKELEY TECH. L.J. 123, 124 (2006). The utility requirement is also expressed in 35 U.S.C. § 112, ¶ 1 (2006).
[44] *See* Am. Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. 566 (1874); Farbenfabriken Co. v. Kuehmsted, 171 F. 887 (C.C.N.D. Ill. 1909).

Circuit's decision, *Merck & Co. v. Olin Mathieson Chemical Corp.*[45]

Since 1874, the Supreme Court has inherently recognized that an isolated and purified substance may be patentable via the novelty doctrine.[46] In *American Wood-Paper Co. v. Fibre Disintegrating Co.*, the patentee asserted two main claims: a manufacture claim for cellulose extracted from wood and vegetable substances and purified and a method claim for the process of extracting and purifying it.[47] The cellulose claimed by the patentee, as the Court explained and the patentee did not dispute, was previously known in the art, but it was never purified to the same degree as the patented manufacture.[48] The claimed manufacture and the prior art differed in degree of purity – they did not differ in kind, substance, and uses.[49] Both the prior art and the claimed cellulose were suitable for the manufacture of paper and the end paper product was identical.[50] Because the prior art and the claimed manufacture differed solely in degree of purity, the Court held that the manufacture itself was not sufficiently novel to be patentable.[51] As the *American Wood-Paper* Court eloquently quoted from old English law, "[w]hat the law looks to . . . is the inventor and the discoverer who finds out and introduces a manufacture which supplies the market for useful and economical purposes with an article which was previously little more than the ornament of a museum."[52] While the Supreme Court did not uphold the manufacture claims in *American Wood-Paper*, its discussion prompted, at the very least, the concept that isolated and purified substances *could* be patented, *so long as the claimed substance differs from the known art more substantially than simply degree of purity.*

Immediately following the *American Wood-Paper* decision, circuit courts began expressly upholding the patenting of both process and manufacture claims for isolated and purified substances.[53] In 1909, the Court of Appeals for the Seventh Circuit considered whether pure aspirin ("asperin") was patentable.[54] Aspirin is a product of coal tar known by its chemical name, acetyl salicylic

[45] 253 F.2d 156 (4th Cir. 1958).
[46] *Am. Wood-Paper Co.*, 90 U.S. 566.
[47] *Id.* at 593.
[48] *Id.* at 594.
[49] *Id.* at 595 ("[Cellulose] had been used in the arts, a manufacture which was the same in kind and in substance, and fitted for the same uses as the article of which the complainants now claim a monopoly.").
[50] *Id.*
[51] *Id.* at 596.
[52] *Am. Wood-Paper Co.*, 90 U.S. at 596 (quoting Young v. Fernie, 10 L.T. 861 (1866)).
[53] *See, e.g.*, Blumenthal v. Burrell, 53 F. 105 (2d Cir. 1892) (upholding a patent for pure chymosin, used to curdle milk in cheese manufacturing, for having a "distinctive nature" not present in the impure prior art).
[54] Farbenfabriken Co. v. Kuehmsted, 171 F. 887, 887 (C.C.N.D. Ill. 1909).

acid, and was known in its impure chemical form for many years prior to the patentee's filing of a patent application in August of 1898.[55] The prior art, impure acetyl salicylic acid, contains a small percentage of free salicylic acid and other impurities which render the aspirin injurious to the stomach.[56] The prior known methods of purification of aspirin included heat and boiling water, which would split the resulting product into two acids: acetic and salicylic acid, creating the impurities.[57] The patentee's process circumvented the existence of impurities by engaging in a waterless purification process not previously known in the art.[58] The new product differed *in kind* from the old, because aspirin's therapeutic benefit could be achieved *only* in the absence of the free acids. The Seventh Circuit held aspirin was patentable because the acid in its impure state was worthless; however, through discovering a method that would remove its impurities, the comparative worth was "immediately successful to an extraordinary degree."[59]

The assertion founded in the *American Wood-Paper* decision was extended to isolated and purified substances derived from *organic* matter in 1911, with the decision in *Parke-Davis v. H.K. Mulford & Co.*[60] In *Parke-Davis*, Judge Learned Hand considered, *inter alia*, whether an isolated and purified form of adrenalin was patentable.[61] The adrenalin, as patented in U.S. Patent No. 753,177, was extracted from suprarenal glands as a salt,[62] and then further purified as a base.[63] The defense asserted four pieces of prior art, none of which specifically extracted the base, although all four prior works hoped to extract from the glands the active principle for which adrenalin was responsible: increasing blood pressure and controlling or ceasing internal bleeding.[64] Though it is interesting to note, as the court did,[65] that the extracted and purified adrenalin has the same physiological properties that the gland itself was responsible for, what made the patented adrenalin novel was that the danger of injecting the impure substance into a hu-

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[55] *Id.*
[56] *Id.* at 888.
[57] *Id.*
[58] *Id.*
[59] *Id.* at 890.
[60] Parke-Davis & Co. v. H.K. Mulford Co., 189 F. 95 (C.C.S.D.N.Y. 1911), *aff'd in part*, 196 F. 496 (2d Cir. 1912).
[61] *Id.* at 106.
[62] Note that a "salt" is defined as any compound formed by the reaction of an acid with a base, with the hydrogen of the acid replaced by a metal or equivalent group. COMPACT OXFORD ENGLISH DICTIONARY OF CURRENT ENGLISH, *Salt*, (3d ed. 2005).
[63] *Id.*; U.S. Patent No. 753,177 (filed on May 12, 1903). Note that the patentee amended his claims.
[64] '177 Patent.
[65] *Parke-Davis*, 189 F. at 101.

man was severe.[66] Like in *Farbenfabriken*,[67] the isolation and purification of the base produced a novel substance no longer dangerous to the human body that had tremendous therapeutic effects.[68]

In his opinion, Judge Hand noted that the patent examiner originally rejected the plaintiff's original product claims on the basis of his interpretation of *American Wood-Paper Co. v. Fibre Disintegrating Co.*[69] The examiner interpreted *American Wood-Paper* to stand for the proposition that "no product is patentable, however it be of the process, which is merely separated by the patentee from its surrounding materials and remains unchanged."[70] Judge Hand used this statement to examine the amendments filed by the patentee. He noted that the amended claims, as they stood at the time of trial, were sufficient to meet the novelty requirement because the patentee was the first to make the salt available from removing it from the gland-tissues in a non-salt form.[71] In other words, the patentee extracted a salt out of a non-salt and purified it, enabling the product to have a new commercial and therapeutic function. The difference was not merely in degree of purity, but in *degree of kind.*

The jurisprudence that developed following *Parke-Davis* primarily relied on Judge Hand's decision to support the patentability of extracted, isolated, and purified "products of nature" that meet the other statutory requirements of patentability. In the Fourth Circuit's 1958 decision, *Merck & Co. v. Olin Mathieson Chemical Corp.*, the court rejected the defendant's contention that the plaintiff's patent for a vitamin B_{12} extract was invalid on the grounds that the patent was for a product of nature.[72] With regard to the defendant's novelty argument, the court relied on the decision in *Parke-Davis* and determined that the purification of the product provided novelty on a commercial and therapeutic basis.[73] The court found that the active substance, claimed in the product

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[66] *Id.* at 115.
[67] *Farbenfabriken*, 171 F. at 890.
[68] Judge Hand noted that:
[t]he uses of the gland were so great that it became a part of the usual therapy in the best form which was accessible. As soon as [the patentee] put out his discovery, other uses practically disappeared; by that I do not mean absolutely, but that the enormous proportion of use now is of [the patentee's] products. There has been no successful dispute as to that; hardly indeed any dispute at all. What use remains is, so far as the evidence shows, of the old dried glands, which every one concedes to have been dangerous, at least for intravenous use. All this ought to count greatly for the validity of the patent, and [the patentee] has a great start, so to speak, from such facts.
Parke-Davis, 189 F. at 115.
[69] *Id.* at 101.
[70] *Id.*
[71] *Id.* at 102.
[72] Merck & Co. v. Olin Mathieson Chem. Corp., 253 F.2d 156 (4th Cir. 1958). The facts and subject matter argument will be discussed further *infra* in Part I.C.
[73] *Id.* at 163. .

claims by the plaintiff, was unidentified and unknown in the crude fermentate form that existed in nature.[74] The Court relied in part on another, older decision, *In re Merz*, 97 F.2d 599, 601 (1938), to reinforce the idea that simply because an invention may be a purified form of a product of nature, it does not necessarily lack patentability under the novelty doctrine: "[I]f the process produces an article of such purity that it differs not only in degree but in kind it may be patentable. If it differs in kind, it may have a new utility in which invention may rest."[75] Only through isolation and purification of the vitamin was the utility claimed by the plaintiff discovered.[76] This new composition of matter and utility was found to comply with the novelty requirement of 35 U.S.C. § 102.

Since the early twentieth century, courts have neglected to find that the novelty doctrine specifically precludes the patentability of extracted, isolated, and purified substances in cases where all other requirements of the patent statute have been fulfilled. Particularly in cases like *Farbenfabriken* and *Merck*, where the utility of the isolated and purified substance deviated greatly from the substance in its natural form, courts have suggested that the novelty requirement is met. This is both because the purified substance does not simply occur in nature, *and* the extraordinary or unexpected results that are achieved when the substance is isolated or purified is indicative of patentable invention. Since the reformation of the Patent Act in 1952 and the *Merck* decision, the general rule for the patentability of such substances is straightforward: so long as the substance meets all other statutory requirements of the Patent Act, the substance does not naturally occur in its present state, and the result is of commercial value, the substance or process to create it is patentable.

C. *The Subject Matter Requirement*

In 1930, the passage of the Plant Patent Act marked the first instance that a naturally occurring object was explicitly granted patent protection under United States law.[77] The Act grants patent protection to "[a]ny person . . . who has invented or discovered and asexually reproduced any distinct and new variety of plant other than a tuber-propagated plant."[78] In short, the Plant Protection Act conferred rights upon a patentee that allowed him

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[74] *Id.* at 164.
[75] *Id.* (quoting *In re* Merz, 97 F.2d 599, 601 (C.C.P.A. 1938)).
[76] *See Merck*, 253 F.2d 156.
[77] *See* Plant Patent Act, ch. 312, § 1, 46 Stat. 376 (1930) (codified as amended at 35 U.S.C.A. §§ 161-64 (1988)). *See also* Jack Wilson, *Patenting Organisms, Intellectual Property Law Meets Biology*, *in* WHO OWNS LIFE? 27 (David Magnus et al. eds., 2002).
[78] Plant Patent Act, *supra* note 77.

to exclude any other party from asexually reproducing the patented plant.[79] Some argue that because this Act specifically excluded all organisms with the exception of a few species of asexually reproducing plants, Congress never intended it to enable the patentability of any natural subject matter beyond those particular plants.[80] To put things in perspective – in the 1930s, biologists were discovering the functions and structures of various cell parts, but they had yet to determine how chromosomes transmit genetic information.[81] Congress, presumably not comprised of a team of scientists, could not have imagined the progression of science beyond when the Act was passed in 1930.

Despite the statutory patent protection of plant matter, the Supreme Court struggled to delineate the bounds of patentability with regard to other natural elements.[82] In 1948, the Supreme Court addressed the question of whether an "inoculant for leguminous plants comprising a plurality of selected mutually non-inhibitive strains of different species of bacteria of the genus Rhizobium" was patentable in *Funk Bros. Seed Co. v. Kalo Inoculant Co.*[83] In *Funk Bros.*, the Court concluded that the particular strains of bacteria at issue were not patentable on the grounds that the patentee did not disclose an invention within the meaning of the patent statute.[84] The Court found that "patents cannot issue for the discovery of the phenomena of nature" and "[i]f there is to be invention from such a discovery, it must come from the application of the law of nature to a new and useful end."[85] The decision, however, was not unanimous. The dissent noted that although the subject matter sought to be patented was not *exactly* a plant, the material functioned similarly enough to one.[86]

The first major amendments to the patent law doctrine as it is known today were made in 1952.[87] The Plant Patent Act provisions of 1930 were originally designed to serve as amendments to the general patent law, but in 1952, Congress collected the provisions codifying the right to patent certain plants in chapter 15 of title 35

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[79] Wilson, *supra* note 77, at 27.
[80] *Id.* at 30 ("[I]f we presume, as we must, that the Plant Protection Act was not superfluous, then we must conclude that it was the intent of Congress not to include living things other than new varieties of plants as patentable subject matter.").
[81] RESNIK, *supra* note 12, at 14.
[82] *See generally* Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127 (1948).
[83] *Id.* at 128.
[84] *Id.* at 132.
[85] *Id.* at 130.
[86] *See id.* at 138 (Burton, J., dissenting) ("While this patent may not be technically a 'plant patent' in the precise sense in which that term is used in this Section, the references in the Section to the differences in descriptions expected in mechanical patents and plant patents obviously support the position here taken.").
[87] RESNIK, *supra* note 12, at 34.

of the United States Code.[88]

The evolution of the subject matter requirement under the current patent statute supports the patentability of gene sequencing. In 1952, Congress collected all of the provisions relating to plant patents in a separate chapter, and in doing so, they amended the text of 35 U.S.C. § 101, which codifies what subject matter is patentable.[89] The former version of § 101 granted patent protection to any discovery or invention of a "new and useful *art*, machine, manufacture, or composition of matter, or any new or useful improvement thereof."[90] In 1952, the word "art" was amended to "process."[91] The reasoning behind the change was stated in Senate Report 82-1979: to clarify the patentability of certain types of processes or methods.[92] The Senate further elaborated that patentable subject matter includes "anything under the sun that is made by man," so long as the conditions of the title are satisfied.[93] The change of § 102 language from "art" to "process" was well aligned with the subject matter jurisprudence at the time. However, the Senate's elaboration on the definition of patentable subject matter expresses the difficulty courts face, even today.

In 1957, the Court of Appeals for the Fourth Circuit considered whether a patent claiming a vitamin B_{12}-active composition was valid in *Merck*, as briefly discussed *supra* in Part I.B.[94] In that case, Merck filed for a patent containing three product claims for its invention – an isolated and purified form of vitamin B_{12}.[95] The vitamin B_{12} composition, as claimed in the patent, was extracted and purified through the fermentation of a specific strain of

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[88] S. REP. NO. 82-1979, at 2400 (1952). *See* 35 U.S.C. § 161 (2006) (allowing patents on plants that were invented or discovered *and* asexually reproduced "any distinct and new variety of plant, including cultivated sports, mutants, hybrids, and newly found seedlings, other than a tuber propagated plant or a plant found in an uncultivated state"); *see also* Ann K. Wooster, Annotation, *Construction and Application of Plant Patent Act*, 135 A.L.R. FED. 273, § 2 (1996).

[89] *See* S. REP. NO. 82-1979, *supra* note 88.

[90] *Id.* at 2398 (quoting 35 U.S.C. § 101 (2006)) (emphasis added).

[91] *Id.*

[92] *Id.* at 2399.

[93] *Id.*; MANUAL OF PATENT EXAMINATION AND PROCEDURE, *supra* note 10, at § 2105; *See also* Diamond v. Chakrabarty, 447 U.S. 303 (1980).

[94] Merck & Co. v. Olin Mathieson Chem. Corp., 253 F.2d 156 (4th Cir. 1958).

[95] *Id.* at 157-60; U.S. Patent No. 2,703,302 (filed Dec. 8, 1952). Vitamin B_{12} as defined by the *Compact Oxford English Dictionary*, is "any of a group of substances essential for the working of certain enzymes in the body, including . . . cyanocobalamin (vitamin B_{12})." COMPACT OXFORD ENGLISH DICTIONARY OF CURRENT ENGLISH, *supra* note 62, at *Vitamin B_{12}*. Claim 1 of the patent reads as follows:

> 1. A vitamin B_{12}-active composition comprising recovered elaboration products of the fermentation of a vitamin B_{12}-activity producing strain of Fungi selected from the class consisting of Schizomycetes, Torula, and Eremothecium, the L.L.D. activity of said composition being at least 440 L.L.D. units per milligram and less than 11 million L.L.D. units per milligram.

Merck, 253 F.2d at 157-58 (quoting '302 Patent).

fungi.[96] For almost thirty years prior to the filing of the patent in 1952, pernicious anemia patients were being treated by ingesting substantial amounts of cattle liver.[97] Since 1926, scientists struggled to identify and isolate the anti-pernicious anemia factor from liver, without success.[98] In 1947, the patentee, Merck, was able to isolate a relatively pure, crystalline vitamin B_{12} composition from the fermentation products derived from the growth of several species of microorganisms.[99] This substance was claimed in Merck's patent, U.S. Patent No. 2,703,302.[100] It is critical to note, as the court did, that "[t]he claims of [the] patent do not reach pure, crystalline vitamin B_{12}, for they are restricted to compositions having a maximum LLD activity which is less than that of the pure substance. The claims do not cover vitamin B_{12} compositions derived from liver or any source other than the specified fermentates."[101] While crystalline vitamin B_{12} is present in cattle liver, it is only found in very minute quantities, is highly potent, and is highly expensive to extract.[102] The court describes the benefits of the patented product: "[the composition is] available in much more abundant supply and, relatively . . . cheap. [Its] potency and dosage may be precisely controlled. [It is] free of toxic substances and may be readily taken by persons whose idiosyncratic digestions do not permit them to tolerate liver materials."[103]

The defendant's main contention was that the patent should be invalid on subject matter grounds because the invention allegedly covered a "product of nature."[104] The Fourth Circuit considered the subject matter argument in great detail, relying primarily on *American Wood-Paper*,[105] *Funk Bros.*,[106] and *Parke-Davis*.[107] Section 101 of the Patent Act of 1952, 35 U.S.C. § 101, authorizes patents for any "new and useful . . . composition of matter."[108] The *Merck* court considered what the statutory text of the new Patent Act meant when it referred to "composition of matter." The court held that "[a]ll of the tangible things with which man deals and

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[96] *Merck*, 253 F.2d at 157.
[97] *Id.* at 158.
[98] *Id.* at 158-59.
[99] *Id.* at 159. Shortly thereafter, other Merck scientists were able to extract and isolate the same from liver. *Id.* at 160. It was found to be identical in chemical structure to that extracted and purified from the aforementioned fermentates. *Id.*
[100] *Id.* at 159-60.
[101] *Id.* at 160.
[102] *Id.*
[103] *Id.* at 161 n.6.
[104] *Id.* at 160.
[105] Am. Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. 566 (1874).
[106] Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127 (1948).
[107] Parke-Davis & Co. v. H.K. Mulford Co., 189 F. 95 (C.C.S.D.N.Y. 1911), *aff'd in part*, 196 F. 496 (2d Cir. 1912).
[108] Patent Act of 1952, 35 U.S.C. § 101 (2006).

for which patent protection is granted are products of nature in the sense that nature provides the basic source materials. The 'matter' of which patentable new and useful compositions are composed necessarily includes naturally existing elements and materials."[109]

The *Merck* court separated the issue into two main inquiries – first, whether the patent in question is an old product derived by a new and patentable process, and second, whether every step of the purification of a new product is a patentable advance.[110] While considering the first inquiry, the court relied primarily on *American Wood-Paper*[111] to contemplate the line between patentable and unpatentable isolated substances. In *American Wood-Paper*, the claimed cellulose was slightly more pure than its previously known form, with no novel process used to create it.[112] A simple increase in its level of purity did not rise to the level required for patentability.[113] In *Merck*, while B_{12} was a known vitamin, the extraction and the purification of B_{12}-active compositions from substances other than liver were never previously known in the field.[114] Before the patentee invented the claimed composition, there were no known active B_{12} compositions derived from fermentates, particularly the ones specified in the claims.[115] The patented vitamin compositions had many substantial advantages, some of which were discussed earlier.

For the second inquiry, the court relied on *Parke-Davis* to note that an article that differs in degree of purity and kind from its naturally-occurring form is patentable.[116] When an article is purified, but retains all of the same utility and properties as the naturally occurring substance, it is not patentable. The court in *Merck* established the general rule in the subject matter doctrine that still stands today: isolating and purifying a substance derived from nature may be patentable so long as the result differs *in kind* from the naturally occurring substance.[117] The patentability of such substances varies on a case-by-case basis according to their unique facts.

Between 1958 and 1980, the USPTO and federal courts were presented with a new subject matter issue: how to deal with the

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[109] Merck & Co. v. Olin Mathieson Chem. Corp., 253 F.2d 156, 161-62 (4th Cir. 1958).
[110] *Id.* at 162.
[111] Am. Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. 566 (1874).
[112] *Id.* at 567.
[113] *Id.*
[114] *Merck*, 253 F.2d at 161.
[115] *Id.* at 160-61.
[116] *Id.* at 163.
[117] *Id.* at 163-64.

patentability of software.[118] As with all other fields of emerging technologies, many opponents to the patentability of software feared that allowing software to be patented would be detrimental to the development of the field.[119] In 1968, the USPTO issued guidelines regarding the patentability of software, generally stating that software was not patentable subject matter unless it was embodied in a mechanical device.[120] Hardware manufacturers expressed their concern that patents on software might "limit the use of their computers."[121] Other parties voiced their concerns over issues that may arise when those who are trying to develop new programs would not know when their experimental use was infringing, thus possibly inhibiting advancement in the field.[122] Another view was that granting patents in the field would inhibit the growth of the industry as a whole because the larger firms with more resources would monopolize certain concepts and "freeze out" smaller firms, eventually creating an oligopoly.[123] While courts eventually allowed the patenting of software with certain restrictions, the concerns voiced during the 1960s and 1970s about granting software patents were very similar to, if not the same as, the arguments made by opponents to synthetic biology patents today.

The United States Supreme Court visited the issue of what extent to allow the patenting of living microorganisms in 1980, when it issued its landmark decision in *Diamond v. Chakrabarty*.[124] In *Chakrabarty*, the Court found that the bacterial microorganisms produced by Ananda Chakrabarty as the products of genetic engineering were not barred from patent protection under 35 U.S.C. § 101.[125] Chakrabarty filed a patent application in 1972 asserting thirty-six claims relating to Chakrabarty's invention of a particular bacterium from the genus *Pseudomonas*, containing at least two stable plasmids.[126] The decision has since been cited countless

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[118] *See, e.g.*, Gottschalk v. Benson, 409 U.S. 63, 64-73 (1972) (holding that the method for converting numerical information from binary-coded decimal numbers into pure binary numbers, for use in computer programming, is merely a series of mathematical calculations or mental steps; for this reason, this method does *not* constitute a patentable "process" within the meaning of the Patent Act).

[119] *See* James Allan Stuckey, Note, *Patent Law – Process Claim Involving Computer Program Meets Statutory Subject Matter Requirements*, 56 TUL. L. REV. 785, 800 n.83 (1982) (explaining the software patenting debate in greater detail).

[120] Stacy V. Jones, *Computer Software Unpatentable*, N.Y. TIMES 59, Oct. 23, 1968, at 59.

[121] *Id.*

[122] *Id.*

[123] Dale W. Clauson, William E. Spaulding & Thomas R. Wotruba, *Content Analysis: An Approach to the Computer Software Protection Controversy*, 17 AM. BUS. L.J. 175, 189 (Summer 1979).

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

[125] *Id.* at 318; *see also* MANUAL OF PATENT EXAMINING PROCEDURE, *supra* note 10, at § 2105.

[126] *Chakrabarty*, 447 U.S. at 305.

times in the biotechnology arena for the proposition that "anything under the sun that is made by man" is patentable.[127] The Court's decision relied, in part, on the Plant Patent Act of 1930, and the legislature's intent in creating it.[128] What marked the change from *Funk Bros.* to *Chakrabarty*? In *Funk Bros.*, the Court seemed remarkably against the patentability of natural phenomena.[129] Scholars have long pontificated this question and have proposed a variety of ideas, such as factual differences,[130] the breadth of the amended 1952 Patent Act,[131] or the possibility that the Court in *Funk Bros.* was actually speaking to the non-obviousness or "invention" requirements, and not the subject matter doctrine.[132] The general proposition that anything made by man may be patentable begins to support the idea that the isolation and purification of a naturally occurring substance is patentable because it reinforces the concept of the earlier stages of United States patent law.

However, neither *Funk Bros.* nor *Chakrabarty* expressly allows for the patenting of human gene sequences or any other isolated or purified naturally occurring substances. In the years following the *Chakrabarty* decision, as the biotechnology field advanced, the number of patents applied for and issued in the field duly increased. Around the time of *Chakrabarty* through 2002, the USPTO issued approximately 16,000 patents relating to DNA alone.[133] In 1990, the United States Department of Energy and National Institute of Health initiated the U.S. Human Genome Project, which included the goals of identifying all of the genes present in human DNA and determining all the chemical base pairs that make up human DNA.[134] During the project's lifespan,

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[127] *Id.* at 309 (quoting S. REP. NO. 82-1979, at 2400 (1952)).

[128] *Chakrabarty*, 447 U.S. at 310-14.

[129] Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948) ("Their qualities are the work of nature. Those qualities are of course not patentable. For patents cannot issue for the discovery of the phenomena of nature.").

[130] The Court itself makes this argument in its decision, suggesting that the art in *Funk Bros.* was not one of the patentable "laws of nature, physical phenomena, and abstract ideas." *Chakrabarty*, 447 U.S. at 309. Chakrabarty himself also differentiates his own findings from *Funk Bros.* in his appellate brief. Brief of Petitioner at 12-14, *Diamond v. Chakrabarty*, 447 U.S. 303 (1980) (No. 79-136).

[131] Robert Greene Sterne & Lawrence B. Bugaisky, *The Expansion of Statutory Subject Matter Under the 1952 Patent Act*, 37 AKRON L. REV. 217, 218 (2004) ("That decision resulted, at least in part, from the absence of express exclusionary language in the Patent Act. The Court noted that 'in choosing such expansive terms as 'manufacture' and 'composition of matter,' modified by the comprehensive 'any,' Congress plainly contemplated that the patent laws be given wide scope.'"); *see also Patentability of Living Microorganisms:* Diamond v. Chakrabarty, 94 HARV. L. REV. 261, 265 (1980).

[132] Wilson, *supra* note 77, at 32.

[133] *See* RESNIK, *supra* note 12, at 1.

[134] Human Genome Project, About the Human Genome Project, http://www.ornl.gov/sci/techresources/Human_Genome/project/about.shtml (last visited Feb. 7, 2008).

government investment in genes and biotechnology doubled, and the investment by the private sector increased almost tenfold.[135] The explosion of the biotechnology sector did not come without reservation.

Concern about the long-term impact of allowing such biotech patents reached everyone from the USPTO to Congress. On February 18, 1993, Senator Mark Hatfield (R-Oregon) introduced a bill to amend title 35 of the United States Code. This bill proposed a two year cessation of patents with subject matter such as human tissues and organs, human gene cells, and animal organisms in order to "provide time for Congress to fully assess, consider and respond to the economic, environmental and ethical issues raised by the patenting of such entities, and for other purposes."[136] The bill was passed along to the Judiciary Subcommittee on Patents, Copyrights and Trademarks; however, the Clinton administration opposed the bill on the ground that it would adversely affect biotechnology research and investment, and the bill did not proceed past the Subcommittee.[137] The concern did not pass completely unnoticed, because in November of 1999, the USPTO issued new Utility Guidelines, which will be discussed in Part II, *infra*, that addressed the concerns of the public.[138] One such concern alluded to the point that neither *Funk Bros.* nor *Chakrabarty* expressly stated that genetic sequences are patentable, and also that the USPTO should seek guidance from Congress to determine their patentability.[139] The USPTO rejected this proposition, and in response, cited the legislative history of 35 U.S.C. § 101, as well as *Chakrabarty*, to support the patentability of gene sequences and similar inventions or discoveries.[140]

The current text of the United States patent statute appears to support the general proposition that any extracted or purified substance is patentable. Under 35 U.S.C. § 101, "Whoever invents or discovers any new and useful process, machine, *manufacture, or composition of matter, or any new and useful improvement thereof*, may

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[135] See Human Genome Project Budget, http://www.ornl.gov/sci/techresources/Human_Genome/project/budget.shtml for a breakdown of government funding for the project from 1988 to 2003.

[136] 123 CONG. REC. 1887 (1993) (referring to S. 387, 103d Cong. (1st Sess. 1993)); *see also* Anna Lumelsky, Diamond v. Chakrabarty*: Gauging Congress's Response to Dynamic Statutory Interpretation by the Supreme Court*, 39 U.S.F. L. REV. 641, 669 (2005).

[137] 1993 USPTO ANN. REP. 30.

[138] Revised Utility Examination Guidelines, 64 Fed. Reg. 71,440 (Dec. 21, 1999) (with a correction at 65 Fed. Reg. 3425 (Jan. 21, 2000)).

[139] Public Comments on the United States Patent and Trademark Office "Revised Interim Utility Examination Guidelines," http://www.uspto.gov/web/offices/com/sol/comments/utilguide/index.html at cmt. 3 (last visited Oct. 5, 2008).

[140] Revised Utility Examination Guidelines, *supra* note 138.

obtain a patent therefore, subject to the conditions and requirements of this title."[141] The Manual of Patent Examining Procedure ("MPEP") examines 35 U.S.C. § 101 in light of patents for living subject matter, such as microorganisms, gene sequences, or other naturally occurring materials.[142] The MPEP notes that *Chakrabarty* interpreted the term "manufacture" to mean "the production of articles for use from raw materials prepared by giving to these materials new forms, qualities, properties, or combinations whether by hand labor or by machinery."[143] The MPEP currently still quotes *Diamond v. Chakrabarty* to stand for the proposition that living subject matter is patentable so long as all other statutory requirements have been met.[144] Since the decision in *Chakrabarty*, the Supreme Court has not considered the question of patentability of such subject matter, indicating that the law is well-settled and has been for the past twenty-five years. That the MPEP still quotes *Chakrabarty* despite all of its revisions in recent years demonstrates that further subject matter jurisprudence has been curbed.[145]

Those who wish to challenge the patentability of isolated and purified substances on the bases of subject matter and novelty will face a rather formidable challenge: the historically rooted, well-established doctrines. Historically, the subject matter and novelty doctrines have created obstacles and points of contention in the field of biotechnology patents; however, the law appears to be well-settled at this point. The focus of concern should be, and has shifted to, the other two doctrinal hurdles to patentability: utility and obviousness. In the past ten years, both utility and obviousness have undergone major changes, which may, in turn, silence the concerns about gene sequence patenting once placed on the subject matter and novelty doctrines.

II. CURRENT CONCERNS: UTILITY AND OBVIOUSNESS REQUIREMENTS

A. *The Utility Requirement*

A historical analysis of the utility requirement through recent case law suggests that the isolation and purification of any naturally occurring substance can be patentable in light of the utility requirement, so long as its utility *is specific to the claimed invention.* As aforementioned, in November of 1999, the USPTO issued a

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[141] 35 U.S.C. § 101 (2006) (emphasis added).
[142] *See* MANUAL OF PATENT EXAMINING PROCEDURE, *supra* note 10, at § 2105.
[143] *See id.* (quoting Diamond v. Chakrabarty, 447 U.S. 303, 308 (1980)).
[144] MANUAL OF PATENT EXAMINING PROCEDURE, *supra* note 10, at § 2105.
[145] *Cf. In re* Nuijten, 500 F.3d 1346, 1348 (Fed. Cir. 2007) (holding that signals with embedded digital watermarks encoded in accordance with a specific process were not patentable subject matter under 35 U.S.C. § 101).

new set of utility requirements for patents claiming genetic sequences.[146] A final version of the USPTO's revised Guidelines was issued in 2001.[147] This new set of Guidelines raised the requisite level of utility to obtain a biotechnology patent. The heightened standard for utility of DNA-related patents in particular was reinforced in the Federal Circuit's 2005 *In re Fisher* decision, where a split Federal Circuit held that the invention of expressed sequence tags ("ESTs") for identifying nucleic acid in maize plants was not patentable due to lack of utility.[148] The court's decision rested in part upon the fact that "all of Fisher's asserted uses represent merely hypothetical possibilities, objectives which the claimed ESTs, *or any EST for that matter*, could possibly achieve, but none for which they have been used in the real world."[149]

The utility requirement of 35 U.S.C. § 101 is one that is rarely visited by the court system, and when the *In re Fisher* decision came out, the patent world was quick to question the implications of such a decision.[150] However, a careful examination of the decision, and the absence of similar decisions since, suggests that the implications for the biotechnology patent field are, perhaps, not as great as originally anticipated. The USPTO Utility Guidelines increased the general standards for examining patents on human gene sequences, amongst other art.[151] The changes in the Guidelines heavily incorporated the concept that utility for such patents must be "specific and substantial," as derived from the Supreme Court's decision in *Brenner v. Manson*, which judicially created such a requirement.[152] The change may be attributed to the increase in patent applications,[153] the moral and ethical concerns behind the patenting of the *human* genome,[154] as well as the general concerns similar to those raised in Congress regarding the overall patentability of gene sequences.[155]

In the case of *In re Fisher*, the claimed invention was five puri-

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[146] Revised Utility Examination Guidelines, *supra* note 138.
[147] *Id.*
[148] *In re* Fisher, 421 F.3d 1365 (Fed. Cir. 2005).
[149] *Id.* at 1373 (emphasis added).
[150] *See, e.g.*, Bryan J. Boyle, Comment, *Fishing for Utility with Expressed Sequence Tags After* In re Fisher, 23 SANTA CLARA COMPUTER & HIGH TECH. L.J. 589 (2007); Joshua Kim, Comment, *Fisher of Genes: Patentability of Expressed Sequence Tags*, 29 HASTINGS COMM. & ENT. L.J. 401 (2007).
[151] Revised Utility Examination Guidelines, *supra* note 138.
[152] *Id.*; Brenner v. Manson, 383 U.S. 519 (1966).
[153] Carol Lee Johnson, *The Continuing Inability for Judges to Pass Their Markman Tests: Why The Broken System Leaves Judges Behind, Confused and Demoralized*, 941 PRAC. L. INST./PAT. 65, 143 (2008) ("The technical complexity of patent applications has increased significantly, with biotechnology, related patent filings increasing 46 percent and pharmaceutical and chemical related filings increasing 42 percent.").
[154] *See generally*, RESNIK, *supra* note 12.
[155] S. 387, *supra* note 138.

fied nucleic acid sequences that encode proteins and protein fragments in maize plants.[156] The application set forth the following uses in an attempt to meet the utility requirement of 35 U.S.C. § 101:

> (1) serving as a molecular marker for mapping the entire maize genome, which consists of ten chromosomes that collectively encompass roughly 50,000 genes; (2) measuring the level of mRNA in a tissue sample via microarray technology to provide information about gene expression; (3) providing a source for primers for use in the polymerase chain reaction ("PCR") process to enable rapid and inexpensive duplication of specific genes; (4) identifying the presence or absence of a polymorphism; (5) isolating promoters via chromosome walking; (6) controlling protein expression; and (7) locating genetic molecules of other plants and organisms.[157]

The examiner rejected the application, in part, because she found that the aforementioned uses were not of a "specific and substantial" nature.[158] The question of whether an application discloses sufficient utility is one of fact, and on appeal, the Federal Circuit reviews the Board's decisions for being supported by "substantial evidence."[159] The Federal Circuit found that the Board's decision, was, in fact, supported by substantial evidence.[160] The court agreed with the government and the *amici* that the seven utilities alleged by Fisher were "merely starting points for further research, not the end point of any research effort,"[161] meaning that the patent does not meet the "specific and substantial" utility requirement.[162] The court noted that the Supreme Court's *Brenner v. Manson* decision of 1966, while establishing the "specific and substantial" utility requirement, did not fully define what the terms meant.[163] The Federal Circuit found that "specific" meant that "an

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[156] *In re* Fisher, 421 F.3d 1365, 1367 (Fed. Cir. 2005).
[157] *Id.* at 1368.
[158] *Id.*
[159] *Id.* at 1369.
[160] *Id.* at 1379.
[161] *Id.* at 1370.
[162] The Federal Circuit relied upon the Supreme Court's decision in *Brenner v. Manson*, 383 U.S. 519 (1966) to find the "specific and substantial" requirement. *In re Fisher*, 421 F.3d at 1371 ("Following *Brenner*, our predecessor court, the Court of Customs and Patent Appeals, and this court have required a claimed invention to have a specific and substantial utility to satisfy § 101."). *See also, e.g.*, Fujikawa v. Wattanasin, 93 F.3d 1559, 1563 (Fed. Cir. 1996) ("Consequently, it is well established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed.").
[163] *In re Fisher*, 421 F.3d at 1371. In *Brenner v. Manson*, the Supreme Court considered whether "the practical utility of the compound produced by a chemical process is an essential element in establishing a prima facie case for the patentability of the process." 383 U.S. 519, 520 (1966).

application must disclose a use which is not so vague as to be meaningless . . . . [and] must also show that that claimed invention can be used to provide a well-defined and particular benefit to the public."[164] The court found that the substantial requirement can be met if "that claimed invention has a significant and presently available benefit to the public."[165] In assessing the uses asserted by Fisher, the Federal Circuit found that the claimed uses did not meet either requirement, because they did not correlate to an underlying gene of a known function.[166]

While some see the *In re Fisher* decision as being a major roadblock to the patentability of gene sequences,[167] the decision itself need not be read so broadly as to prohibit the patentability of *any* gene sequences. Instead, a careful look at the decision suggests that the Federal Circuit did not wish to go quite so far.[168] Both the government and the *amici* put forth arguments that if such a patent was allowed, there would be an onslaught of patent applications for particular ESTs at the USPTO, and further research would be inhibited.[169] The parties argued that allowing claims like Fisher's "would give rise to multiple patents" for ESTs "relating to the same underlying gene and expressed protein," causing "convoluted licensing environment[s] for those interested in researching that gene and/or protein."[170] Instead of addressing this issue, the court punted the issue "to Congress as the legislative branch of government."[171] Recognizing that the court chose not to address the issue in its decision implies that the *In re Fisher* court merely used the opportunity to define the standards necessary to meet the "substantial and specific" utility requirement, but not address the issue of patentability of expressed sequence tags altogether. What

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[164] *In re Fisher*, 421 F.3d at 1371.

[165] *Id.* The Federal Circuit based these definitions on *Cross v. Iizuka*, 753 F.2d 1040 (Fed. Cir. 1985), *Nelson v. Bowler & Crossley*, 626 F.2d 853 (C.C.P.A. 1980), and *In re Kirk*, 376 F.2d 936 (C.C.P.A. 1967). *Id.*

[166] *In re Fisher*, 421 F.3d at 1374.

[167] *See, e.g.*, N. Scott Pierce, In re Dane K. Fisher*: An Exercise in Utility*, 6 J. HIGH TECH. L. 1 (2006); Lillian Ewing, Note, In re Fisher*: Denial of Patents for ESTs Signals Deeper Problems in the Utility Prong for Patentability*, 8 MINN. J. L. SCI. & TECH. 645 (2007); Kim, *supra* note 150. *Cf.* Boyle, *supra* note 150.

[168] *In re Fisher*, 421 F.3d at 1374.

[169] *See, e.g.*, Brief for Eli Lilly & Co. et al. as Amici Curiae Supporting Appellants at *4, *In re* Fisher, 421 F.3d 1365 (Fed. Cir. 2005) (No. 04-1465), 2004 WL 4996616 ("Fisher seeks a patent covering an 'invention' not yet complete or sufficiently definite to be adequately described, nor explored enough to provide specific benefit in currently available form. Fisher seeks a patent that would deter every other scientist from investigating *any* use of a large number of genetic sequences – none of which Fisher has discovered or adequately described, and which provide only a partial sequence, at best, for unidentified proteins having unspecified uses. Fisher fails to identify any use for these sequences, other than speculative research. In short, Fisher seeks to preempt other scientists from entire fields of research.").

[170] *In re Fisher*, 421 F.3d at 1378.

[171] *Id.*

patent seekers can gain from the *In re Fisher* decision is *not* that gene sequences are unpatentable. Instead, they may gain the understanding that, in order to meet the utility requirement, the patentee must assert uses that are not true of *any* expressed sequence tag, but which are more specific to the function of the underlying gene.[172]

While the utility doctrine remained stagnant for many years, the USPTO's revised Utility Guidelines marked the beginning of a movement to possibly lessen the fears of the opponents to synthetic biology patents. The *Fisher* decision did its part to relieve concern as well. By classifying gene sequences and other products of biotechnology patents as "human life," the opponents to such patents may not be able to imagine how the subject matter and novelty doctrines could possibly allow such patents.[173] However, both doctrines are, at this point in time, well-established.[174] The utility requirement was largely ignored for many years, but as the USPTO examined patent law under the scope of these concerns, the long-ignored doctrine was revisited. In accordance with the revisions to the Utility Guidelines[175] and *Fisher*, the USPTO and Federal Circuit raised the utility bar for biotechnology patents. The change in the doctrine addresses some of the concerns of those who are opposed to the patenting of gene sequences. Like with all emerging fields, one concern is that allowing gene patenting would cause an onslaught of patents that would flood the USPTO, thus inundating an office already understaffed.[176] Another general concern is that "patent trolls" will be granted with patents in an underdeveloped field and seek exorbitant licensing fees once a researcher discovers an actual use for the patented art.[177] The heightened utility guidelines speak to both of these concerns, ensuring that those who seek patent protection for gene sequences with legitimate, established utilities will receive that protection. But those who seek patents on undeveloped or generically useful sequences, or mere incremental advances in the art of gene sequences, will not receive the protections they desire.[178]

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[172] *See* Boyle, *supra* note 150.

[173] *See, e.g.*, Leon R. Kass, *Triumph or Tragedy? The Moral Meaning of Genetic Technology*, 45 AM. J. JURIS. 1 (2000); David B. Resnik, *The Morality of Human Gene Patents*, 7:1 KENNEDY INST. ETHICS J. 43 (1997).

[174] *See, supra*, Parts I.B-C.

[175] Revised Utility Examination Guidelines, *supra* note 138.

[176] *See* RESNIK, *supra*, note 12, at 9, 60.

[177] Lemley, *supra* note 21, at 630. *See also, e.g.*, Brief for Eli Lilly & Co., *supra* note 168, at *4.

[178] *In re* Fisher, 421 F.3d 1365 (Fed. Cir. 2005).

B. *Obviousness Requirement*

Another large obstacle to obtaining biotechnology patents faced at the present will most likely be the Supreme Court's recent decision in *KSR v. Teleflex.*[179] While the decision was based upon a mechanical patent for adjusting the pedal placement in cars, the Supreme Court eliminated the Federal Circuit's strict reliance on the teaching, suggestion, or motivation test ("TSM test"), which applies to obviousness review for all patents, not only mechanical ones.[180] The elimination of such a test has not yet been sufficiently examined in the biotechnology field in order to fully determine the total impact of the decision on patenting extracted or purified naturally occurring substances, such as gene sequences. However, a thorough examination of the decision in *KSR* in light of the prior *In re Fisher* decision demonstrates that, while extracted and purified substances will likely still be patentable, the number of patents that can be obtained in the field will likely decrease. Not only will inventions require a greater level of utility to sustain patentability under *In re Fisher*, but they will also require a more concrete level of non-obviousness under *KSR*.

The Supreme Court in *KSR* released the formerly rigid test for obviousness in patents.[181] In *KSR*, Teleflex held the single license for the asserted patent, an adjustable pedal assembly with electronic throttle control.[182] The asserted claim of the patent, Claim 4, described a mechanism for combining an electronic sensor with an adjustable automobile pedal.[183] KSR's defense against the asserted claim of patent infringement was that a claim for the assembly was obvious, which allowed the Court to revisit the 35 U.S.C. § 103 obviousness standard.[184] The district court initially applied the old standard, known as the *Graham* framework, which requires:

> Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the

[179] KSR Int'l Co. v. Teleflex, Inc., 127 S. Ct. 1727 (2007).
[180] *Id.*
[181] *See id.* at 1734-35.
[182] *Id.* at 1734.
[183] *Id.*
[184] *Id.*

subject matter sought to be patented.[185]

However, the district court, restricted by recent Federal Circuit decisions, was required to apply the TSM test.[186] The district court found that the claim was obvious under both standards, but the Federal Circuit reversed on the grounds that the district court allegedly did not apply the TSM test strictly enough.[187] The Federal Circuit found that the district court failed to make "'finding[s] as to the specific understanding or principle within the knowledge of a skilled artisan that would have motivated one with no knowledge of [the] invention' . . . to attach an electronic control to the support bracket of the Asano assembly."[188] The Federal Circuit held that genuine issues of material fact precluded summary judgment.[189] The Supreme Court granted certiorari to answer the following question: whether a Circuit Court's practice of applying the TSM test is proper in light of 35 U.S.C. § 103, and Supreme Court precedent.[190] The test, as defined by the Court, was that where a patent claim is only proved obvious if "'some motivation or suggestion to combine the prior art teachings' can be found in the prior art, and the nature of the problem, or the knowledge of a person having ordinary skill in the art,"[191]

The Supreme Court rejected the "rigid" standard of applying the teaching, suggestion, or motivation test as applied by the Federal Circuit Court.[192] Instead, the Supreme Court began by reasoning that, as prior obviousness decisions have made clear, "the analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ."[193] In other words, instead of looking for a specific teaching, suggestion, or motivation in the prior art to determine whether an invention is "obvious," a court or patent examiner must reason much like someone with skill in the art – with a reasonable degree of creativity and inferences.[194] The Supreme Court did not go so far as to demand that the test be eliminated.[195] The Court noted that the TSM test was a "helpful insight" but did not need to evolve into the rigid and mandatory

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[185] *Id.* (citations and quotations omitted).
[186] *See id.* at 1737-38.
[187] *KSR*, 127 S.Ct .at 1734.
[188] *Id.* at 1738 (citation omitted).
[189] *Id.* at 1739.
[190] *Id.* at 1734.
[191] *Id.*
[192] *Id.* at 1739.
[193] *Id.* at 1741.
[194] *Id.*
[195] However, the practical effect is that the test really need not be used.

test as applied by the Federal Circuit in this case. Consequently, this test was no longer the standard for obviousness.[196] The Court noted that in many fields of invention, market demand, not scientific literature, will motivate inventors.[197] The Supreme Court characterized the TSM test as a mere benchmark to help determine obviousness, instead of a bright-line rule.[198]

The widespread apprehension about the result in *KSR v. Teleflex* has been rooted in a general concern that U.S. patents will be nearly impossible to obtain.[199] Some have read the *KSR* decision to mean that the Supreme Court is urging lower courts and the USPTO to reject those patents considered to be mere marginal advances or obvious combinations driven by market forces.[200] By reducing the TSM test to an advisory rather than a mandatory measure, the Court requested that patents be examined in the same manner in which they were created: by employing the same level of creativity, ingenuity, and awareness of surroundings as would one who is of ordinary skill in the art.[201] Certainly, patents will be harder to obtain if the TSM test is more liberally applied as advisory or not applied at all; however, one should be cautious to read that the opinion suggests that patents will be nearly impossible to obtain.

In the few months following *KSR v. Teleflex*, federal district and circuit courts have handed down several decisions in the chemical and other non-mechanical fields which suggest that the obviousness standard, as altered by *KSR*, will not prove to have a substantial effect on non-mechanical patents.[202] On June 28, 2007, the Federal Circuit decided *Takeda v. Alphapharm*, the first major pharmaceutical decision related to obviousness following *KSR*.[203] In *Takeda*, Alphapharm filed an Abbreviated New Drug Application ("ANDA") pursuant to the Hatch-Waxman Act for a generic form of pioglitazone, asserting that Takeda's patent was invalid as

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[196] *KSR*, 127 S. Ct. at 1741.

[197] *Id.*

[198] Though, the practical effect of eliminating a test converts the "test" to a suggestion instead of black letter law.

[199] *See* Sarah Herbert & Charles Tansey, Australia: Will A US Patent Be More Difficult To Obtain After KSR v. Teleflex Inc? (Nov. 23, 2007), http://www.mondaq.com/article.asp?articleid=54558; Michael Orey & Arlene Weintraub, *A Higher Hurdle for Investors: Has it become too easy to win and defend patents? The Supreme Court says yes*, BUS. WK., May 14, 2007, *available at* http://www.businessweek.com/print/magazine/content/07_20/b4034049.htm?chan=gl.

[200] *See* Orey & Weintraub, *supra* note 199, at 38.

[201] *See generally* KSR Int'l Co. v. Teleflex, Inc., 127 S. Ct. 1727 (2007).

[202] These decisions include: Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd., 492 F.3d 1350 (Fed. Cir. 2007), Abbott Labs. v. Sandoz, Inc., 500 F. Supp. 2d 846 (N.D. Ill. 2007), and Astrazeneca AB v. Mylan Labs., Inc. (*In re* Omeprazole Patent Litig.), 490 F. Supp. 2d 381 (S.D.N.Y. 2007).

[203] *Takeda*, 492 F.3d 1350.

obvious under 35 U.S.C. § 103.[204] In determining whether Takeda's patent was obvious, the Federal Circuit took the opportunity to examine the *KSR* decision in the chemical field.[205] The court explained that *KSR* rejected a rigid application of the TSM test, and "acknowledged the importance of identifying 'a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does' in an obviousness determination."[206] In other words, the court went on to find that in cases involving chemical compounds, the TSM test can provide "helpful insight" or guidance, and the patent must still identify a reason that would have led a chemist of ordinary skill in the art to modify a known compound.[207]

Following the *Takeda* decision, district courts have not hesitated to cite to *Takeda* as evidence that the *KSR* decision has a limited holding in the field of chemical patents. In *Novartis v. Teva* and *Altana v. Teva*, the District Court of New Jersey cited the language of *Takeda*, requiring the identification of a reason that a chemist of ordinary skill would modify an existing or known compound.[208] Additionally, in both cases, the court noted that the *KSR* decision did appear to be limited in application to non-mechanical patents, particularly given that the *KSR* decision did not expressly overrule any prior precedent.[209]

While it is too soon to predict the consequences of the Supreme Court's decision, the likely result appears that the implications on the biotechnology field might prove to be serious in the long-run, but should not necessarily be severe. *KSR* did not overrule any prior precedent, and it did not completely render the TSM unusable.[210] The Supreme Court acknowledged the usefulness of the TSM test as an indicator and a benchmark, but found that the Federal Circuit's application of the test was improper. The decision in *KSR* reinforced the Supreme Court's view of what the 35 U.S.C. § 103 doctrine was designed to prevent, that one with ordinary skill in the art would not have been obviously lead to

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[204] *Id.* at 1354. An Abbreviated New Drug Application (ANDA) under the Hatch-Waxman Act is a more efficient way for a generic drug company to gain FDA approval after applicable patents on brand name drugs are expired or deemed invalid. Rebecca S. Eisenberg, *Pharma's Nonobvious Problem*, 12 LEWIS & CLARK L. REV. 375, 414 (2008).

[205] *See Takeda*, 492 F.3d at 1356-57.

[206] *Id.* (quoting *KSR*, 127 S. Ct. at 1731).

[207] *Id.* at 1357.

[208] Novartis Pharms. Corp. v. Teva Pharms. USA, Inc., No. 05-CV-1887, 2007 WL 2669338 (D.N.J. Sept. 6, 2007); Altana Pharma AG v. Teva Pharms. USA, Inc., 532 F. Supp. 2d 666 (D.N.J. 2007).

[209] *KSR*, 127 S. Ct. at 1743.

[210] *Id.* at 1731.

the invention seeking patent protection.[211] The Court found that strict adherence to the TSM test undercut the purpose of the § 103 doctrine, particularly in emerging fields of technology; this may present several unexplored questions that have yet to be questioned in scientific publications.[212] In the biotechnology field, which is still relatively new, as evidenced by the recent Watson and Venter discoveries,[213] the obviousness doctrine post-*KSR* would help to exclude the patenting of those advances which were generic and incremental. The *KSR* decision was not meant to make patenting impossible. Instead, the Supreme Court sought to reaffirm the goal of § 103 and reestablish the importance of the *Graham* factors to determine obviousness. Unfortunately, the Supreme Court did not express a particular method for discerning obviousness to replace the TSM test.[214] However, the Court did suggest that the best review of obviousness is to combine the use of the *Graham* factors and the TSM test to assist examiners in discerning what would be obvious to one with ordinary skill in the art at the time of the invention.[215]

Patents in the biotechnology realm may be slightly harder to obtain. However, in the months following *KSR*, the USPTO's Board of Patent Appeals and Interferences have been using *KSR* to reverse an examiner's finding as many times as it has affirmed an examiner's finding.[216] Its impact on the biotechnology sector may instead merely require a slightly higher degree of ingenuity to attain patents, much like what is called for under the utility doctrine.

III. ADDRESSING THE CONCERNS AGAINST PATENTING GENE SEQUENCES

Opponents to the patentability of isolated and purified substances such as gene sequences make many arguments, several of which are not founded on particularly persuasive principles, and others are no longer applicable under the current state of the law. In this section, I will attempt to address these concerns, in turn. My analysis is shaped in part by the recent shift in importance from the novelty and subject matter doctrines to the utility and obviousness doctrines, as discussed *supra* in Parts I & II.

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[211] *See id.* at 1734.
[212] *Id.* at 1743.
[213] *See* Wade, *supra* note 1.
[214] *See generally KSR*, 127 S. Ct. 1727.
[215] *Id.* at 1745.
[216] *See* Mark Nowotarski, Using *KSR* To Overcome an Obviousness Rejection, INTELL. PROP. TODAY, *available at* http://www.iptoday.com/articles/2007-09-nowotarski.asp ("It turns out that the Board is citing *KSR* just as often when it reverses an examiner as when it affirms an examiner. Apparently, the more flexible approach of *KSR* cuts both ways.")

In general, opponents assert two major arguments why gene sequences and other tools of synthetic biology should not be patentable. The first argument is that gene sequences should not be patentable because they are products of nature and the backbone of human life.[217] The second argument is that, by allowing patents on gene sequences, the United States is essentially allowing ownership of human life, which may be abused through hard bargains in licensing.[218]

A. *Product of Nature Argument*

The argument that products of nature cannot be patented has been argued countless times, and the law in the area is well-settled, as discussed *supra* in Part I. The Supreme Court's decision in *Diamond v. Chakrabarty* is the decision most frequently relied upon to suggest that biotechnology patents do, in fact, meet the subject matter requirements of 35 U.S.C. § 101. The MPEP even includes the decision in Section § 2105, which advises patent examiners how to deal with living subject matter.[219] In the case of "products of nature," the subject matter doctrine works closely with the novelty doctrine to require both a certain degree of human intervention – the extracting, isolating, and purifying – as well as an extraordinary difference in degree in kind – for example, extracting adrenalin, a base, from a salt that, without human intervention, would be poisonous to the human body.[220] Another way to look at it: if anything that originated in nature was not patentable, the United States would be granting very few patents. Depending on one's viewpoint, even some mechanical patents may be rooted in "products of nature."

The product of nature argument additionally relies on common misconceptions of what gene sequences are, and what patent protection will provide. A genome refers to an organism's complete set of DNA, deoxyribonucleic acid. A DNA sequence, or a genetic sequence, is the particular side-by-side arrangement of the chemical base pairs along the DNA strand.[221] The smallest organisms, bacteria, have around 60,000 base pairs, while a larger organism, such as a human, has around three million.[222] In other words, genes are made up of complex chemicals not much different than

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[217] See, *supra* note 15, for a list of readings further explaining this argument.
[218] See, *supra* notes 16 & 17, for a list of sources further detailing this argument.
[219] MANUAL OF PATENT EXAMINING PROCEDURE, *supra* note 10, at § 2105.
[220] *See* Parke-Davis & Co. v. H.K. Mulford Co., 189 F. 95 (C.C.S.D.N.Y. 1911), *aff'd in part*, 196 F. 496 (2d Cir. 1912).
[221] Human Genome Project, The Science Behind the Human Genome Project, http://www.ornl.gov/sci/techresources/Human_Genome/project/info.shtml (last visited Feb. 3, 2008).
[222] *Id.*

those of a pharmaceutical. The only main difference is that gene sequences generally will occur naturally without human intervention, and pharmaceuticals require a certain degree of human intervention. However, gene sequences that could possibly warrant patent protection require a similar degree of human effort as the generation of a pharmaceutical. Sequences that are granted patent protection have specific functions that have been found through extensive experimentation.

Some examples of patented gene sequences include a sequence that serves as a marker for non-small cell lung carcinoma enabling detection and treatment of the disease,[223] a gene sequence for a novel strain of fungus *Aspergillus niger* that produces very high levels of a catalase that assists in the neutralization of hydrogen peroxide,[224] and a sequence that functions as an indicator of retinoid action in psoriatic skin.[225] The heightened utility requirements discussed *supra* in Part.II.A ensure that a gene sequence is not patentable unless it meets all the statutory requirements of the patent doctrine, *and* the application discloses a specific and substantial utility such as the ones disclosed by the patents listed above. A gene sequence is not eligible for patent protection if it merely exists in nature. The invention must include an isolating and purifying step in addition to a result that has a commercial value or extraordinary purpose, meaning that patent protection will not be granted to gene sequences as they are discovered by scientists. For example, in U.S. Patent 5,650,279, the sequence claimed is complementary to a sequence that is only expressed in mammalian cells *after* treatment with a specific chemical.[226] If the USPTO were to cease all patenting on gene sequences because technically gene sequences *as a whole* are originally derived from nature or could be naturally occurring, it would need to reconsider patents in the entire chemical and pharmaceutical fields.

Subject matter no longer appears to be the important argument to be made to the USPTO. Since 1980, the Supreme Court and the Federal Circuit have not considered in depth any major adjustments to the current subject matter doctrine. Instead, the USPTO has evaluated 35 U.S.C. § 101 in a new way, through revising the utility doctrine. This notion is best supported by the 1999 Amendments to the USPTO Guidelines[227] and their interpretation

[223] U.S. Patent No. 5,589,579 (filed July 19, 1994).
[224] U.S. Patent No. 5,360,901 (filed Mar. 4, 1992).
[225] U.S. Patent No. 5,650,279 (filed Jan. 27, 1995).
[226] *Id.*
[227] Revised Utility Examination Guidelines, *supra* note 138.

as discussed in the *In re Fisher* decision.[228] What the USPTO attempted to do in the altering of its guidelines was to ensure that the patent application of the gene sequences applied for are "meticulously scrutinized for an adequate written description, sufficiency of the disclosure, and enabled utilities, in accordance with the standards set forth by our reviewing courts."[229] The heightened standard of utility not only provided a different mechanism by which the USPTO was able to deal with the opponents' § 101 products of nature arguments, but it also provides a basis to respond to the opponents' second major argument.

B. *The Moral Considerations*

The second argument, the concern that allowing the ownership over human life will have negative ramifications, particularly with licensing, is a better argument against allowing patenting of gene sequences; however, the doctrinal shift towards more stringent utility and obviousness standards in patent law should help correct the potential negative ramifications.

One fundamental question that has emerged from the growing biotechnology field is: who can, and should, own human life?[230] This general fear is rooted in the idea that with granting patents in the biotechnology sphere, the government would essentially be granting twenty-year monopolies over facets of human life.[231] This fear can be dissected into two main concerns. One concern is that by patenting a gene sequence, one is obtaining a monopoly over the gene sequence, which could confer ownership over a human being.[232] The other concern is a more philosophical one, based in part on the Lockean natural entitlement doctrine, as best explained here:

> I do not deny that humans may legitimately own organisms in certain senses. For example, in order to acknowledge that people have special claims and responsibilities to determine what happens to certain organisms, talk of ownership rights is appropriate. A person has rights and responsibilities to determine what happens to her dog or her child that are not possessed by others. However, I do deny the appropriateness of

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[228] *In re* Fisher, 421 F.3d at 1374.

[229] *Gene Patents and Other Genomic Inventions: Hearing Before the Subcomm. on Courts and Intellectual Property of the H. Comm. on the Judiciary*, 106th Cong. 28 (2000) (statement of Todd Dickinson, Under Secretary of Commerce for Intellectual Property and Director of the United States Patent and Trademark Office, Department of Commerce).

[230] *See, e.g.*, RESNIK, *supra* note 12; Lori B. Andrews, *Genes and Patent Policy: Rethinking Intellectual Property Rights*, 3 NATURE REVIEWS GENETICS 3, 803-08 (2002).

[231] Andrews, *supra* note 230 at 804.

[232] See Mark A. Chavez, *Gene Patenting: Do the Ends Justify the Means?*, 7 COMP. L. REV. & TECH. J. 255, 266 (2003), for a lengthy explanation of the precise monopoly concern.

> the idea of owning organisms in the way that people own their bodies or in the way that artificers own created utilitarian artifacts. A human body exists as a manifestation of a person and, in this sense, exists for the use of that person. A utilitarian artifact exists to serve the purposes of its creator or users. But an organism and its parts are not appropriately understood as existing solely to serve the purposes of its human owner. The characteristics of an organism are not things that people may use for their benefit without also considering the possible conflicting benefits those characteristics provide the organism. There is moral dimension in determining what people may do with organisms because the interests of the owned organism must be considered in this decision. Thus, people are not naturally entitled to use an organism as they please. These points hold true even when humans cause the organism's existence or have manipulated its characteristics.[233]

To address the monopoly concern, while patent protection does offer a practical monopoly of certain rights for twenty years from the date of filing, patents only offer the right to *exclude others* from making, using, offering to sell, selling, and importing the patented item.[234] They do *not* offer the patentee the right to actually make, use, offer to sell, sell, or import the patented product, particularly if it is in violation of law. This prompts the following questions: first, what exactly does it mean to exclude others from making, using, offering to sell, selling and importing a gene sequence without violating American law? Second, would a patent on a gene sequence confer ownership over a human being? To put the argument in context, one could not claim patent infringement on a party who procreated and incidentally "made" another human being whose DNA happened to contain a patented gene sequence because such a prohibition would be in violation of public policy. Similarly, selling, offering to sell, or importing human beings is undoubtedly in violation of American anti-slavery laws. So, even if a patented gene sequence were to exist in a human being, the practical effect would not give the patentee any rights to or control over that human. Thus, the monopolist argument can be quenched with careful consideration of the negative right that is conferred by the patent statutes. Accordingly, the moral argument should more accurately be based upon the philosophical concern rather than the monopoly consideration.

As suggested by the USPTO, with all prior new technological

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[233] Ned Hettinger, *Patenting Life: Biotechnology, Intellectual Property, and Environmental Ethics*, 22 B.C. ENVTL. AFF. L. REV. 267, 281 (1995).

[234] 35 U.S.C. § 271 (2006).

endeavors, opponents will always argue that allowing patents and patent licenses in the field will stifle innovation. However, the argument is not specific to gene patenting. The cornerstone of patent law is that patent law grants monopolies to inventions as an incentive for public disclosure, which will then spur on further discovery. Biotechnology research is a costly endeavor. By awarding innovation through patent protection, researchers are given commercial opportunities to fund further research. Further research will bring the field closer to goals such as personalized medicine and the ability to map personal genomes for less than ten thousand dollars. Additionally, patent protection presents the public with the means necessary to pursue further research through its disclosure. The argument here is not one that is unique to gene patenting. If it were to apply to gene patenting, it would also apply to all patents.

More importantly, the heightened utility and obviousness requirements should, at least partially, address the concern about abuse through hard bargains in licensing. By increasing the level of utility required, as described in *In re Fisher*, patent applications for ESTs and other gene sequences require *specific and substantial* utility.[235] This requirement ensures that inventions that are granted protection are conceptions that are fully developed. While some may argue that requiring a heightened standard for biotechnology patents unfairly discriminates against a particular field of patent law, the 1999 Guidelines simply ensure that these patents comply with the statutory requirements of title 35 of the United States Code. There are thousands of combinations of base pairs that serve as genetic sequences; however, not all of these combinations have a specific function outside of expressing a certain gene. The line between invention and non-invention is thus created by the 1999 MPEP Guidelines and the *Fisher* decision. Instead of granting patent protection to any isolated and purified gene sequence, the USPTO will only grant protection to those isolated and purified gene sequences that have demonstrated a specific utility and result, such as a marker for a specific human disease, which is in line with the historical subject matter requirements for any isolated and purified substance. The more flexible obviousness standard as implemented by *KSR* should also help ensure that gene sequences can only be patented if those skilled in the art would find their invention to be truly innovative. This, in turn, will help prevent a cascading effect of allowing ownership over human life.

[235] *In re Fisher*, 421 F.3d 1365.

C. *Additional Concerns*

Other concerns include the following: a potentially heightened volume of applications that will flood the USPTO; stagnation of discovery in the field; an oligopoly over a sector of the market by those with the largest resources; the filing of provisional applications by patent trolls who have not yet fully invented a gene sequence; and the general moral concern that allowing patenting of gene sequences will have a cascading effect eventually resulting in ownership over human life. All of these concerns are similar to the concerns voiced about new technology patents since the beginning of the patent laws in the United States and abroad. All of these are currently remedied with the changes in the law, as discussed *supra* in Parts I & II, or are general misconceptions over what a gene sequence is and what synthetic biologists and engineers actually do, as discussed *supra* in this Part.

CONCLUSION

The recent discoveries of Watson and Venter prompt us to revisit an old question in light of the new advances in patent law. When the Human Genome Project came underway, there was a great influx of biotechnology patent applications at the USPTO that caused a response from the USPTO and generating major questions in Congress. Certainly, the ability now to sequence personal genomes and the move towards personalized medicine will have an impact on the USPTO. However, as with public concern over all new fields of technology, much of the panic is centered on unfounded misconceptions. The recent advances in the utility and obviousness doctrines may make it more difficult to obtain biotechnology patents, which would implicitly quench some of the concern.

Gene sequences are isolated and purified substances, whose patentability has been questioned since the latter half of the nineteenth century. Isolated and purified substances such as gene sequences have been definitively patentable since the beginning of the twentieth century and should continue to be patentable. Many inventions at some point originated from a "product of nature." The USPTO and the federal courts have drawn the line of invention for such products of nature and have stuck to it for over one hundred years. The level of invention required for isolated and purified substances is much akin to the level of invention required for mathematical algorithms, the precursor for software patents. If we were to eliminate patents of anything that originated in nature, the system would be essentially disservicing the United States Constitution, which provides for patent protection under U.S. Constitution, article I, § 8, clause 8 in promotion of the

science and the arts. Science inevitably encompasses a myriad of fields including biology and chemistry, both of which include inventions rooted in "products of nature."

Patent protection is awarded in exchange for public disclosure, which is said to, in turn, promote and incentivize further invention. In the field of gene sequencing, further invention is crucial if society hopes to move towards personalized medicine. On its face, it may sound absurd to think that DNA sequences, the fundamental building blocks of our genome, may be patentable. But if you compare the patentable sequences to the aspirin extracted from coal tar or the adrenalin extracted from the salt of a gland, it should begin to sound less absurd. That the four major hurdles to patentability must still be met precludes, or should preclude, concerns that United States patents will be issued that will exclude the "making, using, offering for sale, or selling" the personal sequence comprising you, I, or any other human being.

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