Patenting Genomic Technology - 2001 Utility Examination Guidelines: An Incomplete Remedy in Need of Prompt Reform

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SUMMARY

The patent system protects a patentee's work-product from potential infringers by preventing others from copying, making, using, offering for sale, or selling another's work without consent. Consequently, researchers and their funding organizations seek protection in the regulations of the United States Patent and Trademark Office (USPTO). However, in addition to protection from unlicensed future use of their inventions, genomic companies use the patent system offensively as a sword rather than a shield. Most prospective gene patentees seek patent rights on genetic sequences, which lack intrinsic marketability or definite utility. Genomic researchers employ their patents in the hope of exploiting royalties from future researchers who use the claimed fragment in ways uncontemplated by the original patentee.

The USPTO tried to address the economic, scientific, and ethical problems introduced by gene patenting via the

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5. See id.
amendment of its utility examination guidelines. Although these revisions speak to the need for a more stringent patent policy, this paper discusses how the USPTO's new guidelines fall short of adequately addressing the numerous problems emanating from the patentability of genes. Tenets of basic molecular biology and a description of DNA sequencing, including the advent of DNA sequencing machines, introduce the topic. The dilemma inherent in the privatization of genes provides a lens for analysis of the future of the USPTO's patent policies governing biotechnology. Finally, this paper will examine the shortcomings of the USPTO's revised utility guidelines for patentability and will suggest several proposals for reform, such as more stringent policies against obviousness, heightened utility standards for gene patents, and the institution of morality requirements.

I. INTRODUCTION

The field of biotechnology has grown exponentially in the past twenty-five years, with significant public benefit. In particular, genetic research contributes to the development of many of today's breakthrough pharmaceuticals and diagnostic tests, such as the genetic screening test for Canavan disease and recombinant techniques for producing human insulin. Research can take many years of commitment and immense capital to successfully bring an innovation from the laboratory bench to the marketplace. Some research can re-
quire companies to invest $500 million on the mere probability of a product's success. Patentees can justify the enormous financial backing necessary to their research by charging royalties on a claimed invention during the life of the patent. Thus, patent protection provides companies with a foothold for commercial success in the biotech industry.

Despite high initial costs, patents in the gene industry have proven to be quite lucrative. Even at the current success rate of 40% for biotechnology patents, most biotechnology companies will more than quadruple their patent portfolios. In addition, these companies often charge other researchers consultation fees ranging from five thousand dollars to five million dollars just to view the company's data. Currently, the biotech industry generates over $22 billion per year. This figure piques the interests of many biotech companies to obtain more patents. In 1990, the USPTO received over 16,000 patent applications. In 2000, that figure more than doubled to 33,000.

Gregory Williams, the general counsel of New England Biolabs, Inc., stated: “Technology feeds on itself. As the level of technology and the level of skill is raised, it opens more doors. I don't see it slowing down any time soon.”

Modern, more efficient methods of discovery may explain

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15. See Haseltine, supra note 13, at 59.
16. See Enserink, supra note 4, at 1196.
17. See id.; see also Adam Bryant & Gregory Beals, Who Will Own the Code of Life?, NEWSWEEK, Apr. 10, 2000, at 67 (stating that Miami Children's Hospital owns the rights to a patent on the Canavan gene and has developed a genetic screening test for this disorder, but charges $12.50 to anyone who uses this test).
20. See Aoki, supra note 18, at D1.
22. See Richard Willing, Gene Patents Get Tougher, USA TODAY, Nov. 15, 2000, at 14A.
24. See Willing, supra note 22, at 14A.
25. See id.
26. See Aoki, supra note 18, at D1.
this boom.\textsuperscript{27} Results are obtained in a much shorter time\textsuperscript{28} because computer searching replaced much of the book research and discussions between scientists.\textsuperscript{29} Cloning and DNA sequencing research greatly expanded in genomics.\textsuperscript{30} As a result, a single machine now does the same work as a traditional team of researchers in a shorter amount of time.\textsuperscript{31}

The advent of these sequencing machines fueled the race to sequence genes.\textsuperscript{32} The 6,000 gene patents already approved by the USPTO office,\textsuperscript{33} 1,000 of which are for human genes or gene fragments,\textsuperscript{34} reflect the biotech rush to capitalize on these efforts and innovations.\textsuperscript{35} Because the human genome consists of over three billion chemical units\textsuperscript{36} each with potentially significant medical, health, or research benefits,\textsuperscript{37} researchers scramble to stake a commercial claim in their work.\textsuperscript{38} In fact, more than 40,000 gene patent applications are still pending approval of the USPTO.\textsuperscript{39} Of these 40,000, more than half relate to human genes.\textsuperscript{40} Millennium Pharmaceuticals, Inc., a biotechnology company that specializes in gene-based drug discovery, has over 1,500 pending patent applications.\textsuperscript{41} Incyte Pharmaceuticals (Incyte) already holds over 500 gene patents and has over 6,000 pending, while Celera Genomics (Celera) has more than 6,500 gene patents filed

\begin{thebibliography}{10}
\bibitem{27} See Merrill Goozner, \textit{Patenting Life; Public Science Financed Breakthroughs in Genetic Research -- So Why Are Private Firms Allowed to Patent Genes?}, AM. PROSPECT, Dec. 18, 2000, at 23.
\bibitem{28} See Dastgheib-Vinarov, \textit{supra} note 11, at 159.
\bibitem{29} See Goozner, \textit{supra} note 27, at 23.
\bibitem{30} See Dastgheib-Vinarov, \textit{supra} note 11, at 158-62.
\bibitem{31} See Deborah Josefson, \textit{Biotechnology Company Claims to Have 97\% of Human Genes on Its Database; Celera Genomics Group, W. J. MED., Apr. 1, 2000, at 228.
\bibitem{32} See Goozner, \textit{supra} note 27, at 23.
\bibitem{33} See Jenna Greene, \textit{PTO to Rein in Gene Patents}, LEGAL TIMES, July 24, 2000, at 12.
\bibitem{34} \textit{See id.}
\bibitem{37} See Dastgheib-Vinarov, \textit{supra} note 11, at 145-47.
\bibitem{38} See Knox, \textit{supra} note 35, at G1.
\bibitem{39} See Willing, \textit{supra} note 22, at 14A.
\bibitem{40} See Goozner, \textit{supra} note 27, at 23.
\bibitem{41} See Aoki, \textit{supra} note 18, at D1.
\end{thebibliography}
Both public and private researchers likened this offensive gene patenting to a genetic gold rush. Substantially burdensome to the limited resources of the USPTO, this increase in the number of gene patent applications also raises basic questions. What do the patent claims look like? Are they too broad? How can the right to gene ownership be justified? Are frivolous applications being filed? To address the many issues surrounding the patentability of genes and partial gene sequences, or expressed sequence tags (ESTs), the USPTO revised the utility requirement for patent applications in January 2001. Accordingly, the U.S. presently validates applications for isolated genes and gene fragments, provided three utility criteria for patents are satisfied—specificity, substantiality, and credibility. These new requirements aim to narrow patent claims as well as reduce the number of unsubstantiated applications. However, when viewed from the perspective of EST patent applications, the new utility requirements are not stringent enough. Many genome researchers are uncertain about an EST’s genomic functioning or simply fail to realize other possible uses. These researchers lack a sufficient claim to the genes, yet still will gain commercial rights to their ESTs. The acquisition of rights in gene fragments may have an effect counter to the goals of patent law to promote science and

42. See Goozner, supra note 27, at 23.
43. See, e.g., Saltus, supra note 3, at D3; Goozner, supra note 27, at 23.
44. See, e.g., Dastgheib-Vinarov, supra note 11, at 143; Jenna Greene, The Changing Climate PTO Faces New Workload and IP Challenges, INTELL. PROP. STRATEGIST, Jan. 2001, at 5.
45. See generally Goozner, supra note 27.
46. See Jenna Greene, PTO Set to Tighten Standards for Gene Patents, RECORDER, July 27, 2000, at 3.
47. See id.
48. See generally Saltus, supra note 3.
50. See id.
51. See Elizabeth Howard & William Anthony, New PTO Guidelines Only Say ESTs Are Protectable, Courts Must Now Decide Reach of Patents for Expressed Sequence Tags, 23 NAT’L L.J. C3, C10 (2001) (discussing the PTO’s concern over EST patents and the PTO’s new requirements in evaluating ESTs for patentability).
53. See Enserink, supra note 4, at 1196.
the useful arts.\textsuperscript{54}

The following sections will first give some background on genetics and DNA sequencing.\textsuperscript{55} The paper will then analyze some issues raised by the privatization of genes and ESTs.\textsuperscript{56} Next, the paper will discuss patent protection in relation to genes.\textsuperscript{57} The subsequent section will review the new utility guidelines by the USPTO and address their shortcomings as applied to gene patents.\textsuperscript{58} Part V will propose reform measures that may better address the existing problems with the purpose and scope of patent laws and the unanticipated boom of biotechnology research.\textsuperscript{59} These reforms include heightening the standard for nonobviousness, re-instituting a Brenner-type standard, and imposing a morality requirement.\textsuperscript{60}

II. BACKGROUND

A. The Patent Act

In the words of Abraham Lincoln, “[Patents] couple the fuel of interest to the fire of genius.”\textsuperscript{61} The Venetians originally developed the concept of a patent system as a social contract between society and the inventor.\textsuperscript{62} With this system, the Venetians aspired to promote trade and commerce, while eschewing the notions of trade secrets.\textsuperscript{63} Congress’ enactment of the Patent Act parallels that of the Venetians.\textsuperscript{64}

The advancement of science relies upon the sharing of new knowledge and innovations to allow others to build upon them and create new knowledge and innovations of their own.\textsuperscript{65} In Article I, drafters of the U.S. Constitution sought to encourage this dissemination of ideas when they stipulated that Congress has the power “to promote the progress of Science and useful Arts, by securing for limited Times to Au-

\textsuperscript{54} See id.
\textsuperscript{55} See discussion infra Part II.A-B.
\textsuperscript{56} See discussion infra Part III.
\textsuperscript{57} See discussion infra Parts II.A-B, IV.A-B.
\textsuperscript{58} See discussion infra Part IV.C-D.
\textsuperscript{59} See discussion infra Part V.
\textsuperscript{60} See id.
\textsuperscript{61} Haseltine, supra note 13, at 59.
\textsuperscript{62} See id.
\textsuperscript{63} See id.
\textsuperscript{64} See CHISUM, supra note 2, at 11.
\textsuperscript{65} See id. at 70.
thors and Inventors the exclusive Right to their respective Writings and Discoveries. Thus, in 1790 the Patent Act was born. Although the Act has been amended and recodified, it continues to enumerate the requirements for obtaining a patent and explains the ensuing rights of a patentee.

The patent system is structured around several theories. It provides an incentive to invent, to disclose, to commercialize, and to design around. As a patent creates temporary commercial monopolies for the patent holder, it provides an economic incentive for researchers to invent. Dissemination of a patentee's written disclosure of the invention furthers innovative research so that others are able to then reproduce, use, and build upon the patent's ideas.

Patent rules require the inventor to state a specific usefulness for the invention. In the seminal case of Brenner v. Manson, the inventor applied for a process patent for making certain steroids. Although Manson's process produced steroids with no known utility, he argued that an adjacent homologue of his steroidal process demonstrated tumor-inhibiting effects in mice that met the utility requirement for patentability. The Supreme Court refused to extend Manson patent protection unless his invention had a specific usefulness in its present state. "Unless and until a . . . specific benefit exists in currently available form -- there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Justice Abe Fortas explained that a patent is "not a hunting license," but, is the "compensation for [research's] successful conclusion" and "must be re-

67. See CHISUM, supra note 2, at 18.
69. See CHISUM, supra note 2, at 70.
70. See id.
71. See id. at 70-71.
72. See id. at 75.
75. Id. at 520.
76. Id. at 531.
77. Id. at 534-35.
78. Id.
lated to the world of commerce." A patent is the quid pro quo for the public's deriving an invention with substantial utility.

Of course, this limited monopoly entitles the original patentee to receive royalties from others who may use the work during the term of the patent. In turn, downstream researchers may further promote the sciences with innovations, which they hope eventually to patent. As the demand for a patented product increases in the marketplace, downstream researchers have even more incentive to create non-infringing substitutes or improvements. Hence, the patent system greatly benefits society by expediting the discovery of new medications, technologies, and non-infringing improvements while decreasing consumer costs through the development of non-infringing substitutes.

B. The Advent of Biotechnology Patents

In the seminal case of *Diamond v. Chakrabarty*, the Supreme Court confronted the issue of the patentability of genetically engineered bacterium. The patent applicant in this case claimed to have invented "a bacterium from the genus *Pseudomonas* containing therein at least two stable energy-generating plasmids." Ordinarily, a single *Pseudomonas* bacterium is incapable of breaking down oil. Chakrabarty, however, discovered plasmids capable of degrading individual components of oil and developed a process whereby these plasmids could transfer into a single bacterium capable of

79. *Id.* at 536 (quoting *In re Ruschig*, 343 F.2d 965, 970 (C.C.P.A. 1965) (posing philosophical questions regarding what constitutes the "invention" of a new compound and concluding that a patent system must be related to the world of commerce rather than to the realm of philosophy)).


81. *See* CHISUM, supra note 2, at 70-71.

82. *See id.* at 70-75.

83. *See id.* at 75.

84. *See also* Saltus, supra note 3, at D3 (noting the statement of Chuck Ludlam, Vice President for Government Relations for the Biotechnology Industrial Organization: "For patients awaiting therapies and cures for deadly disease, there is hardly a more important issue than patents... without patents private-sector research leading to gene-based medicines will be very, very limited.").


86. *Id.* at 307.

87. *Id.* at 305 (quoting the patent application at issue in *Chakrabarty*).

88. *Id.*
multiple component oil degradation. Through an analysis of 35 U.S.C. § 101, the Court held the statute to mean that patentable subject matter “include[s] anything under the sun made by man.” However, manifestations of nature, such as the laws of nature, physical phenomena, and abstract ideas, are free to all and consequently are not patentable. In this case, Chakrabarty’s bacteria were not the “handiwork of nature,” but the result of human ingenuity and research. Thus, Chakrabarty paved the way for genetic technology patents.

In In re Deuel, the U.S. Court of Appeals for the Federal Circuit questioned whether a patent could claim a DNA sequence when at least part of the amino acid sequence of the encoded protein is known. The court reiterated an earlier opinion stating that in the absence of prior art suggesting the claimed DNA sequence, Deuel’s DNA sequence was nonobvious and, therefore, patentable because of the redundancy of the genetic code and the enormous number of sequences that could code for one protein.

Consequently, “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 therefore.” As long as the patentee can overcome anticipation and obviousness, he can patent anything that does not occur in nature. Therefore, the question now is whether genes constitute a “manufacture” or a “composition of matter.”

C. Genetics and Molecular Biology Basics

To better explain the legal issues surrounding the patenting of genes, some background information on genetic research and DNA sequencing is helpful.

89. Id. at 305-06.
90. Id. at 309 (quoting S. REP. NO. 82-1979, at 5 (1952)).
92. Id. at 310-13.
93. In re Deuel, 51 F.3d 1552, 1557 (Fed. Cir. 1995).
94. Id. at 1558-59; see also In re Bell, 991 F.2d 781 (Fed. Cir. 1993) (holding that the proper issue for determining patentability is the obviousness of the DNA sequence claimed, not the method by which it is made).
96. See Chakrabarty, 447 U.S. at 309.
Individual cells compose the human body and all of its organs. Although different cells have different biological roles, most consist of the same genetic material and have the same biochemical structures. Genes control these various cellular functions and serve as the cells' genetic blueprint. DNA is the code for this blueprint. The language of the DNA code is expressed through four deoxyribonucleotide bases: adenine (A), guanine (G), cytosine (C), and thymine (T). Different combinations of these bases dictate the properties and functions of a gene. Genes control protein synthesis within a cell. Because virtually everything is made of protein or by protein via enzyme activity, proteins direct almost every cellular function.

The base sequences are serially arranged along two complementary DNA strands. A gene can be identified by its DNA strands and by the specific order of base sequences DNA strands contain. A codon, which is a sequential grouping of three nucleotide bases, encodes for one out of a possible twenty amino acids. A particular sequence of amino acids codes for a particular protein. For example, if a sequence of nucleotides is known, then an amino acid sequence can be determined and used to sequence a protein. However, since there are more possible triplet groupings to form a codon than there are amino acids, a particular amino acid can be coded for in more than one way. Thus, knowledge of a protein and

99. See id. at 41.
100. See id. at 104-05.
102. See id. at 76-79.
103. See id. at 71-74.
104. See Alberts, supra note 98, at 104-05.
105. See id. at 111-30.
106. See id. at 76-82.
107. See id. at 86-87.
108. See id. at 86-88, 213-15. A DNA sequence can also have non-coding regions, which do not play a role in protein synthesis, and regulatory regions, which basically inform the gene when to start or stop the process of protein synthesis. See id.
109. See id. at 8-13. Proteins differ from one another due to their unique sequence of amino acids. See id.
110. See Alberts, supra note 98, at 111-30.
111. See Lewin, supra note 101, at 213-15. A codon consists of three of the four nucleotide bases. Since there are only twenty natural amino acids, there are sixty-four possible codons. See id. at 213.
its amino acid sequence does not necessarily mean that its nucleotide sequence can be inferred.\textsuperscript{112} Scientists refer to this phenomenon as redundancy or degeneracy of the genetic code.\textsuperscript{113}

Each unique amino acid sequence consequently affects a protein's biochemistry.\textsuperscript{114} Proteins affect the phenotypic and genotypic expressions of a particular genetic trait\textsuperscript{115} and influence just about every cellular function and biological process within a living organism.\textsuperscript{116} Clearly, DNA sequencing is extremely important in our understanding of life and how living organisms function.\textsuperscript{117}

\textbf{D. DNA Sequencing and Sequencing Machines}

When gene analysis first began, the process was painstakingly slow compared to modern methods.\textsuperscript{118} In the past, scientists extracted genetic material from persons already identified as carriers for a particular disease.\textsuperscript{119} Then, they tried to manually identify the particular gene and its function for the next several years.\textsuperscript{120} The scientists inserted the genes into artificial bacterial chromosomes and mapped and sequenced their positions on these chromosomes.\textsuperscript{121} Today, the process starts with the genomic code and ends with a particular protein and its function.\textsuperscript{122}

Gene sequencers, which are comparable in size to small refrigerators, "speed-read" genes.\textsuperscript{123} Basically, these machines: 1) fragment genes, 2) propagate millions of copies of each fragment, 3) reassemble these fragments using linking DNA fragments of known length to close any gaps, 4) delete these linkers once missing pieces are found, and finally 5) re-

\textsuperscript{112} See ALBERTS, supra note 98, at 111-30.
\textsuperscript{113} See LEWIN, supra note 101, at 213-15. Genotype refers to the genetic constitution of an individual. Phenotype refers to the visible characteristics of the individual produced by the genotype and the environment.
\textsuperscript{114} See ALBERTS, supra note 98, at 8-13.
\textsuperscript{115} See LEWIN, supra note 101, at 61-63.
\textsuperscript{116} See ALBERTS, supra note 98, at 111-30.
\textsuperscript{117} See id. at 291.
\textsuperscript{118} See Goozner, supra note 27, at 23.
\textsuperscript{119} See id.
\textsuperscript{120} See id.
\textsuperscript{121} See Josefson, supra note 31, at 228.
\textsuperscript{122} See Goozner, supra note 27, at 23.
\textsuperscript{123} See Saltus, supra note 3, at D3.
assemble the base pairs. The machines subsequently download the sequences to a computer library of existing ESTs. With very little manpower, these machines provide a rapid, large-scale method for sequencing the genetic code and a reasonable extrapolation of the functions of ESTs. Unlike human researchers, these machines can run twenty-four hours a day, seven days a week. For example, Celera's gene machine sequences roughly two billion base pairs each month.

The biotechnology companies employing this technology are private and are not obligated to share their information. Yet, publicly funded institutions such as the National Institutes of Health (NIH), which funds the Human Genome Project, are compelled to publish newly sequenced genes within twenty-four hours. Consequently, although Celera sequenced a majority of the human genome using its own resources, it inferred almost 10% of the genome using the data published by the NIH. Given a genome size of about 80,000 genes, roughly 8,000 were sequenced using NIH's work-product. Thus, the research done by the NIH benefits private companies, but not vice-versa. This dichotomy further complicates the patentability of genes by questioning the propriety of private companies with exclusive rights to an EST, which may have been successfully sequenced in part due to previously disclosed, but unpatented, NIH research.

III. LEGAL ISSUES CONCERNING THE PRIVATIZATION OF GENES AND GENE FRAGMENTS

A complete set of DNA provides extremely useful infor-
mation with a lucrative promise of patent royalties. From these gene sequencing and characterization efforts, one learns how genes interact with each other, how their regulatory functions work, how disruption of these regulatory interactions trigger genetic diseases like cancer or Alzheimer's, or how diseases such as AIDS can be transmitted. Researchers hope to develop safer, more effective drugs, new treatments, and various diagnostic tools. With both fame and fortune at stake, researchers and biotech companies clamor to identify genes and their corresponding proteins.

Competition among companies, along with the accelerated research capabilities of the gene sequencing machines, brought an incredible number of new technologies to fruition in a short amount of time. For example, Celera began its sequencing project in September 1999 and completed the venture in June 2000. The company's original schedule was remarkably outpaced, and the media toted Celera's efforts as an example of the value of competition. However, this gene competition is not necessarily framed around the incentive to invent, but the desire for the temporary exclusionary period in the commercial market, which patents afford their holders.

Gene patents allow companies with novel information to charge others who may later use this technology, whether in treatments or screening tests, in order to recoup the large investment capital used to fund the original research. Without patent protection, marketable products are less likely to arrive on the shelves. Further, patents and their written descriptions ensure that completed research enters the public

135. See Reichard, supra note 19, at 3.
136. See LEWIN, supra note 101, at 1131-72.
137. See Tatjana Dragic et al., HIV-1 Entry into CD4+ Cells Is Mediated by the Chemokine Receptor CC-CKR-5, 381 NATURE 667 (1996).
140. See Goozner, supra note 27, at 23.
141. See, e.g., id.; Josefson, supra note 31, at 228.
142. See Goozner, supra note 27, at 23.
143. See Knox, supra note 35, at G1.
145. See id.
arena and that others can build upon the technology. However, "there [always] exists a dangerous combination of power, money, and market economy" as patents confer the right to exclude others from benefiting from the technology.

Patentees may prevent competitors from using their technology, specify conditions of use, and charge royalties. Public health may suffer because of these economic and academic prohibitions. For example, Celera plans eventually to make its gene sequences publicly available, but currently intends first to turn a profit by licensing certain gene sequences of particular diseases to large pharmaceutical companies such as Pfizer, Novartis, and Rhone-Poulenc or to its genome library's paid subscribers. Restriction on the use of a gene to one or a limited number of laboratories will retard further research efforts, and the public will suffer as a result. Unlike the practices of the NIH, many of these gene-sequencing companies do not immediately publish their work in an attempt to be the first to generate a profit. These gene sequencing companies work on securing a patent and using the information to solicit funding from drug companies. These practices may cause delay in the development of new drugs and diagnostic tools, causing the public to lose quick

146. See CHISUM, supra note 2, at 70-75.
147. Mary Kwang, Should Genes Be Patented?, STRAITS TIMES (SINGAPORE), June 5, 2000, at 17 (quoting Dr. Xu Zhi-Wei, Professor of Bioethics at the University of British Columbia in Vancouver).
148. See CHISUM, supra note 2, at 70-71.
149. See id. at 75.
150. See Knox, supra note 35, at G1.
151. But see Enserink, supra note 4, at 1196 (claiming that gene-based drugs would never reach the market without intellectual property protection).
152. See Josefson, supra note 31, at 228.
153. See id.; see also Goozner, supra note 27, at 23 (describing this situation as monopolistic). But see Aoki, supra note 18, at D1 (explaining that companies are not trying to squeeze out competition, but instead simply trying to claim competitive advantages).
154. See Knox, supra note 35, at G1; see also Aoki, supra note 18, at D1 (quoting Dr. Aubrey Milunsky, Director of the Center for Human Genetics at the Boston University School of Medicine: "By doing so, they would ultimately exclude someone else from working on that gene."). But see id. (noting that patents do not impede science because patent applications require detailed written descriptions that allow for replication and freedom to use the technology in a non-commercial way).
155. See Josefson, supra note 31, at 228.
156. See id.
access to new drugs.\textsuperscript{157} Such pecuniary practices may “substitute the judgment of profit-making companies for our judgment as physicians.”\textsuperscript{158}

Many critics of gene patenting argue that human genes are an intrinsic part of the human body, thus ownership of a gene is like ownership of any other part of the body.\textsuperscript{159} However, patents do not confer ownership, but merely confer a right to preclude others from using the claimed invention.\textsuperscript{160} Furthermore, one does not patent a gene, but patents the code of symbols, which describe that gene and the methods to manipulate the gene.\textsuperscript{161} Thus, no one ever “owns” a human gene.\textsuperscript{162}

Although humans have only one genome, the genetic information contained in the genome can exist in two different formats.\textsuperscript{163} One format is the raw sequence of the human genome, consisting of the entire sequence of nucleotide bases that either code for amino acids or do not code for anything at all.\textsuperscript{164} The raw sequence is a natural manifestation of nature, not made by the human hand.\textsuperscript{165} The other format consists of the cloned or isolated and purified partial DNA fragments.\textsuperscript{166} Unlike the raw sequence, which exists as a purely natural substance and thus remains unpatentable, the DNA fragments must be excised from the natural context of the human genome, isolated, purified, and cloned before scientists can study them.\textsuperscript{167} Since the sequenced gene fragments, like ESTs, do not exist in their natural state and are therefore “not nature’s handiwork,” they are “patentable subject matter

\textsuperscript{158} Knox, supra note 35, at G1 (quoting Dr. Debra Leonard, Chief of the Molecular Pathology Laboratory at the Hospital of the University of Pennsylvania).
\textsuperscript{159} See Penny Fannin, Patent Critics Try to Stop Human-Gene Slave Trade, SUNDAY AGE (MELBOURNE), Mar. 19, 2000, at 6.
\textsuperscript{160} See CHISUM, supra note 2, at 70-75.
\textsuperscript{161} See 35 U.S.C. § 101 (2001); see also Haseltine, supra note 13, at 59 (explaining the misconceptions regarding gene patents).
\textsuperscript{162} See Saltus, supra note 3, at D3.
\textsuperscript{163} See id.
\textsuperscript{165} See Saltus, supra note 3, at D3.
\textsuperscript{166} See In re Bergstrom, 427 F.2d 1394, 1397 (C.C.P.A. 1970) (holding that proteins purified from their natural setting were patentable).
Hence, gene patentees can circumvent the “anything in nature” prohibition for patents.  

IV. AN ANALYSIS OF GENE PATENTS UNDER THE REVISED GUIDELINES

Scholars, patentees, physicians, and patients hotly debate whether the USPTO should grant portions of the human genome patent protection.  

A. Legal Issues Concerning Gene Patents

There was little debate in the field when gene patents first began to issue in the late 1970s. As a result of the painstaking process of taking a gene and its protein expression and linking them backwards to a genomic code, scientists closely correlated a gene to a specific cause of a disease or developed a treatment for a particular disease, and eventually patented their gene sequence.

Today, computer searches characterizing genes based on probability replace experimental laboratory data. Because gene machines compare the gene fragments to a library of known ESTs, they only infer protein expression and function from the code, yielding largely theoretical information. Unfortunately, these inferred utilities might result in an inaccurate or underinclusive characterization of the EST's true functions. For example, an unknown gene may have striking similarity to a gene known to have hydrophobic qualities. Hence, the sequencer will infer that the unknown gene

168. Diamond v. Chakrabarty, 447 U.S. 303, 310 (1980); see also Amgen v. Chugai Pharm., 927 F.2d 1200 (Fed. Cir. 1991) (limiting patents to cloned DNA sequences and refusing to grant generic claims for all possible DNA sequences).
169. See Parke-Davis & Co. v. H.K. Mulford Co., 189 F. 95, 103 (C.C.S.D.N.Y. 1911) (stating that through the process of isolating and purifying a hormone, the hormone “becomes for every practical purpose a new thing.... That is a good ground for a patent.”).
170. See Haseltine, supra note 13, at 59.
171. See Greene, supra note 33, at 12.
172. See id.
174. Contra Enserink, supra note 4, at 1196 (explaining that homology searches are an accepted way of ascribing a gene's function and virtually 100% correct).
175. See Jacobs & Gosselin, supra note 23, at A1.
176. Hydrophobic, or nonpolar, parts of molecules attract each other in the presence of water or other polar fluids. Because water repels hydrophobic molecules, these molecules form clumps with one another so that the clumped interi-
probably will produce a protein that floats in a cell membrane. But, scientists must perform more research to conclusively determine its cell membrane function and possibly other, more significant functions.

Those opposed to gene patents argue that isolated genes are not invented, but discovered. The "researchers" are really the gene sequencing machines that run twenty-four hours a day to determine the ESTs and to infer the expression of a protein. Thus, the product of human ingenuity is in fact the gene sequencer, and the genomic sequences are the handiwork of these machines. Nevertheless, statutory law ensures that the USPTO cannot reject a patent application based on the manner in which the invention was developed.

However, once an inventor files a patent application, others can oppose it on the grounds of novelty. An inventor can never invent a gene because genes existed since the beginning of time and are not new compositions. Furthermore, genes are not novel because they are closer to being discoveries than new compositions. One can argue that if the USPTO granted gene patents, then anyone carrying a patented gene in his or her body would infringe on the gene patentee's rights. However, the USPTO disagrees with this argument because a gene patent covers an isolated, purified gene, not a naturally occurring gene that exists within the human

ors face away from, and thus exclude water or other polar molecules. See Enserink, supra note 4, at 1196.

177. See id.
178. See id.
179. See, e.g., M. Scott McBride, Comment, Patentability of Human Genes: Our Patent System Can Address the Issues Without Modification, 85 MARQ. L. REV. 511, 518-20 (2001); Greene, supra note 46, at 3; see also Saltus, supra note 3, at D3 (quoting Bob Franza, biologist at Washington University in St. Louis, who stated that "DNA in the genes is a product of evolution, not of man").
180. See Jacobs & Gosselin, supra note 23, at A1 (quoting Tanya Dragic of the Albert Einstein College of Medicine in New York). "[S]ophisticated equipment and computers analyze the utility of a gene sequence. It isn't... hard work...[or] innovative work." Id.
181. 35 U.S.C. § 103(c) (2001); see also Carter-Wallace v. Gillette, 675 F.2d 10, 13-14 (1st Cir. 1981) (explaining that for an invention to be patentable, "it is immaterial whether it resulted from long toil and experimentation or from a flash of genius").
183. See McBride, supra note 179, at 518.
184. See id.
185. See id.

B. Theoretical Issues Concerning Gene Patents Based on Fundamental Reasons for Patent Law

Some argue that the granting of patent monopolies for genes restricts the promotion of science and research. One gene contains many ESTs, each of which can code for a functional protein.187 Thus, one gene may code for several various protein functions.188 Problems arise when different researchers want use to the same gene to find treatments for different diseases. The inability to assert patent rights to an already patented gene fragment may deter other researchers from further investigating the same fragment.189 In addition, the original patentee may not choose to license the EST to another competitor. Alternatively, the commercial incentive to invent or further discover may decrease due to the royalty payments by researchers to the patentee or the possible reduction in profits. In this way, patents discourage research on the function of genes and their relation to various diseases and stifle the development of new medicines or other technologies.190

The methodology of modern sequencing represents an additional problem with gene patentability. The high-speed search machines neither infer possible useful drugs or therapeutics nor investigate the possible interactions of ESTs with other sequences.191 Consequently, the utility disclosure needed for patent protection may be inadequate, because a potential gene patentee may not fully understand the gene’s function. In this case, a patent grant not only would be counterintuitive to the basic requirements of patents, but also would be unfair to later researchers and harmful to the pub-

188. See id. at 111-30.
189. See, e.g., Gesteland, supra note 144, at 18; Enserink, supra note 4, at 1196.
190. Cf. McBride, supra note 179, at 525-27. Gene patenting does not discourage invention because 1) patents are time-limited, 2) most inventions have favorable licensing terms, 3) a second researcher who discovers a new use can patent that process, and 4) cross-licensing needs cause researchers to share information. Id.
191. See Enserink, supra note 4, at 1196.
lic.\textsuperscript{192}

By promising recoupment of investments and royalty profits, patents give an economic incentive to invent.\textsuperscript{193} Giving patent rights to a researcher who lacks a clear understanding of the EST's function would allow gene patentees to unfairly benefit from future studies conducted with or related to the same EST.\textsuperscript{194} For instance, Human Genome Sciences (HGS) received a patent on the CCR5 gene by describing its utility as a screening tool for receptor agonists and antagonists\textsuperscript{195} as well as for gene mutation detection.\textsuperscript{196} At the time of the application, HGS neither claimed nor contemplated an anti-viral utility.\textsuperscript{197} However, through subsequent research, the NIH determined that the gene played a role in the transmission of the AIDS virus and identified CCR5 as the docking mechanism on cell surfaces used by the virus to infect cells.\textsuperscript{198} HGS will collect a windfall if this mechanism becomes part of a new therapy to fight the deadly disease.\textsuperscript{199} In fact, in early 2000, HGS executed a licensing agreement with Praecis Pharmaceuticals for the development of a HIV therapy based on CCR5 and already began to reap rewards.\textsuperscript{200}

Moreover, if the USPTO cannot guarantee intellectual property protection for one's work-product based on a patented EST, pharmaceutical companies may not be willing to invest the capital needed to develop useful drugs and innovative therapies from the EST.\textsuperscript{201} The emergence of new technologies, especially in the field of genomics, forced the USPTO to address a number of the aforementioned issues in its revi-

\textsuperscript{192} See also Greene, supra note 33, at 12 (quoting Harold Varmus, President of Memorial Sloan-Kettering Cancer Center and former Director of the National Institutes of Health, 1993-1999). “Overly enthusiastic protection of intellectual property, too early in the process of product development, can impede the delivery of public health benefits.”\textit{Id.}

\textsuperscript{193} See CHISUM, supra note 2, at 70-71.

\textsuperscript{194} See Enserink, supra note 4, at 1196.

\textsuperscript{195} An agonist is a chemical substance capable of combining with a nervous receptor and initiating a response. An antagonist is a chemical substance that reduces the physiological activity of another chemical substance by combining with and blocking its nervous receptor.


\textsuperscript{197} See id. at 354.

\textsuperscript{198} See id.

\textsuperscript{199} See id.

\textsuperscript{200} See id.

\textsuperscript{201} See Enserink, supra note 4, at 1196.
sion of the Utility Examination Guidelines. However, these guidelines remain inadequate.

The revised guidelines specifically address the utility and written description requirements for patentability. The guidelines not only assist patent examiners, but also assist the public with standards for patentability, especially for emerging technologies such as genomic research. However, because the USPTO is bound by 35 U.S.C. § 101 and case law, the revised guidelines only reflect the USPTO’s understanding of § 101. Thus, the revisions do not constitute legislative action and lack the force and effect of law. Consequently, an appeal cannot be based on a USPTO examiner’s failure to follow the guidelines, but must have a basis in substantive law.

C. Statutory Requirements

All patent applications must meet certain statutory requirements of utility (application in commercial or real-world use), novelty (no previous disclosure of the work), and nonobviousness (inventiveness). Additionally, the invention disclosure must sufficiently enable one skilled in the art to make and use the invention without undue experimentation.

Because the USPTO faced many problems with the patenting of gene fragments and needed stricter policies, the USPTO revised its utility and written description require-

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203. See id. at 1097-99.
204. See id. at 1092-98.
205. See id. at 1096.
206. See id. at 1098.
207. See id.
208. See 35 U.S.C. § 101 (2001). This section ensures that a patentee provides society with an invention that operates in accordance with its intended purpose or a purpose discernible to a person skilled in the art. See CHISUM, supra note 2, at 707.
210. See 35 U.S.C. § 103 (2001). This section prevents a patent applicant patent protection on an invention which could be derived or obtained from available technical literature or other public sources. See CHISUM, supra note 2, at 514.
ments for patentability.\textsuperscript{212}

However, many companies with access to a gene-sequencing machine and a genomic library can sequence genes and extrapolate EST functions almost instantaneously.\textsuperscript{213} Thus, two unrelated companies could sequence the same gene and infer the same functions, directly conflicting with the definition of nonobviousness. In other words, the scientific information available about proteins, DNA, amino acids, and extrapolated EST functions renders the gene fragment obvious as soon as any sequencer splices up the gene.

\textbf{D. The Revised Guidelines Addressing the Utility and Written Description Requirements}

Since the USPTO's guidelines mainly serve to train its examiners and inform the public, they do not have any power within the legal system itself.\textsuperscript{214} As such, courts must determine the scope of claims under the new guidelines.\textsuperscript{215} The USPTO solicited volunteer applicants to test the sufficiency and legal applicability of its new guidelines.\textsuperscript{216} As a result, a test case involving a volunteer private company with a gene patent application most likely will go to the federal court.\textsuperscript{217}

The new guidelines do not greatly affect the former patentability standards of genomic technologies, and the privatization of genes has not slowed.\textsuperscript{218} For instance, despite the advent of the new rules for patentability, the general counsel of Incyte expressed his confidence in the patentability of the company's 1.2 million EST applications by stating, "We never filed applications where we didn't know what the EST did."\textsuperscript{219}

The utility requirement is met if "a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention" and if "the utility is specific, substantial, and credible."\textsuperscript{220} The

\begin{footnotesize}
\begin{enumerate}
\item[212.] See Goozner, supra note 27, at 23.
\item[213.] See id.
\item[215.] See id.
\item[216.] See Greene, supra note 44, at 5.
\item[217.] See id.
\item[218.] See Goozner, supra note 27, at 23.
\item[219.] Enserink, supra note 4, at 1196.
\end{enumerate}
\end{footnotesize}
USPTO defines “credible” as whether someone of ordinary skill in the art would believe the asserted utility based on the totality of evidence.221 However, the guidelines specifically state that an applicant only needs to provide one credible utility for each claimed invention222 and that a patent cannot be withheld “until another, or better, use is discovered.”223 Any higher, better, or more practical use is an inurement of the starting point provided by original disclosure, and a benefit of the patent system.224

Specific and substantial utility refers to usefulness for any particular, practical purpose.225 This requirement excludes “throw-away,” “insubstantial,” or “nonspecific” uses226 and refers to practical, real-world uses.227 However, commercial viability of a product is not required to establish usefulness.228

The requirements for written description are embodied in 35 U.S.C. § 112. In general, the applicant must show that he actually invented what he claims and that he possessed the claimed invention at the time of application.229 Under the guidelines, rejection for inadequate written description should be rare because of the strong presumption that the requirements embodied in § 112 are present in patent applications.230 In relation to gene fragments, the guidelines state that description of the “complete chemical structure, i.e., the DNA sequence, of a claimed DNA is one method of satisfying the written description requirement, but it is not the only method.”231 “There is no basis for a per se rule requiring disclosure of complete DNA sequences or limiting DNA claims to only the sequence disclosed,” since DNA can be described by its structure, formula, chemical, name, or physical proper-

221. See id.
222. See id.
223. Id. at 1094.
224. See id.
225. See id. at 1098.
227. See id. at 1094.
228. See id.
231. Id. at 1101.
ties.  

Issues of inequity are unresolved because private companies based some of their gene patent applications on prior, publicly disclosed NIH research. The USPTO still would grant Human Genome Sciences' original patent application for the CCR5 gene under the revised standards. As such, holders of gene patents can continue to receive a windfall from more thorough, subsequent research.

Although the institution of a compulsory licensing system may combat this problem, companies would no longer control their profits and thus, may not invest the large capital needed to conduct research. Alternatively, the USPTO could institute an exception to patent rights granted for gene fragments. The commercial monopoly rights given to a patentee of an EST could be not only time-limited, but also disclosure-limited. Researchers may be inspired to make further discoveries in order to have broader disclosures and thus broader monopoly claims. However, this proposal also may have the opposite effect. Often, research companies recoup their investments through licensing agreements with subsequent researchers. Companies may no longer want to invest large amounts of money into projects with such limited potential for future commercial rights. Further, the USPTO may not be able to distinguish the breadth of disclosure claims or to argue against the patent's increased presumption of validity when later attempting to narrow a claim against the patentee. Tougher requirements will lead to stronger, more enforceable patents. Once the USPTO grants a gene patent under the new rules, opposers will have more difficulty invalidating the patent.

V. PROPOSALS FOR FURTHER REFORM

The new guidelines do not preclude EST patents and do not adequately address the aforementioned issues concerning

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232. Id.
233. See Josefson, supra note 31, at 228.
234. See Luukkonen, supra note 196, at 354.
235. See McBride, supra note 179, at 534.
236. See Luukkonen, supra note 196, at 366.
237. See id.
239. See id.
them. Although the USPTO's revisions are a step in the right direction, the USPTO would benefit from raising the bar on patentability soon. Because the patent system originated in the Constitution, the founders could not have predicted the innovations in biotechnology. History shows that legal doctrines change with time. Thus, changes in USPTO regulations cannot be too prescriptive in a single reform, especially in view of the biotechnology field where new inventions may present new problems to existing laws. Similar to Congress, which aptly responds to a problem at the time the problem presents itself, the USPTO should take small, reformatory steps. In the words of Justice William Douglas, "[R]eform may take one step at a time, addressing itself to the phase of the problem which seems most acute . . .".

The present controversy also suggests an immediate need for government intervention. When ideas and innovations such as novel gene therapies or diagnostic tests remain out of the public domain, society's health and welfare suffer. These overriding national interests demand attention from the legislature and implementation of substantive laws and restrictions on gene patentability. Meanwhile, genetic applications continue to stream into the USPTO. Thus, the USPTO needs to take prompt action to strengthen its requirements for patents.

A. Raise the Nonobviousness Bar

Recent USPTO revisions only encompass issues of utility and written description, and do not raise the bar for nonobviousness. A higher standard under 35 U.S.C. § 103 provisions would require researchers to better understand genomic function and could spur companies to relate the EST to a particular disease, drug therapy, or diagnostic test. With increased quality of disclosure, comes the strengthening of pat-

241. See Enserink, supra note 4, at 1196.
243. See Enserink, supra note 4, at 1196.
244. See Greene, supra note 44, at 5.
245. See also Dastgheib-Vinarov, supra note 11, at 179 (arguing for the elevation of the nonobviousness standard for genomic inventions set forth in In re Deuel).
ent validity. 246

B. Require Different Standards for Different Technologies

To raise the bar, the USPTO also could require different standards or protection for different technologies. Although the new guidelines target gene patents, these provisions are unlikely to deter research companies from pursuing gene patents 247 and actually may hinder the pursuit of other types of technology patents. To address the issues presented by these EST patents, the USPTO must link a concrete, technical effect with the revised utility assessment for gene patents only. Thus, companies could not claim use as a probe for an unspecified target for gene patentability, and companies like Celera would have to invest more time and effort into researching its gene fragments after their promulgation by a machine.

C. Return to Brenner

The advent of patented genomic technologies and inequities that may ensue provides an impetus for the USPTO and patent law to return to the standard set forth by the Brenner court. 248 Brenner stipulated that before a patent may issue, an invention must have a specific benefit in a currently available form. 249 This heightened utility standard should narrow the overbroad protection of a gene patent with non-precise functions or gene patents with utilities insufficient to justify broad product claims. Limitations on the claimed subject matter will also facilitate subsequent researchers who could either invent around the patent or develop technologies entirely novel from the original claims of the patent. In turn, the public will benefit from decreased cost, because of large companies' inability to demand royalties for the basic EST of previously unclaimed therapeutic uses. Additionally, a return to the Brenner standard would deter companies from filing applications with the USPTO until they have performed further research beyond the use of a sequencing machine.

247. See Enserink, supra note 4, at 1196.
248. See also Zuhn, supra note 52, at 998 (discussing the utility requirement in relation to the patentability of DNA sequences with no known function).
D. Institute a Morality Requirement

The U.S. patent system may also benefit from emulating the additional requirements adopted by the European Patent Convention (EPC). Under the codes of the EPC, an applicant must show that his or her invention (1) is susceptible to industrial invention, (2) is new, and (3) involves an industrial step. These provisions correlate to the USPTO’s requirements of utility, novelty, and nonobviousness. In contrast to the U.S. patent system, which fails to address any of the moral or ethical concerns from genomic inventions, the EPC regulates the patentability of the human genome and does not grant patents, which would be contrary to ordre public or morality. Specifically, the human body, its elements, and the complete or partial structure of a gene at any stage are not patentable. However, the EPC can grant a patent to the function of a gene if the possibility of a useful drug or therapy can be shown, or if the patent sufficiently and specifically identifies the intended use of the gene.

Although a morality requirement may help address the issue of gene patentability in the U.S., this requirement fails to account for the resources and funding used during research. Because morality is rooted within the accepted norms of a society, it comprises a somewhat intangible quality that may change over time. Knowledge that a patent may not issue based on an intangible, variable standard may deter companies from investing money into genomic research without the significant assurance of exclusive commercial rights. Thus, a definite move towards imposing a morality standard may hinder the goals of patent law. However, Europe’s system may provide helpful guidance for the U.S. as the USPTO tries to further reform its guidelines. Small steps rather than giant leaps are necessary for effective reform.

E. Post-Patent Issuance Remedies

As previously stated, an aggressive, initial reformatory
step will not help. If the USPTO moves towards a policy of rejecting the patentability of genes, commercial incentive to invent would wane, and the promotion of sciences would not occur. Because the USPTO should not have to bandage problems after issuance of a gene patent, the USPTO should make reforms during the review of patent applications.

VI. CONCLUSION

The economic, scientific, ethical, and practical implications over the patentability of genes influenced the USPTO to revise its guidelines, resulting in higher standards for utility and written description. Despite the changes, many of the same issues continue to face researchers and U.S. patent examiners. Although the 2001 amendments speak to the need for harmonization between the legislative goals of patent laws and the inconsistencies with emerging technologies, much more change is needed.

Though the USPTO could attempt post-patent issuance remedies, the patent office should address the problems well before legal battles over validity arise. Reforms should include raising the bar for nonobviousness, requiring stricter standards for gene-related patents, going back to a stricter Brenner standard, instituting a morality requirement, and perhaps limiting the commercial scope to claimed utilities. In order to avoid problems such as complete subject matter exclusion, these small steps will lead to effective reform in gene patenting and a much more equitable patent system for individual researchers, biotechnology companies, and society.

256. See McBride, supra note 179, at 534.
257. See discussion infra Part IV.D.