



THE U.S. PTO'S NEW UTILITY GUIDELINES:
WILL THEY BE ENOUGH TO SECURE GENE PATENT RIGHTS?

ANNA E. MORRISON

Abstract

This Comment examines the newly revised PTO utility examination guidelines for biotechnology patents. The race for patenting human genes is well underway. When complete sequences of human genes are found, researchers have been quick to seek patents. This “patent grab” has been driven less by the expectation that a particular gene sequence will result in production of a useful protein and more by the idea that enough patenting will create a protectable “haystack” in which one will find a few “genetic needles of value.” The new utility guidelines may not completely aid the underlying and fundamental policies on patenting. While the guidelines may possibly provide some surety that DNA patents will hold up under challenges in the courts, the solution to gene patenting problems will require something more. Help is needed in the areas of public misconception, legislation for licensing agreements, and possible limits on claims involving drugs of extreme medical importance.

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THE U.S. PTO'S NEW UTILITY GUIDELINES: WILL THEY BE ENOUGH TO SECURE GENE PATENT RIGHTS?

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INTRODUCTION

The race for patenting human genes is well underway. Dubbed as the “great gene grab,” patent attorneys have been frenzied in their attempts to secure patent rights for their research university and biotechnology company clients.¹ Already, Human Genome Sciences of Rockville, Md. holds patents to over 100 genes, with patents pending on another 7,500.² Celera, the company to first announce completion of the human genome, has filed patent claims on more than 6,500 gene sequences.³ Yet the United States Patent and Trademark Office (PTO) has only

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¹ Antonio Regalado, *The Great Gene Grab*, TECH. REV., Sept./Oct. 2000, available at <http://www.technologyreview.com/magazine/sep00/regalado.asp> (last visited Nov. 3, 2001).

² *Id.*; David Malakoff, *Will a Smaller Genome Complicate the Patent Chase?* 291 SCIENCE 1194, 1194 (2001).

³ *Id.*; see also *Celera—Welcome*, at <http://www.celera.com> (last visited Oct. 26, 2001) (offering information about the company and new developments). One recent patent belonging to Celera covers the nucleotide molecule and peptide amino acid sequence of a Human Metalloprotease and methods for obtaining peptide para- and orthologs. U.S. Patent No. 6,294,368 (issued Sept. 25, 2001). Though perhaps not as well known in the popular press, metalloproteases are thought to perform a role in regulating levels of proteins with structural, enzymatic, and regulatory function and could contribute to such diseases as “cancer, arteriosclerosis, and degenerative disorders.” *Id.* at col. 1. Celera claims the following:

1. An isolated nucleic acid molecule consisting of a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence that encodes an amino acid sequence shown in SEQ ID

NO:2;

(b) a nucleic acid molecule consisting of the nucleic acid sequence of SEQ ID No: 1;

(c) a nucleic acid molecule consisting of the nucleic acid sequence of SEQ ID No: 3;

and

(d) a nucleotide sequence that is completely complementary to a nucleotide sequence of (a)-(c).

2. A nucleic acid vector comprising a nucleic acid molecule of claim 1.

3. A host cell containing the vector of claim 2.

4. A process for producing a polypeptide comprising culturing the host cell of claim 3 under conditions sufficient for the production of said polypeptide, and recovering the peptide from the host cell culture.

5. An isolated polynucleotide consisting of a nucleotide sequence set forth in SEQ ID NO:1.

6. An isolated polynucleotide consisting of a nucleotide sequence set forth in SEQ ID NO:3.

7. A vector according to claim 2, wherein said vector is selected from the group consisting of a plasmid, virus, and bacteriophage.

recently begun to address the potential problems in allowing claims to genes of unknown functions. Under the new guidelines, issued in January of 2001, patent examiners must reject patents that do not describe a "specific, substantial and credible" use for DNA sequence.⁴ Thus, doomed are the majority of expressed sequence tags (ESTs) and those gene sequences which "finesse the utility requirement" by using computer programs which merely guess at the likely function of a given DNA sequence.⁵ In a midst of public controversy, how the PTO applies the new utility examination guidelines, may be an essential step in establishing with some surety that gene patents will not be invalidated upon challenge in the courts. The new utility guidelines, applied in addition to the standards for novelty, usefulness, and non-obviousness, aim to assist courts in determining the ultimate worth of patented genomic information.

This comment focuses on the newly revised PTO utility examination guidelines for biotechnology patents. Part I includes a brief background in the field of genetic research, highlighting major accomplishments that have lead to the current gene patenting controversy. Part II analyzes the effect of competing public and private interests in the rush to patent genetic sequences. Parts III and IV, provide a brief history of patenting in the field of biotechnology and explain how gene patent abuse prompted the new utility guidelines. Part V examines the new utility guidelines in the context of patent law policy. Part VI discusses pending cases and their effect on public perception. Finally, Part VII analyzes the PTO's likelihood of success in applying the new utility guidelines and proposes a number of measures including legislation on licensing agreements for patents with significant medical importance and efforts toward correcting public misconceptions for the ultimate end of ensuring patent rights to genetic information.

I. BACKGROUND TO GENE RESEARCH

But what exactly is the human genome and why the rush to patent? Said esteemed molecular biologist David Baltimore, "I've seen a lot of exciting biology emerge over the past 40 years. But chills still ran down my spine when I first read the paper that describes the outline of our genome."⁶ The human genome is the set of

8. A vector according to claim 2, wherein said isolated nucleic acid molecule is inserted into said vector in proper orientation and correct reading frame such that the protein of SEQ ID NO: 2 may be expressed by a cell transformed with said vector.

9. A vector according to claim 8, wherein said isolated nucleic acid molecule is operatively linked to a promoter sequence.

Id. at cols. 65-66.

⁴ Utility Examination Guidelines, 66 Fed. Reg. 1092, 1092 (Jan. 5, 2001).

⁵ *Genetics and Patenting*, at <http://www.ornl.gov/hgmis/elsi/patents.html> (last modified Sept. 27, 2001) (giving a general explanation of genetics and patenting).

⁶ David Baltimore, *Our Genome Unveiled*, 409 NATURE 814, 814 (2001). A native New Yorker, David Baltimore is an esteemed molecular biologist and Nobel laureate. *Baltimore, David*, in MICROSOFT® ENCARTA® ONLINE ENCYCLOPEDIA (2001), at <http://encarta.msn.com/find/Concise.asp?z=1&pg=2&ti=761582601> (last visited Oct. 27, 2001). In 1975, Baltimore shared the Nobel prize in physiology/medicine with Renato Dulbecco and Howard M. Temin for genetic studies in tumor causing viruses. *Id.* Baltimore is also well known for his work in discovering the process of retroviral transcription, essential in understanding how the AIDS virus initiates replication. *Id.*

essential blueprints used in creating a human being.⁷ Elucidating the function of any one of its yet unknown genes may lead to a cure for cancer, heart disease, diabetes, and more.⁸ The potential social and commercial value is overwhelming.

Nearly all organisms, including humans, store their genetic information in a genome based on deoxyribonucleic acid (DNA).⁹ The human genome is organized into 23 pairs of chromosomes, each chromosome comprised of thousands of genes, each gene comprised of a particular stretch of DNA sequence.¹⁰ Now known as the primary molecule of life, DNA was actually discovered by Frederick Miescher in the early 19th century.¹¹ But it was not until 1958 that researchers James Watson and Francis Crick proposed a working model for how DNA enables our genome to pass hereditary information to subsequent generations.¹²

The development of 'Recombinant DNA Technology' in 1973 was another landmark discovery in the field of genetics.¹³ Herbert Boyer and Stanley Cohen established that a gene of one bacterial organism could be removed and recombined in vitro with the DNA of a different bacterial organism.¹⁴ The recombined DNA could then be re-introduced into the first organism to confer the gene's characteristic trait.¹⁵ Although this discovery prompted the "birth of the biotechnology era," by today's standards, use of recombinant DNA technology is trivial when applied to

⁷ *Id.*; see also National Center for Biotechnology Information, *NCBI HomePage*, at <http://www.ncbi.nlm.nih.gov/> (revised Oct. 24, 2001) (allowing a user to browse through sequences of the government-sponsored human genome map).

⁸ Regalado, *supra* note 1.

⁹ Baltimore, *supra* note 6, at 814.

¹⁰ *Id.*

¹¹ Lisa A. Karczewski, Comment, *Biotechnological Gene Patent Applications: The Implications of the PTO Written Description Requirement Guidelines on the Biotechnology Industry*, 31 MCGEORGE L. REV. 1043, 1048 (2000) (citing JAMES D. WATSON ET AL., RECOMBINANT DNA 13 (2d ed. 1992)). Miescher was born in 1844 and is now best known for discovering nucleic acids. Max-Planck-Society, *The Friedrich-Miescher-Laboratory*, at <http://www.fml.tuebingen.mpg.de/fml.htm> (last modified Jan. 14, 2000). However, his work in science was not limited to this. *Id.* Miescher also showed that the regulation of breathing depends on bloodstream levels of CO₂. *Id.*

¹² Karczewski, *supra* note 11, at 1048. Structurally, DNA molecules form a double helix in the shape of a long, twisted ladder. *Id.* Chemically, a sugar-phosphate backbone makes up the 'sides' of the ladder while the 'rungs' are comprised of one of the four nucleotide bases, adenine, cytosine, guanine, or thymine. *Id.* These rungs hydrogen bond complementarily, adenine to thymine and cytosine to guanine, with rungs on the adjacent side. Complementary base pairing is what allows DNA to be structurally defined by any given stretch of sequence. *Id.*

¹³ *Id.* at 1049.

¹⁴ *Id.*; see also Massachusetts Institute of Technology, *7.001 Hypertextbook: Recombinant DNA Chapter Directory*, at <http://esg-www.mit.edu:8001/esgbio/rdna/rdnadir.html> (last visited Oct. 27, 2001) (offering a brief history and picture description of cloning technology). It was through the use of Boyer's enzyme, capable of cutting DNA into discrete fragments, and Cohen's method of introducing a portion of genetic material encoding antibiotic resistance, that cloning was born. *Id.*

¹⁵ Karczewski, *supra* note 11, at 1049, 1051. The technique of Recombinant DNA Technology requires the production of a complementary DNA (cDNA) sequence that encodes a protein. *Id.* at 1051. Here, DNA must initially be cloned. Cloning includes: 1) selecting a DNA source for cloning (chromosomal DNA or cDNA); 2) producing DNA fragments for insertion into a plasmid vector (the collection of cloned DNA fragments is called a library); and 3) screening the newly created library for expression of a desired protein. *Id.*

simplistic bacterial systems.¹⁶ Manipulating the genes of higher organisms, like humans, has posed a more significant challenge.¹⁷

As the biological dogma goes, DNA encodes mRNA, which encodes protein.¹⁸ Messenger ribonucleic acid (mRNA) acts as an intermediate transcriber while proteins are the functional molecules of a cell.¹⁹ Yet in higher organisms, not all DNA encodes protein.²⁰ It has been estimated that protein is made from only 1.1% to 1.4% of the entire human genome.²¹ The rest is thought to be ignored, regulatory or remnants from our evolutionary past.²² Protein production relies on cellular machinery that must find these selected portions of chromosomal DNA to create a protein encoding sequence.²³

For researchers, this complication means that raw genomic information must be scanned with fragments of known gene sequence, compared to back calculated sequence from proteins, or run through computer programs that predict encoding regions.²⁴ The task of finding a human gene is rarely trivial.²⁵ Hence, when the complete sequence of one of the 30,000 to 50,000 anticipated human genes is found, researchers have been quick to patent.²⁶

¹⁶ *Id.* Mammalian DNA has more elements than bacterial DNA, including what some have referred to as "junk DNA," which most likely functions in regulation of gene expression but does not encode protein. Baltimore, *supra* note 6, at 814.

¹⁷ Baltimore, *supra* note 6, at 814; *see also* Georgia Institute of Technology, *Software Program Developed at Georgia Tech Adds New Capabilities to Decipher Genomes of Higher Organisms* (Dec. 02, 1998) (describing new software for predicting gene encoding regions in higher organisms), at <http://www.sciencedaily.com/print/1998/12/981202075222.htm>.

¹⁸ Karczewski, *supra* note 11, at 1051; *see also* Massachusetts Institute of Technology, *The Central Dogma of Biology*, at <http://cyberbio.mit.edu:8001/esgbio/dogma/dogma.html> (last visited Oct. 27, 2001) (giving detailed information about the different forms of encoding and non-encoding RNA).

¹⁹ *Id.*

²⁰ Baltimore, *supra* note 6, at 814.

²¹ *Id.*

²² *Id.*

²³ *Id.*; *see also* Craig G. Livingston & Martin E. Nobel, *The Molecules of Life*, at http://biop.ox.ac.uk/www/mol_of_life/Molecules_of_Life.html (last visited Oct. 15, 2001) (providing an interactive demonstration of biotechnology techniques and on how proteins function in living cells).

²⁴ Gerald M. Rubin, *Comparing Species: The Draft Sequence*, 409 NATURE 820, 820 (2001); *see* Howard Hughes Medical Institute, *Gerald M. Rubin*, at <http://www.hhmi.org/research/investigators/rubin.html> (last updated Apr. 16, 2001). Dr. Gerald Rubin has contributed much to the field of drosophila genetics through use of computer programs used to predict genes from genomic information. *Id.*

²⁵ Rubin, *supra* note 24, at 820; *see also* Biowriters, *The Gene Discovery Page*, at <http://www.biowriters.com/bioinformatics/gdp.html> (most recently updated Feb. 21, 2001) (discussing various type of bioinformatic tools for use by scientists with little computer training, from identifying a gene sequence of interest to predicting possible protein structures and functions).

²⁶ Martin Brow & Sandy Thomas, *Patents in a Genetic Age: The Present Patent System Risks Becoming a Barrier to Medical Progress*, 409 NATURE 763, 763 (2001). The authors urge caution in the absence of legislative action to protect public interest before allowing unfettered gene patenting. *Id.*

II. PUBLIC V. PRIVATE INTEREST

The rush to capitalize on gene patents may also be explained by competing efforts of the public and private sectors. The publicly funded Human Genome Project began in 1990, aiming to decode what became the 3.2 gigabases of human genome sequence.²⁷ This multibillion-dollar project was the coordinated effort of twenty “laboratories and hundreds of people” from around the world.²⁸ Announcement of the Human Genome Project’s first draft sequence came in February of 2001.²⁹ However, that same week, Craig Venter—founder of Celera Genomic, Inc., announced the completion of Celera’s own genome sequence.³⁰ The privately owned company had begun sequencing only one year earlier.³¹

Fear that private companies might try to destroy public efforts to make genomic information freely available was evidenced by the apparently critical statements regarding human genome patents made by former U.S. President Bill Clinton and British Prime Minister Tony Blair.³² Yet in the words of Craig Venter, “Speed matters—discovery can’t wait.”³³ Celera’s rapid success in completing its version of the human genome demonstrated the power of private funding to spur discovery.³⁴ Venter believes such discovery is deserving of reward, specifically in the form of a patent.³⁵

²⁷ Baltimore, *supra* note 6, at 814.

²⁸ *Id.*; see U.S. Department of Energy Office of Science, Office of Biological and Environmental Research, Human Genome Program, *Human Genome Project Information*, at http://www.ornl.gov/TechResources/Human_Genome/home.html (last modified Oct. 19, 2001) (discussing the “next step” in using the information obtained from the Human Genome Project to better understand human biological functions).

²⁹ Baltimore, *supra* note 6, at 814.

³⁰ See Alan Hall, *Craig Venter: The Bad Boy of Genomics Makes Good*, BUS. WK. ONLINE, Apr. 7, 2000, at <http://www.businessweek.com/bwdaily/dnflash/apr2000/nf00407e.htm>.

³¹ *Id.*

³² See BMA, *Gene Patenting: A BMA Discussion Paper* (July 2001), at <http://www.bma.org.uk/public/ethics.nsf/39f32339ff78cd6b802566a6003f3311/8b561223c9e754b880256a9300531f61?OpenDocument> (last visited Oct. 27, 2001). According to the authors:

To realize the full promise of this research, raw fundamental data on the human genome, including the human DNA sequence and its variations, should be made freely available to scientists everywhere. Unencumbered access to this information will promote discoveries that will reduce the burden of disease, improve health around the world, and enhance the quality of life for all humankind. Intellectual property protection for gene-based inventions will also play an important role in stimulating the development of important new health care products.

Id.

³³ See Hall, *supra* note 30.

³⁴ *Id.* Ironically, Venter began researching at the publicly funded National Institutes of Health (NIH) in the early 1990s. *Id.* His departure from the government agency followed a heated controversy over an NIH decision to patent partial gene sequences identified by Venter’s research. *Id.*

³⁵ *Id.* With \$70 million dollars of funding from Healthcare Management Investment Corp., Venter demonstrated his own method of sequencing called “shotgun cloning”—10 times less expensive and much faster than methods used by the government, on the pathogenic bacterium *Hemophilus influenzae*. *Id.* As early as 1995, Venter ‘wowed’ the scientific community by publishing the genome of *H. influenzae*, as the first complete sequencing of a free-living organism. Venter formed Celera with Perkin-Elmer, when the company agreed to fund Venter’s 1997 proposal

In March of 2000, Celera announced that it had begun sequencing with the intention of creating a computer database.³⁶ The company insisted this database would be free and open to all researchers via the Celera web site, but vehemently stated that all genes discovered in the Celera human genome should qualify for patents.³⁷ This statement directly opposed the publicly funded Human Genome Project whose aim was to make all genomic information unpatentable.³⁸ By April 2000, despite wide criticism from the scientific community, Celera's company reports revealed over 6,500 "provisional patent applications," meaning that Celera was indeed staking its claim.³⁹

III. BACKGROUND TO GENE PATENTING

Why allow gene patenting? The government's purpose in granting patent protection can be found in Article I, Section 8, Clause 8 of the United States Constitution. This clause empowers Congress, "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."⁴⁰ Since their beginning, legislated patent acts have maintained a broad scope regarding issuance "includ[ing] anything under the sun that is made by man."⁴¹

However, the reward of patentability comes at a price. In exchange for the right to exclude others from making, using, selling, offering for sale, or importing an invention, for a period of time measured twenty years from the filing date, an inventor must disclose the invention with sufficient detail to enable its reproduction by one skilled in the art.⁴² For the PTO to issue a patent, an invention must meet requirements for statutory subject matter, utility, novelty, and non-obviousness.⁴³ With the addition of new utility guidelines, a gene patent applicant must also teach others how to use the invention in at least one way.⁴⁴

to sequence the entire human genome for only \$300 million, a small sum considering what was spent on the publicly funded effort. *Id.*

³⁶ *Id.*

³⁷ *Id.*

³⁸ Baltimore, *supra* note 6, at 814.

³⁹ *See* Hall, *supra* note 30 (noting that patent applications must be filed within one year of discovery).

⁴⁰ U.S. CONST. art. 1, § 8, cl. 8.

⁴¹ Karczewski, *supra* note 11, at 1051. The Patent Act of 1793, was among the first of these U.S. patent laws. *Id.* at 1054. Subsequent statutes came in 1836, 1870, and 1874 and maintained the founders' broad philosophy regarding issuance. *Id.* Even the change in 1952 which replaced the word "art" with "process" intended to keep this broad scope by "includ[ing] anything under the sun that is made by man." *Id.*

⁴² *Id.* Section 112 states in relevant part:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

35 U.S.C. § 112 (2000).

⁴³ Karczewski, *supra* note 11, at 1051.

⁴⁴ Utility Examination Guidelines, 66 Fed. Reg. 1092, 1092 (Jan. 5, 2001).

Patenting a gene differs from patenting a chemical compound or process for using or altering the genetic produce, although such uses may be part of the claims.⁴⁵ Gene patents cover the molecule of DNA, but not the code for its genetic sequence.⁴⁶ And as with any patent, for a gene patent to issue it must comply with the requirements in 35 U.S.C. §§ 101, 102, and 103.⁴⁷ Although utility is typically never an issue under § 101, usefulness is often the deciding factor for inventions such as methods of doing business, chemical compounds, and now DNA.⁴⁸

The biotech industry's first concerns came under the statutory subject matter requirement in § 101, which is read to include "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof."⁴⁹ Statutory subject matter does not include natural phenomena or products of nature.⁵⁰ Early on, many in the biotech industry feared that genes, as products of nature, would be excluded from patent protection.⁵¹

However, these fears were assuaged following a landmark decision in *Diamond v. Chakrabarty*.⁵² There, the Supreme Court held that a genetically engineered microorganism was patentable under 35 U.S.C. § 101.⁵³ Although the bacterial

⁴⁵ *Id.*

⁴⁶ *Id.* at 1094

⁴⁷ According to the Patent Act, the following inventions are patentable: "[A]ny new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of [Title 35]." 35 U.S.C. § 101 (2000).

The Patent Act requires that an invention must be novel to qualify for a patent: "A person shall be entitled to a patent unless— (a) the invention was known or used by others . . ." 35 U.S.C. § 102 (2000).

The Patent Act also requires that an invention be based on non-obvious subject matter to qualify for a patent. 35 U.S.C. § 103 (2000). In particular, for biotechnological processes, the Act states:

(3) For purposes of paragraph (1), the term "biotechnological process" means—

(A) a process of genetically altering or otherwise inducing a single- or multi-celled organism to—

(i) express an exogenous nucleotide sequence,

(ii) inhibit, eliminate, augment, or alter expression of an endogenous nucleotide sequence, or

(iii) express a specific physiological characteristic not naturally associated with said organism;

(B) cell fusion procedures yielding a cell line that expresses a specific protein, such as a monoclonal antibody. . . .

35 U.S.C. § 103 (2000).

⁴⁸ 35 U.S.C. § 101 (2000).

⁴⁹ *Id.*

⁵⁰ Karczewski, *supra* note 11, at 1055.

⁵¹ *Id.*

⁵² 447 U.S. 303, 305-06 (1980). The Court stated:

Chakrabarty's patent claims were of three types: first, process claims for the method of producing the bacteria; second, claims for an inoculum comprised of a carrier material floating on water, such as straw, and the new bacteria; and third, claims to the bacteria themselves. The patent examiner allowed the claims falling into the first two categories, but rejected claims for the bacteria. His decision rested on two grounds: (1) that microorganisms are "products of nature," and (2) that as living things they are not patentable subject matter under 35 U. S. C. § 101.

Id.

⁵³ *Id.*

organism was merely transformed with genes encoding proteins used in breaking down crude oil, the classification of the bacterium as “human-made,” verses that “made by nature” fulfilled the requirement for statutory subject matter because the organism did not exist in nature with the additional genes.⁵⁴ The genes contained in the new organism were protected under patent law.⁵⁵

A second concern expressed by the biotech industry involved the novelty requirement of § 102. Researchers feared that a gene would not meet the novelty requirements of 35 U.S.C. § 102 because genetic sequence, as it exists in a database, is prior art.⁵⁶ Reasoning found in *Chakrabarty* also served to establish novelty for isolated genes because their use in an expression system, which in *Chakrabarty* was a bacterium used in cleaning up oil spills, made the inventor “first to confer the benefit of the invention on the public.”⁵⁷ With the understanding that a patented gene differs from what can be found in a database or in genomes of naturally existing organisms, the standard for novelty could be met where the patented gene is removed from its natural environment.⁵⁸

The PTO guidelines state that a patentable gene sequence exists when a researcher separates the protein coding section from extraneous information in the gene sequence.⁵⁹ As applied to the human genome, a researcher must make significant alterations in the raw genetic sequence to isolate, let alone patent, a gene of interest.⁶⁰ Here, current gene patenting policy treats newly isolated gene sequence like naturally occurring chemicals, which may be patented in an isolated or purified form, a concept that is familiar to patent law.⁶¹

Statutory subject matter and novelty aside, a patent must also fulfill the requirement of non-obviousness under 35 U.S.C. § 103. Confusion arose when applying the standard of non-obviousness to gene sequences.⁶² Section 103 of the Patent Act may be read (1) to apply to the method of acquiring a sequence or (2) to the sequence itself.⁶³ Given that the non-obviousness standard requires courts to establish the scope and content of the prior art, ascertain differences between the prior art and the claimed invention, and determine the level of ordinary skill in the

⁵⁴ *Id.*

⁵⁵ *Id.* at 318. However, the court was careful to point out the limits of their authority. *Id.* “Our task, rather, is the narrow one of determining what Congress meant by the words it used in the statute; once that is done our powers are exhausted. Congress is free to amend § 101 so as to exclude from patent protection organisms produced by genetic engineering.” *Id.*

⁵⁶ Regalado, *supra* note 1.

⁵⁷ Karczewski, *supra* note 11, at 1048, 1055 (citing Andrew T. Knight, Note, *Pregnant with Ambiguity: Credibility and the PTO Utility Guidelines in Light of Brenner*, 73 IND. L.J. 997, 1008 (1998)) (noting that information is not in the hands of the public when it has not been “published, publicly sold or used, or previously invented and not abandoned”).

⁵⁸ Karczewski, *supra* note 11, at 1057; *see also* Utility Examination Guidelines, 66 Fed. Reg. 1092, 1092 (Jan. 5, 2001). This reasoning is an extension of a relatively recent case dealing with the isolation of prostaglandins PGE2 and PGE3 from human and animal prostrate glands. *Id.* at 1093. There, the court held that the appellants’ claim to PGE2 and PGE3 was neither overly broad to encompass what has previously existed in “nature’s storehouse” nor merely discovered since these compounds do not exist in pure form in nature. *Id.*

⁵⁹ Utility Examination Guidelines, 66 Fed. Reg. at 1092.

⁶⁰ Karczewski, *supra* note 11, at 1057.

⁶¹ Utility Examination Guidelines, 66 Fed. Reg. at 1094.

⁶² *Id.*

⁶³ Karczewski, *supra* note 11, at 1057.

art, the patent language was too vague to determine the proper application.⁶⁴ To most researchers, the reasonable assumption was to apply novelty to the gene sequence itself, given that methods used to remove a gene from genomic sequence are known to those with ordinary skill in the art (i.e., scientists), thereby making prior art useful only in establishing that a particular gene sequence has not already been isolated.⁶⁵ Nonetheless, a patent amendment in 1995 applied non-obviousness to both the process and subject matter.⁶⁶ Discouraged gene patentees breathed a sigh of relief when the Court of Appeals for the Federal Circuit, in *In re Deuel*,⁶⁷ held that “general motivation to search for some gene that exists does not necessarily make obvious a specifically-defined gene that is subsequently obtained as a result of that search.”⁶⁸ Hence, it was possible to obtain a gene patent using an obvious method.⁶⁹

Fulfilling the requirements for statutory subject matter, novelty, and non-obviousness, according to the new guidelines, gene patent applicants must also pay particular attention to the utility requirement of § 101.⁷⁰ Utility is perhaps the most important and by far the most abused requirement in gene patent applications.⁷¹ Stemming from the rise in gene patenting following technological advancements in the 1980’s, and most recently following the first draft release of the human genome, such abuses were the instigators for change in current patent applicant requirements.⁷² The PTO aimed these guidelines at companies making frivolous attempts to patent genes before they have determined use.⁷³ Utility now contains “specific, substantial, and credible” requirements.⁷⁴

Similar to what has been done in the past for patents in the computer industry, a four prong test has now been established to better enable PTO examiners to judge the usefulness of a given gene patent.⁷⁵ First, the claims and supporting written description must be read to determine exactly what is being claimed.⁷⁶ This prong looks to whether the claims meet statutory subject matter requirements and whether the claims show an apparent well-established utility.⁷⁷ A claim may not be rejected for lack of utility if this first prong is satisfied.⁷⁸ Second, the claims and written description must be reviewed for specific and substantial utility that is credible.⁷⁹ Here, a claim is not rejected if its usefulness would be obvious to one skilled in the art.⁸⁰ The claim may only be rejected if the specified utility is for a “throw away,”

⁶⁴ *Graham v. John Deere*, 383 U.S. 1, 37 (1966).

⁶⁵ *Karczewski*, *supra* note 11, at 1057.

⁶⁶ *Id.*

⁶⁷ 51 F.3d 1552 (Fed. Cir. 1995).

⁶⁸ *Id.* at 1557.

⁶⁹ *Id.*

⁷⁰ Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (Jan. 5, 2001).

⁷¹ *New Gene Patent Guidelines Issued* (Jan. 5, 2001), at <http://www.msnbc.com/news/512245.asp?cp1=1>.

⁷² *Regalado*, *supra* note 1.

⁷³ Utility Examination Guidelines, 66 Fed. Reg. at 1094.

⁷⁴ *Id.*

⁷⁵ *Id.* at 1097.

⁷⁶ *Id.* at 1098.

⁷⁷ *Id.*

⁷⁸ *Id.*

⁷⁹ *Id.*

⁸⁰ *Id.* “If at any time during the examination, it becomes readily apparent that the claimed invention has a well-established utility, do not impose a rejection based on lack of utility. . . .” *Id.*

“insubstantial,” or “nonspecific” utility such as a “complicated invention for use as landfill.”⁸¹ Credibility may be attained by asserting just one specific and substantial utility supported by test data, expert affidavits, or printed publication.⁸² If no such assertion is made, then the patent will be rejected under § 101, because it lacks utility, and under § 112 for lack of enablement.⁸³ Third, if an examiner rejects a claim for lack of utility, he must respond with a detailed explanation as to why the invention lacks a substantial, credible utility.⁸⁴ The response must include clear reasoning, support from factual findings, and evaluations of the closest prior art.⁸⁵ Finally, the examiner must view all the evidence of record and determine whether the utility would be considered specific, substantial, and credible by one exhibiting ordinary skill in the art.⁸⁶ The examiner should assume that a specific, substantial, and credible utility has been asserted unless one of ordinary skill in the art would have legitimate reason to doubt this assertion.⁸⁷ Likewise, if a patent applicant offers expert testimony, an examiner is to set aside personal disagreements regarding the significance or meaning of the given facts, and allow a finding of utility.⁸⁸

IV. GENE PATENTING ABUSE

What prompted the utility guidelines and how were gene patents abused? The new guidelines state that it is not enough to simply purify a gene from its natural position in the genome and guess at a function.⁸⁹ A patented gene must have “specific, substantial, and credible” use.⁹⁰ This “new” standard derives in part from the earlier Supreme Court ruling of *Brenner v. Manson*,⁹¹ which held that patent utility is not established simply by proving that a given product was the result of scientific investigation.⁹² In *Brenner*, the product was not a gene, but a chemically synthesized compound claimed by the respondent.⁹³ The Court reasoned that, “[a] patent is not a hunting license. It is not a reward for the search, but compensation

⁸¹ *Id.*

⁸² *Id.*

⁸³ *Id.*

⁸⁴ *Id.*

⁸⁵ *Id.*

⁸⁶ *Id.*

⁸⁷ *Id.*

⁸⁸ *Id.* The guidelines describe the elements of a prima facie case for rejection as follows: The *prima facie* showing must contain the following elements: (1) An explanation that clearly sets forth the reasoning used in concluding that the asserted specific and substantial utility is not credible; (2) Support for factual findings relied upon in reaching this conclusion; and (3) An evaluation of all relevant evidence of record, including utilities taught in the closest prior art.

Id.

⁸⁹ *New Gene Patent Guidelines Issued, supra* note 71.

⁹⁰ Utility Examination Guidelines, 66 Fed. Reg. at 1094.

⁹¹ 383 U.S. 519 (1966).

⁹² *Id.* at 532.

⁹³ *Id.* at 536.

for its successful conclusion.”⁹⁴ The public would not reap any benefit in creating a vast monopoly on future scientific knowledge.⁹⁵

The change in patenting guidelines was by no means undeserved. Many agree that the “patent grab” has been driven less by the expectation that a particular gene sequence will result in production of a useful protein and more by the idea that enough patenting will create a protectable “haystack” in which one will find a few “genetic needles of value.”⁹⁶

Even before completion of the human genome, 1990’s DNA sequencing technology enabled patenting of gene fragments known as expressed sequence tags (ESTs).⁹⁷ Generally, ESTs had no known biological function, but represented what was thought to be a portion of the full-length gene.⁹⁸ An average EST contains 300-500 bases, which is 10-30% of the full-length gene in its spliced form, and only 3-5% of its full genomic size.⁹⁹ Patent applications have claimed ESTs for use as scientific probes, for finding a gene or another EST, or to map a gene to a chromosome.¹⁰⁰ However, some patent applications have gone so far as to claim ESTs as probes for use in dog food and shampoo (an unlikely “specific, substantial, and credible” use for lack of commercial viability).¹⁰¹ Researchers voiced strong opposition to EST claims because ESTs required little effort to obtain and researchers feared that an EST patent holder could block other researchers from obtaining patents to the entire gene sequence, which could impose undue research costs through sequence licensing agreements.¹⁰² Much like the *Brenner* arguments for chemicals obtained in a research screen, ESTs had the potential to create “vast monopolies” with little societal profit.¹⁰³ Under the new guidelines, many previously issued EST patents are not likely to pass the “specific, substantial, and credible” use requirements.¹⁰⁴ Nor is it likely that gene patents will prevail where researchers have relied on computer programs to construct what was believed to be a gene, rather than physically testing the gene sequence products in a lab.¹⁰⁵ The new utility guidelines are at least a start in remedying past patent problems.

⁹⁴ *Id.*

⁹⁵ *Id.* at 537.

⁹⁶ *Genetics and Patenting*, *supra* note 5.

⁹⁷ *Id.* ESTs are still useful scientific tools and can be used to identify any number of genes in compiled genomic databases. Giuseppe Borsani, *The EST Machine*, at <http://www.tigem.it/ESTmachine.html> (last visited Oct. 27, 2001) (linking several databases for analysis of such express sequence tags).

⁹⁸ *Genetics and Patenting*, *supra* note 5.

⁹⁹ *Id.*

¹⁰⁰ *Id.*

¹⁰¹ *New Gene Patent Guidelines Issued*, *supra* note 71; *cf.*, *e.g.*, UNITED STATES PATENT AND TRADEMARK OFFICE, REVISED INTERIM UTILITY GUIDELINES TRAINING MANUAL 7 (1999) (“[U]sing transgenic mice as snake food is a utility that is neither specific . . . nor substantial . . .”), *available at* <http://www.uspto.gov/web/offices/pac/utility/utilityguide.pdf>.

¹⁰² *Id.*

¹⁰³ *Brenner v. Manson*, 383 U.S. 519, 537 (1966).

¹⁰⁴ Regalado, *supra* note 1.

¹⁰⁵ Sara Dastgheib-Vinarov, Comment, *A Higher Nonobviousness Standard for Gene Patents: Protecting Biomedical Research from the Big Chill*, 4 MARQ. INTELL. PROP. L. REV. 143, 170-171 (2000).

V. WILL THE CURRENT PATENT LAW WORK?

Keeping in mind the goals of our patent system, we must also consider whether the new utility guidelines will aid the underlying and fundamental policies on patenting by (1) rewarding researchers for their discoveries by giving them a 'first crack' at commercial production, (2) allowing best resource allocation and preventing research redundancy, (3) promoting research into new areas, and (4) allowing public access to knowledge of the patented information.¹⁰⁶ Different conclusions are reached when applying the new utility guidelines to genes as compositions of matter, partial gene sequences, non-encoding regions, and entire genomes.

Enforcement of the new utility guidelines will allow patents issued for DNA sequences as "compositions of matter" to meet all four goals.¹⁰⁷ Researchers who have invested significant time, effort, and money are given the reward of exclusive rights to the DNA molecule and its constructs.¹⁰⁸ Combining best resource allocation with reward, the new utility guidelines strike a delicate balance between the likelihood of commercial success and the potential for abuse and wasted resources.¹⁰⁹ Were it not for the utility requirement, researchers could be wasting valuable 'patent time' while research and development attempts to find a specific, substantial, and credible use for an isolated gene sequences.¹¹⁰

Yet, the utility requirement is not so restrictive as to create an undue burden of expense or a risk of revealing important knowledge too soon. The PTO merely requires evidence as to the patent holder's potential for one specific, substantial, and credible use.¹¹¹ It need not be ready for commercial use at the time of application.¹¹² Indeed, certain marketable gene products, or derivative gene products, may require considerable testing between the period of patent application and commercial use.¹¹³ This potential lag in marketability, as often required for FDA approval in medical therapies, still promotes adequate reward to the patent holder in that a gene product's published positive result will undoubtedly influence company stocks where an already obtained patent will ensure at least some period of exclusivity in studying and developing the gene product for its particular use.¹¹⁴ Hence, the value of the exclusive right to genes encoding commercially valuable proteins is still larger than what is lost by revealing the sequence and its use to the public.¹¹⁵

Likewise, were it not for the new utility guidelines, other researches could be wasting valuable research time finding a use for their own isolated DNA molecules.¹¹⁶ Recall that patents on gene sequences do not prevent the public from studying the DNA of other researchers, i.e., viewing, using, or analyzing the actual

¹⁰⁶ *Genetics and Patenting*, *supra* note 5.

¹⁰⁷ *Id.*

¹⁰⁸ *Id.*

¹⁰⁹ *Id.*

¹¹⁰ *Id.*

¹¹¹ Utility Examination Guidelines, 66 Fed. Reg. 1092, 1094 (Jan. 5, 2001).

¹¹² *Id.*

¹¹³ *Genetics and Patenting*, *supra* note 5.

¹¹⁴ *Id.*; see *The FDA Drug Approval Process*, at http://idid.essortment.com/fdadrugapprova_rrgy.htm (last visited Oct. 27, 2001) (discussing the phases involved in clinical research).

¹¹⁵ *Genetics and Patenting*, *supra* note 5.

¹¹⁶ *Id.*

genomic DNA sequence.¹¹⁷ Nor do they prevent others from viewing the detailed written description of how the DNA will be used.¹¹⁸ This serves both to prevent redundancy and to promote discovery.¹¹⁹ Scientists will know what genes are already being researched and will gain insight into those stretches of the genome that potentially encode protein sequence, or researchers will discern uses for recently isolated genes that have yet to be patented for lack of an appropriate use.¹²⁰ Hence, for those who aim to produce a commercially viable protein or derivative product, the current patent system works.¹²¹

Although capable of promoting the same four goals, patents issued for partial gene sequences would have significant difficulty in achieving these goals were it not for the new utility guidelines.¹²² Despite past abuse, the new guidelines do not expressly prohibit patents to partial gene sequences.¹²³ In fact, ESTs with legitimate use can be patented as diagnostic probes or for use in studying the information in non-coding regions of DNA molecules.¹²⁴ Since the use of an EST probe differs from the use of the full-length DNA molecule, both are patentable.¹²⁵ However researchers must use caution in constructing claim language.¹²⁶ In the case of a disease diagnostic probe, a claim must specify that the DNA molecule serves as a marker for a disease gene to prevent *per se* unpatentability.¹²⁷ PTO examiners will carefully scrutinize such claims.¹²⁸

Patenting other types of useful, yet non-encoding, genetic information will likewise serve the goals of promoting discovery and reducing research redundancy.¹²⁹ Single nucleotide polymorphisms (SNPs), as their name implies, are genomic sequences in which a single nucleotide has been altered.¹³⁰ Occurring naturally every 100 to 1000 bases in the genome, SNPs are found in both coding and non-coding regions.¹³¹ Hence, many have no effect on gene function, but are believed to predispose an individual to certain diseases or affect their responses to drugs.¹³² The creation of SNP maps may allow scientists to identify multiple genes associated with

¹¹⁷ Utility Examination Guidelines, 66 Fed. Reg. at 1094. A patent is issued on the isolated DNA molecule, not the DNA sequence itself. *Genetics and Patenting*, *supra* note 5.

¹¹⁸ *Genetics and Patenting*, *supra* note 5.

¹¹⁹ *Id.*

¹²⁰ *Id.*; *see also* Utility Examination Guidelines, 66 Fed. Reg. at 1094 (“An isolated and purified DNA molecule may meet the statutory utility requirement if, *e.g.*, it can be used to produce a useful protein or if it hybridizes near and serves as a marker for a disease gene.”).

¹²¹ Rebecca S. Eisenberg, *Re-examining the Role of Patents in Appropriating the Value of DNA Sequence*, 49 EMORY L.J. 783, 790 (2000).

¹²² *Genetics and Patenting*, *supra* note 5.

¹²³ Utility Examination Guidelines, 66 Fed. Reg. at 1094.

¹²⁴ *Id.*

¹²⁵ *Id.*

¹²⁶ Dastgheib-Vinarov, *supra* note 105, at 170-171.

¹²⁷ Utility Examination Guidelines, 66 Fed. Reg. at 1094.

¹²⁸ *Id.*

¹²⁹ *Genetics and Patenting*, *supra* note 5.

¹³⁰ *Id.*

¹³¹ *Id.*

¹³² *Id.*

cancer, diabetes, heart disease, and mental illness.¹³³ U.K. Wellcome Trust philanthropy, a non-profit foundation, established in April 1999, has aimed to find and map some 300,000 common SNPs.¹³⁴ With the goal of generating a publicly available map, the trust has announced that it will be patenting their SNPs, not for purposes of enforcement, but to discourage others from wasting valuable resources researching the same information.¹³⁵ Application of the utility guidelines to SNPs will also promote the goals of our patent system.¹³⁶

Patenting raw genomic sequence is one example of how the current patent system does not work, but for good reason.¹³⁷ Genomic sequencers like Celera or Human Genome Sciences would argue that the creation of a computer-readable medium is indeed a product of 'human hands' and should be allowed patent rights.¹³⁸ To exclude information in a computer database from patent protection ignores the PTO's definition of "non-functional descriptive material" as distinct from that which is "merely carried off by" the computer readable medium.¹³⁹ This was precisely the reason Human Genome Sciences filed patent rights to their *H. influenza* genome.¹⁴⁰ However, a genome in its raw form is currently considered a natural substance¹⁴¹ Granting "full-blown" rights to an entire genome would produce undue reward, destroy the goals of best allocation, and prevent discovery in new areas by creating prohibitive licensing fees for future researchers.¹⁴² Because the alternative produces a more desirable result, it is unlikely that any entity will ever obtain patent rights on an entire genome.

Logic dictates that a patent may reasonably be restricted from discoveries or products of a modified process—as in the case of Human Genome Sciences' *H. influenza* or Celera's human genome database, when there is an alternative means of profiting which does not interfere with the goals of the patent system.¹⁴³ Since raw genomic sequence is considered to be outside the scope of subject matter patentability, Celera has opted to charge subscribers a fee to search its genomic database.¹⁴⁴ Celera is neither inhibited by nor intruding upon the free information provided in the publicly funded Human Genome Project.¹⁴⁵ Despite both genomes being termed 'complete,' they actually contain only 90% of the entire sequence of the human genome, and in many areas are complementary.¹⁴⁶ The publicly funded government agency has fulfilled its goal in providing unrestricted genetic information

¹³³ *Id.*; see also *Single Nucleotide Polymorphism: bSNP Search Options*, at <http://www.ncbi.nlm.nih.gov/SNP/> (revised Oct. 2, 2001) (giving access to various search engines used by scientists to identify genes or families of genes associated with a given SNP).

¹³⁴ *Single Nucleotide Polymorphism: bSNP Search Options*, *supra* note 133.

¹³⁵ *Id.*

¹³⁶ *Id.*

¹³⁷ *Id.*

¹³⁸ Eisenberg, *supra* note 121, at 790.

¹³⁹ *Id.*

¹⁴⁰ Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (Jan. 5, 2001).

¹⁴¹ *Genetics and Patenting*, *supra* note 5.

¹⁴² *Id.*

¹⁴³ *Id.*

¹⁴⁴ Hall, *supra* note 30.

¹⁴⁵ *Id.*

¹⁴⁶ Baltimore, *supra* note 6, at 814.

to the public.¹⁴⁷ Celera offers a complementary service for a price.¹⁴⁸ Also, given the slow and expensive nature of publicly funded genome sequencing, and the profit to be made from private subscribers, it is also unlikely that publicly funded genomic efforts will halt future sequencing by companies wishing to compare the genomes of different human populations.¹⁴⁹ Disallowing patents in this area would neither prevent profits, encourage redundancy, discourage further genome sequencing, nor completely restrict genomic information.¹⁵⁰ Hence, disallowing patents on entire genome sequences, regardless of a stated use, does not contradict the goals behind patent protection.¹⁵¹

Yet, the real question over which there is much disagreement is whether the current patent guidelines will provide adequate patent protection for claims directed to genes upon challenge in the courts. The argument stems partly from the history of the written description guidelines established in *Regents of the University of California v. Eli Lilly & Co.*¹⁵² There, gene patents were granted only narrow protection and patent claims could be only as broad as the gene sequence disclosed.¹⁵³ Patent holders now fear that because minor changes in the DNA sequence often lead to insignificant changes in the protein, patent protection may be essentially useless.¹⁵⁴

However, this argument may be overcome both by application of the new utility guidelines and the standard of non-obviousness.¹⁵⁵ Such a patent could be issued only if a new, “specific, substantial and credible” use could be shown by the applicant.¹⁵⁶ Given what is known of DNA sequence ‘wobble’ and amino acid substitution, infringement might not be as difficult to enforce as first suspected.¹⁵⁷ If a patent applicant attempts to change every third nucleotide in the coding sequence, thereby producing a different gene sequence which encodes the exact same amino acid sequence, he must still demonstrate that one with adequate skill in the art would not have predicted the product of the proposed gene sequence to be the same as that expressed by the original DNA molecule.¹⁵⁸ Such a patent is unlikely to issue without proof that the researcher is also claiming a specific, substantial, and credible use that is different than the use claimed for the original DNA molecule.¹⁵⁹ Without

¹⁴⁷ *Id.*

¹⁴⁸ Hall, *supra* note 30.

¹⁴⁹ *Id.*

¹⁵⁰ *Genetics and Patenting*, *supra* note 5.

¹⁵¹ *Id.*

¹⁵² 119 F.3d 1559 (Fed. Cir. 1997); *see* Karczewski, *supra* note 11, at 1076.

¹⁵³ Karczewski, *supra* note 11, at 1076-77.

¹⁵⁴ *Id.* at 1081.

¹⁵⁵ *Id.*

¹⁵⁶ Utility Examination Guidelines, 66 Fed. Reg. 1092, 1094 (Jan. 5, 2001).

¹⁵⁷ Dastgheib-Vinarov, *supra* note 105, at 160. In discussing degeneracy of the genetic code, amino acids are specified by a triplet codon of nucleotides. BRUCE ALBERTS, ET AL., *MOLECULAR BIOLOGY OF THE CELL* 230-31 (3d ed. 1994). However, absolute specificity is not required due to the ability of the tRNA (transfer RNA, a molecule used in translation of nucleotide to amino acids) to tolerate such mismatching in the third base pair. *Id.* at 231. The phenomenon is called *wobble base pairing* and explains why “so many of the alternative codons for an amino acid differ only in their third nucleotide.” *Id.*

¹⁵⁸ Utility Examination Guidelines, 66 Fed. Reg. at 1096-97.

¹⁵⁹ *Id.*; *see also In re Deuel* 51 F.3d 1552, 1555 (Fed. Cir. 1995) (“[A] gene probe for potentially isolating DNA or cDNA encoding a protein may be designed once the protein’s amino acid sequence,

sufficient evidence through experimental tests or expert testimony, the new utility guidelines would not allow patent issuance.¹⁶⁰ Similarly, were the researcher to change the molecular gene sequence to encode a single amino acid whose substitution would not predictably affect the structure or function of the protein product, he must prove that the substitution does cause a functional difference in addition to specifying its use.¹⁶¹ Similar to the addition of an active or inactive chemical linkage onto a commercially viable drug, an amino acid change must show some utility other than what may be found in the prior art.¹⁶²

VI. COURT CASES AND PUBLIC PERCEPTION

What does the public think? Perhaps the most frightening aspect of gene patenting involves public policy. Amid public misconceptions of what is actually meant by patenting a gene and in an environment of constantly progressing technologies, there are patent infringement lawsuits drawing national attention.¹⁶³ A good guess at how the PTO's utility guidelines will hold up under challenge in the courts is likely to be demonstrated in the pending case where the University of Rochester sued G.D. Searle for patent infringement.¹⁶⁴

The University of Rochester obtained a patent to the Cox-2 gene in April 2000. Almost immediately thereafter, Rochester filed suit against Pharmacia and its subsidiary, G.D. Searle.¹⁶⁵ Searle, a major pharmaceutical company, produces Celebrex, better known as 'super aspirin,' which acts as a chemical inhibitor to the protein encoded by the Cox-2 gene.¹⁶⁶ Rochester asserts patent rights to not only the sequence and protein product of the Cox-2 gene, but also to the method of using a drug to block the gene product and alleviate pain.¹⁶⁷ Although Searle admits to having used scientific findings on Cox-2 during its search for a pain-inhibiting drug, attorneys for Searle believe that the Rochester patent is invalid on grounds that the university has not given precise instructions for finding the drug inhibitor.¹⁶⁸

or a portion thereof, is known.'). Although this case highlights the court's broader acceptance of gene patents with respect to using known methods, in its description of the involved technology, the court does recognize the fact that several different gene sequences could code for the same protein and this could be an important factor in allowing claims directed to a given gene. *Id.* at 1554.

¹⁶⁰ Utility Examination Guidelines, 66 Fed. Reg. at 1096-97.

¹⁶¹ *Id.*

¹⁶² *Id.*

¹⁶³ Regalado, *supra* note 1.

¹⁶⁴ *Id.*

¹⁶⁵ *Id.*

¹⁶⁶ *Id.*

¹⁶⁷ *Id.*

¹⁶⁸ *Id.* The specific claim language is as follows:

(1) A method for selectively inhibiting PGHS-2 activity in a human host, comprising administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product to a human host in need of such treatment.

(2) The method of claim 1 in which the compound inhibits the enzymatic activity of the PGHS-2 gene product, and has minimal effect on enzymatic activity of PGHS-1.

(3) The method of claim 1 in which the activity of PGHS-1 is not inhibited.

(4) The method of claim 3 in which the compound is a non-steroid anti-inflammatory drug.

Although issued before release of the new utility guidelines, the challenged claims are being examined in a manner similar to prong two of the new utility test.¹⁶⁹ This prong rejects patents for failing to adequately teach others how to use the claimed invention.¹⁷⁰ The court's ruling in this matter should reveal whether the new utility standards are sufficient to ensure patentability, or whether the guidelines will need some refining.

Given the number of academic institutions protesting patent applications on the grounds that university researchers will not be able to afford licensing fees, Rochester lends itself to an intriguing brand of hypocrisy when one of its attorneys states that “[s]omehow there is a school of thought that different rules should apply to basic research in medicine, and I don’t think that washes under any kind of scrutiny.”¹⁷¹ Nonetheless, the University’s tactics raised eyebrows when it asked a judge to force Searle to take the drug, which is currently being used by seven million people, off the market because Searle would not pay royalties.¹⁷² Meanwhile, a “giddy” University of Rochester official remarked that this patent might be “the most lucrative in U.S. history.”¹⁷³

In the recent case of *Amgen v. Hoechst Marion Roussel, Inc.*,¹⁷⁴ the District Court for the District of Massachusetts dealt with the issues of invalidity and lack of enablement regarding a recombinant DNA patent held by Amgen.¹⁷⁵ There, Amgen was seeking a declaration that the defendants had infringed certain patents rights to

(5) A method for selectively inhibiting PGHS-2 activity in a human host, comprising administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product in a human host in need of such treatment, wherein the activity of the non-steroidal compound does not result in significant toxic side effects in the human host.

(6) A method for selectively inhibiting PGHS-2 activity in a human host, comprising administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product in a human host in need of such treatment, wherein the ability of the non-steroidal compound to selectively inhibit the activity of PGHS-2 gene product is determined by:

(a) contacting a genetically engineered cell line that expresses PGHS-2, and not PGHS-1, with the compound for 30 minutes, and exposing the cell to a pre-determined amount of arachidonic acid;

(b) contacting a genetically engineered cell that expresses human PGHS-1, and not human PGHS-2, with the compound for 30 minutes, and exposing the cell to a pre-determined amount of arachidonic acid;

(c) measuring the conversion of arachidonic acid to prostaglandin metabolite; and

(d) comparing the amount of the converted arachidonic acid converted by control cells that were not exposed to the compound, so that the compounds that inhibit PGHS-2 and not PGHS-1 activity are identified.

(7) The method of claims 1, 3, or 4 which is used to treat inflammation.

(8) The methods of claim 1, 3, or 4, in which the inhibition of prostaglandin synthesis has anti-inflammatory action in the human host.

U.S. Patent No. 6,048,850 (issued April 11, 2000).

¹⁶⁹ Utility Examination Guidelines, 66 Fed. Reg. 1092, 1098 (Jan. 5, 2001).

¹⁷⁰ *Id.*

¹⁷¹ Regalado, *supra* note 1.

¹⁷² *Id.*

¹⁷³ *Id.*

¹⁷⁴ 126 F. Supp. 2d 69 (D. Mass. 2001).

¹⁷⁵ *Id.* at 77.

its best selling drug, EPOGEN®.¹⁷⁶ Amgen was first to discover and manufacture the recombinant DNA product, which is similar to human isolated erythropoietin and is currently used in a number of medical treatments.¹⁷⁷ Sales of EPOGEN® reached \$1.76 billion in 1999.¹⁷⁸

As pointed out by the court, arguments were predictable on both sides.¹⁷⁹ The patentee, Amgen, argued that the court should adopt the broadest possible interpretation of its claims.¹⁸⁰ Defendant Hoescht sought to capitalize on recent advancements in genetic technology and attempted to limit interpretations and distinguish its products and process from the scope of Amgen's claim language.¹⁸¹

Although the court upheld the majority of Amgen's claims, Amgen's phrasing of "glycosylation which differs" in the '933 patent was problematic.¹⁸² In its patent application, Amgen referred to the placement and number of glycosylation sites found on its claimed, recombinant protein.¹⁸³ Amgen argued that it used established methods, which were similar to those used in distinguishing healthy patient-derived EPO from the EPO of aplastic anemia patients, to distinguish its own recombinant EPO.¹⁸⁴ For this reason, Amgen asserted that its patent claim was valid.¹⁸⁵

The court held that Amgen's claim language did not specify which type of human urinary EPO was meant, and that by applying the "plain and ordinary meaning" to the phrase "human urinary erythropoietin," Amgen had included all EPOs and the patent was therefore invalid.¹⁸⁶ Additionally, the court stated that Amgen's failure to limit the claim by a description of specific tests, knowing that Amgen indeed knew of the specific tests for distinguishing glycosylation, would result in lack of enablement.¹⁸⁷ All disputed claims in the '933 patent were found to be invalid.¹⁸⁸

¹⁷⁶ *Id.*

¹⁷⁷ *Id.*; see *About EPOGEN®*, at <http://www.amgen.com/product/AboutEpogen.html> (last visited Oct. 27, 2001) (offering information about the product itself including sales and stock information). Epogen® stimulates red blood cells and is used in patients undergoing frequent kidney dialysis, suffering from anemia, and may be given to cancer patients to prevent anemia. *Id.*

¹⁷⁸ *Amgen*, 126 F. Supp. 2d at 77. The court pointed out that the very details regarding how such a "useful result" has come about are at the "heart" of a process patent. *Id.* at 101. Additionally, the court made mention of an eight-factor test regarding enablement, and whether necessary experimentation would be considered "undue". *Id.* at 157. The eight enablement factors include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, and (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* In addition to several findings of infringement for Amgen, the court held that claims 1, 2, and 9 of the '933 patent were not infringed, but if in error, these claims were invalid for lack of adequate written description, indefiniteness, and lack of enablement. *Id.* at 164-65.

¹⁷⁹ *Id.* at 81-82.

¹⁸⁰ *Id.* at 83 (characterizing the defendant as arguing its proposed interpretation "in order to 'sweep within its patents' span the greatest possible amount of its competitor's activities").

¹⁸¹ *Id.* at 115

¹⁸² *Id.* at 122.

¹⁸³ *Id.* at 122, 129-32.

¹⁸⁴ *Id.* at 110.

¹⁸⁵ *Id.* at 93. Amgen's claim construction did not limit the manner by which glycosylation differences are proven. *Id.* at 92. Defendant's construction required proof by the two sets of tests stated in the prior art, and no others. *Id.*

¹⁸⁶ *Id.* at 92.

¹⁸⁷ *Id.* at 165.

Comparing this result to the aforementioned pending University of Rochester case,¹⁸⁹ the Rochester claim language is seemingly more specific given the number of methods listed for developing an inhibitor to the Cox genes, in addition to specifying the intended purpose for each desired compound. Regardless, the outcome of the Rochester case may still depend on the court's interpretation of the exacting claim language and the exacting method used by Searle in creating its own inhibitor.¹⁹⁰ It is even more difficult to say how the courts will incorporate public policy when upholding Rochester's patent could adversely affect millions of medically dependent persons.¹⁹¹

VII. LIKELIHOOD OF SUCCESS

Will the PTO's new utility guidelines provide some surety that DNA patents hold up under challenges in the courts? Possibly. However, the solution to gene patenting problems will require something more than new utility examination guidelines. Help is needed in the areas of public misconception, legislation for licensing agreements, and possible limits on claims involving drugs of extreme medical importance.¹⁹²

Given the rapid pace of technology, it is difficult for many scientists, let along the general public, to keep up with biotechnology advancements. Thus, it was not surprising to see the PTO addressing public concerns over what is actually covered by a gene patent in the Federal Notice announcing the new utility examination guidelines.¹⁹³ Public arguments against issuing gene patents included the fear that a person whose body contained a patented gene would be guilty of infringement.¹⁹⁴ The PTO explained that patent claims to a purified DNA molecule would cover only that which was excised, isolated, and purified.¹⁹⁵ The system in which the patented DNA is to be expressed would be drastically different from the expression as it occurs in the human body.¹⁹⁶ With numerous accounts of people attempting to patent their own genomes, it is likely that more efforts aimed at public misconceptions will be necessary before a clear understanding is achieved.¹⁹⁷

Not unlike the controversy surrounding *Moore v. Regents of the University of California*,¹⁹⁸ where cells were removed from a cancer patient and used to create a cell line for the purposes of scientific research, the court holding demonstrated that

¹⁸⁸ *Id.*

¹⁸⁹ See *supra* notes 164-73 and accompanying text.

¹⁹⁰ Regalado, *supra* note 1.

¹⁹¹ *Id.*

¹⁹² Donald G. McNeil, Jr., *Demand for Antibiotic May Alter U.S. Patent Policies*, INT'L HERALD TRIB., October 18, 2001, available at <http://www.ihl.com/articles/36074.html>.

¹⁹³ Utility Examination Guidelines, 66 Fed. Reg. 1092, 1092 (Jan. 5, 2001).

¹⁹⁴ *Id.* at 1093.

¹⁹⁵ *Id.*

¹⁹⁶ *Id.*

¹⁹⁷ *Id.*; see *Briton Applies to Patent Her Own Genes*, REUTERS WORLD REP., Mar. 4, 2000, available at <http://www.netlink.de/gen/Zeitung/2000/000304d.html>; see also *Patent Thyself: Claim Your Own Body* (June 21, 2001), at <http://www.kuro5hin.org/story/2001/6/21/104713/229>.

¹⁹⁸ 793 P.2d 479 (Cal. 1990).

public gain outweighed the personal right to ownership of the excised cells.¹⁹⁹ Again, although many argue that patents should not be allowed on something so basic to human life, the reality is that a patent does not confer ownership of a gene.²⁰⁰ It merely confers certain rights to the inventor, which are intended to promote discovery, and in turn, all of society.²⁰¹

Clear rules regarding cross-licensing agreements are crucial in posing a solution to gene patenting problems.²⁰² The current U.S. patent system will allow a different researcher, here a researcher who does not hold patent to the gene itself, to obtain patents for a new and different use of an old invention.²⁰³ For example, the nine patents issued on the BRCA1 and BRCA2 genes, which are associated with breast cancer, may be separately patented for an entirely new use.²⁰⁴ However, for the new use and gene to be used together, the patent holders must cross-license.²⁰⁵ Because forced licensing agreements are outside the jurisdiction of the PTO, legislation could be enacted to ensure that second use patentee would be in a fair bargaining position and able to market medically important patents.²⁰⁶

Also, in a manner similar to the limits placed on infringement remedies for medical or surgical procedures, Congress may wish to limit the infringement remedies for uses to gene patents, such as the Cox gene inhibitors.²⁰⁷ An appropriate measure of damages for infringement in these cases might be best measured as reasonable royalties, that is, what the patentee would be willing to accept in an arms length bargaining position at the time of infringement.²⁰⁸ Many agreements may be reached independently between patent holders and those seeking to make or use their patented products, as the patent holder may choose such an agreement for fear of government seizure under the Fifth Amendment.²⁰⁹

However, it is most important to remember that although allowing patent rights to genetic information initially restricts the public's use, information and drug

¹⁹⁹ Dastgheib-Vinarov, *supra* note 105, at 170-71.

²⁰⁰ Utility Examination Guidelines, 66 Fed. Reg. at 1093.

²⁰¹ Dastgheib-Vinarov, *supra* note 105, at 170-71.

²⁰² *New Gene Patent Guidelines Issued*, *supra* note 71.

²⁰³ *Id.*

²⁰⁴ *Id.*

²⁰⁵ *Id.*

²⁰⁶ *Id.*

²⁰⁷ Regalado, *supra* note 1. Currently, the Patent Act currently provides the following for damages for patent infringement:

Upon finding for the claimant the court shall award the claimant damages adequate to compensate for the infringement, but in no event less than a reasonable royalty for the use made of the invention by the infringer, together with interest and costs as fixed by the court.

When the damages are not found by a jury, the court shall assess them. In either event the court may increase the damages up to three times the amount found or assessed. Increased damages under this paragraph shall not apply to provisional rights under section 154(d) of this title.

The court may receive expert testimony as an aid to the determination of damages or of what royalty would be reasonable under the circumstances.

35 U.S.C. § 284 (2000).

²⁰⁹ Gregory G. Katsas, *Intellectual Property Rights and State Sovereign Immunity: The Recent Supreme Court Decisions* (2001), at <http://www.fed-soc.org/Publications/practicegroupnewsletters/intellectualproperty/iprightsipv3i2.htm> (last visited Nov. 3, 2001).

developments gained from researchers willing to invest time and money into isolating patentable gene sequence is profound. The new utility restrictions may ultimately represent a mere stepping-stone to future restrictions in gene patenting. Given that we are only in the beginning stages of finding uses for the expressed products of patented genes, let alone finding out how they work in conjunction with the other proteins in a cell, it is likely that PTO examiners and the courts will be able to demand a more specific use, and heightened restrictions will follow as knowledge increases. For now at least, the new utility examination guidelines establish that a gene is eligible for patent protection, provided that its use is “specific, substantial, and credible.”²¹⁰ How useful these guidelines will be in protecting biotechnology patents remains to be seen.

²¹⁰ Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (Jan. 5, 2001).