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Should Congress Do Something About Upstream Clogging Caused by the Deficient Utility of Expressed Sequence Tag Patents?

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SHOULD CONGRESS DO SOMETHING ABOUT UPSTREAM CLOGGING CAUSED BY THE DEFICIENT UTILITY OF EXPRESSED SEQUENCE TAG PATENTS?

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I. PREFACE

Patents on upstream discoveries, if sufficiently broad in scope, impede follow-on research and development, because access to the foundational tools is blocked or restricted.

Congress possesses the power to "promote the Progress of . . . *useful* Arts by securing . . . exclusive Right[s] to . . . Discoveries."[1] The question is whether granting patents to the discoverers of deoxyribose nucleic acid (DNA) sequence fragments is useful. The U.S. Supreme Court, the Court of Appeals for the Federal Circuit (CAFC), and the U.S. Patent and Trademark Office (PTO) have set a precedent that patents on DNA or genes are proper subject matter, novel, and nonobvious; thus, utility is the only remaining standard left to test the validity of an application for a DNA or gene patent.[2] Though typically a lenient and slight barrier to patentability, the utility requirement has gained significant importance in biotechnology and chemistry.[3] The utility doctrine is "a timing device, helping to identify when an invention is ripe for patent protection," concerning itself with "patenting 'too close to the laboratory bench.'"[4]

To sum up the controversy addressed in this Article, the following analogy from a critic of the current system highlights the ease with which applicants have obtained patents related to gene sequence fragments:

> Entities that claim patents on a gene with a particular utility is akin to a company that tries to patent the word "the." The company claims to have isolated the word by taking it out of the sentence that usually surrounds it. The company has discovered that it can give a description of the word "the" — it has three letters in a specific order, etc. In this way, the company has also proven it is a new and novel invention because "the" does not occur naturally in language without at least a noun. The company says its researchers have isolated and copied the word. As well, with its computers, the

1. U.S. CONST. art. I, § 8, cl. 8 (emphasis added).

2. *In re* Deuel, 51 F.3d 1552, 1559-60 (Fed. Cir. 1995) (DNA sequences encoding human and bovine protein were not invalid as obvious where prior art only disclosed partial amino acid sequence); *In re* Bell, 991 F.2d 781, 784 (Fed. Cir. 1993); Amgen v. Chugai Pharm. Co., 927 F.2d 1200, 1209 (Fed. Cir. 1991) (holding that a unique probing and screening method employed by the inventor in isolating the human erythropoietin (EPO) gene was not obvious).

3. FEDERAL TRADE COMM'N, TO PROMOTE INNOVATION: THE PROPER BALANCE OF COMPETITION AND PATENT LAW POLICY, ch. 4, at 33 (Oct. 1993).

4. *Id.* at 34. The utility requirement's use relates to concerns that patents on basic research, very far upstream, may impede follow-on innovation by virtue of effects on inventive and on access to upstream technology. *Id.* Allowing too early patenting will create an "anticommons," where inadequately or insufficiently developed follow-on technology is separately owned by too many upstream owners. *Id.*

> company claims to have discovered that the word "the" occurs in, say, 5% of sentences that are "soothing." The company says it has found a correlation between "the" and soothing sentences. In its patent application, therefore, the company claims that the "utility" of the word "the" is that it has a correlation to soothing sentences. This company hopes to produce products from the word "the," perhaps a whole series of sentences that are soothing.[5]

Though this analogy may seem far-fetched, since the word "the" has only three letters, it should be noted the genetic code is composed of three-letter words, known as "codons."[6] Like the word "the," every single living organisms' genetic code uses "words" that are three letters long. In simplistic terms, this Article contemplates the appropriateness of patenting the word "the."

II. INTRODUCTION

A. *Scope of Article*

Because DNA sequences are genetic "information," should that not distinguish them from other chemical compounds in the context of a patent system?[7] This wide-ranging question continues to be hotly debated by

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5. MATTHEW ALBRIGHT, PROFITS PENDING: HOW LIFE PATENTS REPRESENT THE BIGGEST SWINDLE OF THE 21ST CENTURY 123-124 (2004).

6. DNA is made up of nucleic bases composed of nucleotides (molecules) that each have three components: (1) a sugar, (2) a phosphate, and (3) a base. *See* LARRY GONICK & MARK WHEELIS, THE CARTOON GUIDE TO GENETICS 120 (1st ed. 1991). The bases are adenine, guanine, cytosine and thymine. *Id.* Scientists decided to identify the bases with letters *A*, *G*, *C*, and *T*, respectively. *Id.* Their "letters" (as a part of a nucleic acid base) make up DNA. *See id.* at 120-22. From your DNA, the messenger RNA (mRNA) takes a "message" out from the nucleus (where your chromosomes/DNA (DNA makes up your chromosomes) reside) into the cytoplasm (the area in the cell surrounding the nucleus of the cell) where the ribosomes work with the transcription or transfer RNA (tRNA). *Id.* at 133-34. The mRNA is also made up of nucleotides like DNA with one difference: its letters are *A*, *G*, *C*, and *U*. GONICK & WHEELIS, *supra*, at 132. The *U* substitutes for the *T*. *Id.* Regardless, the ribosomes' and tRNAs' jobs are to read the mRNA's message, which the mRNA copied from the DNA, to turn the message into amino acids that become proteins and enzymes. *Id.* at 136-37. Each three letter "codon" is a code for a specific amino acid. *Id.* at 136.

7. NUFFIELD COUNCIL ON BIOETHICS, THE ETHICS ON PATENTING DNA: A DISCUSSION PAPER, EXECUTIVE SUMMARY xi (July 2002); *cf.* Hitzman v. Rutter, 243 F.3d 1345, 1349 n.1 (Fed. Cir. 2001) ("DNA is deoxyribonucleic acid, a generic term encompassing the many chemical materials. . . ."); Burroughs Wellcome Co. v. Barr Labs., Inc., 40 F.3d 1223, 1229 (Fed. Cir. 1994) ("DNA encoding a human protein [is a] chemical compound."); *Amgen*, 927 F.2d at 1206 ("A gene is a chemical compound. . . .").

individuals in every walk of life.[8] There is a distinct lack of agreement, even among the Justices of the U.S. Supreme Court, the CAFC, and the Board of Patent Appeals and Interferences (BPAI). Though several cases have held that DNA sequences are mere chemicals,[9] more recent cases have addressed the distinction between the written description and enablement requirements for patentability. The courts in those cases have found sufficient differences between chemical compositions and genetic material to conclude that, in genetic material cases, there is more basis for a separate written description requirement than in a chemical composition case.[10] Nevertheless, because of the breadth of this question, which many believe requires a profound and deliberate examination of fundamental aspects of life, this Article only examines the following: (1) whether fragments of "a copy of DNA" (cDNA) sequences can and should be patented under current policy and law; and (2) what the legal consequences and implications may be for continuing research and development and public health in the biotechnology field, if the PTO and courts continue to allow patents on cDNA sequence fragments.

B. *Confusion Caused by Loose Terminology in a New Field*

It must also be noted at the outset that, because of the relative newness of the sequencing of the human genetic code, terminology is used quite loosely. The terms DNA sequences, cDNA, gene fragments, DNA fragments, DNA or gene fragment sequences, and cDNA fragments generally mean the same thing: a copy of a fragment of DNA containing the code for a portion of a gene. Therefore, to correctly quote or reference other cases, articles, and papers, this Article will, likewise, use these same terms interchangeably, citing no difference in their definitions.

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8. Public Comments on the United States Patent and Trademark Office "Revised Interim Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112, ¶1 'Written Description' Requirement," 64 Fed. Reg. 71427 (Dec. 21, 1999), *available at* http://www.uspto.gov/web/offices/com/sol/comments/utilitywd/index.html (last visited Mar. 30, 2005); Public Comments on the United States Patent and Trademark Office "Revised Interim Utility Examination Guidelines," 64 Fed. Reg. 71440 (Dec. 21, 1999), corrected 65 Fed. Reg. 3425 (Jan. 21, 2000) [hereinafter Revised Interim Utility Examination Guidelines] (in response to comments complaining of broad patents that might issue on DNA sequences, the PTO states that "patents for genes are treated the same as for other chemicals. . . ."), *available at* http://www.uspto.gov/web/offices/com/sol/comments/utilguide/index.html (last visited Mar. 30, 2005).

9. *Hitzman*, 243 F.3d at 1349 n.1; *Burroughs*, 40 F.3d at 1229; *Amgen*, 927 F.2d at 1206.

10. Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 925 (Fed. Cir. 2004) ("[I]n fact, where there might be some basis for finding a written description requirement to be satisfied in a genetics case based on the complementariness of a nucleic acid and, for example, a protein, that correspondence may be less clear in a non-genetic situation.").

Loose use of the terminology is sometimes harmless and easily corrected. Yet, in other situations, it can be problematic. This is easily illustrated in a recent case where a court had to define terms used by the parties. In *Monsanto Co. v. Good*, the district court had to assume and define what one of the parties meant when referring to a "DNA construct." The district court defined it as "DNA sequences, in light of the context."[11]

However, in a situation where loose use of terminology was not as easily corrected, a former director for the PTO, the Honorable Todd Q. Dickinson, testified before Congress, "[r]aw DNA sequenced data, such as that recently generated by the Human Genome Project and various corporate endeavors, is not patentable."[12] However, the "raw DNA sequenced data" generated by the Human Genome Project was cloned DNA, not "raw data," unless Dickinson meant something else.[13] Since the CAFC had, at that time, concluded a gene was a mere chemical compound and patentable, Dickinson must have meant otherwise.[14] Dickinson meaning something different is also demonstrated through reports revealing that, at the time of Dickinson's statement, up to six thousand DNA fragment sequence patents had already been granted.[15] Surely then, this statement must have been merely a result of a lack of universal agreement on terminology. Indeed, Dickinson himself stated that

11. Monsanto Co. v. Good, No. Civ. A. 01-5678 FLW, 2004 WL 1664013, at *4 n.3 (D.N.J. July 23, 2004).

12. *On Gene Patents and Other Genomic Inventions: Oversight Hearing Before the Subcomm. on Courts and Intellectual Property, House Comm. on the Judiciary*, 106th Cong. 26 (D.C. 2000) [hereinafter Dickinson Statement] (statement of Honorable Todd Dickinson, Under Secretary of Commerce for Intellectual Property and Director of the U.S. Patent and Trademark Office, Dept. of Commerce), *available at* http://commdocs.house.gov/committees/judiciary/hju66043.000/hju66043_0.htm (last visited Mar. 30, 2005).

13. The Human Genome Project sought to unveil the human genetic code in two stages: (1) DNA from each chromosome was studied and organized; and then (2) the chromosomes (from which the DNA is derived) were broken up into pieces that were then recovered as DNA clones. THE GENOMIC REVOLUTION, UNVEILING THE UNITY OF LIFE 37 (Michael Yudell & Robert DeSalle eds. 2002).

14. *Amgen*, 927 F.2d at 1206 ("A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it."); *Utility Examination Guidelines*, 66 Fed. Reg. 1092, 1093 (2001); Andrew T. Kight, Note, *Pregnant with Ambiguity: Credibility and the PTO Utility Guidelines in Light of* Brenner, 73 IND. L.J. 997, 1003 (1998).

15. Tanya Wei, Comment, *Patenting Genomic Technology — 2001 Utility Examination Guidelines: An Incomplete Remedy in Need of Prompt Reform*, 44 SANTA CLARA L. REV. 307, 310 (2003).

misinformation is the fuel behind the debates surrounding patents on genes and genetic inventions.[16]

Nevertheless, despite the confusion on terminology, the most important fact is that human genes, as produced and used in the human body, are viewed as different from the "genes, DNA, nucleotide sequences, nucleic acids, etc.," currently being patented, because patents are allowed only on genetic substances in their isolated and purified state, which requires "human intervention."[17] The U.S. Supreme Court has held that raw products of nature, such as human DNA in its natural state, are not patentable.[18] It is this difference that allows a patent to issue and defines the limits of the patent.[19] "Gene" patents do not grant "inventors" property rights of genes in other people's bodies.[20] Nevertheless, this limit on patenting raw products of nature has not resolved the escalating controversies caused by continuing patenting of DNA sequence fragments.

C. *The Beginning of the "Gene" Patent Controversy*

Indeed, this controversy began when J.D. Watson and F.H.C. Crick submitted an article to *Nature* magazine on April 25, 1953. Watson and Crick "suggested a structure for the salt of deoxyribose nucleic acid (D.N.A.)."[21] More intriguing, however, was their announcement containing a suggestion that triggered an unexpected chain of events more quickly than anticipated. Watson and Crick noted: "It has not escaped our notice that the specific pairing we have postulated immediately suggests *a possible copying mechanism for the genetic material.*"[22] Though Watson

16. Dickinson Statement, *supra* note 12; *see also* Amgen v. Chugai Pharm. Co., 13 U.S.P.Q.2d 1737, 1759 (D. Mass. 1989) ("The invention claimed in the '008 patent is *not* . . . the DNA sequence encoding human EPO . . . [r]ather, the invention . . . is the 'purified and isolated' DNA sequence encoding erythropoietin."), *aff'd in part, rev'd in part, Amgen*, 927 F.2d at 1209 (involving U.S. Patent No. 4,703,008, entitled "DNA Sequences Encoding Erythropoietin").

17. ROBERT P. MERGES & JOHN F. DUFFY, PATENT LAW AND POLICY: CASES AND MATERIALS 104 (3d ed. 2002).

18. Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980) ("[A] new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter."); Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948) ("The qualities of these [unpatentable] bacteria [are] like the heat of the sun, electricity, or the qualities of metals, [and they] are part of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men and reserved exclusively to none.").

19. MERGES & DUFFY, *supra* note 17, at 104.

20. *Id.* (citing *Utility Examination Guidelines*, *supra* note 14).

21. J.D. Watson & F.H.C. Crick, *Molecular Structure of Nucleic Acids*, 4356 NATURE 737, 737 (1953).

22. *Id.* (emphasis added).

was a proponent of interpreting the sequence of DNA, he did not appear to support the patenting of DNA sequences.[23]

III. DEFINITION OF TERMS

Nonetheless, before delving much further, some genetic terminology requires explanation. Though genome, genes, and their elements are admittedly best understood after a course on genetics, alongside a view through a high-resolution cooled CCD camera connected to a Zeiss Axioplan 2 epifluorescence microscopesome, a few basic definitions are necessary.

A. *Genome*

A genome is a collection of all genes in a cell. It is defined as the "[t]otal genetic information carried by a cell or organism."[24] The smallest genome for a free-living organism (a bacterium) contains 600,000 DNA base pairs.[25] The human genome has 3 billion DNA base pairs.[26]

The DNA in the human genome is arranged into 23 distinct chromosomes, and each of these chromosomes is a physically separate molecule that ranges in length from about 50 million to 250 million DNA base pairs.[27] Each chromosome contains many genes, which are the basic physical and functional units of heredity.[28] What is surprising, however, is that genes comprise only about 2% of the human genome; the remainder consists of non-coding regions whose functions may include providing chromosomal structural integrity and regulating where, when, and how many proteins are made.[29] The human genome is estimated to contain 20,000 to 25,000 genes.[30]

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23. Kight, *supra* note 14, at 1004 (quoting Watson in context of the National Institute of Health seeking patents on Dr. Craig Venter's automated cDNA sequences: "'[V]irtually any monkey' can run an automated sequencing machine, and to allow patents on such sequences is 'pure lunacy.'").

24. HARVEY LODISH ET AL., MOLECULAR CELL BIOLOGY, Glossary (W.H. Freeman ed., 4th ed. 2000), *available at* http://www.ncbi.nlm.nih. gov/books/bv.fcgi?rid=mcb.glossdiv.7880#7519 (last visited Mar. 30, 2005).

25. *Genomics and Its Impact on Science and Society: 2003 Primer: Early Insights from the Human DNA Sequence*, Oak Ridge Nat'l Lab (The Human Genome Project and Beyond, Oakridge, TN), 2003 [hereinafter *Genomics*], *available at* http://www.ornl.gov/sci/techresources/Human_Genome/publicat/primer2001/primer11.pdf (last visited Mar. 30, 2005).

26. *Id.*

27. *Id.*

28. *Id.*

29. *Id.*

30. *Genomics*, *supra* note 25.

In a multicellular organism, every cell has a copy of the same genome, but not all cells express the same genes.[31] It is for this reason that we are all different. What expressed means, in the context of genes, is explained below.

B. *Gene*

A gene is a subsection of a chromosome that encodes a specific protein.[32] It is an entity of a genome consisting of sequences that define the gene product, and additional sequences directing its expression. Genes are specific sequences of bases (nucleotide bases make up DNA) that encode instructions about how to make proteins.[33] In general terms, a gene is a physical and functional unit of heredity that carries information from one generation to the next.[34] In more specific, or molecular, terms, it is the entire DNA sequence, including exons,[35] introns (a.k.a. "junk DNA"),[36] and non-coding transcription-control regions necessary for production of a functional protein or RNA.[37] The genetic code is the set of rules by which nucleotide triplets in DNA or ribonucleic acid (RNA) specify amino acids in proteins.[38]

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31. *Id.*

32. Michael D. Kane, Ph.D., Introduction to Computational Life Sciences 4 (1997) (unpublished presentation, on file with Purdue Univ.), *available at* http://www.tech.purdue.edu/Cpt/Courses/tech581V-Kane/lecture1_intro.ppt (last visited Mar. 30, 2005).

33. *Genomics*, *supra* note 25.

34. LODISH ET AL., *supra* note 24.

35. An exon is "a region of a gene that is present in the final functional transcript (mRNA) from that gene." It is also "any non-intron section of the coding sequence of a gene." Together "the exons constitute the mRNA and are translated into protein." Mark Lefers, MA, Glossary Definition of Exon, maintained by Holgrem Lab, *available at* http://www.biochem.northwestern.edu/holmgren/Glossary/Definitions/Def-E/exon.html (last visited Mar. 30, 2005).

36. An intron is a meaningless sequence that is in the middle of a gene that can be several hundreds of nucleotides long, and is sometimes lovingly referred to as "junk." GONICK & WHEELIS, *supra* note 6, at 148; *see also* Gane Ka-Shu Wong et al., *Is "Junk" DNA Mostly Intron DNA?*, 10 GENOME RES. 1672-78 (2000), *available at* www.genome.org/cgi/doi/10.1101/gr.148900 (last visited Mar. 30, 2005); Carole Nottenburg, Ph.D., J.D., *Analysis of "Junk DNA" Patents*, *available at* http://lorac.typepad.com/patentblog/files/simons_patents_analysisf.pdf (last visited Mar. 30, 2005). The phrase "junk DNA" is attributed to Dr. Susumu Ohno, a very highly-regarded researcher at the City of Hope in Duarte, California. *See* T.R. Gregory, The C-Value Enigma ch. 1 (unpublished Ph.D. thesis, University of Guelph, Ontario, Canada), *available at* www.genomesize.com/rgregory/thesis/ (last visited Mar. 30, 2005). In 1972, in an attempt to explain the paradox that there was much more coding capacity in genomes than the number of genes, Ohno proposed that much of the genome of more advanced eukaryotes was functionless. *Id.* He called this DNA "garbage" or "junk" DNA. *Id.*

37. LODISH ET AL., *supra* note 24.

38. *Id.*

C. *DNA (including RNA, cDNA, mRNA, tRNA)*

Two different kinds of genetic material exist: DNA and RNA.[39] Most organisms' genetic code is made of DNA, but a few viruses have RNA as their genetic material.[40] The biological information contained in an organism is encoded in its DNA or RNA sequence.[41]

1. The Material Composition of DNA

The three-dimensional structure of DNA, first proposed by Watson and Crick about fifty years ago, consists of two long helical strands that are coiled around a common axis forming a double helix.[42] Each strand of DNA is composed of just four different types of monomers,[43] called nucleotides.[44] Nucleotides are the building blocks for nucleic acids.[45] An individual nucleotide has three components: a sugar, a phosphate, and a base.[46] At a molecular level, the sugar, phosphate, and base are hooked together to make a long sugar-phosphate "backbone," with a sequence of "bases" sticking off of the "backbone."[47] The bases are composed of adenine, cytosine, guanine, and thymine (uracil, instead of thymine, in RNA).[48]

As a result, a DNA molecule consists of two long polynucleotide chains that are composed of the four types of nucleotide subunits.[49] Each of these chains is known as a DNA chain, or a DNA strand.[50] Hydrogen bonds between the base portions of the nucleotides hold the two chains together.[51] In the case of the nucleotides in DNA, the sugar, deoxyribose,

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39. National Center for Biotechnology Information, *A Science Primer — Just the Facts: A Basic Introduction to the Science Underlying NCBI Resources, What is a Cell?* [hereinafter *What is a Cell?*], *available at* http://www.ncbi.nlm.nih.gov/About/primer/genetics_cell.html (last visited Apr. 15, 2005).

40. *Id.*

41. *Id.*

42. LODISH ET AL., *supra* note 24, § 1.2.

43. A monomer is any small molecule that can be linked with others of the same type to form a polymer. *Id.* Examples include amino acids, nucleotides, and monosaccharides. *Id.* A polymer is any large molecule composed of multiple identical or similar units (monomers) linked by covalent bonds. *Id.*

44. *Id.*

45. GONICK & WHEELIS, *supra* note 6, at 106.

46. *Id.*

47. *Id.*

48. BRUCE ALBERTS ET AL., MOLECULAR BIOLOGY OF THE CELL, pt. II, § 4 (4th ed. 2002), *available at* http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=mboc4 (last visited Mar. 30, 2005).

49. *Id.*

50. *Id.*

51. *Id.*

is attached to a single phosphate group (hence the name deoxyribonucleic acid), and the base may be either adenine (*A*), cytosine (*C*), guanine (*G*), or thymine (*T*).[52] Because only the base differs in each of the four types of subunits, each polynucleotide chain in DNA is analogous to a necklace (the backbone) strung with four types of beads (the four bases *A*, *C*, *G*, and *T*).[53] These same symbols (*A*, *C*, *G*, and *T*) are also commonly used to denote the four different nucleotides (that is, the bases with their attached sugar and phosphate groups).[54] These symbols, ascribed by scientists, created the alphabet of the genetic code.

2. The Principle of Complementarity

One very important characteristic of DNA that has made its sequencing possible is the "principle of complementarity."[55] Before Watson and Crick, scientist Erwin Chargraff found that in any DNA, the number of *A*s was the same as the number of *T*s; and the number of *C*s was equal to the number of *G*s.[56] In cracking this code, Watson and Crick realized each base (*A*, *G*, *C*, or *T*) can only pair with one other base, called its complement. Only *G* and *C* can pair, and likewise, only *A* and *T* can pair.[57] This is due to the composition of the molecules and their "attraction," which is created by the atoms that have a negative or positive charge.[58]

3. The Self-Replication of DNA

Gene-copying, or DNA replication, occurs when each strand (or chain) of the DNA double helix, which contains the information necessary to make its complementary strand, pulls apart.[59] In the neighborhood of the "pulling-apart process," there are plenty of free nucleotides, which are the building blocks for the new strand.[60] Of course, because of the principle of complementarity, what comprises the new strand is dictated by the strand that just pulled apart.[61] When a free nucleotide meets its complementary base on the DNA, it sticks because its hydrogen bonding creates a weak attraction between a hydrogen atom on one nucleotide molecule, and a

52. *Id.*
53. ALBERTS ET AL., *supra* note 48.
54. *Id.*
55. GONICK & WHEELIS, *supra* note 6, at 124.
56. *Id.* at 121.
57. *Id.* at 122.
58. *Id.*
59. *Id.* at 125.
60. GONICK & WHEELIS, *supra* note 6, at 126.
61. *Id.* at 125.

non-hydrogen atom on the other molecule.[62] If the wrong nucleotide comes along, it will bounce away because of the required hydrogen bond.[63]

The principle of complementarity is the key to DNA's replication and its code, which programs for creation of enzymes and proteins.[64] In fact, the sequence of DNA parallels or reflects the sequence necessary to build a protein.[65] The sequence of the base pairs can be thought of as a series of "words" specifying the order of amino acids in each protein.[66] Through a complex process, the "words" of the DNA are translated into instructions specifying particular amino acids.[67]

4. The Role of RNA and DNA in Creating Proteins

RNA comes into the picture when the DNA words are translated into amino acids. RNA is also a sugar-phosphate backbone with a series of bases.[68] RNA is made up of four bases, but instead of *A*, *C*, *G*, and *T*, the *T* is substituted by uracil (*U*), so RNA is composed of *A*, *C*, *G*, and *U*.[69]

Protein synthesis begins when a region of DNA splits apart, just as in DNA replication, except that a molecule of RNA, instead of a complementary strand of DNA, is built along one strand.[70] Just as in DNA replication, each base of the RNA is complementary to the corresponding DNA base, but instead of *A* and *T* matching up, it is *A* and *U*. This RNA is called messenger RNA (mRNA) because it carries the genetic message from the DNA to the protein factory.[71] Since cells use proteins (enzymes) to make other molecules like sugars or fats, DNA indirectly leads the synthesis of many small molecules as well as proteins.[72] DNA also contains a coded set of instructions that dictates when various proteins must be made, and in what quantities.[73]

The replication occurs in the nucleus of the cell. To do its job, however, the mRNA gets its "code," or instructions, from the DNA by "copying" it, and then moving from the nucleus of the cell to the cellular cytoplasm

62. *Id.* at 127.
63. *Id.*
64. *Id.* at 128.
65. GONICK & WHEELIS, *supra* note 6, at 130.
66. *Id.*
67. *Id.* at 131.
68. *Id.* at 132.
69. *Id.*
70. GONICK & WHEELIS, *supra* note 6, at 133.
71. *Id.* at 132-33.
72. LODISH ET AL., *supra* note 24, § 1.2.
73. *Id.*

outside the nucleus, where it serves as the template for protein synthesis.[74] The mRNA is translated, through the help of tRNA (t stands for transcription) and ribosomes, into a string of amino acids that will constitute the protein molecule for which it codes.[75]

5. The Role of RNA's Replication of DNA in Creating DNA Copies

The genetic code is obtained by using mRNA, since mRNA is essentially a copy of the coding regions of DNA.[76] In the laboratory, the mRNA molecule can be isolated and used as a template to synthesize a cDNA strand.[77] The cDNA refers to the other strand in a double helix and often describes the cDNA strand to mRNA. Many mRNAs are published as cDNA. The cDNA is made to solve the problem of mRNA being very unstable outside of a cell.[78] Scientists use special enzymes called reverse transcriptase to convert the mRNA into cDNA.[79] This process is called "reverse" because using the cDNA is the reverse of the usual process of transcriptions in cells.[80] The usual process involves the mRNA "reading" the DNA sequence as the template, but the reverse process involves scientists using the mRNA as the template.[81] Because mRNA is a reverse copy of DNA, the cDNA represents only the "expressed," or coding regions, of the DNA sequence.[82]

D. *Expressed Sequence Tags*

Expressed Sequence Tags (ESTs) are partial sequences of cDNA clones corresponding to mRNA.[83] They are small copied pieces of DNA and are

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74. Denise Casey, A Primer on Molecular Genetics 6, DOE Human Genome 1991-92 Program Report, *available at* http://www.genome.iastate.edu/edu/doe/prim1.html#1 (last visited Mar. 30, 2005).

75. *See id.* at 7-8.

76. *See id.* at 8.

77. *Id.*

78. National Center for Biotechnology Information, *A Science Primer — Just the Facts: A Basic Introduction to the Science Underlying NCBI Resources, ESTs: Gene Discovery Made Easier* [hereinafter *ESTs*], *available at* http://www.ncbi.nlm.nih.gov/About/primer/est.html (last visited Mar. 30, 2005).

79. *See generally What is a Cell?*, *supra* note 39.

80. *See* D. Benjamin Borson, *The Human Genome Projects: Patenting Human Genes & Biotechnology is the Human Genome Patentable?* 35 IDEA 461, 465-67 (1995).

81. *See ESTs*, *supra* note 78.

82. *See id.*

83. Press Release, HUGO Statement on the Patenting of DNA Sequences (Jan. 1995) [hereinafter HUGO Statement], *available at* http://www.gene.ucl.ac.uk./hugo/patent.htm (last visited Feb. 21, 2005). HUGO is the Human Genome Organisation, an international membership organization whose goal is to coordinate and enhance efforts in genome research. *Id.*

considered mere research tools.[84] They are usually 200 to 500 nucleotides long,[85] and are generated by sequencing either one or both ends of an expressed gene.[86] An EST can be used to identify an expressed gene and can also be used as a sequence-tagged site marker to locate a particular gene on a physical map of a genome.[87] ESTs are called "tags" because they are "sequenced" (i.e., the order, or sequence, of the deoxyribonucleic acids, *AGTCTTAGA*, has been determined) bits of DNA that represent genes expressed in certain cells, tissues, or organs.[88] These "tags" are then used to fish a gene out of a portion of chromosomal DNA by matching base pairs.[89]

According to many commentators, a "mere wisp of a gene sequence from brain tissue, with almost nothing known about its function . . ." should not be a patentable product.[90] Knowing the whole genome, will not lead directly to cures for cancer and other killers.[91] The whole genome can lead to new drugs, but it, much less an EST, cannot cure anything.[92] Among the issues that have emerged during discussions of the members of Human Genome Organisation (HUGO), a nongovernmental agency that coordinates genetic research among countries,[93] are the nature and extent of scientific work involved in:

(1) the generation of ESTs;
(2) the use of ESTs to obtain full-length cDNA and gene sequences;
(3) the use of ESTs or full-length sequences to obtain expression of proteins;
(4) the use of ESTs or full-length gene sequences to determine their normal biological functions, association to disease(s) and their RNA and protein products; and
(5) the use of genes or gene fragments for categorizing; mapping; tissue typing; individual or forensic identification; production of antibodies; antisense, triple helix and ribozyme applications; or locating gene regions associated with genetic disease, etc.[94]

84. *ESTs*, *supra* note 78.
85. *Id.*
86. *Id.*
87. HUGO Statement, *supra* note 83.
88. *ESTs*, *supra* note 78.
89. *Id.*
90. JAMES SHREEVE, THE GENOME WAR 84 (2004).
91. *Id.* at 16.
92. *Id.*
93. HUGO Statement, *supra* note 83.
94. *Id.*

The concern generated by EST or DNA sequence fragment patents has even led companies to sue companies in other countries and even the countries themselves.[95] But understanding how the genetic code is being patented is necessary to fully understand the legal and policy issues created.

IV. HOW GENE (DNA) FRAGMENTS (A.K.A. ESTS) ARE BEING PATENTED

Every person's DNA is approximately 99.9% identical.[96] Therefore, it does not matter "whose" DNA is selected.[97] In fact, the publicly funded Human Genome Project (HGS) created a BAC[98] library made from a series of anonymous individuals.[99]

Nonetheless, in a non-exhaustive list, the Nuffield Council on Bioethics, has explained that genes or DNA sequences can, and do, appear in patent claims in the following ways:

- the DNA sequence, whether comprising a complete or partial gene;
- promoters;
- enhancers;
- individual exons;
- expressed sequences as expressed sequence tags (ESTs) or cDNAs;
- whole transcribed genes as cDNAs;
- individual mutations known to cause disease;
- variations between people not associated with disease (polymorphisms);
- cloning vectors, formed from bacterial DNA, which are used to replicate DNA sequences;
- expression vectors, also formed from bacterial DNA, which are used to express proteins in replicated DNA sequences;
- isolated host cells transformed with expression vectors, which are cells that have been created to express particular proteins;

95. *Infra* Part IX.

96. THE GENOMIC REVOLUTION, *supra* note 13, at 39.

97. *Id.* at 39-40.

98. At a very simplified level, a BAC is the resulting cloned DNA that was created by inserting small pieces of DNA into bacteria that then replicated this portion of a chromosome through division of itself. *Id.* at 39-40; *see also* GONICK & WHEELIS, *supra* note 6, at 185-86. Therefore, a BAC library is based on replication through bacteria. *Id.*

99. THE GENOMIC REVOLUTION, *supra* note 13, at 40.

- amino acid sequences (proteins);
- the use of such proteins as medicines;
- antibodies, which are used as markers;
- nucleic acid probes, which are fragments of DNA that are used to locate particular parts of DNA sequences;
- methods of identifying the existence of a DNA sequence or a mutation or deletion in an individual;
- testing kits for detecting genetic mutations; and
- whole genomes.[100]

Many of these listed items contain DNA sequence fragments, and the PTO has issued a few patents for gene fragments.[101] To get these fragments, the traditional method used reverse transcription of mRNA to make cDNA (a.k.a. cloning). The steps for making cDNA are the following:

1. Create bacteria that transcribes the mRNA that codes for the protein of interest.
   a. Extract mRNA from cells that are making the protein of interest.
   b. Use reverse transcriptase to create a "library" of cDNA molecules from the mRNA.
   c. Insert these cDNA molecules into viral "vectors."
   d. Infect bacteria in culture with the vectors containing the desired cDNA.
2. Synthesize cDNA "probes" that can recognize the cDNA that codes for the protein of interest.
   a. Identify, isolate and purify the protein of interest.
   b. Determine some of the exact sequence of the protein.
   c. Predict codons which can code for the protein.
   d. Manufacture DNA "probes" complementary to codons predicted for the protein. This set may require making many different probes to account for the redundancy in the genetic code.
3. Identify colonies of bacteria whose DNA "hybridizes" to the probe. These colonies contain cDNA that codes for the protein of interest. Grow large amounts of, or "clone," this specific bacterium, and finally isolate and purify the cDNA.

100. NUFFIELD COUNCIL ON BIOETHICS, *supra* note 7, at 25.
101. Wei, *supra* note 15.

4. Remove the cDNA from the bacterial vector and insert it into a vector suitable for expression in mammalian cells.[102]

Though cloning was the main method for identifying gene DNA sequences, computational techniques have evolved, and they have now become the main method.[103] These techniques rely on libraries like HGS's BAC library, and they have sped up the sequencing process.

V. How the Newness and Complexities of Genetics May Have Led to the Problematic "Patentability" of EST Patents

Because computational techniques have sped up the process and volume of sequences being discovered, the number of patent applications being filed on whole gene sequences and DNA fragment sequences has increased, and may be one of the reasons the PTO has granted patents on ESTs. In addition, the complexities inherent in this area of science and technology are also likely to blame for the PTO granting patents on DNA fragments.

A. *The Problem of the Sheer Volume and Cost of Examining DNA Multi-Sequence Patents*

With regard to the sheer volume of patents being filed, in a press release dated October 23, 1996, the Honorable Bruce Lehman, a former Commissioner of the PTO declared that:

> the costs for determining even the initial patentability of the some 350 pending multi-sequence gene applications are prohibitive. [The] PTO estimates that if one patent examiner were to tackle this task, it would take approximately 200 years. To initially examine these applications, the entire biotechnology group of some 200 examiners would take over one full year at a cost of over $34 million.[104]

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102. "Rarely does a single cDNA contain the entire sequence needed for protein expression. Usually, many different pieces of cDNA, each of which codes for apart of the protein must be linked together to create the 'full-length' sequence, which can be used to express the full-length protein." Borson, *supra* note 80, at 465-66 n.9.

103. Nuffield Council on Bioethics, *supra* note 7, at 25

104. PTO Press Release, PTO Announces New Policy to Process Gene-Sequence Biotechnology Patents (Oct. 23, 1996), *available at* http://www.uspto.gov/web/offices/com/speeches/96-21.txt (last visited Apr. 15, 2005).

At the time of this press release in October of 1996, the number of pending gene patent applications contained 500,000 isolated DNA and RNA sequences of nucleotides.[105] This presented the PTO with "an unprecedented search and examination challenge . . . even with the most modern equipment."[106] As a result, the PTO subsequently required applicants for multi-sequence gene patents to claim no more than ten independent and distinct nucleotide sequences for each application.[107] Furthermore, on top of the sheer volume, Lehman explained the PTO simply did not have,

> the resources to tackle this challenge under current policy. PTO costs greatly exceed the $350,000 in application fees that we've collected for these applications; we receive no taxpayer dollars and simply cannot subsidize the applications of biotechnology inventors. It's just not fair to the majority of our customer base, inventors pursuing other worthwhile advances in different technologies.[108]

Since approximately 2000, the filing of applications for DNA/RNA-based patents has overwhelmed the PTO. In 1990, the PTO received 16,000 patent applications.[109] In 2000, the number of patents had more than doubled to 33,000.[110] According to the National Research Council, in 2001, the approximate number of patents issued by the PTO on DNA/RNA fragments was 1400.[111] In 2002, the number of patents was between 1300-1350, and in 2003, the approximate number was between 1200-1300.[112] In 2003, the two largest filers of these types of patent applications were Incyte Pharmaceuticals, Inc. (Incyte) and HGS.[113] The high point for DNA/RNA fragment patents occurred in approximately 1999, when the USPTO granted Incyte nearly 100 patents on DNA/RNA fragments, and between 20 and 30 patents to HGS.[114]

The exact number of patents that are currently issued on ESTs or gene fragments is difficult to ascertain, however, because of the lag between

105. *Id.*
106. *Id.*
107. *Id.*
108. *Id.*
109. Wei, *supra* note 15, at 309.
110. *Id.*
111. A PATENT SYSTEM FOR THE 21ST CENTURY, NAT'L RESEARCH COUNCIL OF THE NAT'L ACADEMIES 56, 57 (Stephen A. Merrill et al. eds., 2004).
112. *Id.*
113. *Id.* at 58.
114. *Id.*

application filings and patent grants.[115] Nevertheless, in the context of patents that contain any claims to DNA, the most current information suggests that as of February 5, 2004, the PTO has granted 12,074 patents to the 50 entities holding the largest number of DNA-based patents.[116] This number accounts for only the 50 entities with the largest DNA-based patent holdings. This number was generated from a search engine containing a recently created, and apparently more effective, algorithm. In fact, it may have been because of the problem of ascertaining the number of DNA patents that are issued, that Dr. LeRoy Walters refined this new search algorithm, allowing the PTO to more effectively search DNA-based patents that are issued.[117]

B. *The Problem of the Complexity of Examining DNA Multi-Sequence Patents*

To provide readers a sense of the complexities involved in merely searching the gene patents, the following is reported as the algorithm Dr. Walters used and developed to search for DNA-based patents and their total number:

> ((047???* OR 119* OR 260???* OR 426* OR 435* OR 514* OR 536022* OR 5360231 OR 536024* OR 536025* OR 800*) <in> NC) AND ((antisense OR <case><wildcard>cDNA* OR centromere OR deoxyoligonucleotide OR deoxyribonucleic OR deoxyribonucleotide OR <case><wildcard>DNA* OR exon OR "gene" OR "genes" OR genetic OR genome OR genomic OR genotype OR haplotype OR intron OR <case><wildcard>mtDNA* OR nucleic OR nucleotide OR oligonucleotide OR oligodeoxynucleotide OR oligoribonucleotide OR plasmid OR polymorphism OR polynucleotide OR polyribonucleotide OR ribonucleotide OR ribonucleic OR "recombinant DNA" OR <case><wildcard>RNA* OR <case><wildcard>mRNA* OR <case><wildcard>rRNA* OR <case><wildcard>siRNA* OR <case><wildcard>snRNA* OR <case><wildcard>tRNA* OR

115. *Id.* at 56.

116. LeRoy Walters, *DNA Patent Project: Database and Survey, Kennedy Institute of Ethics at Georgetown University* (powerpoint presentation), *at* http://www7.nationalacademies.org/step/Walters_ppt.ppt (last visited Mar. 30, 2005). Data is based on two research projects supported by Grant No. R03 HG02683-02, "DNA Patent Policies at Academic Institutions," from the National Human Genome Research Institute, NIH; and Grant No. DE FG 01ER63171, "Enhancing the DNA Patent Database," from the U.S. Department of Energy.

117. *See* Biographical Sketch of LeRoy Walters, PhD., *available at* http://philosophy.georgetown.edu/faculty/bios/cvs/walters.pdf (last visited Mar. 30, 2005).

> ribonucleoprotein OR <case><wildcard>hnRNP* OR <case><wildcard>snRNP* OR <case><wildcard>SNP*) <in> CLAIMS)[118]

What this algorithm means in plain English is:

> Search US Patent classes 047 (plant husbandry), 119 (animal husbandry), 260 (organic chemistry), 426 (food), 435 (molecular biology and microbiology), 514 (drug, bio-affecting and body treating compositions), 536/subclasses 22 through 23.1 (nucleic acids, genes, etc., but not peptides or proteins), subclasses 24 and 25 (various nucleic acids, variants, and related methods), and class 800 (multicellular organisms).[119]

The algorithm further searches patents in a group that includes one or more of the following terms in their claims: "antisense, cDNA, centromere, deoxyoligonucleotide, deoxyribonucleic, deoxyribonucleotide, DNA (with or without following letters, such as DNAs), exon, gene or genes (exact match only), genetic, genome, genomic, genotype, haplotype, intron, mtDNA (with or without following letters such as mtDNAs) — exact case match only, nucleic, nucleotide."[120]

To further underscore the multifaceted difficulties faced by patent examiners, the Honorable Todd Dickinson described to Congress the size of some of the DNA-related patent applications being received in 2000.[121] He testified that one patent application contained a DNA sequencing, which if submitted on paper, would have totaled more than 400,000 pages.[122] Incredibly, however, more recent reports state that "one recent biotech patent application contained the equivalent of six million pages of data."[123]

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118. Walters, *supra* note 116, at 4.

119. *Id.* at 5.

120. *Id.* at 6.

121. *See generally* Dickinson Statement, *supra* note 12.

122. *Id.*

123. Dashka Slater, *Humouse™*, LEGAL AFF., Nov./Dec. 2002, *at* http://www.legalaffairs.org/issues/November-December-2002/feature_slater_novdec2002.html#top (last visited Mar. 30, 2005).

VI. HOW THE LAWS HAVE ALLOWED PATENTS ON DNA FRAGMENTS: THE CONSTITUTION, THE STATUTES, TREATIES, AND AN ANALYSIS OF PERTINENT CASES SINCE *BRENNER V. MANSON*

The next question that arises is how the law allows DNA fragment patents to issue when an examination of the potential problems they raise is, ironically, the very reason for which the law exists.

A. *Statutory Patenting Requirements*

The U.S. Constitution grants power to Congress to "promote the Progress of . . . *useful* Arts by securing . . . exclusive Right[s] to . . . Discoveries."[124] In addition, in lay terms, to obtain a patent, the invention must meet the following requirements:

(1) it must be an invention or a discovery;
(2) that is a process, machine, manufacture, composition of matter or improvement thereof;
(3) that is new, i.e., not already invented or discovered;
(4) that when compared to other inventions or discoveries in the same field does not lead to the conclusion that the invention or discovery sought to be patented would have been obvious to a person of ordinary skill in that field (or the most closely related);
(5) that is useful; and
(6) for which a proper patent application has been filed with the PTO, which means that a person of ordinary skill in the field of the invention (or the most closely related) could read the application and understand:
  (a) what it is through the full and precise description of the invention in full, clear, concise, and exact words;
  (b) how to make and use it through the full and precise description of its makeup and use in full, clear, concise, and exact words; and
  (c) which is the best way of making and using it.[125]

B. *Interpretation of the Laws by the Courts*

Historically, the U.S. Supreme Court has taken a conservative view of "utility."[126] This conservative view is exemplified in *Brenner*, where the Court denied an applicant's request to patent a process for making a

124. U.S. CONST. art. I, § 8, cl. 8 (emphasis added).
125. *See* 35 U.S.C. §§ 101-103 & 112.
126. *See generally* Brenner v. Manson, 383 U.S. 519 (1966).

steroid and the steroid composition itself.[127] However, depending on the meaning of one of the last statements in the decision, one wonders if, perhaps, it is possible the Court might now be amenable to allowing EST patents.

In *Brenner*, the Patent Office denied the applicant's request for a patent. Manson appealed to the Court of Customs and Patent Appeals (CCPA),[128] which held the patent applicant, Manson, showed sufficient utility for his claimed process because it "produce[d] a known product, [making] it [un]necessary to show utility for the product. . . ."[129] The Patent Office then sought a writ of certiorari, which the U.S. Supreme Court granted in order to "resolve th[e] running dispute over what constitute[d] 'utility' in chemical process claims."[130]

In its written opinion, the Court applauded the Patent Office for "remain[ing] steadfast in its view" that a patent should not be granted upon a product or process, if neither are useful.[131] However, it did not treat the CCPA as kindly, criticizing it for reversing the Patent Office's rejection of a claim for a process that yielded mere chemical intermediates that were only "useful to chemists doing research on steroids."[132] Noting the mood of the Court, Manson took a reasonable position, and arguing that his claimed process was useful enough to, at least, entitle him to an interference proceeding under the Patent Office's utility standard because a scientific article said an "adjacent homologue" of the steroid that his process produced showed "tumor-inhibiting effects in mice."[133] Manson reasoned that this article disclosed sufficient utility, but despite this article, the Patent Office rejected Manson's process because his application failed to disclose "a sufficient likelihood" his steroid would have the same ability to inhibit tumors as the "adjacent homologue."[134] In addition, Manson conceded that merely because the steroid yielded by his process was an adjacent homologue to the one identified in the article, the field of steroids was unpredictable.[135] The Court, thus, reversed the CCPA's reversal of the PTO's rejection, concluding, "Unless and until a process [and its product] is refined and developed to [the] point where *specific benefit exists in*

127. *See id.* at 522.
128. The CCPA is the predecessor to the CAFC.
129. *Brenner*, 383 U.S. at 522.
130. *Id.*
131. *Id.* at 530.
132. *Id.*
133. *Id.* at 531.
134. *See generally Brenner*, 383 U.S. at 531-32.
135. *Id.* at 532.

currently available form — there is insufficient justification for permitting an applicant to monopolize what may prove to be a broad field."[136]

However, the Court concluded its opinion with a vague statement. The Court stated it is not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public."[137] In context of the first part of the sentence that preceded this statement, the Court made clear it was not disparaging the importance of compounds and processes like Manson's. Immediately following this ambiguous statement, the Court made its famous "a patent is not a hunting license" statement.[138] Therefore, it is unclear whether the Court was suggesting that compounds and processes producing intermediates may one day be patentable, or whether it was trying to make Manson feel better. Regardless, though this statement is only dicta, the Court chose to print it for some unknown reason.

Nonetheless, very soon thereafter, the CCPA confronted the patentability of more steroid compounds in *In re Joly*.[139] Having been castigated "on the record" only a year earlier by the Court, the CCPA followed the Court's directives, expressly declaring it was "particularly concerned with the applicability of the decision of the Supreme Court in *Brenner v. Manson*."[140]

Joly[141] involved a claim for "esters of 2-enols of steroids and preparation thereof" that the applicants said would be useful as starting materials to make "2, 3-keto compounds," which would be intermediates for preparing other compounds.[142] However, neither the starting materials nor the subsequently produced "intermediates" had any value, other than to make compounds of unknown use.[143] The applicants contended that the steroids produced by the "esters" in their process were "closely related," in chemical structure to other compounds of known usefulness, but they presented no evidence that these "2,3-diketo steroids" possessed any "*properties* or *activities*" in common with the alleged "closely related" useful compounds.[144] The court rejected the argument that "disclosure of a steroid as useful as an intermediate to make other steroids by specified reactions [was] an adequate disclosure of utility."[145] The CCPA affirmed

136. *Id.* at 534-35 (emphasis added).
137. *Id.* at 536.
138. *Brenner*, 383 U.S. at 536.
139. *In re* Joly, 376 F.2d 906, 907 (C.C.P.A. 1967).
140. *Id.*
141. *Id.*
142. *Id.* at 907.
143. *Id.* at 907-08.
144. *Joly*, 376 F.2d at 908.
145. *Id.*

the PTO examiner's rejection on the basis of utility.[146] It also declared there was no utility in a disclosure, claiming an intermediate existed that worked, reacted, or could be used to produce an intended product of no known use.[147] Furthermore, the CCPA pointed out it would also find insufficient utility for a product obtained from intermediates belonging to some class of compounds that now is, or might in the future be, the subject of research.[148]

In a companion case, *In re Kirk*, the CCPA confronted additional similar claims for steroid compounds the applicants claimed had valuable "biological properties," value in "the furtherance of steroidal research," value as "intermediates in prepar[ing]" other steroids and "biologically active compounds," and that could "be applied to veterinary or medical practice in the form of tablets, elixirs, injections, implants or other pharmaceutical preparations."[149] Despite the fact that the applicants submitted an affidavit showing "one skilled in the art [could] determine biological uses," the examiner rejected the patent application because the specification lacked disclosure of utility.[150] The BPAI agreed, pointing out that "biological properties" of the claimed compounds was "so general and vague as to be meaningless."[151]

The CCPA affirmed the rejection on the grounds that it seemed the applicants made "nebulous expressions of 'biological activity' or 'biological properties,'" which were set out in their specification gave no more indication of the usefulness of the compounds, or how to use them, than did the equally obscure expressions of "useful for technical and pharmaceutical purposes," unsuccessfully relied on by another applicant in a prior case.[152] The CCPA treated the submitted affidavit as an irrelevant "*ex post facto* affirmation" and characterized its content as merely showing that a PHOSITA[153] would know how to use the compounds to figure out whether the compounds are useful.[154] The CCPA also mentioned that even if the specification had stated that the claimed compounds were similar to other useful compounds, such a statement would have been incredible since steroids are known to be unpredictable.[155]

146. *Id.* at 909.
147. *Id.* at 908.
148. *Id.*
149. *In re* Kirk, 376 F.2d 936, 938 (C.C.P.A. 1967).
150. *Id.* at 940.
151. *Id.*
152. *Id.* at 941 (citing *In re* Diedrich, 318 F.2d 946 (C.C.P.A. 1963)).
153. PHOSITA stands for a "Person Having Ordinary Skill In The Art."
154. *Kirk*, 376 F.2d at 940.
155. *See id.* at 942.

Furthermore, perhaps because of the vehement dissent or to bolster its opinion, the *Kirk* majority declared that the *In re Nelson*[156] case relied on by the applicant, which fully supported the applicants' position, was overruled by *Brenner*.[157] It also declared "a specification that disclosed a steroid that was an intermediate that 'work[ed],' reacted, or could be used to produce some product of no known use," would, nonetheless, fail the utility requirement.[158] As it declared in *Joly*, it was also not enough that the product obtained from the intermediate belonged to some class of compounds that now is, or might in the future be, the subject of research.[159] But in the next sentence, the CCPA did not overrule, and instead invited the reader to compare, *Reiners v. Mehltretter,* where the CCPA held, "[C]ompounds employed as intermediates to produce other *directly* useful compounds were found to be themselves useful."[160] A "compare" introductory signal means the CCPA thought the holding in *Reiners* was sufficiently analogous to lend support to its previous statement that the disclosed product would not meet the utility requirement if the product produced by the intermediate was not immediately useful.[161] This implies the CCPA would consider an application disclosing intermediates that produced directly useful compounds as meeting the utility requirement.

Nonetheless, it took another thirteen years before the CCPA was again confronted with the utility issue in the context of chemical compositions. Perhaps because it was thirteen years later, and fourteen years since the *Brenner* case, the CCPA decision appears to completely contradict its *Kirk* and *Joly* decisions, while ignoring *Brenner*. However, *In re Jolles*[162] can be reconciled.

Jolles filed a patent application for pharmaceutical compositions and methods useful for the treatment of acute myeloblastic leukemia in human patients.[163] The examiner rejected the claims on the grounds of "no utility," citing as her reason insufficient evidence of the compositions' "operativeness" and safety and efficacy "to treat acute myeloblastic leukemia in human patients."[164] She said the claims were "incredible."[165]

156. *Id.* at 943 (citing *In re* Nelson, 280 F.2d 172 (C.C.P.A. 1960)).

157. *Id.* at 946.

158. *Id.* at 945.

159. *Kirk*, 376 F.2d at 945.

160. *Id.* (citing Reiners v. Mehltretter, 236 F.2d 418, 421 (C.C.P.A. 1956)).

161. *Id.* at 946 n.11; *id.* at 950 (citing Reiners v. Mehltretter, 236 F.2d 418, 421 (C.C.P.A. 1956)); THE BLUEBOOK: A UNIFORM SYSTEM OF CITATION R. 1.2(a), at 23 (Columbia Law Review Ass'n et al. eds., 17th ed. 2000).

162. *See In re* Jolles, 628 F.2d 1322 (C.C.P.A. 1980).

163. *Id.* at 1322-23.

164. *Id.* at 1325.

165. *See id.* at 1327.

Furthermore, no methods of treatment or pharmaceutical compositions for use in humans were set out in the specification, no dosages were described, and how the invention was to be used was left "to speculation."[166] However, as the losing applicant did in *Kirk*, the *Jolles* applicant filed affidavits indicating one of eight compounds had "substantial activity against experimental tumors in mice in tests customarily used for the screening of anti-cancer agents of potential utility in the treatment of humans," but the examiner rejected these references.[167] The timing of the affidavits, however, is crucial to note: in *Kirk*, the affidavit was filed *after* the final rejection, whereas in *Jolles*, the affidavits were filed "in" the application.[168] Therefore, in reversing the examiner's and BPAI's decision, the CAFC relied heavily on the *Jolles* affidavits to show that a PHOSITA would find the claimed uses credible.[169] The CAFC concluded that evidence of efficacy of the compound in laboratory animals, as shown in the affidavits, was sufficient to show closely related compounds had the requisite utility for treating humans.[170] In reaching this conclusion, the CAFC also cited *In re Buting*[171] and *In re Bergel*,[172] which support the proposition that testing in animals or mice was relevant to the utility of the components in humans.[173] Furthermore, in reaching this conclusion, the CAFC held the BPAI erred in dismissing evidence in one of the affidavits that declared the testing in mice was routinely used to screen anticancer agents of potential utility in humans.

In addition, in another "utility" case, *Cross v. Iizuka*,[174] involving a priority contest, the CAFC rejected the argument that *in vivo* tests were necessary to establish a practical utility. Instead they held that the demonstration of the *in vitro* activity of a novel pharmaceutical agent was enough to establish statutory utility.[175] More importantly, as in *Jolles*, the Court pointed to expert testimony to uphold the examiner's and BPAI's disputed finding of utility.[176] This seems to conflict with *Kirk*, where the expert evidence was rejected as an "ex post facto affirmation."[177]

166. *Id.*
167. *Jolles*, 628 F.2d at 1324.
168. *In re* Kirk, 376 F.2d 936, 939 (C.C.P.A. 1967); *Jolles*, 628 F.2d at 1323-24.
169. *Jolles*, 628 F.2d at 1327.
170. *Id.* at 1327-28.
171. *In re* Buting, 418 F.2d 540 (C.C.P.A. 1969).
172. *In re* Bergel, 292 F.2d 955 (C.C.P.A. 1961).
173. *Jolles*, 628 F.2d at 1327.
174. Cross v. Iizuka, 753 F.2d 1040 (Fed. Cir. 1985).
175. *Id.* at 1051.
176. *Id.* at 1049.
177. *See In re* Kirk, 376 F.2d 936, 940 (C.C.P.A. 1967).

A more careful reading of *Cross*, however, reveals that after the examiner's final decision, the expert testimony was presented during a priority contest, and the evidence presented through the testimony was the "fact" that, in essence, the utility, though not as detailed as desired, was nonetheless actually "there" because a PHOSITA would know the utility at the time the application was filed.[178] According to the Court, the BPAI found the application "disclosed some activity or utility. . . .," yet the appellant argued this was insufficient to show practical utility.[179] In citing that cases holding "[e]vidence of any utility is sufficient when the court does not recite any particular utility," the Court agreed with the BPAI that the application "disclosed that it was generally known in the art, as of the critical date, that the parent . . . compounds possessed" use; this was further supported by the expert testimony.[180] The Court, likewise, concluded that the same expert testimony also proved a PHOSITA would know "how to use" the compound even though the application did not specify how, because the PHOSITA had, on the critical date, "information as to the approximate dosage levels. . . ."[181] In addition, citing *Brenner* as a source for "broad guidelines," the CAFC declared, "[T]here is a reasonable correlation between the disclosed *in vitro* utility and an *in vivo* activity, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence."[182]

In addition, in *Amgen, Inc. v. Chugai Pharmaceutical Co.*,[183] which is known more for its obviousness analysis, the Court briefly addressed utility in the context of enablement. The Court invalidated broad claims that were unsupported by a sufficient number of examples of use the Court felt were needed to validate Amgen's broad claims. In recognizing the lack of predictability in the art of isolating and using purified, isolated DNA sequences encoding human Erythropoietin (EPO), the court declared that "[f]or DNA sequences, [an applicant must disclose] how to make and use enough sequences to justify grant of the claims sought."[184] This result occurred because, in deposition, the head of Amgen's EPO analog program confessed they did not know whether the EPO analogs "had the [useful] biological property of causing bone marrow cells to increase

178. *Cross*, 753 F.2d at 1044-45.
179. *Id.* at 1045.
180. *Id.* at 1049.
181. *Id.* at 1051.
182. *Id.* at 1050.
183. Amgen v. Chugai Pharm. Co., 927 F.2d 1200, 1212-15 (Fed. Cir. 1991).
184. *Id.* at 1213.

production. . . ."[185] And in its specification, Amgen made extensive statements concerning all of the EPO gene analogs that could be made, yet disclosed how to make and use only a few.[186] Furthermore, the Court knew and noted, "There may be many other genetic sequences that code for EPO-type proteins."[187] Therefore, because Amgen was trying to claim all EPO analogs, but only disclosed how to make and use a few, the Court invalidated Amgen's claims.[188] This suggests that, if an applicant fully enables the applicant's invention or discovery, the Court will be less stringent in applying section 103 utility. However, if the enablement is weak, the Court will strictly demand complete and specific descriptions of section 103 utility.

Nevertheless, in the most recent chemical composition case, *In re Brana*, the CAFC ruled in favor of the applicant, reversing the PTO's rejection of no utility of an antitumor agent.[189] The PTO based its rejection on the specification's failure to describe any specific disease against which the claimed compounds were active, and the fact only *in vitro* tests had been performed, requiring the applicant to cite to similar compounds showing *in vivo* activity.[190] In disregarding a reference showing some laboratory oncologists were skeptical about the predictive value of *in vivo* models for human therapy, the CAFC declared human clinical testing was not necessary to establish practical utility for an invention having therapeutic utility.[191] The CAFC also gave little weight to the fact that changes in chemical compounds could radically alter the chemical's effect on humans; at the time, it accepted prior art references that disclosed structurally similar compounds proven, *in vivo*, to be effective anticancer agents against various tumor models.[192] Seemingly contrary to *Kirk* and *Joly*, the CAFC stated evidence of success in structurally similar compounds was relevant in determining whether one skilled in the art would believe an asserted utility.[193]

Though many have interpreted *Brana* as conflicting with *Brenner* and its progeny, the cases can be read as consistent with one another. Both decisions set forth the standard for determining a specific utility: an appropriate use of homologous art can provide credible support or a well-

185. *Id.*
186. *Id.*
187. *Id.*
188. *Amgen*, 927 F.2d at 1213.
189. *In re* Brana, 51 F.3d 1560 (Fed. Cir. 1995).
190. *Id.* at 1564 (the examiner cited § 112 as grounds for rejection, but § 101 would have also been proper).
191. *Id.* at 1568.
192. *Id.* at 1567.
193. *Id.*

established utility. Indeed, in *Brana*, the applicants relied on more than mere evidence from structurally similar compounds.[194] The applicants relied on *in vivo* and *in vitro* mouse model systems to test the antitumor activities of their compounds.[195] The applicants also submitted an affidavit containing evidence of the utility of the claimed compounds *in vivo*, even though they only tested *in vitro*.[196] In fact, before making it to the CAFC, the applicants already overcame the section 103 utility rejection.[197] They were before the CAFC, on the examiner's final rejection based on the specification failing to show "how-to-use" the compound under section 112.[198] However, relying again on the affidavit, the CAFC reversed the section 112 rejection because prior art and the submitted affidavit showed several compounds within the scope of the applicants' claims did exhibit antitumor activity *in vivo*.[199] This is unlike Mason's claims and evidence in *Brenner*. In *Brenner*, where the Court reached an opposite result, the context was highly unpredictable compounds, and Mason failed to provide evidence to show his steroids possessed any of the same useful tumor-inhibiting properties as the prior art homologues. Therefore, though *Brenner* is not mentioned in *Brana*, perhaps it was not raised because of the critical factual differences. These differences might have made the cases so dissimilar that, if the CAFC had mentioned *Brenner*, its mention could have been viewed as inapposite.

Summing up the meaning of these cases, in context of DNA sequence fragments, can one predict how the Court or the CAFC would rule? Though the Court in *Brenner* invalidated the patent claiming steroids, it recognized "that what [in 1966] seems without 'use' may tomorrow command the grateful attention of the public."[200] Could this be viewed as the Court hinting it might, in the future, be amenable to loosening its strict application of the utility requirement? At this time, it is unknown. Based on its holdings, however, the Court has been historically opposed to patents. Therefore, the odds are that it would maintain its strict interpretation.

The CAFC and its predecessor, the CCPA, however, have been quite liberal in upholding and enforcing patents in the pharmaceutical and biotechnology fields.[201] In fact, as long as the slightest evidence has been

194. *Brana*, 51 F.3d at 1563.

195. *Id.*

196. *Id.*

197. *Id.*

198. *Id.*

199. *Brana*, 51 F.3d at 1563, 1565-66.

200. *Brenner*, 383 U.S. at 536.

201. *See* ADAM B. JAFFE & JOSH LERNER, INNOVATION AND ITS DISCONTENTS: HOW OUR BROKEN PATENT SYSTEM IS ENDANGERING INNOVATION AND PROGRESS AND WHAT TO DO ABOUT

put forward to support a disclosure of utility, the CCPA has ruled in favor of the applicant.[202] Only in those cases where the applicant was unable to come forward with any relevant evidence of utility did the CCPA rule against the applicant.[203] In addition, it has been the CAFC's position that minimal utility is all that is required to obtain a patent.[204] The CAFC tends to give expert and PHOSITA evidence great weight.[205] If any of this evidence is credible, it seems to find in favor of the applicant, regardless of the PTO's ruling.[206] Though the CAFC has rejected gene-related applications under the written description and enablement requirement, the CAFC has intimated it might take a more lenient approach. It believes that, by having only the amino acid sequence of a protein, one can be in possession of the entire genus of DNA sequences that encode a disclosed partial protein sequence, "even if individual species within that genus might not have been rendered obvious."[207] To meet the written description requirement, the CAFC does not require a patent applicant to list every possible permutation of nucleic acid sequences that can encode a particular protein for which the amino acid sequence is disclosed.[208] This approach recognizes the degeneracy of the genetic code, but it also means once a protein is claimed through a DNA or amino acid sequence, the applicant obtains a monopoly on all nucleic acid sequences that code for the particular protein. Since these sequences do not have to be expressly identified in the patent application it is unclear how another person is supposed to know what sequences have already been patented.

IT 9-11 (2004). The CAFC has "significantly broadened and strengthened the rights of patent holders." *Id.* at 10. "Patents have become so easy to get, and are enforced so ruthlessly by the courts that the winners of the technological competition in crucial industries are sometimes those with the best lawyers, or those simply lucky enough to have been awarded a key patent they did not really deserve, rather than those that have created the best products or services." *Id.* at 19.

202. *See, e.g.*, Nelson v. Bowler, 626 F.2d 853 (C.C.P.A. 1980); *In re* Malachowski, 530 F.2d 1402 (C.C.P.A. 1976); *In re* Gaubert, 524 F.2d 1222 (C.C.P.A. 1975); *In re* Gazave, 379 F.2d 973 (C.C.P.A. 1967); *In re* Hartop, 311 F.2d 249 (C.C.P.A. 1962); *In re* Krimmel, 292 F.2d 948 (C.C.P.A. 1961).

203. *See, e.g.*, *In re* Citron, 325 F.2d 254 (C.C.P.A. 1964) (uncharacterized biological extract not supported with scientifically credible utility); *In re* Buting, 418 F.2d 540, 542 (C.C.P.A. 1969) (credible basis not established for the claim that the single class of compounds has utility in treating different kinds of cancers); *In re* Novak, 306 F.2d 924 (C.C.P.A. 1962) (grounds proffered for utility of claimed compounds could not affect claimed physiological activity).

204. Brenner v. Manson, 383 U.S 519, 522 (1966); *contra* Envirotech Corp. v. Al George, Inc., 730 F.2d 753, 762 (Fed. Cir. 1984) ("[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding lack of utility."); Brooktree Corp. v. Advanced Micro Devices, Inc., 977 F.2d 1555 (Fed. Cir. 1992).

205. *See supra* text accompanying notes 161-98.

206. *Id.*

207. *In re* Wallach, 378 F.3d 1330, 1333 (Fed. Cir. 2004).

208. *Id.* at 1334.

More recently, criticizing the CAFC, a publication decrying the "broken patent system" has complained that "certain aspects of biotechnology such as genetic sequences are all technologies for which the courts have expanded the range of patentable subject-matter beyond what was perceived to be patentable at the end of the 1970."[209] As a result, if utility is the only issue before the CAFC on a DNA fragment application, it is likely the CAFC would rule in favor of the applicant.

C. *Application of the Law by the PTO*

The PTO has historically been more conservative. In *Ex parte Aggarwal*,[210] the BPAI found no utility for an antitumor pharmaceutical agent on grounds that the applicant failed to disclose "evidence showing substantial activity in screening tests customarily used and accepted as predictive of human activity for the type of chemical tested."[211] Though the applicant's specification contained many broad statements regarding utility, and it described administration of the chemical, lymphotoxin, via virtually all known routes available for administering anticancer substances, the actual illustrations and explanations of utility were sparse.[212] The application was virtually devoid of teachings to support the broad scope of its claims.[213] Additionally, even though the applicant submitted an affidavit to support his claimed utility, as reported by the BPAI, the affidavit seemed neutral to negative.[214] In addition, the BPAI agreed with the examiner that there was "considerable doubt that those skilled in the art would be willing to accept [the applicant's] *in vitro* tests

209. JAFFE & LERNER, *supra* note 201, at 198.

210. 23 U.S.P.Q.2d 1334 (Bd. Pat. App. & Interf. 1992).

211. *Id.* at 1339.

212. *Id.* at 1337-38.

213. *Id.* at 1338.

214.

> The declaration admits that it is not possible, particularly in the early stages of development of a given candidate chemotherapeutic agent, "to predict in advance whether a selected tumor is susceptible to treatment with the agent." The Sherwin declaration does not state that lymphotoxins are useful against tumors or that practitioners skilled in the art know how to use lymphotoxin. All that is said is that (1) oncologists will "not be misled" by the assertion of broad anti-tumor activity, (2) routine and conventional clinical studies will be conducted to "more fully refine the activity of the agent," and (3) though "extensive and burdensome," the studies involve nothing more than "routine manipulations."

Id. at 1339.

and *in vivo* tests as established models predictive of utility against tumors in humans."[215]

Additionally, though *Aggarwal* has been cited as conflicting with *Cross*, it does not necessarily conflict, since the basis for the rejection in *Aggarwal* was the breadth of the claims that were unsupported by the prior art or the submitted affidavit.[216] In addition, according to the BPAI, the specification was "virtually devoid of teachings that indicate[d] the broad scope of lymphotoxins claimed has the broad scope of utility asserted."[217]

In the more recent case of *Ex parte Fisher*,[218] the BPAI also took a more conservative approach, rejecting an EST patent application that did not meet the utility standards set out by the PTO.[219] In *Fisher*, which involved plant ESTs, the examiner rejected an application on more than 32,236 ESTs, commenting that the uses specified by the applicants were "non-specific uses that are applicable to nucleic acids in general and not particular or specific to the nucleic acids being claimed."[220] The applicants had stated the DNA sequences might be useful, essentially, as a probe.[221] Though the BPAI upheld the examiner's rejection on utility and enablement grounds (but reversed on the written description requirement), it made a statement that suggests ESTs might have utility.[222] The BPAI said, even if it agreed that monitoring the expression of uncharacterized nucleic acids would be useful, each sequence is not necessarily useful.[223] "A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities."[224] However, the BPAI was in some ways equivocal on whether it would ever allow a patent like the applicants'

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215. *Aggarwal*, 23 U.S.P.Q.2d at 1338.

216. *See id.* at 1338 n.8 (distinguishing Cross v. Iizuka, 753 F.2d 1040 (Fed. Cir. 1985)).

217. *Id.* at 1339.

218. 72 U.S.P.Q.2d 1020 (Bd. Pat. App. & Interf. 2004).

219. *See* Mary Ann Liebert, *ESTs Fail to Make the Grade, Again*, 23 BIOTECHNOLOGY L. REP. 571, 571-72 (2004).

220. *Fisher*, 72 U.S.P.Q.2d at 1022; *see also* Liebert, *supra* note 219, at 571.

221. Liebert, *supra* note 219 at 571.

> [The applicants] stated that their sequences might be useful for several purposes, such as producing a plant that synthesized lower than normal amounts of a given protein, determining an association between a genetic polymorphism and a particular trait, isolating a particular genetic region, detecting mutations, as molecular tags, and for identification of tissues.

Id.

222. *See id.* at 571-72.

223. *Id.* at 572.

224. *Ex parte* Xuanchuan Yu, Appeal No. 2004-1761, 2004 WL 2733632, at *12 (Bd. Pat. App. & Interf. 2004) (unpublished opinion).

application, perhaps indicating its rulings will land somewhere in between the loose utility guidelines of 1995 and the stricter utility guidelines of 2001.

In fact, the more recent utility guidelines, put in effect in January 2001, are stricter than the utility guidelines of 1995, but a PTO examiner may still grant a DNA fragment patent, since there is a lack of much needed guidance.[225] Many maintain that the guidelines do not address the issuance of DNA fragment patents.[226] Nevertheless, according to Dickinson, the asserted utility of a gene patent will be considered credible by patent examiners "unless the logic underlying the assertion is seriously flawed, or the facts upon which the assertion is based are inconsistent with the logic underlying the assertion."[227] Because this statement is somewhat murky, Dickinson provided an example: "at least some nucleic acids might be used as probes, chromosome markers, or diagnostic markers. Therefore, the *per se* credibility of assertions regarding the use of nucleic acids is not usually questioned."[228]

According to the *2001 Utility Guidelines*,

> [t]he patentee is required to disclose only one utility, that is, teach others how to use the invention in at least one way. The patentee is not required to disclose all possible uses, but promoting the subsequent discovery of other uses is one of the benefits of the patent system.[229]

In addition, the patent applications must show a well established utility defined as specific, substantial and credible.[230] This means the patent examiner must "determine if the assertion of utility is credible (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided)."[231] To determine credibility, the examiner must look to the reliability of the patent applicant's assertion based on the logic and facts offered to support

225. *See* USPTO Revised Interim Utility Guidelines Training Materials, ex. 10, at 53-55 (1999) [hereinafter USPTO Revised Training Materials] (DNA Fragment encoding a Full Open Reading Frame), *available at* http://www.uspto.gov/web/menu/utility.pdf (last visited Mar. 30, 2005).

226. *See, e.g.*, Wei, *supra* note 15, at 311, 327.

227. Dickinson Statement, *supra* note 12, at 27.

228. *Id.*

229. *Utility Examination Guidelines*, *supra* note 14, at 1094.

230. USPTO Revised Training Materials, *supra* note 225, at 3; *see also* USPTO MANUAL OF PATENT EXAMINING PROCEDURE § 2107.01 (ed. 8, rev. 1, Feb. 2003).

231. USPTO Revised Training Materials, *supra* note 225, at 5.

the assertion of utility.[232] Accordingly, an assertion of utility for nucleic acids, claiming they could be used as probes, chromosome markers, forensic markers, or diagnostic markers is credible, but such a use might fail the specific and substantial utility tests.[233]

To be a specific utility means the utility asserted is specific to the subject matter claimed, which is contrasted with a "general" utility that would only apply to the invention's broad class.[234] If a claimed polynucleotide use is disclosed simply as a "gene probe" or "chromosome marker," then it would not be considered a specific utility in the absence of a disclosure of a specific DNA target.[235] Likewise, general statements of diagnostic utility, such as diagnosing an unspecified disease, would be insufficient unless a specific condition for diagnosis is disclosed.[236]

A "substantial utility" is a "real world" use, which means that if further research must be performed to identify or reasonably confirm a "real world" use, there is no substantial utility.[237] A "well established utility" is a specific, substantial, and credible utility that is well-known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.[238] It does not encompass a nonspecific utility that would apply to virtually every member of a general class of materials, such as proteins or DNA.[239]

However, the CAFC seems to contradict the requirement for a well established utility since it allows statements of nonspecific utility. By having only the amino acid sequence of a protein, the CAFC says one can be in possession of the entire genus of DNA sequences that encode a disclosed partial protein sequence, "even if individual species within that genus might not have been described or rendered obvious."[240] Though the Guidelines disallow broad nonspecific utilities that would apply to every member of a general class, the CAFC's statement implies that the Guidelines are wrong, since if one is not required to identify all of the sequences that encode for the protein, a statement of a specific utility for each unidentified sequence need not be specified, and a broad statement would suffice. As confusing as it is, the CAFC is lenient and may very well disagree with the PTO's Guidelines. Despite the fact that, in fleshing out the guidelines for both the utility and written description requirements,

232. *See id.*
233. *Id.*
234. *Id.*
235. *Id.*
236. USPTO Revised Training Materials, *supra* note 225, at 5-6.
237. *Id.* at 6.
238. *Id.* at 7.
239. *Id.*
240. *In re* Wallach, 378 F.3d 1330, 1333 (Fed. Cir. 2004).

the PTO has applied case law based on chemical fact issues,[241] the CAFC may still reverse the PTO on an EST patent.

Furthermore, the PTO's use of chemical composition-based case law results in questionable conclusions. The guidelines state that, if a patent application claims a "nucleic acid" that bases its utility on "homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted . . . unless . . . rebut[ted]."[242] Likewise, the guidelines allow one protein's function to be imputed to another based on homology.[243] These statements, however, contradict chemical practice, and furthermore, risk the issuance of a patent on an EST displaying a high degree of homology to other DNA fragment sequences that could actually exert the opposite, or a very different, effect.[244] The utility of DNA fragment patents is not always known.[245] This leaves broad gaps, and it has likely predisposed the utility guideline training materials to errors in application through the examples it provides.[246]

In conjunction with the *Revised Interim Utility Guidelines Training Materials*, the PTO also issued the Synopsis of Application of Written Description Guidelines.[247] These guidelines have limited relevance to the utility inquiries because "the specification must teach those of skill in the art 'how to make and *how to use* the invention as broadly as it is claimed.'"[248] They also lack sufficient guidance, and in one of the more controversial examples, the PTO rejects (for the wrong reasons) a claim directed to "A DNA comprising the EST of SEQ ID NO: 1," stating substitution of the word "gene" for "DNA" would solve the problem.[249] The PTO says use of the term "gene" in the preamble of an EST claim

241. J. Timothy Meigs, *Biotechnology Patent Prosecution in View of PTO's Utility Examination Guidelines*, 83 J. PAT. & TRADEMARK OFF. SOC'Y 451, 474 (2001).

242. *Utility Examination Guidelines*, *supra* note 14, at 1096.

243. *Id.*

244. *See* Natalie A. Lissy, Note, *Patentability of Chemical and Biotechnology Inventions: A Discrepancy in Standards*, 81 WASH. U. L.Q. 1069, 1078 (2003).

245. *See* Wei, *supra* note 15, at 311.

246. *See* Revised Interim Utility Examination Guidelines, *supra* note 8, cmt. 44, at 81-89 (NIH, Jack Spiegel, Ph.D.); *accord* Joshua C. Benson, Note, *Resuscitating the Patent Utility Requirement, Again: A Return to* Brenner v. Manson, 36 U.C. DAVIS L. REV. 267, 291 (2002) (citing Timothy A. Worrall, Note, *The 2001 PTO Utility Examination Guidelines and DNA Patents*, 16 BERKLEY TECH. L.J. 123, 133 (2001)).

247. USPTO Synopsis of Application of Written Description Guidelines (1999), *available at* http://www.uspto.gov/web/menu/written.pdf (last visited Mar. 30, 2005).

248. *In re* Goodman, 11 F.3d 1046, 1050 (Fed. Cir. 1993) (quoting *In re* Vaeck, 947 F.2d 488, 496 (Fed. Cir. 1991) (emphasis added)).

249. *See* Stephen G. Kunin, *Written Description Guidelines and Utility Guidelines*, 82 J. PAT. & TRADEMARK OFF. SOC'Y 77, 91-92 (2000).

may raise a written description issue because of the ambiguity of what an accurate description of a "gene" really is.[250]

Nevertheless, it is still unclear what practical impact the guidelines have had on the examiners' behavior.[251] Because of the lag between application filings and patent grants, the PTO output is difficult to measure.[252] Additionally, to provide a full assessment of the effect of the written description and utility guidelines on DNA patents would require analysis of the scope of issued claims and the types of nucleic acids claimed (full-length coding sequences, ESTs, and antisense fragments), in addition to an analysis of the number of DNA sequence patent applications the USPTO forced applicants to separate into individual sequences.[253]

Furthermore, the utility guidelines have not yet been interpreted or applied by a court. On July 23, 2004, in *Monsanto Co. v. Good*, the District Court for the District of New Jersey rejected one party's interpretation of the utility guidelines. [254] However, the district court did not interpret the guidelines; it merely quoted them.[255]

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250. *See* KENNETH J. BURCHFIEL, BIOTECHNOLOGY AND THE FEDERAL CIRCUIT 55 (Dale H. Hoscheit & Lisa M. Hemmendinger eds., Cumm. Supp. 2000). This is supported, however, by the fact that not all molecular biologists and geneticists agree that a "gene" really exists at all. *See, e.g.*, EVELYN FOX KELLER, IS THERE AN ORGANISM IN THIS TEXT?, *in* CONTROLLING OUR DESTINIES: HISTORICAL, PHILOSOPHICAL, ETHICAL, AND THEOLOGICAL PERSPECTIVES ON THE HUMAN GENOME PROJECT 273-76 (Phillip R. Sloan ed., 2000). The word "gene" was a term chosen by a scientist to identify various interesting regions of nucleic acids or genomic text. *See id.* at 273-75. In fact, the concept of "genes" has never been stable, "unitary, comprehensive, or 'clean.'" *Id.* at 275. Questions have arisen as to whether a gene really even tangibly exists, since a gene is the sequence of nucleotides transcribed and translated into a polypeptide chain, and may not come into existence until after the DNA has been read by the mRNA, and the mRNA has been spliced. *See id.* at 275-76. As such, the "gene" does not really reside on the chromosome, and perhaps not even in the nucleus. *Id.* at 276.

251. A PATENT SYSTEM FOR THE 21ST CENTURY, *supra* note 111, at 56.

252. *Id.*; *accord* ALBRIGHT, *supra* note 5, at 2 n.5.

> The number of life patents waiting and already awarded by the U.S.P.T.O. seems to vary greatly depending on who is asked in the patent office. . . . [One source] claimed that 20,000 patents on genes or gene-related molecules [had issued]. . . . One year earlier, the former director of the U.S.P.T.O. told a Congressional subcommittee that there had been only 6,000 patents awarded. . . .

Id.

253. A PATENT SYSTEM FOR THE 21ST CENTURY, *supra* note 111, at 57-58.

254. *See* Monsanto Co. v. Good, No. Civ. A. 01-5678 FLW, 2004 WL 1664013, at *5 (D.N.J. July 23, 2004).

255. *See id.*

D. *Relevant Treaties — TRIPs*

Finally, in addition to the U.S. Constitution, the statutes, case law and the PTO guidelines, there are standards set out in a treaty that specifically addresses patents. In the last few years, the United States, along with hundreds of other countries joined the World Trade Organization and signed the Agreement Trade Related Aspects of Intellectual Property (TRIPs). Therefore, the United States must now comply with its provisions. The enforcement of TRIPs takes place through the World Trade Organization, which authorizes the application of compelling penalties to ensure compliance. The provisions applicable to the problem of EST patents are TRIPs articles 8 and 27. Article 27 of TRIPs allows patents to be granted for inventions that are "new, involve an inventive step and are capable of *industrial application.*"[256] It also disallows any member country to discriminate against patent rights due to field of technology.[257] However, article 27(3) specifically excludes from the anti-discrimination provision a country's treatment of patents on "diagnostic, therapeutic and surgical methods for the treatment of humans."[258]

Presently, no cases construe the meaning of "field of technology." The only complaint pending before the World Trade Organization regarding discrimination on the basis of field of technology involves a complaint made by Canada on December 7, 1998, alleging that a patent term extension scheme was implemented under the European Community regulation Nos. 1768/92 and 1610/96, and that this patent term extension scheme was limited to pharmaceutical and agricultural chemical products.[259] However, the pharmaceutical and agricultural chemical products field is far broader than the discrete portion of DNA gene fragments that are in the field of biotechnology. So, one could argue that mere modification of laws regulating the granting of patent rights on DNA sequence fragments is not a discrimination against an entire field of technology. ESTs are a miniscule part of the field of genetics, biotechnology, and biology. Therefore, modifying only the area affecting DNA fragment sequence patents does not affect an entire field of technology.

Furthermore, in context of the issue presented herein, the relevant TRIPs provisions arguably conflict with each other. Although, if read in

256. Agreement on Trade-Related Aspects of Intellectual Property Rights, Apr. 15, 1994, 33 I.L.M. 92, art. 27(1) (emphasis added) [hereafter TRIPs Agreement].

257. *Id.*

258. *Id.* art. 27(3)(a).

259. *See* Request for Consultations by Canada, European Communities — Patent Protection for Pharmaceutical and Agricultural Products, WT/DS153/1, 1998 WL 842152 (W.T.O. Dec. 7, 1998).

a vacuum, they do not appear to conflict, once applied to EST patents there is a good argument they do conflict. Under article 27(1) of TRIPs, if the U.S. grants patents on fragments of DNA, such patents would arguably violate the provision requiring patents to be granted on inventions that "are capable of industrial application."[260] It would seem that DNA sequence fragments for which no well established (i.e., credible, substantial and specific) utility can be adequately described, or fragments that are identified as merely probes or research tools, cannot meet the TRIPs requirement that patents be granted only on inventions capable of industrial application. Therefore, arguably, to come into compliance with TRIPs, Congress must change the law to prohibit granting patents on ESTs. However, if Congress did modify the laws applying to EST patents, TRIPs might be equally violated since modification of the current U.S. patent laws could violate the TRIPs provision disallowing discrimination against patent rights in a "field of technology."[261]

However, pursuant to article 27(3), countries are specifically allowed to exclude from patents inventions involving "diagnostic [or] therapeutic methods . . . for the treatment of humans."[262] Moreover, article 8(1) of TRIPs, which sets forth the general principles behind TRIPs, states that members "may, in formulating or amending their laws and regulations, adopt measures necessary to protect public health . . . and to promote the public interest in sectors of vital importance to their socio-economic and technological development."[263] Clearly, many in the medical, genetics and biotechnology fields, including other countries, have been troubled by the PTO's allowance of DNA fragment sequence patents.[264] This concern has been raised because of the potential problem of the "anticommons."[265]

Therefore, though at first blush compliance with TRIPs can be a concern, there are three provisions that could support changes in the law with regard to ESTs: Article 8(1), 27(1)(a), and 27(3). As a result, Congress could arguably modify the law governing issuance of DNA fragment patents without violating TRIPs.

260. TRIPs Agreement, *supra* note 256, art. 27(1).

261. *Id.*

262. *Id.* art. 27(3)(a).

263. *Id.* art. 8(1).

264. *See infra* Part VIII.

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

VII. WHY EST PATENTS HAVE CAUSED PUBLIC OUTCRY

Though the utility and written description guidelines are helpful, they are not stringent enough to prevent the granting of patents on ESTs, DNA sequence fragments, for which there is no real known utility, or objects on which the most valuable utility, among many other unknown utilities, has yet to be determined.[266] Furthermore, it seems the CAFC and the PTO have decided to gloss over the real issues of whether gene fragment patents are proper subject matter, novel, nonobvious, and useful.[267] By focusing on the technicalities of claim drafting, the attention has been removed from the subject matter and utility requirement and has made them "toothless."[268]

This has compelled many nongovernmental organizations to publicize their opinions. The Nuffield Council on Bioethics points to a common criticism of DNA sequence patenting: the sequences only carry information telling the body how to construct and produce proteins, and therefore cannot be patented, but can only be discovered as a product of nature.[269] Another main concern about granting patent rights over DNA sequences is that in a composition of matter patent, the patent owner has exclusive rights over all subsequent uses of that sequence.[270]

Though significant amounts of information about identification of one DNA sequence can be obtained from a partial DNA sequence (one can infer the presumed protein function between a DNA sequence that is similar to a previously characterized and identified gene, known as a full-length DNA sequence), the process of getting from an identified EST to a full-length cDNA or gene sequence is not simple.[271] A "full-length" cDNA is an image of the entire sequence of the mRNA it copies or "mirrors."[272] However, according to HUGO, using these partial DNA sequences to find full-length cDNA is an important research activity, even though it is not always successfully accomplished.[273] To properly and successfully obtain a full-length cDNA or gene sequence requires the development of methods, strategies, and techniques to deal with the many

266. *See generally* Wei, *supra* note 15.

267. *See* John M. Conley & Roberte Makowski, *Back to the Future: Rethinking the Product of Nature Doctrine as a Barrier to Biotechnology Patents (Part I)*, 85 J. PAT. & TRADEMARK OFF. SOC'Y 301, 301-06 (2003).

268. *See id.* at 304-05 (quoting John M. Golden, *Biotechnology, Technology Policy, and Patentability: Natural Products and Invention in the American System*, 50 EMORY L.J. 112, 127 (2001).

269. *See* NUFFIELD COUNCIL ON BIOETHICS, *supra* note 7, at 27.

270. *Id.* at 53.

271. HUGO Statement, *supra* note 83.

272. *Id.*

273. *Id.*

issues and problems that occur in the process, and such efforts may take from a matter of weeks (when extremely short, or easily cloned genes are involved), to more than a year.[274] In addition, it may also be necessary to screen multiple cDNA libraries and tissue sources, or to use a variety of cloning-based and polymerase chain reaction-based techniques.[275]

Furthermore, in addition to the difficulties faced in obtaining a useful DNA fragment or sequence, there are further obstacles that can complicate the generation of this fragment into a useful product that correctly expresses a gene.[276] Successful cloning of this fragment to produce the correct expression construction does not always occur easily because finding the right host to correctly reproduce the DNA fragment's expression creates many other problems.[277]

As a result, not only is the review and examination of gene fragment patents a difficult, complex, expensive, and time-consuming task for the PTO, it is also controversial because with new technologies, the effort required to isolate and characterize an EST is small compared to the work of isolating and characterizing a gene and gene product, finding out what it does, and developing a commercial product.[278] Furthermore, because a gene can be expressed as mRNA many times, ESTs ultimately derived from mRNA may be redundant.[279] "Redundant" means there may be many identical or similar copies of the same EST.[280] This redundancy and overlap means a person searching for a particular EST in a computer

274. *Id.*

275. *Id.*

276. HUGO Statement, *supra* note 83.

277.

> For instance, it may be necessary to attempt cloning in multiple hosts, including bacterial, yeast, insect, and mammalian cells, to find a usable host. There is no guarantee as to what expression vector and gene structure will be adequate for the task. Moreover, there is little way to know in advance what cell types will produce the appropriate post-translational modifications. Each expression construction must also allow for appropriate promoters, high affinity translation sequences, and often enhancers and splice junctions.

Id.

278. *Genetics and Patenting*, Human Genome Project Information, Genome Management Information System of the Dept. of Energy, Office of Biological and Environmental Research (formerly Office of Health and Environmental Research) Genome Programs Task Group, *at* http://www.ornl.gov/sci/techresources/Human_Genome/elsi/patents.shtml#2 (last visited Feb. 21, 2005).

279. *See What is a Cell?*, *supra* note 39.

280. *See id.*

database may retrieve a long list of tags, many of which represent the same gene.[281]

Therefore, those who do attempt to, and sometimes successfully, obtain gene fragment patents are said to own "gatekeeper" patents allowing them to exercise undue control over the commercial fruits of genome research.[282] Though only recently occurring, this will likely result in multiple patents on different parts of the same genome sequence, adding undue costs to a researcher who wants to examine the sequence.[283] This is because multiple patents may have issued on a gene fragment, the gene, and the protein.[284] As a result, if a researcher wants to examine the sequence, she will have to pay each patent holder a fee for the opportunity to study the sequence.[285] Of course, she would first have to pay someone to research the patents to determine which ones apply to the sequence she wants to study, and then hope that the patent holders would be willing to allow her to examine the sequence for a fee.[286] If she is lucky, she will locate all of the patents, be allowed to pay a reasonable license fee, and not miss a patent that she would infringe and for which she would likely be sued.

VIII. WHY CONGRESS HAS THE POWER TO DO SOMETHING ABOUT EST PATENTS

As a result of the above, Congress must do something to protect the public health of this country. The problem probably has its origin in the PTO's application of the law Congress created. With only one or two exceptions, the PTO treats all patent applications the same way: "From gear shifts to genomics, [the PTO] applies the same norms to all inventions and technologies. . . . Just as the patent system has nurtured the development of telephony, aeronautics, and computers, so, too, will it

281. *See id.*

282. *See Genetics and Patenting, supra* note 278. In the context of bioengineered and genetically engineered food, ActionAid, which is a charitable organization active in more than thirty countries, is one of a number of organizations calling for a complete rethink of the provisions of the TRIPs Agreement that apply to the patenting of life forms. Joff Wild, The Future for Patents on Life, Jan. 2000, *available at* http://thomsonscientific.com/ipmatters/patlife/8180006 (last visited Feb. 21, 2005). Alex Wijeratna, the international food rights campaign coordinator in the UK branch of ActionAid, claims "there should be no patents on staple crops. Food security in the south needs to be ring fenced, it is too important to leave to intellectual property and the private sector." *Id.*

283. *Genetics and Patenting, supra* note 278.

284. *Id.*

285. *Id.*

286. *Id.*

ensure that the new discoveries in genomics lead to healthier, longer lives for all of humankind."[287]

However, because "Congress is free to amend § 101 so as to exclude from patent protection organisms produced by genetic engineering,"[288] it is, likewise, free to amend section 101 to impose regulations, conditions or more stringent requirements on the issuance of DNA sequence fragments. "Or it may choose to craft a statute specifically designed for such . . . things."[289] In fact, Congress has once before taken action on genetic research by imposing conditions under which such research could be performed.[290] It has also continued to do so indirectly, by charging the NIH with the task of publishing its Guidelines for Research Involving Recombinant DNA Molecules.[291]

IX. WHY THE QUESTIONABLE "UTILITY" OF ESTS IS IMPORTANT ENOUGH TO ASK CONGRESS TO IMPLEMENT CHANGES

Because the functions are unknown for more than 50% of discovered genes,[292] it reasonably follows that their utility cannot be identified, and the patenting of ESTs, with even less known functions, must be restricted. Furthermore, because the human genome sequence is almost (99.9%) identical in all humans,[293] allowing patents on DNA fragment sequences has caused, and will likely continue to cause overlapping, therefore blocking patent rights.[294] Only about 2% of the genome encodes instructions, and genes appear to be concentrated in random areas along the genome, with vast expanses of non-coding DNA in between.[295]

On pending applications, the utility of gene fragments has been identified by vague terms, like providing "scientific probes" to help find a gene or another EST, or to help map a chromosome.[296] Questions have

287. Dickinson Statement, *supra* note 12, at 18, 21.

288. Diamond v. Chakrabarty, 447 U.S. 303, 318 (1980).

289. *Id.*

290. *See id.* at 317 n.11 (citing 41 Fed. Reg. 27902 (1976)).

291. *See* Notices, Department of Human Health and Services, 66 Fed. Reg. 57970 (Nov. 19, 2001). In these guidelines, the NIH was, *inter alia*, resolving how to balance the need for disclosure of information to the public about gene transfer research with the desire to keep trade secret information confidential. *See id.*

292. *Genomics*, *supra* note 25.

293. *Id.*

294. *See* Donald L. Zuhn, Jr., *DNA Patentability: Shutting the Door to the Utility Requirement*, 34 J. MARSHALL L. REV. 973, 994 (2001).

295. *Genomics*, *supra* note 25.

296. *Genetics and Patenting*, *supra* note 278.

arisen over the issue of when, from discovery to development into useful products, exclusive right to genes can, if ever, be claimed.[297]

A. *The Granting of EST Patents Rewards the Wrong Entity*

Initially the method for identifying and cloning a gene cost between $40,000 and $50,000, and required a researcher to work backwards from a known biological function.[298] After identifying a known biological function, the researcher would isolate and purify the responsible proteins, and then use degenerate DNA probes to locate the corresponding gene.[299] This was not only expensive, but also time consuming.

Subsequently, though highly criticized, Dr. Craig Venter found a way to resolve the time and money issue of sequencing DNA. His approach was so modern that most had never heard of it: it was driven by reductionism.[300] His strategy of discovery was based on the belief that, the more he divided natural phenomena into its constituent parts, and those parts into subparts and so forth, the more he could learn how nature really works.[301] But because it was too simplified, many were stunned to hear that Venter sought patents on DNA fragments sequenced by his automated machine.[302] When James Watson[303] heard Venter was seeking patents on the EST sequences, he was stunned. He said that allowing patents on these cDNA sequences was "pure lunacy," and further commented that "virtually any monkey" could run the automated sequencing machines.[304]

Indeed, Venter relied on the many cDNA libraries that had been constructed since the mid-1970s from many sources, including different organisms, tissues, and functional cellular states.[305] The idea of coupling

297. *Id.*

298. Kight, *supra* note 14, at 1003.

299. *Id.*

300. SHREEVE, *supra* note 90, at 7.

301. *Id.*

302. Venter, developed an improved approach by using cDNA sequencing to identify genes. *See* Kight, *supra* note 14, at 1003. Venter used an automated sequencer that, instead of identifying a full-length gene or DNA sequence, identified an edited copy of a gene that contained only the protein-coding regions. *Id.* This edited gene, known as cDNA, is much shorter, and can be characterized more quickly. *Id.* Venter identified and copied only the mRNA molecules into sturdier strands of what he termed cDNA, and this cDNA would then be processed in the sequencing machine. *Id.* Venter's process of identifying cDNA cost only approximately twenty dollars a piece. *Id.* Venter sought patent protection for these sequences while working at NIH. Kight, *supra* note 14, at 1003.

303. Watson and Crick identified the double helix structure of DNA. *See supra* Part II.C.

304. Kight, *supra* note 14, at 1004 (citing Leslie Roberts, *Genome Patent Fight Erupts*, 254 SCIENCE 184, 184 (1991) (quoting James Watson).

305. *See* HUGO Statement, *supra* note 83.

DNA sequencing to cDNAs was discussed as early as 1986.[306] Nevertheless, many issues and problems still plague the use of ESTs to obtain full-length cDNA and gene sequences.[307] In addition, HUGO does not agree with the patenting of partial and uncharacterized cDNA sequences because it believes those grants will reward those who make routine discoveries, but penalize those who determine biological function or application.[308] Allowing patents on DNA fragments will impede the development of diagnostics and therapeutics.[309] Partial and uncharacterized cDNA sequences (ESTs) constitute research tools that should not be patented.[310]

B. *The Granting of EST Patents Has Blocked the Dissemination of Knowledge Creating the "Anticommons"*

One of the purposes of the patent system is "to encourage dissemination of information concerning discoveries and inventions."[311] The government wants to encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge.[312] Unfortunately, it appears the contrary is occurring in the case of gene fragments.

The granting of a patent that has not been sufficiently developed so as to disclose a specific utility creates a "monopoly of knowledge which should be granted only if clearly commanded by the statute."[313] Such a

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306. *Id.*

307. *See id.*

> [I]t remains a task that is fraught with uncertainty. In some cases known techniques such as specific primer extensions may be successful; in others extraordinary skill will be required to overcome obstacles such as secondary structure. Foreseeable obstacles include the difficulty or impossibility of cloning mRNAs that are large or that encode poorly clonable sequences; the problems posed by immature, or incorrectly or alternatively spliced messages; the difficulties posed by cross-hybridization among members of gene families; and the rare but extremely challenging problems posed by post-transcriptional alternations of RNA sequence.

Id.

308. *Id.*

309. *Id.*

310. *See* HUGO Statement, *supra* note 83; NUFFIELD COUNCIL ON BIOETHICS, *supra* note 7, at 81-82.

311. Brenner v. Manson, 383 U.S. 519, 533 (1966).

312. *Id.*

313. *Id.* at 534.

monopoly without being useful may, nonetheless, "engross a vast, unknown, and perhaps unknowable area."[314] It appears patents that have issued on DNA sequence fragments have obtained a monopoly on a grossly vast and unknown area.

The Nuffield Council on Bioethics reports three concerns with the patenting of DNA arguing human DNA sequence patents should not be allowed because: (1) human DNA sequences have a special status; (2) the patent applications do not meet the legal criteria for patenting; and (3) there are possible negative effects on health care and research related to health care.[315] To support the argument that genes have an inalienable nature, it cites a European Community Directive.[316]

In addition, according to the National Research Council during deliberations for creation of the report, "A Patent System for the 21st Century," the realm of biotechnology research and development, as primarily applied to human health, was repeatedly raised as an area where there might be "a significant problem of access to patented technology."[317] Patents on upstream discoveries, if sufficiently broad in scope, can impede follow-on research and development if access to the foundation in intellectual property is restricted.[318] Indeed, "[p]atents of dubious quality only invite legal challenges that divert money and other resources from more productive purposes . . . such as raising venture capital, commercializing inventions and creating jobs."[319]

Currently, because the PTO has already awarded patents on 162 human genes to HGS, and the PTO has applications pending on 7,500 more,[320] there is little left to patent. The top gene-patent holders, Incyte, Celera Genomics, Hyseq (now known as Nuvelo, Inc.), Millennium Pharmaceuticals, and HGS, own nearly 1,000 life patents, and have

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314. *Id.*

315. NUFFIELD COUNCIL ON BIOETHICS, *supra* note 7, at 21.

316. *See id.* at 22; Council Directive 98/44/EC, 1998 O.J. (L 213) 13, *available at* http://europa.eu.int/scadplus/leg/en/lvb/l26026.htm (last visited May 5, 2005) "The human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions." Council Directive 98/44/EC, art. 5(1). However, the EC does differentiate between copies of DNA through section two, which states: "An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element." *Id.*, art. 5(2).

317. A PATENT SYSTEM FOR THE 21ST CENTURY, *supra* note 111, at 71.

318. *Id.*

319. *Patent Quality Improvement: Hearing Before the Subcomm. on Courts, the Internet, and Intellectual Property, of the House Comm. on the Judiciary*, 108th Cong. 2 (2003) (opening statement by Rep. Smith, Chair, Subcomm. On Courts, the Internet and Intellectual Property).

320. ALBRIGHT, *supra* note 5, at 29.

applied for 25,000 more.[321] Considering these companies are all biopharmaceutical companies that base their pharmaceuticals on genetics, and that there are only about 32,000 genes, one must wonder if there will be any "upstream territory" left in the public domain.[322]

Allowing DNA sequencing patents means research on genetic testing has been inhibited.[323] Almost half of the research laboratories in the United States surveyed have ceased to pursue some research because of existing patents.[324] The patenting of research tools has already occurred, and the result is that researchers now need to pay royalties on multiple distinct research tools in order to market a given product, thereby retarding the inventive process.[325]

The World Health Organization has begun to investigate how to deal with the blockage of information flow and data access, and it is evaluating whether an "open genomics" might be a viable option.[326] In 1997, 34% of the 2,167 life science (not just genetic) researchers surveyed by Dr. David Blumenthal, of Massachusetts General Hospital, reported they had been denied access to research results from other institutions.[327] More troubling, however, is that in 2002, a survey found that 47% of university geneticists were denied access to other scientists' research results.[328] Many geneticists have delayed release of their own research results by more than 6 months in the past 3 years giving as their main reason, "the need to wait for a patent application."[329] Contrast this with one biologist's comment, "At one time, if you found something exciting, you would run down the corridor

321. *Id.* Albright uses the term "life patents" which include patents on human genes, deadly diseases, whole animal species, plants, seed and foodstuffs (genetic makeup of rice and corn). Each of these companies' main products are based on gene patents. For more information, see Incyte Corporation Web Site, *at* http://www.incyte.com/ (last visited Mar. 30, 2005); Celera Genomics Web Site, *at* http://www.celera.com/celera/about (last visited Mar. 30, 2005); HGS Web Site, *at* http://www.hgsi.com/ (last visited Mar. 30, 2005). In January 2003, Hyseq, Inc. and Variagenics, Inc. (U.S.) merged, and changed their name to Nuvelo, Inc. (U. S.). Nuvelo Company Overview, *at* http://www.nuvelo.com/about/index.html (last visited Mar. 30, 2005); Millennium Pharmaceuticals Web Site, *at* http://www.mlnm.com/ (last visited Mar. 30, 2005).

322. *See supra* text accompanying note 321.

323. *See* NUFFIELD COUNCIL ON BIOETHICS, *supra* note 7, at 50.

324. *Id.*

325. JAFFE & LERNER, *supra* note 201, at 203.

326. World Health Organization, *Genomics and World Health: Navigating the Information Jungle — From DNA Sequence to Human Welfare* (powerpoint presentation), *at* http://www.who.int/ethics/topics/en/cook-deegan-Jul04.pdf (last visited Mar. 30, 2005).

327. ALBRIGHT, *supra* note 5, at 24-25.

328. *Id.* at 25.

329. *Id.*

to talk about it."[330] This is not so anymore, and geneticists are wondering if "the attitude of withholding data is eroding the scientific method in genetic research."[331]

Furthermore, there is the problem of the anticommons for biotechnology.[332] Renowned organizations, composed of leading scientists engaged in genome research, scientific advisors to biotechnology companies engaged in genome research, and representatives from government agencies involved in genome research, oppose the patenting of partial and uncharacterized DNA sequences for this reason.[333] Dr. Abdallah Daar, an ethicist at the University of Toronto who commented on Utah-based Myriad Genetics' threat to sue Canadian provinces if they used breast cancer genes (BRCA1 and BRCA2) to screen patients, said Myriad was like an inventor of a mousetrap that claims he owns any device that traps mice.[334] Daar says, "'Nobody can own our genes. They are property of us human beings.'"[335] Groups like the Canadian Cancer Society (CCS) fear that "as more genetic therapies come into use, gene-patent owners may stop others from making new, possibly better tests."[336] CCS president Julie White says gene-patenting "'really puts a chilling effect on research.'"[337] However, BioteCanada, claiming to represent 85% of all Canadian genetic researchers, defends gene patents, saying patents balance the risk and high costs of genetic research with the hope of financial returns.[338]

C. *The Granting of EST Patents Has Already Created Litigation Because of Upstream Clogging*

Though the motivating concern behind complaints is the anticommons problem, and its dampening effect on vital therapeutic or curative research, there is also the high cost of litigation. The early twentieth century gives a predictive example of patent infringement litigation over patented natural substances.

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330. *Id.* at 25-26 (citing Jennifer C. Christiansen, *The Price of Silence*, SCI. AM., Nov. 1996 (quoting biologist Derry Roopenian at Jackson Laboratory)).

331. *Id.* at 25.

332. *See* Heller & Eisenberg, *supra* note 265, at 698.

333. *See* HUGO Statement, *supra* note 83.

334. Ken Ernhofer, *Ownership of Genes at Stake in Potential Lawsuit*, CHRISTIAN SCI. MONITOR, Feb. 27, 2003.

335. *Id.* (quoting Dr. Abdallah Daar).

336. *Id.*

337. *Id.* (quoting Julie White).

338. *Id.*

In *Parke-Davis & Co. v. H.K. Mulford Co.*, a "purified" form of adrenaline was patented, and litigated by a subsequent inventor who found a different process for obtaining a less purified adrenaline.[339] Recognizing that one patent was a product patent for a composition of matter ("purified" adrenaline), and the other for a different process that produced less pure adrenaline, Judge Learned Hand concluded that, "considering the similarity of the processes, the use of each substance practically, and the approximation of result physiologically, the two are near enough to be an infringement one of the other."[340] It appears gene fragment patents will, likewise, have to "duke it out" in court.

A recent example involves what scientists have called "junk DNA,"[341] which is apparently not junk, and for use of which biotechnology companies are now being sued.[342] Since it was considered junk DNA, which had no function, it is really ironic that someone actually obtained a patent on it.[343] The happy owner of the "junk DNA" patents is Genetic Technologies Limited (GTL), and it claims to have a "strong intellectual property portfolio" that includes two key DNA-related patents: the first on "DNA analysis, covering non-coding regions of DNA from any species" (misleadingly known until recently as 'junk DNA') and the second on a method for gene mapping.[344] Because the "coding" regions of DNA take up only two percent of DNA,[345] it is reported that GTL owns 95% of the DNA in humans, plants, and animals, and that these patents were awarded before anyone had really found a specific function for the DNA.[346]

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339. *See* Parke-Davis & Co. v. H.K. Mulford & Co., 189 F. 95, 97-98 (S.D.N.Y 1911), *aff'd*, 196 F. 496 (2d Cir. 1912).

340. *Id.* at 99.

341. *E.g.*, GONICK & WHEELIS, *supra* note 6, at 147; *see also* Wong et al., *supra* note 36; ALBERTS ET AL., *supra* note 48, pt. IV, § 14; EUGENE V. KOONIN & MICHAEL Y. GALPERIN, SEQUENCE-EVOLUTION-FUNCTION: COMPUTATIONAL APPROACHES IN COMPARATIVE GENOMICS § 9.2 (2003).

342. *See* ALBRIGHT, *supra* note 5, at 27.

343. GeneType AG (CH) is the assignee of the "junk DNA" patents, but its parent company is an Australian company called Genetic Technologies Limited, which owns eleven companies located in Australia, Switzerland, Canada, and the USA. *See* Biotechnology Directory, Business and Research Organisation Contact and Links Directory [hereinafter Biotechnology Directory], *at* http://www.biotechnology.vic.gov.au/directory/search_results.asp?id=5261 (last visited Mar. 30, 2005). The local company is called GeneType Corp., and it owns U.S. Patent Nos. 5,612,179 ('179) (issued Mar. 18, 1997); 5,851,762 ('762) (issued Dec. 22, 1998); and 5,192,659 ('659). Patent '179 was a C-I-P of '659 (issued Mar. 9, 1993). *See* United States Patent and Trademark Office Web Site [hereinafter Patent Office Web Site], *at* http://www.uspto.gov (last visited Mar. 30, 2005).

344. Biotechnology directory, *supra* note 343.

345. *Genomics*, *supra* note 25.

346. ALBRIGHT, *supra* note 5, epilogue.

Nevertheless, GTL guards their patents zealously. In July 2003, Dr. Francis Collins, the director of the National Human Genome Research Institute (NHGRI) at the National Institutes of Health (NIH), interrupted his keynote speech at the International Congress of Genetics in Melbourne, Australia, in order to publicly rebuke GTL.[347] Dr. Collins charged the firm with hijacking drug research with "flimsy patents" covering huge strips of so-called junk DNA, which are "biological bits" once thought insignificant, but are now central to the work of disease hunters.[348]

But it gets worse, because now this "junk DNA" plays a crucial role in telling genes when to express, and when not to express.[349] Scientists are now shocked when they discover that an obscure company actually has a patent on the "junk."[350] Unfortunately, many are finding out upon receipt of cease and desist letters or lawsuits. Dr. Mervy Jacobson, GTL's chairman, has compiled a list of more than 1,800 companies whose work he thinks infringe GTL's patents, and he says "[t]he world has become our research lab."[351] In about 14 months, GTL, whose gross revenues were $3 million the year before, has taken in $7 million for licensing fees alone; if you do not pay, GTL will sue you.[352] In October 2003, three U.S. firms faced infringement suits for refusing to pay licensing fees.[353] One of the threatened companies, Applera, was using the non-coding DNA for cystic fibrosis diagnostic tests.[354] GTL is also demanding $1,000 for academic licenses, and $5.7 million in licensing fees from the New Zealand Department of Health.[355]

D. *The Granting of EST Patents Has Been Done When the EST's Use Was Unknown*

There is also the problem of "owning a gene you know nothing about."[356] "'It's like patenting an airplane that doesn't have a tail. They

347. Zina Moukheiber, *Junkyard Dogs*, FORBES.COM, Oct. 6, 2003, *at* http://www.forbes.com/global/2003/1006/022.html (last visited Mar. 30, 2005).

348. *Id.*

349. *See id.*

350. *Id.*

351. *Id.*

352. Moukheiber, *supra* note 347.

353. *Id.*

354. *Id.*

355. *Id.*

356. ALBRIGHT, *supra* note 5, at 26.

know it won't fly, but they'll stop everyone who has an airplane with a tail.'"[357]

Commenting on its patented CCR5 gene, which subsequent to patenting was discovered to have potentially lifesaving use for HIV/AIDS patients, the CEO of Human Genome Sciences (HGS), William Haseltine, told the *Los Angeles Times*: "'If someone uses [the CCR5] gene in a discovery program . . . and does it for commercial purposes, they have infringed the patent.' . . . 'We'd be entitled not just to damages, but to double and triple damages.'"[358] Within eight months of Mr. Haseltine's threat, HGS's stock rose 111%.[359] But the CCR5 gene was one of hundreds submitted to the PTO by HGS while it did mass-sequencing of the human genome, and when it applied for the patent, HGS had no clue that CCR5 had any connection to AIDS, or that it was possibly the first step toward developing a cellular "block" against AIDS.[360] In fact, the patent application for the CCR5 gene claimed its utility "could be a receptor for a virus (a claim that could be made for any cell surface molecule)."[361] Furthermore, soon after the PTO awarded the patent, serious mistakes were found in the original patent application, and it was also discovered that HGS incorrectly mapped the gene.[362] Yet now all research and possible new drugs that might be developed to block the HIV viruses' entry into a cell will be controlled by one corporation.[363] Unless challenged in court, HGS retains the patent.[364]

Furthermore, a review of patents issued on ESTs is disheartening. For example, U.S. Patent 5,817,479 ('479) was granted to Incyte in 1998 for human kinase homologues that were based on 12 EST sequences claimed to predict the function of the genes from which the ESTs were derived.[365] The '479 patent states that the nucleotide sequences may be used in molecular biology techniques that have not yet been developed, to

357. *Id.* (quoting John P. Moore, Aaron Diamond AIDS Research Center, commenting on the CCR5 patent by Human Genome Sciences).

358. *Id.* at 27 (quoting Paul Jacobs & Peter G. Gosslin, *Robber Barons of the Genetic Age: Experts Fret Over Effect of Gene Patents of Research*, L.A. TIMES, Feb. 28, 2000; BLOOMBERG.COM FINANCIAL MARKET COMMODITIES NEWS, retrieved from Company Graphs, Oct. 26, 2000).

359. *Id.* at 27.

360. *Id.*

361. ALBRIGHT, *supra* note 5, at 28 (quoting Letter from National Advisory Council for Human Genome Research, National Institutes of Health, to Commissioner of Patents and Trademarks, Mar. 21, 2000).

362. *Id.* at 28-29.

363. *Id.* at 27.

364. *Id.* at 29.

365. NUFFIELD COUNCIL ON BIOETHICS, *supra* note 7, at 33 n.27.

generate probes for mapping the native genomic sequence, to design oligonucleotide primers for the extension of the cDNAs to full length, and to produce a kinase kit for diagnosing disorders or diseases associated with altered kinase expression.[366] This seems to directly contravene even the CAFC's most liberal opinion. Something must be done.

X. PROPOSALS

Human genes are special. Genes are our common heritage.[367] Perhaps one extreme remedy would be to approach DNA fragment patents as Louis Pasteur approached his novel discoveries, obtaining patents on substances like yeast (which now would likely not be allowed).[368] He placed them in the public domain.[369] But because of the profit motive, this could never happen today.[370] However, the current state of affairs in genomic patenting must be fully elucidated and the consequences addressed. The recommendations proposed below are not final solutions. To find the appropriate solution would require cooperation between organizations on both sides of the fences (i.e., not-for-profit research versus for-profit research). However, the ideas proposed below contain elements that should provoke discussion and action by those who are in a position to reverse the inertia of doing nothing.

A. *Use Patents*

Because little, or nothing, of a chemical nature would be found lacking in utility,[371] not every use asserted can be sufficient to satisfy section 101 and 112 of title 35 of the U.S. Code. Indeed, since the outset, commentators have argued potential patentees should be forced to commit to uses for the ESTs, and EST-related products, in the specification and claims of patent applications.[372] If not, when other researchers discover other critical uses for the genes and their products, they will not be able to

366. *See* U.S. Patent No. 5,817,479 (issued Oct. 6, 1998).

367. *See* NUFFIELD COUNCIL ON BIOETHICS, *supra* note 7, at 21 ("It is argued that the human genome is unique and distinctive, so it should be treated differently from others such as the genomes of mice or maize, for example.").

368. MERGES & DUFFY, *supra* note 17, at 95.

369. *Id.*

370. *See generally* ALBRIGHT, *supra* note 5; SHREEVE, *supra* note 90.

371. *See* Brenner v. Manson, 383 U.S. 519, 530 (1966).

372. Joseph P. Pieroni, *The Patentability of Expressed Sequence Tags*, 9 FED. CIR. B.J. 401, 412 (2000).

patent those uses without conflict, as already seen with the HGS CCR5 gene and the GTL "junk DNA" patents.

The Nuffield Council on Bioethics identifies three different types of patents: (1) product patents; (2) process patents; and (3) use patents.[373] A "use" patent is a patent on the use of the patented invention for a specific purpose, and only the specified use is covered.[374] Because of the degeneracy of the genetic code, one way to avoid the negative effect of composition of matter patents on DNA sequence patents is to limit the patent rights granted on DNA sequence claims to only use patents, which do not assert rights over the DNA sequence itself or all unknown uses of it.[375]

Allowing only patents on use is historically valid. Since the early nineteenth century, the U.S. Supreme Court has reiterated the need for a use or utility before granting a patent. According to Judge Story, "the original elementary principles of motion, which philosophy and science have discovered" is not patentable; but "the modus operandi, the peculiar device or manner of producing any given effect" is patentable.[376] Historically, cases of patentability have turned less on the patentability of the metaphysical definitions and distinctions about principles and laws of nature, and more on the fit between the inventor's claims and his inventive contribution to the subject.[377] In the nineteenth century, the patentability of natural principles was mainly concerned with ensuring "(1) that the inventor specified a practical utility, and (2) that the patent bore some relation to the inventor's contribution to the useful arts."[378] "The mere discovery of a new element, or law, or principle of nature, without any valuable application of it to the arts, is not the subject of a patent."[379] The discoverer of a new rule or force of nature could not obtain a patent unless, and until, he also identified a useful end.[380] Though an appreciation of all uses is not necessarily implied or required under current law, it makes

373. NUFFIELD COUNCIL ON BIOETHICS, *supra* note 7, at 24. Using a pharmaceutical product as an example, a product patent would cover the active ingredient or a particular formulation; and process patents would cover the making of the active ingredient or particular formulation. *Id.*

374. *Id.*

375. *Id.* at 53, 66.

376. MERGES & DUFFY, *supra* note 17, at 96 (citing Whittemore v. Cutter, 29 F. Cas. 1123, 1124 (C.C.D. Mass. 1813) (Story, J.); Barrett v. Hall, 2 F. Cas. 914, 923 (C.C.D. Mass. 1818) (endorsing Story's view)).

377. *Id.*

378. *Id.*

379. O'Reilly v. Morse, 56 U.S. (15 How.) 62, 132 (1853) (Grier, J., dissenting in part).

380. MERGES & DUFFY, *supra* note 17, at 95 (citing 1 WILLIAM C. ROBINSON, THE LAW OF PATENTS § 136, 195-96 (1890); GEORGE TICKNOR CURTIS, A TREATISE ON THE LAW OF PATENTS § 136, 149 (4th ed. 1873)).

sense in the realm of ESTs, since the genetic code contains more value in it than any other "chemical composition" known to man, in terms of universal public health, and since so little is currently known about this supremely complex tool.

Pragmatic inquiries governed then, and they should govern now. Research will not come to a stand still. As the Supreme Court pointed out many years ago,

> [t]he grant or denial of patents on micro-organisms is not likely to put an end to genetic research or to its attendant risks. The large amount of research that has already occurred when no researcher had sure knowledge that patent protection would be available suggests that legislative or judicial fiat as to patentability will not deter the scientific mind from probing into the unknown any more than Canute could command the tides.[381]

Limiting the patent applicant's monopoly on the specifically identified use set out in the application would quickly solve any new patents that are issued. As set out above, DNA patents cannot be treated the same as chemical composition patents since chemical compositions that do not use genetic information are generally based on how the body reacts, whereas DNA patents are based on the code that dictates how the body will function.

B. *"Gene" Patents Issued Only When Utility Disclosed is in Currently Accessible and Deliverable Form*

Another option would be to modify the current definition of utility. In the new definition, the standard of credibility required for a claimed utility of a DNA sequence would need to be set higher than the mere theoretical possibility of this utility.[382] Some positive evidence showing the DNA sequence has the claimed utility should be required, and the utility should be more than just a biological function.[383] Biological functions are only a description of a fact of nature and are not a practical utility in the usual sense applied to invented products.[384]

Congress should define as useful an invention that has "'substantial and specific utility that is in currently deliverable form.'"[385] This would, in

381. Diamond v. Chakrabarty, 447 U.S. 303, 317 (1980).

382. NUFFIELD COUNCIL ON BIOETHICS, *supra* note 7, at 70.

383. *Id.*

384. *Id.*

385. Daniel L. McKay, Comment, *Patent Law and Human Genome Research at the Crossroads: The Need for Congressional Action*, 10 SANTA CLARA COMPUTER & HIGH TECH. L.J.

essence, be a codification of the *Brenner* standard, and would solve the problem of companies obtaining patents on gene fragments for which they know no function or utility.[386] Researchers have been apprehensive because the breadth of claims granted on mere fragments of a gene would prevent them from gaining protection for the entire gene when the complete structure was discovered.[387] In addition, a very broad claim might cover the actual protein coded for by that gene, again based on very little of the gene itself.[388] This would prevent patent owners from later claiming uses not currently available or deliverable, and it would leave open to others the option of obtaining a patent on a later discovered use.

Of course, some system would need to be put in place on the matter of whether a subsequent researcher or inventor would be required to pay licensing fees on the same EST before she discovers the new use. As a result, the best combination would be to make the definition of utility more strict, then combine this with a use patent limiting the patent owner's rights, and right to demand payment, to only uses of the EST that are the same or sufficiently similar, under the doctrine of equivalents.

C. *"Gene" Patents Issued Only When Beneficial Utility or Use Requirement Met*

Because the most critical problem with EST patents is their prohibitive effect on research that is in the best interests of public health, the concept of beneficial utility may be perfectly suited to limiting the scope of patents granted for ESTs. In addition, the story of filing the chimera (sometimes called the huMouse) patent application must be told, since this horror story succinctly describes the slippery slope that can result from granting any type of gene patents.

Dr. Stuart Newman and Jeremy Rifkin jointly filed an application for animal-human hybrids named "chimeras,"[389] and for the process of making these creatures.[390] The patent application disclosed creatures that melded human and animal embryos such as "the huMouse, a mixture of man and mouse; the humanzee, a cross between a human and chimpanzee; and blends of human with pig and human with baboon."[391] Disclosed uses were

465, 495 (1994) (quoting Thomas Kiley, *Patents on Random Complementary DNA Fragments?*, 257 SCIENCE 915, 920 (1992)).

386. *See id.*

387. Pieroni, *supra* note 372, at 411.

388. *Id.*

389. The name "chimeras" is from the mythical Greek monster with a goat's body, a lion's head, and a serpent's tail. Slater, *supra* note 123.

390. MERGES & DUFFY, *supra* note 17, at 225.

391. Slater, *supra* note 123.

to study embryonic development, raise organs for transplants, or test new drugs.[392] This patent application clearly identified the problems associated with the fact that under the laws currently in place, and the PTO's policy that it does not engage in ethical or moral evaluations of patent applications, this application could have been granted. In indirectly addressing this application, the Commissioner of the PTO made the following statement:

> No patent is granted for an invention that does not meet the strict patentability requirements set forth in patent laws contained in title 35 of the United States Code. These include requirements that the invention have utility, be novel and non-obvious, and be adequately described and disclosed so as to enable the making and using of the invention. The PTO will not, therefore, issue a patent for an invention of incredible or specious utility or for inventions whose utilization is not adequately disclosed in the application. Additionally, the courts have interpreted the utility requirement to exclude inventions deemed to be "injurious to the well being, good policy, or good morals of society."[393]

In directly addressing the chimera patent application, the PTO Commissioner stated, "[T]here will be no patent on monsters, at least not while I'm commissioner."[394] What is most frightening about the Commissioner's statement is that he could not cite to any portion of the patent statute as grounds for rejecting the patent application. The Commissioner had to cite to a case from 1817 that had been quoted by a case in 1991. Furthermore, the PTO never raised the utility requirement, since it merely rejected the application on grounds that human hybrid creatures were not patentable subject matter, without further comment.[395]

It must be noted, too, that Newman's and Rifkin's purpose for filing the chimera patent application was to prevent anyone else from filing such an application.[396] Indeed, Newman is both a developmental biologist and a founding member of the Council for Responsible Genetics, a

392. *Id.*

393. Media Advisory, U.S. Patent and Trademark Office, Apr. 1, 1998 (quoting Lowell v. Lewis, 15 F. Cas. 1018, 1019 (C.C.D. Mass. 1817) (No. 8,568)), *available at* http://www.uspto.gov/web/offices/com/speeches/98-06.htm (last visited Mar. 30, 2005).

394. MERGES & DUFFY, *supra* note 17, at 225 (citing *"Morality" Aspect of Utility Requirement Can Bar Patent for Part-Human Inventions*, 55 PAT. TRADEMARK & COPYRIGHT J. (BNA) 555 (1998)).

395. *Id.*

396. *See* Slater, *supra* note 123.

biotechnology watchdog group.[397] Both applicants reasoned that, if they obtained the patent they could "lock up" any subsequent attempts to patent chimeras, but if the patent was rejected the PTO could use the rejection to block other similar applications.[398]

If modified to require beneficial utility, the patent applications on genetic information could be tested in a way that would protect public health and, incidentally, also fall in line with articles 8 and 27 of TRIPs. Then-Judge Story interpreted the word "useful" to mean, generally, beneficial to the public, in the sense that it would not, *inter alia*, injure the "well-being, good policy or sound morals of society."[399] He also explained that an invention that would poison people would not be useful; but in his interpretation, anything not hurtful would likely be patentable even if not "extensively useful," since the market could deal with this lack of utility.[400] Interestingly, as applied to inventions in the early nineteenth century, Story's view of utility was quite liberal. However, as applied to DNA sequence fragments, it is strict. If a patent application on an EST could cause blockages or unreasonable increases in the cost of lifesaving therapies to a price out-of-reach of the average human, the application would be injurious to the well-being, good policy and sound morals of society. As a result, the application should be rejected or tailored to prevent a violation of beneficial utility. Requiring a beneficial utility would greatly minimize the danger of any patents like Newman's from issuing. It would also deal with the issuance of patents that would cause public health, anticommons, and undeserved monopoly problems.

D. *Compulsory Licensing of EST Patents*

Though it may seem silly at first glance, perhaps EST patents should be treated like computer code, and placed in a single searchable database, like music. The genetic code, after all, is referred to and identified by letter and three-letter codons. In addition, according to Venter, who sequenced the human genome by using ESTs and automated computers, his company

397. The story begins with a phone call, over ten years ago, from Jeremy Rifkin, who asked Dr. Stuart Newman if he could design a genetically engineered invention that was technically feasible, scientifically useful, and yet "so disturbing that it would draw the public's attention to the possibilities of genetically engineering humans." Slater, *supra* note 123. After several years of work, in December 1997, Newman and Rifkin jointly submitted their application to the patent office. *Id.*

398. *See id.*

399. Lowell v. Lewis, 15 F. Cas. 1018, 1019 (C.C.D. Mass. 1817) (No. 8,568).

400. *See id.*

was "not a biotech,"[401] but in fact, something closer to an information technology company. In August of 1998, Venter said,

> [Celera is] an information company, like LexisNexis. If you had the time, you could find the same information they have on your own. So why do they have two million subscribers? Because they've already done the legwork for you, so you can find what you want in seconds rather than hours. We're going to do the same for genomic information, on a global scale.[402]

At that same time, Venter also maintained "'I am not the Bill Gates of the genome.' . . . 'At least not yet.'"[403] Though a little boastful, Venter's statements reveal the nature of the genetic code, as at its core, being pure information. It is information used by the bodies of humans, animals, and plants to live.

The problem with allowing patents on this information, as opposed to copyrights, is that the code can be used for so many different things. In other words, the uses for each EST can be myriad. As a result, infringements occur, research is stopped and lawsuits get filed. A system modeled on the compulsory licensing provision of the Copyright Act[404] may provide a way for tracking who owns a particular EST, and allowing a for-profit or not-for-profit researcher to pay a fee for use of the EST.

Like the compulsory licensing statute of the Copyright Act, an EST compulsory licensing system could define the rights held by the owner of the EST and the limited rights to which the EST licensee would be entitled. A notice provision to the owner could be included, with penalties provided for the failure to notify. A royalty provision could contain initial royalties for nonprofit research uses, and a subsequent, more remunerative royalty for any composition or process that generates income from the use of the patented EST. The non-profit research royalty could be designated by length of time used, and could be nominal. The subsequent royalty for compositions or processes that generate income could be based on a percentage of the profit made from composition or process. The compulsory licensing scheme of the Copyright Act could be the starting point for a method of dealing with the difficulty of finding out if a particular patent has issued on an EST, who to contact to get permission to use the EST, and how to fairly license the EST.

401. SHREEVE, *supra* note 90, at 120.
402. *Id.*
403. *Id.*
404. *See* 17 U.S.C. § 115.

XI. CONCLUSION

Patents have issued on ESTs. Problems are surfacing because of the EST patents. The Courts have taken a liberal view, and the PTO has been overwhelmed. In addition, because of the nature of the patent system, the complete consequences of granting patents on ESTs will take time to fully develop. However, as described in this Article, examples of those repercussions are beginning to surface; EST patents are having a detrimental effect on public health and are creating litigation for the Courts. The question, then, is whether EST applications are still pending at the PTO for which some remedy could be created by Congress. Because of the difficulty and complexity, described above, of searching issued patents, and the inability of third parties to review pending patent applications. a congressional inquiry is needed to determine if there are any remaining applications on which changes in the law might have an impact. If there are pending applications, then Congress should consider changing the definition of utility to include a requirement that either the invention or discovery and its use be beneficial. Alternatively, Congress should limit patents on those ESTs to only the uses identified by the applicant and uses in currently deliverable form at the time the application is filed. If all applications on ESTs are out of the reach of Congress, then a compulsory licensing scheme could minimize the problems these patents have created in limiting research and increasing litigation by fairly licensing them to those who want to provide beneficial inventions to the public.