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INTERNATIONAL CONFLICTS OVER PATENTING HUMAN DNA SEQUENCES IN THE UNITED STATES AND THE EUROPEAN UNION: AN ARGUMENT FOR COMPULSORY LICENSING AND A FAIR-USE EXEMPTION

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The thought of a large biotech company holding an exclusive right to research and manipulate human genetic material provokes many reactions—from moral revulsion to enthusiasm about the possibilities for therapeutic advancement. While most agree that such a right must exist, debate continues over the appropriate extent of its entitlements and preclusive effects. In this Article, Professor Donna Gitter addresses this multidimensional problem of patents on human deoxyribonucleic acid (DNA) sequences in the United States and the European Union. Professor Gitter chronicles not only the development of the law in this area, but also the array of policy and moral arguments that proponents and detractors of such patents raise. She emphasizes the specific issue of patents on DNA sequences whose function has not fully been identified, and the chilling effect these patents may have on beneficial research. From this discussion emerges a troubling realization: While the legal framework governing "life patents" may be similar in the United States and the European Union, the public perceptions and attitudes toward them are not. Professor Gitter thus proposes a dual reform: a compulsory licensing regime requiring holders of DNA sequence patents to license them to commercial researchers, in return for a royalty keyed to the financial success of the product that the licensee develops; and an experimental-use exemption from this regime for government and nonprofit researchers.

INTRODUCTION

In February 2000, the United States Patent and Trademark Office (PTO)[1] granted to Human Genome Sciences Incorporated (HGS), a publicly traded biotechnology company based in Rockville, Mary-

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[1] The PTO is the federal administrative agency charged with the review and grant of patents. 35 U.S.C. § 1 (Supp. V 2000). PTO patent examiners review patent applications

land,[2] a patent for the CCR5 receptor gene,[3] described in an HGS press release as one "that produces what is believed to be the critical entry point [into cells] for the AIDS virus."[4] While patenting the CCR5 receptor gene may represent an important technological achievement, the patenting of human deoxyribonucleic acid (DNA) sequences in general is quite common under current biotechnology patent law. Since the 1980s, thousands of human DNA sequences have been patented worldwide.[5] As of September 1, 2001, HGS alone held 180 patents on human gene-based inventions and had filed applications for many more, both in the United States and abroad.[6] Given the extent of such patenting activity, it is no surprise that biotechnology patent law and policy provoke such controversy. Indeed, the patenting of human DNA sequences generates intense international debate, particularly in the technologically advanced United States and European Union (E.U.).[7] The HGS patent on the CCR5 receptor gene serves as a quintessential example of how complex the legal issues surrounding patents on human DNA sequences have become.

Debate has centered on several key issues. First, there is sharp international disagreement as to whether the genetic code that defines human life satisfies the threshold criteria of patentability—that an in-

in order to determine whether the claimed inventions satisfy the legal requirements of patentability. 1 Donald S. Chisum, Chisum on Patents, at OV-1 (2000 & Supp.).

[2] Human Genome Sciences, Inc., LEXIS, News Library, Hoover's Company Profile Database File. HGS was founded in 1992. Id.

[3] See infra Part I.C for a general discussion of the composition and function of genes, the methods geneticists employ to identify them, and what geneticists hope to accomplish by understanding their role.

[4] Nell Boyce & Andy Coghlan, Your Genes in Their Hands, New Scientist, May 20, 2000, at 15; see also Sabra Chartrand, A Human Gene is Patented as a Potential Tool Against AIDS, But Ethical Questions Remain, N.Y. Times, Mar. 6, 2000, at C9; Eliot Marshall, Patent on HIV Receptor Provokes an Outcry, Sci. Now, Feb. 23, 2000, at http://sciencenow.sciencemag.org/cgi/content/full/2000/223/1; Paul Smaglik, Could AIDS Treatments Slip Through Patents Loophole?, 404 Nature 322, 322 (2000); Michael Waldholz, Rights to Life: Genes Are Patentable; Less Clear Is If Finder Must Know Their Role, Wall St. J., Mar. 16, 2000, at A1.

[5] Molly A. Holman & Stephen R. Munzer, International Property Rights in Genes and Gene Fragments: A Registration Solution for Expressed Sequence Tags, 85 Iowa L. Rev. 735, 750 (2000); Telephone Interview with Brigid Quinn, Deputy Director of the Office of Public Affairs, United States Patent and Trademark Office (July 11, 2001) (stating that PTO has granted approximately 1200 patents for full-length genes).

[6] Human Genome Sciences-Patents, at http://www.hgsi.com/patents/index.html (last modified Sept. 10, 2001). As of November 2000, HGS had more than 7500 patents pending for human genes. Tim Radford, Human Genetic Patenting: Microbes Make Millions in a New Klondyke of Microfactories, Guardian (U.K.), Nov. 15, 2000, at 4.

[7] The fifteen member states of the E.U. are Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, the Netherlands, Portugal, Spain, Sweden, and the United Kingdom. See Richard Schaffer et al., International Business Law and Its Environment 88 (4th ed. 1999).

vention constitute patentable subject matter and be novel.[8] In the United States, judicial law and administrative law have affirmed the patentability of human DNA sequences in general. Certain E.U. member states, however, continue to harbor moral and ethical objections to such patents, despite a recent E.U. legislative enactment that provides that human DNA sequences are indeed patentable. The difference in perspective between the United States and the E.U. with respect to patents on human DNA sequences threatens international scientific collaboration, and, consequently, harmonious international relations. This tension is heightened as U.S. biotech companies increasingly seek patent protection in Europe in order to recoup their considerable costs of research and development.

Second, even assuming arguendo that human DNA sequences are patentable, U.S. and E.U. institutions continue to grapple with how liberally to interpret the second patent law criterion, "utility," which requires a patent applicant to articulate the function of the claimed invention.[9] Many patent applications are for DNA sequences of unknown function. For example, HGS was unaware of the CCR5 gene's role in the HIV virus at the time the company applied for its patent.[10] HGS knew only of CCR5's general role as a receptor, or entry point into the cells, and "was expecting instead to exploit the patent primarily in the development of anti-inflammatory therapy."[11] Not until about a year after HGS filed its patent application did several independent research teams, working without help from HGS, publish

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[8] See infra Part II for a description of this threshold criteria.

[9] See infra Part III.B for a discussion of the utility criterion of patentability, termed "industrial applicability" in the E.U.; see also infra note 146.

[10] Quirin Schiermeier, German Agencies Sound Alarm on Risks of Broad Gene Patents . . . , 406 Nature 111, 111 (2000). One writer has explained the functioning of the CCR5 receptor as follows:

> Receptors are found on the surface of cells, much like pins sticking out of a pin cushion, and act as a sort of docking port, sometimes for lethal viruses. But the receptor and the virus have to match, like a key and a lock. CCR5 is known to fit the AIDS virus. The virus binds to the receptor, then fuses to the cell, and fusion allows HIV to work its way inside.

Chartrand, supra note 4.

[11] Smaglik, supra note 4, at 322. HGS filed its patent application for the CCR5 gene as a so-called "homologous sequence," i.e., a gene sequence of unknown utility whose biological function can be predicted because it is similar to a separate sequence whose function is already understood. See David Dickson, NIH Opposes Plans for Patenting 'Similar' Gene Sequences, 405 Nature 3, 3 (2000). Scientists locate such sequences by using computers to hypothesize "the identity and function of a protein encoded by a gene based on the similarity of a [gene] fragment to other known genes." Id.; see also Martin Enserink, Patent Office May Raise the Bar on Gene Claims, 287 Science 1196, 1197 (2000). HGS had deduced the CCR5 gene's general role as a receptor by performing computer analysis of sequence information made public by the Human Genome Project. See Boyce & Coghlan, supra note 4, at 15. For a description of the Human Genome Project, see infra note 16.

pivotal experiments demonstrating that CCR5 is required for efficient replication of the HIV virus.[12]

Some scholars and researchers contest, on the grounds of utility, HGS's right to a patent for the CCR5 receptor gene, given that HGS was unaware of the gene's role in the HIV virus at the time the company obtained its patent.[13] This dispute over how to interpret the utility criterion transcends national borders and pits U.S. and E.U. scholars and researchers from the public and nonprofit sectors,[14] on one hand, against private biotech companies on the other. The former contend that excessively lenient application of the utility criterion with respect to human DNA sequences ultimately will hinder research, because the need to pay licensing fees to the patentee will dissuade scientists from conducting further experimentation relating to patented genes. For example, a University of Pennsylvania bioethicist has warned that HGS's patent on the CCR5 receptor gene, and the company's attendant right to collect royalties from subsequent researchers working on the gene, will impede others from developing therapeutics based on the gene.[15] The biotech industry counters that, absent the limited monopoly furnished to inventors through the extant patent system, firms will not invest in the costly research and development that is so vital to the creation of new pharmaceutical products. This tension between the for-profit and nonprofit communities replicates itself on a meta-international scale, pitting international bodies such as the Human Genome Project (HGP)[16] against multinational biotech companies.

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12 Boyce & Coghlan, supra note 4, at 15; Smaglik, supra note 4, at 322; Waldholz, supra note 4. HGS, in contrast, did not disclose its work publicly because it had contracted to provide its gene database exclusively to SmithKline Beecham PLC in return for a payment of $135 million. Id.

13 Waldholz, supra note 4.

14 This group sometimes includes academic researchers, although academic research has become increasingly commercialized since the mid-1980s. See Arti Kaur Rai, Regulating Scientific Research: Intellectual Property Rights and the Norms of Science, 94 Nw. U. L. Rev. 77, 110 & n.186 (1999) (noting increase in academic-industrial biotech partnerships since 1980s and citing examples); see also Sheldon Krimsky, The Profit of Scientific Discovery and Its Normative Implications, 75 Chi.-Kent L. Rev. 15, 15-22 (1999) (describing trend toward alliances among for-profit and academic researchers).

15 Boyce & Coghlan, supra note 4, at 15.

16 The HGP, also called the "public project," is an international, publicly financed consortium of academic centers that are sequencing and studying the human genome. Alex Berenson & Nicholas Wade, A Call for Sharing of Research Causes Gene Stocks to Plunge, N.Y. Times, Mar. 15, 2000, at A1; Richard Preston, The Genome Warrior, New Yorker, June 12, 2000, at 66, 66. The HGP began in 1990, funded with public money allocated by Congress and coordinated by the National Institutes of Health (NIH), a governmental biomedical research institute, and the U.S. Department of Energy. See Leslie Roberts, DOE's Genome Project Comes of Age, 252 Science 498, 498 (1991); J. Craig Venter et al., The Sequence of the Human Genome, 291 Science 1304, 1305 (2001). Now

Finally, U.S. and E.U. scholars and scientists from the public and nonprofit sectors assert that a patent such as the one held by HGS on the CCR5 receptor gene fails to satisfy the third major patent criterion: "nonobviousness."[17] They contend that the methods employed by biotech companies to isolate the genes that these companies then seek to patent are obvious in light of the "prior art."[18] Specifically, HGS employed computerized homologous sequencing techniques to identify the CCR5 receptor gene by comparing the gene to other similar, or homologous, genes.[19] Many researchers who perform genetic analysis through experimental, rather than computational, work reject these computerized research methods that do not involve "'getting your pipette wet,'"[20] contending that they "'require little scientific insight or creativity.'"[21] Dr. William Haseltine, HGS's chief executive officer, has responded by arguing that computational gene searches require much effort.[22]

This Article will explore the aforementioned legal and public policy issues raised by patents on human DNA sequences. Part I is a basic primer on the science of human DNA sequencing and the uses to which it is applied. Part II examines the law and policy relating to the patentability of life forms in general, and human DNA sequences in particular, under U.S. and E.U. law. This Part concludes that while the United States and the E.U. both have responded to the competitive pressure to increase patent protection for human DNA sequences, an abiding E.U. suspicion of such patents lingers. The fundamental differences between the U.S. and E.U. positions on the propriety of patenting human DNA create significant international

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the HGP is largely financed by the NIH and the Wellcome Trust of London, the largest nonprofit medical research foundation in the world. Berenson & Wade, supra; Preston, supra, at 71. Richard Preston points out that "[o]ne of the founding principles of the Human Genome Project was the immediate release of all the human genetic code that was found, making it available free of charge and without any restrictions on who could use it...." Id. The HGP posts its findings daily on GenBank, a World Wide Web site available to the public. GenBank Overview, at http://www.ncbi.nlm.nih.gov/Genbank/GenbankOverview.html (last visited July 5, 2001).

17 See infra Part IV. In the E.U., nonobviousness is termed "inventive step." See infra note 146.

18 Prior art "includes any relevant knowledge, acts, descriptions and patents which pertain to, but predate, [the] invention in question." Black's Law Dictionary 1193 (6th ed. 1990).

19 See supra note 11.

20 Enserink, supra note 11, at 1197 (quoting critic of computerized process).

21 Dickson, supra note 11, at 3 (quoting Jordan J. Cohen, president of Association of American Medical Colleges).

22 See Smaglik, supra note 4, at 322.

tension,[23] and limit the potential for effective U.S.-E.U. harmonization of biotech patent protection. Part III examines the utility criterion and the international conflict that arises as a result of opposition by members of the public sector and nonprofit research communities in the United States and Europe to the patenting of human DNA sequences of unknown utility. The implementation of a solution acceptable in both the United States and Europe is necessary to foster international scientific collaboration. Part IV discusses the criterion of nonobviousness. As with utility, this criterion has provoked a pitched debate among the public sector and nonprofit research communities in the United States and the E.U. This debate must be resolved in order to facilitate the sharing of cross-border research data. Finally, Part V proposes a means of addressing the conflicts engendered by patents on human DNA sequences: Congressional enactment of compulsory-licensing legislation, coupled with codification of an experimental-use exemption. A compulsory-licensing scheme, with fees set on a sliding scale depending upon the commercial value of the invention, would ensure royalties for inventors while permitting further use of their research. An experimental-use exemption would guarantee public sector and nonprofit scientists the opportunity to engage in research for noncommercial purposes. The combination of these remedies effectively would protect intellectual property rights while simultaneously fostering international scientific cooperation.

I
THE SCIENCE OF HUMAN DNA SEQUENCING

A. The Distinction Between Genome Patenting and Gene Patenting

To understand the controversy in the United States and the E.U. surrounding the patenting of human DNA sequences, it is essential to distinguish between the human genome—the total human complement of DNA present in each of our cells[24]—which cannot be pat-

[23] Much of the pressure to liberalize European gene patenting law comes from the United States. The chairman of the U.S. pharmaceutical firm Pfizer has criticized Europe's reluctance to do so, stating: "Europe seems to be entering a period of the dark ages, where witchcraft and sorcery are prevailing." James Meek, The Race to Buy Life: Carve Up of the Human Heart: Universities and Charities Are Rushing to Isolate and Patent Human Genes Before It Is Even Understood What They Do, Guardian (London), Nov. 15, 2000 (internal quotation marks omitted), available at LEXIS, Nexis Library, The Guardian File; see also infra notes 194-212 and accompanying text (describing conflicts between United States and various E.U. member states over patents on human DNA sequences).

[24] R. Scott Hawley & Catherine A. Mori, The Human Genome: A User's Guide 8 (1999). The genome consists of forty-six deoxyribonucleic acid (DNA) molecules, which contain the chemical units that determine an individual's hereditary characteristics. Id. at

ented,[25] and particular sections of DNA, called genes,[26] which can be patented.[27] Many people in the United States and the E.U. erroneously conflate the terms "genome" and "gene."[28] For example, on March 14, 2000, former U.S. President Bill Clinton and British Prime Minister Tony Blair issued a joint statement addressing patent policy with respect to sequencing the human genome.[29] Clinton and Blair declared that "raw fundamental data on the human genome, including the human DNA sequence and its variations, should be made freely available to scientists everywhere."[30] Interpreting the statement as a policy shift toward greater restrictions on the patentability of human DNA sequences, investors dumped the stocks of biotechnology companies around the world, eliminating tens of billions of dollars in market value.[31] In fact, Clinton and Blair merely had intended to clarify the existing patent regimes in their respective nations at a point in time when scientists were drawing close to completing a working draft of the genome's entire sequence.[32] In short, in both the United States and the E.U., patents can be granted based upon particular human

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17-19; see also Nicholas Wade, Genetic Code of Human Life Is Cracked by Scientists: A Shared Success, N.Y. Times, June 27, 2000, at A1.

25 Robert Langreth, Decoding the Patent Battle, Wall St. J., Mar. 16, 2000, at A18.

26 Hawley & Mori, supra note 24, at 3, 17-19. Genes instruct the cell to make proteins, which perform all the body's essential tasks, such as digestion, and determine physical features, such as eye color. Id. at 3-5.

27 Langreth, supra note 25.

28 See infra Parts I.B and I.C for an explanation of these terms and the science of human DNA sequencing.

29 To sequence the human genome means to determine the order of the entire genetic code, and particularly the location of genes, so as to elucidate their function. See generally Hawley & Mori, supra note 24, at 21-27; Wade, supra note 24; see also infra note 49 and accompanying text.

30 Charles Arthur, Celera Leads Way in High Stakes Chase to Patent Our Genes, Independent (London), Mar. 16, 2000, at 21 (internal quotation marks omitted); see also Berenson & Wade, supra note 16.

31 Berenson & Wade, supra note 16. Indeed, this statement elicited the second-largest point loss in the history of the Nasdaq composite index. Id.

32 See id. Indeed, the Clinton-Blair statement also provided that "[i]ntellectual property protection for gene-based inventions will play an important role in stimulating the development of important health care projects." Arthur, supra note 30 (internal quotation marks omitted). Moreover, the White House insisted immediately afterward that the intention of the statement was to "make raw data available so private companies can innovate, create new medicine and treatment and make a profit" and to "foster competition." Id. (internal quotation marks omitted) see also Robert Langreth & Bob Davis, Plunge in Biotech Stocks Linked to Press Briefing, Wall St. J., Mar. 16, 2000, at A19 (stating that Clinton-Blair joint announcement was "intended to confirm a longstanding policy that federally funded researchers must release gene sequence data to the public as soon as they find it," not to signal any restriction in patents on individual genes).

DNA sequences[33] but not upon the sequence of the entire human genome.[34]

Part of the reason for investors' confused reaction to the Clinton-Blair statement was the contemporaneous public attention to the celebrated race to decode the human genome. Just over three months after the Clinton-Blair statement, on June 26, 2000, two independent teams of scientists, one from the HGP and the other from Celera Genomics Group (Celera),[35] jointly announced that, working separately, each had completed a working draft of the genome's entire sequence.[36] Although the joint announcement indicated a spirit of cooperation between the two groups, which have had an antagonistic rivalry,[37] they nonetheless will continue to pursue their independent

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33 See supra note 5 and accompanying text.

34 See Commission of the European Communities, RAPID, Legal Protection of Biotechnological Inventions: Frequently Asked Questions on Scope and Objectives of the EU Directive (98/44) (July 3, 2000), available at LEXIS, World News Library, European News Sources File [hereinafter Frequently Asked Questions] (noting that human genome cannot be patented because it is discovery, not invention, and thus not product of human innovation); see also Arthur, supra note 30; Langreth, supra note 25.

35 Celera Genomics Group (Celera) is a publicly traded company based in Rockville, Maryland. Celera Genomics Group, LEXIS, News Library, Hoover's Company Profile Database File.

36 Wade, supra note 24.

37 A primary source of tension between Celera and the HGP is the circumstances surrounding the departure of Dr. Craig Venter from his former employment at the NIH, one of the principal sources of HGP funding. See supra note 16. Venter's departure from the NIH was due in large part to the NIH's rejection of Venter's grant proposal for funds to pioneer a controversial, speedy method of gene sequencing, known as whole-genome shotgun sequencing, which would later bring Venter much success at Celera. Preston, supra note 16, at 72. In shotgun sequencing, "the genome is broken into small, random, overlapping pieces, and each piece is sequenced .... Then the jumble of pieces is reassembled in a computer that compares each piece to every other piece and matches the overlaps, thus assembling the whole genome." Id. This process is entirely automated, so the sequencing can run continuously. Rai, supra note 14, at 114 n.206 (citations omitted). A second source of tension is that, in completing its own genome sequence, Celera used HGP's raw sequence data, which was posted each day on HGP's GenBank Web site, see supra note 16, and thus in the public domain. See Declan Butler, US/UK Statement on Genome Data Prompts Debate on 'Free Access,' 404 Nature 324, 324-25 (2000). For its part, Celera published its research on the human genome sequence in the February 16, 2001 issue of *Science* and made the data available free of charge, but with some restrictions on its use. See Celera and *Science* Spell Out Data Access Provisions, 291 Science 1191, 1191 (2001). According to a statement released by *Science*,

> [A]cademic users may access it, do searches, download segments up to one megabase, publish their results, and seek intellectual property protection. ... Commercial users may access data freely upon executing a Material Transfer Agreement stating that they will not commercialize their results or redistribute the sequence.

Human Genome Row Draws in Journals, 357 Lancet 81, 81 (2001). In addition, while Celera's business plan is to offer subscriptions to its full collection of genomic data, software tools, annotation and supercomputing power, see infra notes 58-60 and accompanying text, Celera promised to set annual subscription fees for academic institutions very

approaches to studying the human genome.[38]

Despite their disagreements on many issues, the leaders of the HGP and Celera are united in their view that a human DNA sequence should be patentable not on the basis of its sequence alone, but only after researchers clearly can describe its role and utility.[39] This shared view makes uncomfortable allies of the HGP and Celera, pitting them against Celera's two chief rivals, HGS and Incyte Genomics, Incorporated (Incyte).[40] In contrast to the HGP and Celera, which have been focusing on sequencing the human genome, Incyte and HGS have been seeking to patent as many genes as possible.[41] At an April 7, 2000 hearing before a congressional subcommittee, both Celera and the HGP criticized Incyte and HGS for simply "downloading the public consortium's genome data every night and filing patent applications for any genes they found."[42]

Thus, the race to decode the human genome inevitably raises the issue of patents on human DNA sequences. The following scientific discussion summarizes the differences between the human genome and human genes.

B. A Scientific Primer on the Genome

The term "human genome," which refers to all the hereditary material contained in each cell of the human body,[43] is unique for each individual, except in the case of identical twins. The human body consists of trillions of cells: inside each cell is a nucleus, which contains twenty-three pairs of chromosomes.[44] Each chromosome is a mole-

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low, at about $5000 to $15,000. Butler, supra, at 324; Nicholas Wade, Assembling of the Genome Is at Hand, N.Y. Times, Apr. 7, 2000, at A20. For a history of the HGP, Celera, and their rivalry, see generally Kevin Davies, Cracking the Genome (2001); Preston, supra note 16.

[38] See Wade, supra note 24.

[39] See Wade, supra note 37. Although Celera does patent some genes, its principal business plan is to offer subscriptions to genomic data, software tools, annotation, and supercomputing power. See supra note 37.

[40] Incyte, founded in 1991, is a publicly traded company based in Palo Alto, California. Incyte Genomics, Inc., LEXIS, News Library, Hoover's Company Profile Database File.

[41] See Antonio Regalado, The Great Gene Grab, Tech. Rev., Sept.-Oct. 2000, at 50, 50. As of Summer 2000, Incyte led in the human gene patent race with 397 U.S. patents issued, followed by the University of California (253); Glaxo SmithKline (248); the U.S. government (205); and Novo Nordisk (196). Id. at 55.

[42] Wade, supra note 37.

[43] See supra note 24 and accompanying text.

[44] Matt Ridley, Genome 6 (1999). Each cell, no matter where it is located in the human body, contains the same genetic information. The mechanism which makes some cells behave differently from others is that "[s]pecific genes are flipped on at different times in different tissues." Ellen Licking, The Genome Explained, Bus. Wk., June 12, 2000, at 152, 152; see also Hawley & Mori, supra note 24, at 3 ("[T]he development of a human being

cule of DNA shaped like a double helix.[45] The sides of the ladder are made up of long chains of sugar and phosphate, while the rungs are made up of the chemical compounds (known as bases) adenine, thymine, guanine, and cytosine.[46] There are estimated to be over three billion base pairs[47] in the human genome.[48] Sequencing, or decoding, the genome means putting the base pairs in order.[49]

The genome has been called the "Book of Life,"[50] and one commentator, developing this literary analogy further, explains that, if we imagine the genome is a book, "[t]here are twenty-three chapters, called chromosomes. Each chapter contains several thousand stories, called genes.[51] Each story is made up of paragraphs, called exons,[52] which are interrupted by advertisements called introns.[53] Each paragraph is made up of words, called codons.[54] Each word is written in letters called bases."[55] There are one billion words in this book, making it about as long as two hundred telephone books of one thousand pages each.[56] Of course, while English books are written in words of variable length using twenty-six letters, genomes are written entirely in three-letter words, called codons, made up of the letters A, C, G, and T.[57]

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from conception to death is the result of a complex program of expressing genes in some cell types and not in others at specific times . . . .").

45 Ridley, supra note 44, at 7. In 1953, James Watson and Francis Crick discovered the double helical structure of human DNA, for which they won a Nobel Prize. Hawley & Mori, supra note 24, at 24.

46 Ridley, supra note 44, at 6. For a helpful graphic illustrating the structure of human DNA, see Wade, supra note 24. A subunit of this DNA chain consisting of a single base linked to a sugar is called a nucleotide. The polarity of the nucleotides causes them to attach to each other, creating the double helix shape. See Hawley & Mori, supra note 24, at 21-24.

47 A base pair is a chemical linkage of two bases which attach to each other due to their polarity. Oxford Dictionary of Biology 62 (Elizabeth Martin & Robert S. Hine eds., 4th ed. 2000). Adenine pairs with thymine and cytosine with guanine. Id.

48 Wade, supra note 24.

49 See supra note 29. As of June 27, 2000, when the HGP and Celera jointly announced that they had sequenced the human genome, the sequence was not actually complete. According to Dr. Francis Collins, the leader of the HGP, the consortium had sequenced approximately eighty-five percent of the genome. Meanwhile, Celera was mostly finished, having ordered all the bases, but with many small gaps in its sequence. Celera expected to fill in such gaps in part by using the HGP's data. See Wade, supra note 24.

50 Natalie Angier, A Pearl and a Hodgepodge: Human DNA, N.Y. Times, June 27, 2000, at A1.

51 See infra notes 59-63 and accompanying text.

52 See infra notes 64-65 and accompanying text.

53 See infra notes 66-68 and accompanying text.

54 See infra note 57 and accompanying text.

55 Ridley, supra note 44, at 6.

56 Seth Shulman, Owning the Future 179 (1999).

57 Ridley, supra note 44, at 7. A codon is a triplicate of nucleotides that functions as a unit of genetic coding. See supra note 46; see also Oxford Dictionary of Biology, supra

C. A Scientific Primer on the Genes

Now that a working draft of the genome has been sequenced, the first task at hand is "annotating" the genome,[58] which includes finding and analyzing all of its genes,[59] particular sequences of DNA letters containing around 1500 base pairs on average.[60] The sequence of base pairs within each gene determines the type of protein that a given gene produces. These proteins are "the business end of cellular processes," structuring cells, directing and catalyzing biochemical reactions, facilitating intercellular communication, aiding in the detection of color and smell, and controlling the movement of heart and skeletal muscles—to name just a few of their functions.[61]

Scientists do not yet know exactly how many genes there are—though recent data from both the HGP and Celera give the number as about 30,000 to 40,000[62]—nor precisely where the genes are located along the DNA chains.[63] Each gene is broken into several separate parts, known as exons,[64] "and the exons are strung out along the ribbon of DNA so sparsely that they account for only three percent of the genome's three billion letters."[65] The gene sequences comprising the remaining ninety-seven percent are called introns.[66] While some

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note 47, at 131. The letters A, C, G, and T represent the bases adenine, cytosine, guanine, and thymine, respectively. See supra note 46 and accompanying text.

[58] One commentator has noted that the term "annotating" is "borrowed from computer programmers' practice of writing explanations alongside the major routines in a piece of software." Nicholas Wade, Now, the Hard Part: Putting the Genome to Work, N.Y. Times, June 27, 2000, at F1.

[59] Wade likens the genome to "biological programming" for which "evolution has neglected to provide even the punctuation to show where genes stop and start, let alone any helpful notes as to what each gene is meant to do." Id. "Annotation is achieved with computer programs that analyze the DNA sequence, pinpoint the components of genes, and guess their biological role from comparison with known genes of other species that are already in the databases." Wade, supra note 37. For a graphic illustrating genes' placement on the chromosome, see Wade, supra note 24.

[60] Hawley & Mori, supra note 24, at 43. Some genes, however, can be much longer. Id.

[61] Id. It is not a damaged gene that causes disease, but rather the consequences of that defect, in terms of the gene's inability to produce a vital protein. See id. at 7-8.

[62] Int'l Human Genome Sequencing Consortium, Initial Sequencing and Analysis of the Human Genome, 409 Nature 860, 860 (2001); Venter, supra note 16, at 1317, 1320.

[63] See Venter, supra note 16, at 1317-21 (describing Celera's efforts to locate genes and noting that "[c]onsiderable refinement is still necessary to improve the accuracy" of its findings).

[64] An exon is "a nucleotide sequence in a gene that codes for all or part of the gene product or some control function." Oxford Dictionary of Biology, supra note 47, at 221; see also Hawley & Mori, supra note 24, at 42 (discussing function of exons).

[65] Wade, supra note 58; see also Ridley, supra note 44, at 123-24 (noting "random nonsense" between exons).

[66] An intron is the seemingly nonsensical nucleotide sequence in a gene that does not code for a particular gene product. Oxford Dictionary of Biology, supra note 47, at 323-24; see also Hawley & Mori, supra note 24, at 42 (discussing role of introns).

of the intron material may control the activation or deactivation of certain genes,[67] the remainder are vast stretches of material that appear to lack any function.[68]

Researchers use various methods to identify genes. For example, DoubleTwist Incorporated, an internet startup in Oakland, California, claimed in May 2000 that it had used computer algorithms to locate over 100,000 genes.[69] While Celera also employs this method of locating genes, Celera president Craig Venter insists that human ingenuity is a necessary complement to the computer algorithms.[70]

Ironically, a second method of locating genes that was pioneered by Craig Venter over ten years ago[71] is now used by Celera rivals HGS and Incyte.[72] One commentator described this method, which uses short DNA sequences called expressed sequence tags (ESTs), as follows:

> The E.S.T. approach exploits the fact that humans may not be able to spot the genes in the genome but human cells surely can. They regularly make transcripts of the genes whose information is needed to synthesize the cell's various proteins. Researchers can capture and analyze these transcripts, known as messenger RNA, and from just a small portion of their sequence can identify the corresponding part of the gene from which they come.[73]

Once a human gene has been located on the chromosome, scientists engaged in the field of functional genomics attempt to determine the

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[67] See Licking, supra note 44, at 152.

[68] See Angier, supra note 50. However, as stated by C. Robert Cloninger, a researcher at Washington University in St. Louis, "'I don't know of anything in nature that's just laying around and is not functional.'" Id. (quoting C. Robert Cloinger) Moreover, according to Phil Green of the University of Washington, much of the genome is made up of "'so-called repetitive elements, or transposable elements, which are like little viruses that have taken advantage of the cell's machinery to replicate themselves.'" Id. (quoting Phil Green) Therefore, according to Green: "'Not only aren't we the center of the universe, we're not even the center of our own genome. We only have a small part of our own genome that's really us.'" Id. For a fascinating discussion of this issue, see Ridley, supra note 44, at 122-35.

[69] John Carey, The Genome Gold Rush, Bus. Wk., June 12, 2000, at 147, 152. Now that the number of human genes has been estimated at about 30,000 to 40,000, see supra note 62 and accompanying text, there are many genomics firms whose claims of having located such vast numbers of genes are being regarded with suspicion. See On Human Nature, Economist, Feb. 17, 2001, at 79, 80 (noting suggestions of cynics that genomics companies have inflated number of genes in their databases in order to attract subscribers).

[70] Carey, supra note 69, at 152. In recognition of the importance of human interpretation of computerized gene annotation, Celera has announced its intention to host an international convocation of top geneticists and biologists to decipher the location and role of genes in the human genome. Id.; Wade, supra note 37.

[71] See infra note 207.

[72] See supra notes 40-42 and accompanying text.

[73] Berenson & Wade, supra note 16. Many critics, including Venter, criticize this method as incomplete, or, worse yet, simply inaccurate. Carey, supra note 69, at 152-54.

role the gene performs. They often can guess a human gene's function by comparing its sequence of base letters with that of genes of other species whose role is already known.[74] Because all living creatures descended from one common ancestor approximately four billion years ago,[75] "the sequence of every human gene is recognizably similar to the equivalent gene in other organisms."[76] Thus, biologists expect the genome of the mouse, which Celera has decoded,[77] to be very useful in the endeavor to locate genes on the human genome. Indeed, they "expect that the DNA sequence in the genes will have stayed much the same in the 100 million years since the two species shared a common ancestor but that the rest of the DNA will be different."[78] In addition, the use of laboratory mice will also help to pinpoint genes' functions. Scientists turn off certain genes in mice, creating "knock-out" mice with specific health problems and defects.[79] Researchers then study these mice in order to learn the function of the genes they eliminated.[80]

With this information, geneticists hope to revolutionize the practice of medicine. Already, several pharmaceutical companies use DNA sequences to manufacture various products including human growth hormone, insulin, and erythropoietin, which generate billions of dollars annually in combined sales.[81] In the future, researchers seek to learn more about the body's ability to repair damaged tissue and fight off invaders, so as to develop new therapies that Dr. William Haseltine, president of HGS, has termed "regenerative medicine."[82] They also expect, in time, to develop a system of "personalized medicine," an array of treatment and preventive programs that has been tailored to an individual's needs through genomic analysis.[83]

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74 See Carey, supra note 69, at 154 (describing functional genomics and its practices); Wade, supra note 58 (noting that genomes of many bacteria and two animals, roundworm and fruit fly, already have been sequenced and annotated, and that functions of many of their genes are understood).

75 See Ridley, supra note 44, at 19, 26.

76 Wade, supra note 58.

77 Jonathan Leake, Britain Loses Race to Map the Mouse, Sun. Times (London), Feb. 25, 2001, § 1, at 5.

78 Wade, supra note 58.

79 See id.

80 See Carey, supra note 69, at 154-55 (speculating that researchers' experiments with mouse genes may lead to drugs preventing osteoporosis); see also Wade, supra note 58 (describing role of "knock-out" mice in decoding human genome).

81 Regalado, supra note 41, at 50.

82 Wade, supra note 58.

83 Id. However, knowledge of the genome could be used in harmful ways as well. For example, patients' privacy could be violated if their predisposition to certain diseases were revealed, and they could be discriminated against with respect to health insurance and employment. See, e.g., Comm. on Commerce, U.S. House of Representatives, 105th

II

THE THRESHOLD CRITERION OF PATENTABILITY IN THE UNITED STATES AND THE E.U.: DO (AND SHOULD) HUMAN DNA SEQUENCES CONSTITUTE PATENTABLE SUBJECT MATTER?

The conflict surrounding the patent held by HGS on the CCR5 receptor gene illustrates the irreconcilable positions of those who oppose patents on human DNA sequences per se, and those who support (or, in any event, accept as inevitable) such patents. On the whole, national legislatures, courts, and patent offices in both the United States and the E.U. have tended to increase patent protection over time. The pressure on each of these governmental entities has been to attract biotechnology investment so as to advance the domestic biotech industry, usually at the expense of public policy considerations.[84] Nonetheless, some human rights activists and religious adherents, as well as some medical practitioners who conduct genetic testing, continue to object to human DNA sequence patents on moral and ethical grounds, contending that human DNA sequences should be unpatentable per se. These arguments have more force in the E.U., where citizens and policymakers harbor greater suspicion toward patents on life forms than in the United States. Thus, despite the increasing harmonization of global patent laws noted by Professor Drahos,[85] the fundamentally different U.S. and E.U. perspectives on human DNA patents create international tension.

Cong., Privacy, Confidentiality and Discrimination in Genetics 10 (Comm. Print 1998) ("[A]s knowledge grows about the genetic basis of disease, so too does the potential for discrimination and stigmatization based on genetic information."); Jeremy Rifkin, The Biotech Century 160-69 (1998) ("Now, with the emergence of genetic screening and genetic engineering, society entertains the prospect of a new and more serious form of segregation. One based on genotype."); Larry Gostin, Genetic Discrimination: The Use of Genetically Based Diagnostic and Prognostic Tests by Employers and Insurers, 17 Am. J.L. & Med. 109, 110 (1991) ("As our ability to detect genetic defects or propensities toward illness increases, so too does the threat that such detection will be used to discriminate."); Mary Z. Pelias & Nathan J. Markward, The Human Genome Project and Public Perception: Truth and Consequences, 49 Emory L.J. 837, 849-50 (2000) (noting that genetic testing raises concerns about genetic discrimination); Kathy L. Hudson et al., Genetic Discrimination and Health Insurance: An Urgent Need for Reform, 270 Science 391, 391 (1995).

[84] See Peter Drahos, Biotechnology Patents, Markets and Morality, 21 Eur. Intell. Prop. Rev. 441, 442-43 (1999) (noting that governments have increased amounts of patents granted without considering the "broader public ethic"). According to Professor Drahos, patent offices are increasingly inclined to grant biotech patents because "one of the main uses of patents by companies is as a signalling device to stock markets that they have control of vital or fundamental technologies. . . . The patent system . . . is progressively becoming more and more enmeshed in processes of market valuation." Id. at 446. Patent offices therefore face "further pressures to adopt a liberal attitude towards the grant of patents." Id.

[85] Professor Drahos has observed that

A. The Novelty and Statutory Subject Matter Criteria for Patentability Under U.S. Law

Among Congress's enumerated constitutional powers is the power to grant patents,[86] and Congress has set forth U.S. patent law in the Patent Act of 1952 (Patent Act).[87] A U.S. patent confers a twenty-year exclusive right to prevent others from making, using, offering for sale, selling, or importing the patented invention in the United States,[88] and any invasion of this right is called an infringement.[89] Patents come in three types: utility, design, and plant. Utility patents—the variety applicable to human DNA sequences—fall into two categories: process patents and product patents. The former protects a process of creation but not the end result; other inventors are still free to duplicate that result by means of a different process. The latter provides broader protection to inventors, however, by preventing "others from making or using the final product without compensating the patentholder, regardless of how the product is made."[90]

In order to obtain patent protection under the Patent Act, a claimed invention must be (1) directed to statutory subject matter, (2)

> [t]he patent system has undergone a process of regulatory globalisation and harmonisation. This simply means that more and more countries have adopted patent systems and that those patent systems have progressively become more like each other. Patent systems are not harmonised at the level of rules, but they share common principles. The degree of patent harmonisation is increasing rather than decreasing.

Id. at 442.

86 See U.S. Const. art. I, § 8, cl. 8 (granting Congress power "[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries").

87 Ch. 950, 66 Stat. 797 (codified as amended in scattered sections of 35 U.S.C.).

88 See 35 U.S.C. § 154(a) (1994). Patents, therefore, confer the "negative right" to exclude others, not the "positive right" to make, use, offer for sale, sell, or import the patented invention. For a discussion of "negative" and "positive" rights, see Donna M. Gitter, Led Astray by the Moral Compass: Incorporating Morality into European Union Biotechnology Patent Law, 19 Berkeley J. Int'l L. 1, 7 n.42 (2001). Thus, an inventor, who possesses only negative rights under a patent, must depend upon other laws, extraneous to patent law, in order to exploit an invention. For example, the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301-395 (1994), requires all new drugs to be proved safe and effective before the Food and Drug Administration will approve them for marketing. Id. § 355. Concomitantly, after a patent expires, anyone may use, sell, or import the invention without regard to the inventor's wishes. Nathan Machin, Comment, Prospective Utility: A New Interpretation of the Utility Requirement of Section 101 of the Patent Act, 87 Cal. L. Rev. 421, 423-24 n.1 (1999).

89 35 U.S.C. § 271(a) (1994).

90 Matthew Erramouspe, Comment, Staking Patent Claims on the Human Blueprint: Rewards and Rent-Dissipating Races, 43 UCLA L. Rev. 961, 966 (1996). Thus, a product patent prevents anyone other than the holder, even an unwitting infringer who develops the same invention independently, from using the invention. Rebecca S. Eisenberg, Patenting the Human Genome, 39 Emory L.J. 721, 722 (1990).

novel, (3) useful, and (4) nonobvious to a person of ordinary skill in the art at the time the invention was made.[91] In addition, the inventor must disclose the invention to the public in terms that are sufficient to enable others skilled in the art to make and use the invention.[92] Courts view this enabling disclosure in the patent application as the quid pro quo of the patent monopoly.[93] Thus, an applicant can obtain a patent only after satisfying the obligation to contribute "a measure of worthwhile knowledge to the public storehouse."[94]

U.S. patent law collapses the novelty and statutory subject matter criteria for patents, defining patentable subject matter as "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof . . . ."[95] Thus, in addition to establishing novelty as a criterion of patentability, this provision, as developed by subsequent judicial doctrine, limits patent protection to inventions in the field of applied technology. It precludes patenting of basic scientific research, discovery of a law of nature (e.g., a law of physics), discovery of physical phenomena, abstract ideas, or discovery of something found in nature.[96] The rationale underlying this criterion is that patent law should not operate so as to deprive society of useful knowledge to which it already has access and rights of ownership.[97]

As noted by Professor Eisenberg, the statutory subject matter and novelty criteria taken together form "[a]n intuitively appealing objection to patent protection for DNA sequences in the human genome."[98] Because DNA sequences exist naturally in every cell of the human body[99] and existed in life forms as early as four billion years ago,[100] some opponents of patents on human DNA sequences contend

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91 35 U.S.C. §§ 101-103 (1994).

92 § 112.

93 See United States v. Dubilier Condenser Corp., 289 U.S. 178, 186-87 (1933) (stating that disclosure and consequent benefits to public are consideration for patent); Grant v. Raymond, 31 U.S. (6 Pet.) 218, 247 (1832) (declaring that disclosure is preliminary requirement for issuing patent).

94 Application of Argoudelis, 434 F.2d 1390, 1394 (C.C.P.A. 1970) (Baldwin, J., concurring).

95 35 U.S.C. § 101. Section 102 of the Patent Act expands upon the novelty requirement by establishing several procedural requirements that must be met before an invention can be deemed "novel." See § 102; Philippe G. Ducor, Patenting the Recombinant Products of Biotechnology and Other Molecules 10-11 (1998).

96 David G. Scalise & Daniel Nugent, Patenting Living Matter in the European Community: Diriment of the Draft Directive, 16 Fordham Int'l L.J. 990, 999 (1993).

97 Paul Goldstein, Copyright, Patent, Trademark and Related State Doctrines 402-03 (3d ed. 1993).

98 Eisenberg, supra note 90, at 723.

99 See supra note 44 and accompanying text.

100 See Ridley, supra note 44, at 17-22.

that these sequences are neither the result of an individual's inventive effort nor new. This notion, known as the "products of nature" doctrine, has now been liberalized, so that a significant degree of human intervention may, under U.S. law, transform a naturally occurring "product of nature" into a patentable organism.[101]

The "products of nature" doctrine controlled in the 1948 case of *Funk Bros. Seed Co. v. Kalo Inoculant Co.*,[102] and was used by the PTO for more than thirty years thereafter to challenge almost every patent application that sought inventors' rights in living matter. In *Funk Bros.*, plaintiff Kalo Inoculant Company brought a patent infringement action against the Funk Brothers Seed Company. The plaintiff alleged that Funk Brothers had made unauthorized use of its patent for an inoculant of leguminous plants.[103] The inoculant consisted of six different species of bacteria, each of which existed in nature and was independently known to act as an inoculant in various leguminous plants.[104] Past attempts to create a mixed culture of the bacteria that could inoculate a wide range of crops had failed, because the bacteria inhibited each other's efficacy when combined.[105] The plaintiff was the first to discover strains of each bacterial species that did not impede each other's efficacy as an inoculant and to combine these strains in a single mixed-culture inoculant.[106]

The Supreme Court applied the "products of nature" doctrine to reject Kalo's patent. Justice Douglas, writing for the majority, held the patent claims to the mixed bacterial culture invalid, reasoning that "[t]he combination of species produces no new bacteria, no change in the six species of bacteria, and no enlargement of the range of their utility."[107] Justice Douglas declared that

> patents cannot issue for the discovery of the phenomena of nature. The qualities of these bacteria, like the heat of the sun, electricity, or the qualities of metals, 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.[108]

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101 See Ducor, supra note 95, at 6 (discussing development of this issue in U.S. law).

102 333 U.S. 127 (1948).

103 Id. at 128-30. Leguminous plants are able to take nitrogen from the air and convert it into organic nitrogenous compounds, which constitute nourishment for the plant. Id. at 128. The bacteria contained in Kalo's inoculant increased the plants' ability to take up nitrogen, thereby acting as a fertilizer. Id. at 128-29.

104 Id. at 129 & n.3.

105 Id. at 129-30.

106 Id. at 130.

107 Id. at 131.

108 Id. at 130 (citation omitted).

Although the *Funk Bros.* decision has never been overruled expressly, Professor Eisenberg notes that, "in retrospect it seems to represent the high-water mark in the 'products of nature' doctrine."[109] In 1980, the seminal Supreme Court case *Diamond v. Chakrabarty*[110] demonstrated that courts would cease denying protection to all inventions composed of naturally occurring products or manifesting laws of nature. Specifically, the Court held that a genetically engineered strain of bacteria capable of breaking down multiple components of crude oil was patentable subject matter.[111]

In *Chakrabarty*, the eponymous microbiologist challenged a denial by the PTO of a patent for his invention, a bacterium into which he had introduced certain naturally occurring plasmids[112] that rendered the bacterium capable of breaking down the multiple components of crude oil.[113] Initially, patent examiners at the PTO rejected Chakrabarty's patent application for the organism[114] on the dual grounds that (1) micro-organisms are nonpatentable because they are "products of nature" and (2) living organisms are per se nonpatentable subject matter under section 101 of the Patent Act.[115] The PTO Board of Patent Appeals and Interferences (PTO Board)[116] subsequently concluded that the new bacteria were not products of nature because bacteria containing such plasmids did not occur in nature.[117] Nevertheless, the PTO Board affirmed the rejection of the patent based on the second ground, that Congress had not intended living organisms to be considered patentable subject matter under 35 U.S.C. § 101.[118]

On appeal, the Supreme Court held in a five-to-four decision that a living, genetically altered organism may qualify for patent protection

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109 Eisenberg, supra note 90, at 725.

110 447 U.S. 303 (1980).

111 See id. at 305, 310.

112 A plasmid is a "structure in bacterial cells consisting of DNA that can exist and replicate independently of the chromosome." Oxford Dictionary of Biology, supra note 47, at 467.

113 *Chakrabarty*, 447 U.S. at 305.

114 Chakrabarty's patent application for the process of cleaning up oil spills with the bacterium was approved by the PTO from the outset. Id. at 305-06. See supra note 90 and accompanying text for a discussion of the difference between process and product patents.

115 *Chakrabarty*, 447 U.S. at 306.

116 The PTO Board hears appeals brought by inventors whose patent applications were denied by PTO examiners. The Board may affirm or reverse an examiner's action, and the applicant may either appeal to the Court of Appeals for the Federal Circuit, see infra note 125 and accompanying text, or file a de novo civil suit to obtain a patent against the Commissioner in the District Court for the District of Columbia. 4 Chisum, supra note 1, § 11.06, at 11-277.

117 *Chakrabarty*, 447 U.S. at 306 n.3.

118 Id. at 306.

as a new "manufacture" or "composition of matter" under section 101 of the Patent Act.[119] In distinguishing *Funk Bros.*, the Court noted that the patentholder in that case had not altered the function of any of the species of bacteria in the mixed-culture inoculant, whereas Chakrabarty had created "a new bacterium with markedly different characteristics from any found in nature."[120] Thus, Chakrabarty's discovery was "not nature's handiwork, but his own; accordingly, it is patentable subject matter."[121] The Court also relied upon language in the Committee Reports accompanying the Patent Act, which indicated that Congress desired expansive construction of the patent laws.[122] According to those reports, Congress intended statutory subject matter to "include anything under the sun that is made by man."[123] Pursuant to *Chakrabarty*, the courts suggested in a line of cases that a life form constitutes patentable subject matter so long as it is significantly altered via human intervention.[124]

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119 Id. at 308-10.

120 Id. at 310. Professor Eisenberg has taken issue with this distinction, stating that "[b]oth patents claimed combinations of naturally occurring elements, and in both cases the combination itself did not exist in nature." Eisenberg, supra note 90, at 726 n.21.

121 *Chakrabarty*, 447 U.S. at 310.

122 See id. at 308-09. The Court noted that, when Congress recodified the Patent Act in 1952, it left largely intact the original language authored by Thomas Jefferson, a strong advocate of patent protection. Id.

123 Id. at 309 (quoting S. Rep. No. 1979, at 5 (1952) and H.R. Rep. No. 1923, at 6 (1952)). As suggested by Professor Krimsky, the Supreme Court possibly was influenced as well by "practical consideration of the nascent biotechnology industry." Krimsky, supra note 14, at 25. At the time the court reviewed *Chakrabarty*, there was a backlog of 114 patent applications for living organisms, with an estimated fifty applications added per year, and biotechnology firms were in dire need of venture capital. Id. at 23-24.

124 See Ex Parte Allen, 2 U.S.P.Q. 2d 1425, 1426-27 (1987) (asserting that multicellular organisms such as oysters are patentable, but denying patent to invention at issue on grounds of obviousness); Ex Parte Hibberd, 227 U.S.P.Q. 443, 444 (1985) (accepting that plants are patentable under Patent Act). The PTO conclusively settled the issue by stating just days after the *Allen* decision that the PTO "considers nonnaturally occurring nonhuman multicellular organisms, including animals, to be patentable subject matter." Nonnaturally Occurring Nonhuman Animals Are Patentable Under § 101, 33 Pat. Trademark & Copyright J. (BNA) No. 927, at 664 (Apr. 23, 1987). In April 1988, the PTO issued the world's first patent on a multicellular living organism. See U.S. Pat. No. 4,736,866 (issued Apr. 12, 1988) (patenting mammal with predisposition to develop cancer due to insertion of human gene associated with that disease); see also Thomas A. Magnani, The Patentability of Human-Animal Chimeras, 14 Berkeley Tech. L.J. 443, 448 (1999). With respect to products derived from human beings, courts have followed the *Chakrabarty* holding that sufficient human intervention renders such a product patentable. For example, in Moore v. Regents of the University of California, 793 P.2d 479 (Cal. 1990), the California Supreme Court upheld a patent for a human cell line which was a product of a doctor's "human ingenuity," although the cells existed independently in nature. Id. at 492-93. The cells originated in the body of John Moore, a cancer patient whose doctor used those cells to profit commercially without ever obtaining Moore's informed consent. Id. at 481. Moore then sued his doctor in order to obtain a property right in his own cells. Id. at 482-83. The court found any claim of ownership by the patient in the cell line inconsistent with patent

Employing the "human intervention" standard, the U.S. Court of Appeals for the Federal Circuit[125] upheld the patentability of human DNA sequences in the 1991 case *Amgen, Inc. v. Chugai Pharmaceutical Co.*[126] The court held that even though DNA sequences exist naturally in the human chromosome, they constitute patentable subject matter if they are "purified and isolated" from the original object in nature.[127]

The *Amgen* case originated with allegations of patent infringement brought by Amgen, Inc., a biotechnology firm, against Chugai Pharmaceutical. A researcher at Amgen had conceived of a means to purify and isolate the natural DNA sequence encoding human erythropoietin, a 165-amino-acid-long protein which stimulates the production of red blood cells and is therefore useful in fighting anemia and other blood disorders.[128] In reaching its decision, the court treated DNA molecules as chemical compounds, which are patentable.[129]

Prior to *Amgen*, a body of case law had established that although a biological product is neither patentable subject matter nor novel if it exists in nature,[130] newly purified or isolated preparations of naturally occurring biological materials may be patented if they can be used in a way that the impure product could not.[131] Relying upon this prece-

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law, which seeks to reward human ingenuity of the sort demonstrated by the doctor. Id. at 493-94. While the court denied Moore's property right in his cells, it did, however, hold that Moore had stated cognizable claims for breach of the physician's fiduciary duty and lack of informed consent. Id. at 497.

125 In 1982, Congress created the U.S. Court of Appeals for the Federal Circuit in order to eliminate the problems of forum shopping and uncertainty about patent enforcement. Rai, supra note 14, at 102-03 & n.139. According to Professor Rai, even more than the U.S. Supreme Court, the Federal Circuit has been "[t]he major force behind the shift towards greater patentability, including greater patentability of basic research." Id. at 102.

126 927 F.2d 1200, 1206 (Fed. Cir. 1991).

127 Id.

128 Id. at 1203.

129 See id. at 1206 (stating that "[a] gene is a chemical compound, albeit a complex one").

130 See supra notes 99-108 and accompanying text.

131 See, e.g., In re Bergstrom, 427 F.2d 1394, 1400-02 (C.C.P.A. 1970) (upholding patent for purified prostaglandin although structurally identical impure compounds exist in nature); Merck & Co. v. Olin Mathieson Chem. Corp., 253 F.2d 156, 164 (4th Cir. 1958) (upholding patent for purified Vitamin B12 isolated from fermentation materials, although Vitamin B12 was produced naturally in minute quantities in livers of cattle and in certain microorganisms, because patented product was superior to previously available Vitamin B12 from cattle); Kuehmsted v. Farbenfabriken of Elberfield Co., 179 F. 701, 703-05 (7th Cir. 1910) (upholding validity of patent on acetylsalicylic acid to first inventor to develop process for producing it in sufficiently pure state to render it therapeutically useful); Parke-Davis & Co. v. H. K. Mulford & Co., 189 F. 95, 103 (S.D.N.Y. 1911) (holding purified adrenalin composition patentable because patentholder was first to make adrenalin available for therapeutic use by isolating it from other gland tissue in which it was found), aff'd,

dent, the *Amgen* court held that a human DNA sequence is patentable subject matter only if it is a "novel *purified and isolated* sequence" derived from the original object in nature.[132] The *Amgen* decision rests on the fact that DNA which has undergone the recombinant cloning process[133]—through which DNA sequences are purified and isolated from the human body—may, in fact, have a somewhat different sequence than the corresponding chromosomal DNA from which it was transcribed. The difference between the cloned DNA sequence and the naturally occurring chromosomal DNA lies in the fact that cloned DNA sequences generally are derived from the messenger RNA[134] corresponding to the desired DNA sequence rather than obtained directly from the chromosomes of a cell. Messenger RNA does not contain the regulatory sequences and extraneous information[135] that appear in chromosomal DNA. Therefore, under the *Chakrabarty* standard,[136] cloned DNA,[137] which similarly does not contain such introns, is sufficiently different from its natural analog to be patentable subject matter.[138]

The PTO has incorporated the same standard as the *Amgen* holding into its patent examination practice. According to John Doll, director of biotechnology examination for the PTO, "[i]n order for isolated DNA sequences to be distinguished from their naturally occurring counterparts, which cannot be patented, the patent application must state that the invention has been purified or isolated or is part of a recombinant molecule."[139]

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196 F. 496, 497 (2d Cir. 1912); see also supra notes 110-24 and accompanying text (discussing *Chakrabarty* case).

132 *Amgen*, 927 F.2d at 1206.

133 For a detailed description of this process, see Hawley & Mori, supra note 24, at 177-86.

134 Messenger RNA (mRNA) is a complex organic compound in living cells that is "responsible for carrying the genetic code transcribed from DNA to specialized sites within the cell . . . where the information is translated into protein composition." Oxford Dictionary of Biology, supra note 47, at 522. For a detailed description of the transcription of mRNA and its role in the cell, see Hawley & Mori, supra note 24, at 27-32.

135 See supra notes 66-68 and accompanying text (discussing introns).

136 See supra notes 110-124 and accompanying text.

137 Another term for DNA prepared in the laboratory using mRNA as a template is complementary DNA, or cDNA. See Oxford Dictionary of Biology, supra note 47, at 139 (defining cDNA); Leslie Roberts, Genome Patent Fight Erupts, 254 Science 184, 184 (1991) (describing cDNA).

138 See Eisenberg, supra note 90, at 727 n.25.

139 John J. Doll, The Patenting of DNA, 280 Science 689, 689 (1998).

B. The Novelty and Statutory Subject Matter Criteria for Patentability Under E.U. Law

The basic requirements of E.U. biotechnology patent law, which are comparable to those in the United States,[140] are set forth in the European Patent Convention (EPC)[141] and a 1998 E.U. biotechnology directive (Biotechnology Directive).[142] In order to be patentable under European law, an invention must: (1) comprise patentable subject matter,[143] (2) be new,[144] (3) be "susceptible of industrial application,"[145] and (4) involve an "inventive step."[146]

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[140] See Scalise & Nugent, supra note 96, at 1013 (noting that patent law fundamentals are "essentially the same" in United States and E.U.).

[141] The EPC was signed in Munich as the Convention on the Grant of European Patents, Oct. 5, 1973, 1065 U.N.T.S. 255 [hereinafter EPC]. Signatories to the EPC include all fifteen of the E.U. member states, Switzerland, Liechtenstein, Monaco, and Cyprus. Helen Gavaghan, EU Ends 10-Year Battle Over Biopatents, 280 Science 1188, 1188 (1998). Under the EPC, an inventor can apply for a European patent at the European Patent Office (EPO), an administrative agency headquartered in Munich, as an alternative to filing separate applications with each of the national patent offices throughout Europe. While the EPC reduces the time and cost necessary to obtain patent rights in certain of the signatory nations, "the governing principal of the EPC" remains "that it may not replace or supersede the national patent system already in effect in the contracting states." Scalise & Nugent, supra note 96, at 1012-13. Consequently, under the EPC scheme, the individual contracting countries may interpret and modify a single European patent, thus affording the patentee varying degrees of patent protection. See id. at 1013; Janice McCoy, Patenting Life in the European Community: The Proposed Directive on the Legal Protection for Biotechnological Inventions, 4 Fordham Intell. Prop. Media & Ent. L.J. 501, 509 n.45 (1993). In general, applicants for European biotech patents avail themselves of the EPC patent procedure. R. Stephen Crespi, Chapter 26, in Biotechnology, Patents and Morality 219, 219 (Sigrid Sterckx ed., 1997).

[142] Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the Legal Protection of Biotechnological Inventions, 1998 O.J. (L 213) 13 [hereinafter Biotechnology Directive]. A directive is a type of E.U. legislation that targets one or more specific member states and binds them with respect to the end to be achieved, while allowing each member state some choice as to the method and, sometimes the extent, of implementation. See W.R. Cornish, Intellectual Property: Patents, Copyright, Trade Marks and Allied Rights 20-21 (3d ed. 1996). For a discussion of opposition to the Biotechnology Directive by various segments of the E.U. citizenry and the ramifications of the Biotechnology Directive's morality provision, see generally Gitter, supra note 88.

The EPC and the Biotechnology Directive operate independently of one another in the E.U. The governing bodies of the E.U. do not exercise any control over the EPC, and the EPO is not legally bound to follow the Biotechnology Directive. See Gavaghan, supra note 141, at 1188. However, it is likely that the Biotechnology Directive will influence the EPO's decisions, since fifteen of the nineteen signatories to the EPC are E.U. member states. Id.; see also Gitter, supra note 88, at 30 n.222 (describing instance where Biotechnology Directive has influenced interpretation of EPC).

[143] EPC, supra note 141, arts. 52 & 53, at 271-72; Biotechnology Directive, supra note 142, art. 3, at 18.

[144] EPC, supra note 141, art. 54, at 272; Biotechnology Directive, supra note 142, art. 3.1, at 18.

[145] EPC, supra note 141, art. 57, at 273; Biotechnology Directive, supra note 142, art. 3.1, at 18.

Pursuant to Article 52(2) of the EPC, the categories of unpatentable subject matter in the E.U. are similar to those in the United States. These categories include: (1) discoveries, scientific theories, and mathematical methods, (2) aesthetic creations, (3) schemes, rules and methods for performing mental acts, playing games or doing business, and programs for computers, and (4) presentations of information.[147] European opponents of patents on life forms, especially Green Party members[148] and environmentalists, have contended that living organisms, including human DNA sequences, are not patentable inventions but rather "products of nature."[149] These arguments have failed in Europe under both the EPC and the Biotechnology Directive, just as they have in the United States.[150]

Even an examination of the European case law predating both the EPC and the Biotechnology Directive reveals that the "products of nature" doctrine is not particularly well supported by European precedent. Since the late 1960s, many European nations have been willing to grant patents on life forms.[151] Then, after the enactment of the EPC in 1973,[152] the European Patent Office (EPO)[153] also indicated its approval of such patents. For example, in the 1992 case

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146 EPC, supra note 141, art. 56, at 273; Biotechnology Directive, supra note 142, art. 3.1, at 18. The "susceptible of industrial application" criterion parallels the U.S. "utility" criterion, and the "inventive step" requirement parallels nonobviousness. See Ducor, supra note 95, at 59 n.88; Scalise & Nugent, supra note 96, at 1013.

147 EPC, supra note 141, art. 52(2), at 271-72.

148 The term "Greens," when used in the context of the E.U. debate over patenting biotechnological inventions, refers to "all persons harboring moral or ethical objections to the patenting of living matter," and includes, among others, environmentalists. Scalise & Nugent, supra note 96, at 1024.

149 See generally Hormone Relaxin, 1995 O.J. E.P.O. 388 (Opp. Div.) (summarizing arguments of Greens and others morally opposed to patents on human DNA sequences).

150 See supra notes 109-39 and accompanying text regarding the demise of the "products of nature" doctrine in the United States.

151 See, e.g., Am. Cyanamid v. Berk Pharm., 1976 R.P.C. 231 (1976) (cited in Scalise & Nugent, supra note 96, at 1017 n.125) (approving patents on life forms in United Kingdom); Judgment of Mar. 27, 1969 (Rote Taube/Red Dove), Bundespatentgericht (BPatGE) (federal court for patent matters), 1969, 672, excerpts translated in 1 Int'l Rev. Indus. Prop. & Copyright L. 136 (1970) (cited in McCoy, supra note 141, at 508 n.38) (allowing patents on higher animals in Germany ten years before U.S. Supreme Court's decision in Diamond v. Chakrabarty, 447 U.S. 303 (1980)).

152 See supra note 141.

153 As stated above, see supra note 141, the EPO is the administrative agency charged with the examination and grant of patents under the EPC. The "[a]pplicant must designate at the time of filing the countries of the [EPC] to which he wishes protection of his invention to extend." 3 Peter D. Rosenberg, Patent Law Fundamentals 19-102 (rev. 2d ed. 1999). Examination of a patent application has both a formal and a substantive element. "The substantive examination of each application is conducted by an Examining Division consisting of three technically qualified examiners of different nationality." Id. at 19-104. Within nine months from the date the Examining Division has granted a patent, any person may file a notice of opposition, "which must contain a statement of the extent to which

Harvard/Onco-mouse,[154] the EPO approved the first European patent for a transgenic mammal,[155] the Harvard Onco-mouse. U.S. scientists created this animal to be genetically predisposed to develop breast cancer,[156] intending it to serve as a more effective model for studying how genes contribute to various forms of cancer, as well as for testing drugs for breast cancer.[157] In the 1992 *Harvard/Onco-mouse* decision, the EPO Examining Division[158] affirmed the holding, articulated in a 1990 proceeding in the same matter,[159] that the EPC does not exclude the patenting of animals as a per se category.[160] Nonetheless, it should be noted that legal challenges to the Harvard Onco-mouse

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the European patent is opposed and the grounds on which the opposition is based." Id. at 19-105.

> Oppositions are conducted by an Opposition Division which consists of three technical examiners, at least two of whom must not have taken part in the proceedings for the grant of the patent to which the opposition relates. An appeal to the Technical Board of Appeal lies from a decision of the Opposition Division.

Id. Alternatively, a patent granted under the EPC can be challenged before the national patent offices or courts, in which case the decisions have only a national effect. Gert-Jan van de Kamp, The New Directive on the Legal Protection of Biotechnological Inventions, 7 Eur. Envtl. L. Rev. 234, 235 (1998).

154 Harvard/Onco-mouse, 1992 O.J. E.P.O. 588 (Examining Div.), reprinted in 1991 Eur. Pat. Off. Rep. 525, 525-27.

155 A transgenic plant or animal is one "whose genome incorporates and expresses genes from another species. . . . For example, the gene for rat growth hormone can be inserted into fertilized mouse eggs to produce mice with cells that produce rat growth hormone." Oxford Dictionary of Biology, supra note 47, at 598.

156 Scientists at Harvard University created the Harvard Onco-mouse in the 1980s by inserting into a mouse a gene that renders the mouse highly susceptible to breast cancer. Carrie F. Walter, Beyond the Harvard Mouse: Current Patent Practice and the Necessity of Clear Guidelines in Biotechnology Patent Law, 73 Ind. L.J. 1025, 1029 (1998). The inventors applied for a U.S. patent on June 22, 1984, for the process of producing genetically manipulated animals, as well as for the transgenic animal itself. The patent, granted on April 12, 1988, was the first patent the PTO awarded for a new variety of animal. See id.; see also U.S. Patent No. 4,736,866 (issued Apr. 12, 1988). In 1985, the patentholder applied for an EPC patent. See Harvard/Onco-mouse, 1989 O.J. E.P.O. 451 (Examining Div.), reprinted in 1990 Eur. Pat. Off. Rep. 4, 5 (1989).

157 See Walter, supra note 156, at 1029 (noting usefulness of onco-mice for researching causes of and treatments for cancer); Alun Anderson, Oncomouse Released, 336 Nature 300, 300 (1988) (noting sale of onco-mice that could be used to test human cancer drugs on animals).

158 See supra note 153.

159 See Harvard/Onco-mouse, 1990 O.J. E.P.O. 476 (Tech. Bd. App.), reprinted in 1990 Eur. Pat. Off. Rep. 501, 502.

160 Harvard/Onco-mouse, 1992 O.J. E.P.O. 588 (Examining Div.), reprinted in 1991 Eur. Pat. Off. Rep. 525, 526 (referring to 1990 *Harvard/Onco-mouse* decision, where Technical Board of Appeal declared that "the Examining Division was wrong in refusing the present application" on grounds that EPC "excludes the patenting of animals as such").

continue until the present day in Europe,[161] on the grounds of morality and public policy.[162]

Then, in a 1995 human DNA patent case decided under the EPC, *Hormone Relaxin*,[163] the EPO Opposition Division[164] approved the grant of a patent for a DNA sequence encoding a human protein, produced by pregnant women, that had useful applications during the childbirth process.[165] The Opposition Division rejected the patent opponents' contention that the subject matter of the patent represented a mere discovery and therefore was not patentable. Relying on the Guidelines for Examination in the EPO,[166] the Opposition Division held that "if a substance found in nature has first to be isolated from its surroundings and a process for obtaining it is developed, that process is patentable," and that the substance itself may be patentable if it "can be properly characterised by its structure and it is new in the absolute sense of having no previously recognized existence."[167]

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161 When the EPO announced in 1992 that it intended to approve the Onco-mouse patent application, protests arose throughout Europe. More than two hundred organizations that oppose the patent on moral and ethical grounds, including animal welfare groups, environmental organizations, and religious societies, combined to support seventeen oppositions to the patent. See van de Kamp, supra note 153, at 236 (noting intense legal opposition to Onco-mouse patent); Charles Arthur & Tom Wilkie, Is This the Work of Man or Nature?, Independent (London), Nov. 20, 1995, at 2 (same). In February 1993, under pressure from these groups, the European Parliament revoked the patent and banned further animal patenting until a formal policy could be researched and established. This revocation was nonbinding, resulting in divergent national laws. Estelle J. Tsevdos et al., Law and Nature Collide, Nat'l L.J., June 16, 1997, at C1. At this writing, the outcome of the opposition proceedings has not yet been decided, and it is expected to be affected by the Biotechnology Directive. See Gavaghan, supra note 141, at 1188 (noting that, although "not officially acknowledged, it is widely believed" that final *Harvard/Onco-mouse* decision has been "on hold until the directive was passed").

162 See infra notes 206-32 and accompanying text for a discussion of the E.U. morality doctrine.

163 Hormone Relaxin, 1995 O.J. E.P.O. 388 (Opp. Div.).

164 See supra note 153.

165 See *Relaxin*, 1995 O.J. E.P.O. at 388.

166 Guidelines for Examination in the European Patent Office, at C-IV, § 2.3 (1994). These Guidelines were formulated to direct the EPO staff, as well as to inform patent practitioners and litigants. Id. at General Introduction II.

167 *Relaxin*, 1995 O.J. E.P.O. at 396. As in the United States, the E.U. tends to link inextricably the concepts of patentable subject matter and novelty with respect to biotech inventions. The Opposition Division found the gene sequence encoding human relaxin to be novel for the same reasons that it was patentable subject matter. Again relying on the Guidelines for Examination, the court declared that "[i]t is established patent practice to recognise novelty for a natural substance which has been isolated for the first time and which had no previously recognized existence." Id. at 394; see also Joseph Straus, Patenting Human Genes in Europe—Past Developments and Prospects for the Future, 26 Int'l Rev. Indus. Prop. & Copyright L. 920, 926 (1995) (

> According to the EPO Examination Guidelines, a substance found in nature which must first be isolated from its surroundings and can be properly characterized either by its structure, by the process by which it is obtained or by other

Thus, in *Relaxin*, the EPO expressly limited the applicability of the "products of nature" doctrine, just as the U.S. Court of Appeals for the Federal Circuit had in *Amgen*.[168]

With the enactment of the recent Biotechnology Directive, the E.U. has codified rejection of the "products of nature" doctrine via language providing that a substance isolated from nature cannot be excluded from patentability as a general principle, even if it is identical to its natural equivalent.[169] It also expressly furnishes patent protection for human DNA sequences, providing that although "[t]he 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" is unpatentable,[170] "[a]n 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."[171] Thus, the Biotechnology Directive confirms that a human DNA sequence constitutes patentable subject matter so long as its industrial usefulness can be demonstrated.[172]

The patentability of human DNA sequences has the distinction of being the most controversial provision in one of the most heavily lobbied pieces of legislation that the European Parliament has ever considered.[173] Indeed, although the Member States were required to amend their national laws in compliance with the Biotechnology Di-

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parameters, and is "new" in the absolute sense of having no previously recognized existence, can be patentable per se, provided the inventor discloses the manner of how to obtain it in a repeatable way.) (citations omitted).

168 See supra notes 125-35 and accompanying text. In addition, as the U.S. Federal Circuit did in *Amgen*, the Opposition Division in *Relaxin* treated human gene sequences similarly to other chemical substances in terms of patent law. J. Straus, Patenting of Human Genes and Living Organisms—The Legal Situation in Europe, in Patenting of Human Genes and Living Organisms 12, 19 (F. Vogel & R. Grunwald eds., 1994) (stating that "[d]eoxiribonucleic acid . . . is a biochemical substance and has been treated by patent offices in the same way as other chemical substances").

169 Biotechnology Directive, supra note 142, art. 3.2, at 18 ("Biological material which is isolated from its natural environment or produced by means of a technical process may be the subject of an invention even if it previously occurred in nature.").

170 Id. art. 5.1, at 18.

171 Id. art. 5.2, at 18.

172 Specifically, Article 5.3 of the Biotechnology Directive provides that "[t]he industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application." Id. art. 5.3, at 18. See infra Part III.B regarding the industrial applicability requirement under E.U. law.

173 See Dr. Nick Scott Ram, Biotechnology Patenting in Europe: The Directive on the Legal Protection of Biotechnological Inventions: Is This the Beginning or the End?, 2 Bio-Sci. L. Rev. 43, 43 (1998) (underscoring that "public debate has been highly charged and emotive" with respect to Biotechnology Directive). For a discussion of the ten-year debate

rective no later than July 30, 2000,[174] only four nations have done so, due in large part to their objections to DNA sequence patents.[175] In both the United States and the E.U., judicial rejection of the "products of nature" doctrine has not quelled the arguments of those who are morally and ethically opposed to all patents on human DNA sequences.

C. The U.S. Public Policy Debate as to Whether Human DNA Sequences Satisfy the Patent Criteria of Statutory Subject Matter and Novelty

Notwithstanding the defeat of the "products of nature" doctrine implicit in the *Chakrabarty* court's assertion that patent protection is available for "everything under the sun that is made by man,"[176] some in the United States continue to oppose patents on human DNA sequences. They contend that such patents are inherently immoral and unethical, and therefore fail to satisfy the threshold criterion that a claimed invention must constitute statutory subject matter. These critics divide into three general groups: human rights activists, religious adherents, and members of the medical community.

Human rights activists argue that because DNA holds the key to human life, any claim of intellectual property rights in human DNA sequences is inherently immoral and should therefore be illegal.[177] According to Jeremy Rifkin, a prominent activist[178] and the author of several books critiquing genetic engineering,[179] genomic companies should not be able to "lay claim to the individual genes that make up

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leading up to the enactment of the Biotechnology Directive, see Gitter, supra note 88, at 9-13.

174 Biotechnology Directive, supra note 142, art. 15, at 20-21.

175 As of January 5, 2001, only four member states, Denmark, Finland, Ireland, and the United Kingdom, had amended their national laws in accordance with the Biotechnology Directive. See Patent Laws Re-emerge as Biotech Problem, Chem. Market Rep., Jan. 5, 2001, available at 2001 WL 4368549. See infra notes 221-32 and accompanying text for a discussion of the opposition of many member states to the Biotechnology Directive, even after its enactment.

176 See supra note 123 and accompanying text.

177 Tom Reynolds, Gene Patent Race Speeds Ahead Amid Controversy, Concern, 92 J. Nat'l Cancer Inst. 184, 184 (2000).

178 In 1998, Rifkin, president of the Washington, D.C. Foundation on Economic Trends, and researcher Stewart Newman filed a U.S. patent application for a hypothetical method of making creatures that are part human and part animal by combining the embryos of both and implanting these chimeric embryos into surrogate mothers. The two men explained that they had no intention to commercialize the results of such research, but rather sought to provoke public debate about the morality of patenting such creatures. See David Dickson, Legal Fight Looms Over Patent Bid on Human/Animal Chimeras, 392 Nature 423, 423 (1998). More recently, Rifkin has stated his intent to challenge the legality of gene patents. Andrew Pollack, Is Everything for Sale?, N.Y. Times, June 28, 2000, at C1.

179 See supra note 83.

our common evolutionary legacy."[180] Furthermore, some religious groups warn that "humans and animals are creations of God, not [of] humans, and as such should not be patented as human inventions."[181] Along with human rights activists, members of various religious communities fear that patents on human genes might ultimately lead to a situation "where human embryos and genetically engineered humans are treated as commodities."[182] Finally, many medical practitioners also oppose DNA patents on the grounds that such patents impose unethically high royalty fees on health-care providers who test patients for genetic predisposition to disease.[183]

A particularly controversial example of the high royalty fees imposed on medical practitioners conducting genetic tests concerns two genes, BRCA1 and BRCA2, which are linked to breast cancer.[184] In 1994, a team of scientists from Myriad Genetics (Myriad), working with groups from the University of Utah and the National Institute of Health (NIH), identified and sequenced the BRCA1 gene.[185] In 1996, Myriad scientists identified BRCA2, a second gene related to breast cancer. Ultimately, after settlement of a patent infringement lawsuit with another biotech firm, Myriad gained exclusive patent rights to the genetic tests that screen for mutations in these genes, as well as patent rights in the genes themselves.[186] After an initial period when it did not attempt to enforce its patents against researchers, Myriad

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180 Jeremy Rifkin, Genes Ought to Belong to Us All—Not Just to 'Bio-Prospectors,' Houston Chron., July 2, 2001, at 5C.

181 Ronald Cole-Turner, Religion and Gene Patenting, 270 Science 52, 52 (1995). In 1995, more than eighty religious organizations held a press conference denouncing patents on humans and animals, including patents on human genes. Richard Stone, Religious Leaders Oppose Patenting Genes and Animals, 268 Science 1126, 1126 (1995).

182 Reynolds, supra note 177, at 184.

183 See id. at 185-86. Although U.S. law prohibits the enforcement of patents against those performing medical procedures, "the biotech industry successfully lobbied for an exemption of its products." Id. Similarly, in Europe, although the EPC expressly declares that methods of medical treatment are not patentable inventions, this provision is understood to apply only to those medical-method inventions that are carried out upon a living body, not upon tissue, organs, or fluids which have been removed from the body permanently. Likewise, products that are used in a medical procedure are not excluded from patentability. EPC, supra note 141, art. 52(4), at 272.

184 Mutations in these two genes account for up to ten percent of all breast and ovarian cancers. Christine McGourty, Will the Legal Minefield of Gene Patenting Harm Patients?, Daily Telegraph (London), June 7, 2000, available at 2000 WL 21888555.

185 Reynolds, supra note 177, at 185-86. Ultimately, NIH exclusively licensed its share of the rights to the University of Utah. Id. The university in turn assigned its rights to Myriad, which had been started by one of the university researchers. Phyllida Brown & Kurt Kleiner, Patent Row Splits Breast Cancer Researchers, New Scientist, Sept. 24, 1994, at 4.

186 John Murray, Note, Owning Genes: Disputes Involving DNA Sequence Patents, 75 Chi.-Kent L. Rev. 231, 234-35 (1999); Stephen Naysmith, Gene Tests Could Bankrupt NHS, Sun. Herald (Scotland), June 4, 2000, at 4.

subsequently elected to do so. Because the cost to sequence a woman's DNA in search of BRCA mutation is so high—roughly $2400 to $3500—Myriad eventually agreed to provide investigators funded by the NIH access to the tests at less than half the commercial cost.[187] Although this solution is not acceptable to gene patent opponents, Myriad's patent rights in the breast cancer genes are incontrovertible under U.S. law. Even a University of Pennsylvania cancer researcher who felt strongly enough to resign from Myriad's scientific advisory board after the company barred one of her colleagues from performing BRCA tests in her research acknowledged that "[s]ome people will feel that this is still not satisfactory public policy, . . . but it was the best we could do at this time," given Myriad's intellectual property rights to the gene.[188]

As demonstrated by the events surrounding the BRCA gene patents, opposition to human DNA sequence patents on the part of human rights activists, religious groups, and medical practitioners is not addressed under U.S. law.[189] Indeed, Congress has espoused the view that "patent law is not the place to exercise moral judgments about scientific activity"[190] and has declined to enact bills limiting biotech patenting.[191] Although former President Bill Clinton named members of a National Bioethics Advisory Commission in 1996,[192] this group has been derided as no more than "[s]ymbolic regulation" working with "few resources, uncertain funding futures and difficult deadlines."[193] Thus, arguments against the patentability of human DNA sequences, per se, are a dead letter under U.S. law.

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187 Reynolds, supra note 177, at 185; Tom Reynolds, NCI-Myriad Agreement Offers BRCA Testing at a Reduced Cost, 92 J. Nat'l Cancer Inst. 596, 596 (2000).

188 Reynolds, supra note 177, at 185.

189 The moral and ethical arguments against patenting of human gene sequences command more attention in the E.U. See infra Part II.D.

190 Ronald Schapira, Biotechnology Patents in the United States, in Biotechnology, Patents and Morality 171, 171-72 (Sigrid Sterckx ed., 1997). But cf. Magnani, supra note 124, at 451-58 (discussing infrequently invoked and possibly moribund doctrine in U.S. patent law which bars patent grant on grounds of utility to inventions deemed to contravene morality).

191 See Sigrid Sterckx, European Patent Law and Biotechnological Inventions, in Biotechnology, Patents and Morality 1, 18-19 (Sigrid Sterckx ed., 1997) (describing failure of various congressional bills that would have banned patents on higher life forms).

192 Id. at 19.

193 Drahos, supra note 84, at 446. Professor Drahos cites as an example the fact that in 1997, Clinton asked the Commission to report within a mere ninety days on the issues raised by developments in cloning technology. Id.

D. *Moral and Public Policy Debate in the E.U.: Do DNA Sequences Constitute Unpatentable Subject Matter?*

Ethical objections to patents on human DNA sequences are more robust in the E.U. than in the United States, as demonstrated by the controversy surrounding Myriad's application for European patent rights in the BRCA1 and BRCA2 genes.[194] Myriad not only applied for European patent protection, but also granted the Scottish company Rosgen[195] the exclusive United Kingdom (U.K.) license to test for the BRCA1 and BRCA2 genes.[196] Myriad's actions in Europe alarmed the publicly funded U.K. National Health Service (NHS), which routinely screens patients for predisposition to breast cancer at nonprofit labs for about half the cost of Myriad's $2400 to $3500 test.[197] The NHS feared that, if it were required to pay a licensing fee to Rosgen, a dangerous precedent would be established which threatens the U.K. model of a publicly funded national health service.[198] According to a clinical geneticist at a London hospital that provides breast cancer screening:

> In America, all the other labs have gone out of business. . . . Rosgen is negotiating with the [British] Department of Health, and that will set an enormously important precedent. Myriad is looking to patent methods for predicting other common illnesses such as prostate cancer, testicular cancer and hypertension. If they end up mak-

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194 Myriad must obtain patent rights separately in Europe, as patents are valid only in the jurisdiction that granted them. As noted by one commentator:

> Patent law, like all intellectual property law, has historically been based on the nation-state and the principle of territoriality. National governments grant patents to inventors. The territorial limits of sovereignty preclude a country from giving extraterritorial effect to its patent laws. Obtaining a patent in the United States does not provide patent protection in other countries, nor can the United States grant foreign patents. . . . Thus, each patent has a separate existence in each sovereign state from which it is issued.

Gretchen Ann Bender, Clash of the Titans: The Territoriality of Patent Law vs. the European Union, 40 IDEA 49, 52-53 (2000) (citations omitted).

195 Rosgen is associated with the Roslin Institute of Edinburgh, where scientists cloned Dolly the sheep. See John Chapman & Michael Hanlon, The Race to Control Humanity, Express, Feb. 22, 2000, available at LEXIS, World News Library, European News Sources File; Naysmith, supra note 186.

196 Naysmith, supra note 186.

197 Id.; Reynolds, supra note 177, at 185. Although it concedes that its genetic tests for breast cancer are not as sophisticated as Myriad's, NHS insists that they are more cost-effective. Myriad's method is to analyze the entire gene associated with the cancer, listing all mutations. The British approach instead begins with sites on the gene where mutations are most likely to occur and proceeds to sequence the entire gene only if the initial screening fails to evidence any mutations. James Meek, US Firm May Double Cost of UK Cancer Checks, Guardian (London), Jan. 26, 2000, at 6, available at http://www.guardian.co.uk/Archive/Article/0,4273,3951576,00.html (last visited Oct. 25, 2001).

198 Naysmith, supra note 186; see also McGourty, supra note 184 (describing potential effect on British NHS of Myriad's patent rights in BRCA1 and BRCA2 genes).

> ing people pay through the nose to use their techniques, it could bankrupt the NHS.[199]

Although Myriad's patent applications have yet to be tested seriously in European courts, the recent E.U. Biotechnology Directive, which the U.K. has incorporated into its national law,[200] unambiguously accepts the principle that human DNA sequences can be patented.[201] Rosgen nevertheless has agreed to negotiate with the NHS in order to enable the latter to continue its genetic testing practices. While the parties still are working out the precise terms of the deal, Rosgen has released an interim statement announcing its intent to permit the NHS to conduct an unlimited number of tests without having to pay licensing fees or royalties to Rosgen.[202]

Some of the frustration felt in Britain undoubtedly stems from the fact that much of the research on one of the genes, BRCA2, was originally performed by two British research centers, the Sanger Centre in Cambridge and the Institute of Cancer Research (ICR) in London. Myriad filed its patent application for the gene just hours before the ICR published its discovery in *Nature*, and the ICR maintains that it discovered the gene first.[203] One might surmise that the British scientists object to Myriad's patent simply because they feel that it was wrested improperly from them, and not due to disapprobation, on philosophical and ethical grounds, of human DNA sequence patents. Indeed, the U.K. generally is quite favorably disposed toward patents on life forms.[204]

Yet, it is clear that the tension between the United States and Britain with respect to the BRCA1 and BRCA2 patents reflects a fundamental difference between the respective nations' views of the patentability of human DNA sequences. Indeed, the British and American researchers had initially collaborated as part of an international team of scientists and subsequently ceased working together because of a disagreement over the ethics of patenting DNA. At the time of the split, Mike Stratton, head of the ICR research team, ex-

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199 Naysmith, supra note 186. Indeed, a 1999 poll of U.S. laboratories "revealed that a quarter had received letters from biotech company lawyers ordering them to stop clinical tests because of patents." Patent Yourself, Says British Eco-Activist, Global News Wire, Mar. 7, 2000, LEXIS, World News Library, European News Sources File.

200 See supra note 175.

201 See supra notes 170-72 and accompanying text.

202 Steve Connor, Firm Will Waive NHS Fee for Breast Cancer Test, Independent (London), Nov. 15, 2000, at 11. Naturally, this permission is being offered only to the NHS, and therefore will not benefit any other labs, nonprofit or otherwise, that conduct genetic screening for breast cancer.

203 Chapman & Hanlon, supra note 195.

204 See supra text accompanying note 151; supra note 175 and accompanying text.

plained that he and his British colleagues "do not believe pieces of the human genome are inventions; we feel it is a form of colonisation to patent them," adding that he did not believe it "appropriate for [a disease gene] to be owned by a commercial company because, in contrast to an academic organisation or a charity, there inevitably is a demand for profit."[205]

Indeed, there exists a distinctively European perspective that moral and ethical principles must not be compromised excessively for the purpose of making a profit,[206] and which perspective remains deeply suspicious of patents on life. In a 1991 letter to the journal *Science*, for example, French Minister for Research and Technology Hubert Curien argued that patenting of full or partial gene sequences "would be ethically unacceptable" because "[a] patent should not be granted for something that is part of our universal heritage."[207] This

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[205] Brown & Kleiner, supra note 185, at 4.

[206] For example, during the period of debate leading up to the enactment of the Biotechnology Directive, an E.U. parliamentary committee concluded that facilitating patentability of biotechnological inventions is but one consideration in the restructuring of the biotech industry, and that legal policy in the E.U. "must be more than a set of arrangements aimed at bringing about favorable conditions of competition." Third Report of the Committee on Legal Affairs and Citizens' Rights on the Commission Proposal for a Council Directive on the Legal Protection of Biotechnological Inventions, Eur. Parl. Doc. (PE/92/0286) 27, 35 (1992).

[207] Hubert Curien, The Human Genome Projects and Patents, 254 Science 1710, 1710 (1991). This statement was made in the context of a contemporaneous international debate over the patenting of partial human gene sequences of unknown function, called expressed sequence tags (ESTs). In 1991 and 1992, the NIH filed patent applications for thousands of partial human gene fragments sequenced by a group of researchers led by Dr. Craig Venter, then an NIH employee. Roberts, supra note 137, at 184; Leslie Roberts, NIH Gene Patents, Round Two, 255 Science 912, 912 (1992). The international scientific community decried these applications, lamenting that the award of such patents would foster secrecy among scientists, hamper international collaboration among researchers, and hobble the biotech industry. Robin Herman, The Great Gene Gold Rush, Wash. Post, June 16, 1992, Health, at 11 (describing biotech companies' fear that granting such patents could inhibit investment and some scientists' belief that "protection of property rights 'should be based on uses of sequences rather than the sequences themselves'"). In protest, the U.K. government, supported by the British Medical Research Council, announced that it would seek an international agreement precluding any nation from filing a patent application for gene sequences of unknown function that were discovered during publicly funded research activities. Nonetheless, the U.K. declared that it intended to protect its interests by filing patent applications for decoded DNA sequences, and then to release sequence information quickly to the research community. See Alan Howarth, Patenting Complementary DNA, 256 Science 11, 11 (1992) (declaring, in letter written by Minister of Science of U.K. Department of Education and Science, U.K. government's opposition to NIH patent applications); see also Antonio Ruberti, Patenting Complementary DNA, 256 Science 11, 11 (1992) (stating, in letter written by Italy's Minister of Research, that "all information resulting from efforts made within the framework of the Human Genome Project should be always freely available to the entire scientific community"). French researchers also opposed commercialization of the human genome and protested by granting French research results on the Human Genome Project to the United Nations Educational,

traditional European view finds expression in language, included in both the EPC and the Biotechnology Directive, that provides that it is within the discretion of each member state to deem inventions "unpatentable where their commercial exploitation would be contrary to *ordre public*[208] or morality."[209] During the intense public debate surrounding the enactment of the Biotechnology Directive,[210] the E.U. biotech industry reluctantly agreed to this provision as a political compromise intended to facilitate the Directive's passage. Therefore, the fundamental difference between American and European patent law is that in Europe, biotech inventions may be excluded categorically from patent protection based on their subject matter.[211] Conversely,

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Scientific and Cultural Organization (UNESCO) in Paris. Margaret Llewelyn, Industrial Applicability/Utility and Genetic Engineering: Current Practices in Europe and the United States, 16 Eur. Intell. Prop. Rev. 473, 476 (1994); Declan Butler, Who Owns the Building Blocks of Life?, Independent (London), Nov. 2, 1992, at 14. Ultimately, "[m]ore than two hundred genome scientists from around the world signed a declaration . . . calling for the results of the Human Genome Project to remain . . . freely accessible to all." Id.

The NIH finally abandoned its patent applications in early 1994, not on ethical grounds, but because the PTO had denied them. Rebecca S. Eisenberg & Robert P. Merges, Opinion Letter as to the Patentability of Certain Inventions Associated with the Identification of Partial cDNA Sequences, 23 Am. Intell. Prop. L. Ass'n Q.J. 1, 3 (1995); Michael Waldholz, NIH Gives Up Effort to Patent Pieces of Genes, Wall St. J., Feb. 11, 1994, at B1. The issue is far from settled, however, for numerous private companies the world over since have filed similar patent applications for partial gene sequences of unknown utility. See Holman & Munzer, supra note 5, at 753-54 ("[T]he PTO has received and continues to receive a steady stream of EST patent applications."). After frequent policy changes with respect to the patentability of ESTs, the PTO announced in January 2001 that it would review such applications more stringently in the future. See U.S. Patent and Trademark Office Utility Examination Guidelines, 66 Fed. Reg. 1092, 1098 (Jan. 5, 2001) (requiring patent application for purified and isolated gene to demonstrate "specific, substantial, and credible" utility); U.S. Issues Stiffer Regulations on Frivolous Patenting of Genes, N.Y. Times, Jan. 6, 2001, at C3 (stating that guidelines were "aimed at stopping companies from making frivolous attempts to patent genes before they really have any use for them").

208 The nearest English translation of *ordre public* is "public interest" or "public policy." Cornish, supra note 142, at 195 n.86.

209 Biotechnology Directive, supra note 142, art. 6.1, at 18. The EPC provides that a member state can deny patent protection for "inventions the publication or exploitation of which would be contrary to *ordre public* or morality." EPC, supra note 141, art. 53(a), at 272. The major difference between the language of the two provisions is that the Biotechnology Directive's Article 6.1 omits the word "publication," thereby precluding the body assessing the morality of a patent application under the Biotechnology Directive from denying a patent based upon the morality of the methods used to create the invention. In contrast, under Article 53 of the EPC, the EPO has discretion to reject a patent application based upon the morality of the methods used to create the invention, as well as upon the subsequent use of the invention after the patent has been awarded. Richard Ford, The Morality of Biotech Patents: Differing Legal Obligations in Europe?, 19 Eur. Intell. Prop. Rev. 315, 315-16 (1997).

210 See supra note 173 and accompanying text.

211 See Kevin J. Dunleavy & Milan M. Vinnola, E.U. Biotech Directive Departs from U.S. Practices, Nat'l L.J., May 24, 1999, at C11 (stating that "[t]he most significant differ-

in the United States, there exists "a strong presumption in favor of granting a patent on any invention that satisfie[s] the basic criteria."[212]

The morality provision has been raised in only four EPO suits,[213] including *Harvard/Onco-mouse*[214] and *Relaxin*,[215] and in each case the EPO declined to deny a patent based on morality or public policy.[216] With respect to patenting human gene sequences, at issue in the *Relaxin* case, the EPO Opposition Division rejected the argument that such patents inherently are immoral and alluded to the contemporaneous debate over whether the Biotechnology Directive would permit patenting of human genes (ultimately, it did)[217] to prove that there was no consensus among the contracting states "that the patenting of human genes is abhorrent and hence prohibited under [EPC] Article 53(a)."[218] As for the Biotechnology Directive, since it has been implemented in only four member states,[219] no cases have been brought yet challenging a patent on the grounds of morality. Thus, it is clear that the E.U. feels pressure to provide patent protection comparable to that in the United States so as to prevent the loss of biotech investment.[220]

Notwithstanding the infrequent use of the morality provision under European law, the Biotechnology Directive faces attack on the grounds that patenting human DNA sequences is inherently unethical. The Netherlands has commenced a legal action against the European Parliament demanding annulment of the directive.[221] While this ac-

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ence" between patentability of biological materials in United States and E.U. is assessment of invention's morality when determining whether to grant patent).

212 Beth E. Arnold & Michael J. Malinowski, Patent Protection, in Biotechnology: Law, Business, and Regulation 2-23 to 2-28 (Supp. 2001). But cf. Magnani, supra note 124, at 451-55 (suggesting that there may be some basis under U.S. law to deny patent protection to invention deemed to contravene morality or public policy).

213 For a detailed discussion of these cases, see Gitter, supra note 88, at 21-34.

214 See supra notes 154-62 and accompanying text.

215 See supra notes 163-68 and accompanying text.

216 Gitter, supra note 88, at 40.

217 See supra notes 169-72 and accompanying text.

218 Hormone Relaxin, 1995 O.J. E.P.O. 388, 402 (Opp. Div.).

219 See supra note 175 and accompanying text.

220 See, e.g., Alison Abbott & Ulrike Hellerer, Politicians Seek to Block Human-Gene Patents in Europe, 404 Nature 802, 802 (2000) (noting that patent manager of German biotechnology company Qiagen questioned whether company would remain in Germany if gene patents were not granted).

221 Case C-377/98, Netherlands v. Parliament, 1998 O.J. (C 378) 13, 13; see also Andrew Scott, The Dutch Challenge to the Bio-Patenting Directive, 21 Eur. Intell. Prop. Rev. 212, 212 (1999) ("[U]nhappiness at the Directive's consequences has . . . been manifested in the form of an action for its annulment."). The Netherlands had been the only member state to vote against the Biotechnology Directive, although Belgium and Italy abstained. Patrick Farrant & Vicki Salmon, Netherlands Seeks End to EU Biotech Directive, IP Worldwide, July-Aug. 1999, available at LEXIS, News Library, IP Worldwide File. However, until the

tion challenges the Biotechnology Directive on procedural grounds,[222] the underlying purpose of the suit is to oppose the E.U.'s enactment of a Biotechnology Directive that prohibits these nations from maintaining their traditional opposition to life patents per se[223] and instead creates substantive rights beyond those previously available in national law.[224]

Although the French government is not a party to the lawsuit challenging the Biotechnology Directive, French officials are especially vigorous in their efforts to circumscribe the patenting of human DNA sequences. French President Jacques Chirac has stressed "the need to prevent any 'possibility of patenting the discovery of a gene,' except for its 'therapeutic or diagnostic applications.'"[225] Another French government official declared the Biotechnology Directive "incompatible with French law in general, with the 1994 law on bioethics, with the code on industrial property and with the French code of civil

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European Court of Justice rules on the issue, all member states remain bound by the Biotechnology Directive and therefore are obligated to amend their national laws in conformance with it. Frequently Asked Questions, supra note 34.

222 See *Netherlands*, 1998 O.J. (C 378) at 13-14 (setting forth grounds for Netherlands' legal challenge to Biotechnology Directive). See generally Scott, supra note 221 (examining legal bases for Netherlands' challenge to Biotechnology Directive).

223 See, e.g., Sven J.R. Bostyn, The Patentability of Genetic Information Carriers, 3 Intell. Prop. Q. 1, 14 n.61 (1999) (stating that Dutch government has "often held, in contradiction to the text of the Dutch Patent Act . . . , that plants are not patentable"); id. at 24 n.18 (describing Article 3 of Dutch Patent Act of 1995, which provides that "animals can only be patented in very specific circumstances, i.e. if a licence has been granted for specific types of research pursued on these animals").

224 Although the Recitals of the Biotechnology Directive indicate that E.U. institutions merely are pursuing the goal of harmonization, see Biotechnology Directive, supra note 142, ¶¶ 3, 5, 6, and 7, at 13, without creating a separate body of patent law that offers rights beyond those available under national laws, id. ¶ 8, at 13, some European scholars agree that the Biotechnology Directive indeed does create new rights. According to one commentator, "EU institutions are pursuing the goal not only of harmonising intellectual property legislation, but also, and at least as vigorously, of strengthening it at the same time." Thomas C. Vinje, Harmonising Intellectual Property Laws in the European Union: Past, Present and Future, 17 Eur. Intell. Prop. Rev. 361, 361 (1995). Indeed, this view is supported by language in the Biotechnology Directive, which, despite asserting that "legal protection of biotechnological inventions does not necessitate the creation of a separate body of law in place of the rules of national patent law," nonetheless provides that those national rules "must be *adapted or added to* in certain specific respects in order to take adequate account of technological developments involving biological material which also fulfill the requirements for patentability." Biotechnology Directive, supra note 142, ¶ 8, at 13 (emphasis added).

225 MEPS Clamour for Ad-Hoc Bioethics Committee, Eur. Rep., Sept. 2, 2000, available at LEXIS, World News Library, European News Sources File. President Chirac also emphasized, four days after the joint HGP-Celera announcement regarding the sequencing of the human genome, see supra note 36 and accompanying text, the importance of "the non-marketing of the human body, free access to knowledge about the gene and the sharing of this knowledge." Id.

law which prohibits the commercialisation of the human body."[226] Indeed, France amended its Intellectual Property Code so as to declare unpatentable "the human body and its elements and products, as well as knowledge of the total or partial structure of a human gene."[227]

Support for the Member States opposed to the Biotechnology Directive comes from the Parliamentary Assembly of the Council of Europe,[228] which has called for a moratorium on implementing the Biotechnology Directive, as well as "suspension of all patent attributions on the human genome."[229] Two European politicians, one French and one German, launched the SOS Human Genome initiative, urging parliamentarians throughout the E.U. Member States both to vote against any national attempt to implement the Biotechnology Directive and to persuade the EPO to stop issuing patents on plants, genes, and animals pending a renewed public debate on the Biotechnology Directive.[230]

Thus, the E.U. faces more vigorous public dissent with respect to patents on life forms, including DNA sequence patents, than does the United States. This dissent derives in part from the distinctively European perspective that morality ought not be compromised for the purpose of making a profit. In addition, European law permits individual citizens to challenge a patent on moral and ethical grounds, while U.S. law does not.[231] While both the United States and the E.U. ostensibly regard isolated and purified human DNA sequences as patentable subject matter,[232] the dissent in Europe regarding the morality of such

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226 Biotechnology: Community Law Takes Precedence Over National Law, Eur. Rep., June 21, 2000, available at LEXIS, World News Library, European News Sources File.

227 Law No. 94-653 of July 29, 1994, J.O., July 30, 1994, p. 11,056-59 (Fr.), D.S.L. 1994, 406-09, reprinted in World Health Org., 45 Int'l Dig. Health Legis. 494, 498-99 (1994) (English translation).

228 The Council of Europe, an intergovernmental organization of forty-three nations that have joined to "protect human rights" and "seek solutions to problems facing European society," is distinct from the E.U., though all of the E.U. member states are members of the Council of Europe. Council of Europe, An Overview, at http://www.coe.int (last modified Aug. 22, 2001).

229 Abbott & Hellerer, supra note 220, at 802.

230 Id.; see also Biotechnology: Council of Europe Calls for Revision of Biotechnology Directive, Eur. Rep., July 5, 2000, available at LEXIS, News Library, European News Sources File (describing efforts of Council of Europe's Parliamentary Assembly to urge E.U. member states to delay implementation of Biotechnology Directive pending renegotiation).

231 E.U. citizens, unlike their U.S. counterparts, possess legal standing to challenge the morality of biotech inventions under both the Directive and the EPC. See Breffni Baggot, Legislating a Transgenics Revolution, Intell. Prop. Mag., May 1998, available at LEXIS, News Library, Intellectual Property Magazine File; see also Animal Legal Defense Fund v. Quigg, 932 F.2d 920, 930-31 (Fed. Cir. 1991) (denying U.S. animal rights group standing to challenge PTO's intent to recognize patentability of animals).

232 See supra notes 125-27, 169-72 and accompanying text.

patents threatens to rupture prior U.S.-E.U. agreement on this principle.

E. Moral and Ethical Arguments Supporting Patents on Human DNA Sequences

In response to those human rights activists, religious adherents, and medical practitioners who strongly oppose human DNA sequence patents on moral and ethical grounds, certain bioethicists have advanced countering views. According to utilitarians, patenting of human DNA sequences is moral because it is likely to lead to medical innovations that promote the greatest happiness for the greatest number.[233] Absent the limited monopoly afforded by patent protection, inventors would be discouraged from investing in the costly research and development[234] necessary to bring to market pharmaceutical products and diagnostic tests that promote human health.[235] For ex-

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233 For an overview of the views of Jeremy Bentham, one of the most influential utilitarians, see David Baumgardt, Bentham and the Ethics of Today 171 (1952).

234 It can cost $200 million to $350 million and take from seven to twelve years for development and government approval of a biotechnology drug. Biotechnology Industry Organization (BIO), at http://www.bio.org/aboutbio/guide2000/guide_health.html (last modified Aug. 22, 2001).

235 See Doll, supra note 139, at 690 ("It is only with the patenting of DNA technology that some companies, particularly small ones, can raise sufficient venture capital to bring beneficial products to the marketplace or fund further research."); Frequently Asked Questions, supra note 34 (

> Without the safeguard provided by patents, industry and other inventors would be unwilling to invest their time and money in research and development. . . . Indeed given the considerable amount of high risk investment that is often required in the area of biotechnology, particularly in the field of genetic engineering, adequate patent protection is even more essential to encourage the investment required to create jobs and maintain the European Union's competitiveness in this crucial field.).

Patents also stimulate biotechnological innovation by requiring full disclosure of the patented subject matter to the public. Without such protections, inventors would invoke the trade secrets doctrine, thereby engendering duplicative and superfluous research that might itself be considered immoral. Scalise & Nugent, supra note 96, at 997. Indeed, as noted by Professor Schatz, Scottish researchers delayed their public announcement of Dolly, the cloned sheep, until just before the publication of the European patent application. Without patent protection for biotech engineering inventions, many scientists would continue to pursue such research and simply safeguard their economic interests by shrouding their findings in secrecy. Ulrich Schatz, Patentability of Genetic Engineering Inventions in European Patent Office Practice, 29 Int'l Rev. Indus. Prop. & Copyright L. 2, 2 n.1 (1998).

Finally, the patent system "encourages competition to 'invent around' or improve upon a patented invention." Reid G. Adler, Controlling the Applications of Biotechnology: A Critical Analysis of the Proposed Moratorium on Animal Patenting, 1 Harv. J.L. & Tech. 1, 11 (1988); see also Patents and the Constitution: Transgenic Animals: Hearings Before the Subcomm. on Courts, Civil Liberties, and the Administration of Justice of the House Comm. on the Judiciary, 100th Cong. 27 (1987) (testimony of Dr. Rene Tegtmeyer, Assistant Commissioner for Patents, U.S. Patent and Trademark Office) ("What it really

ample, while Scottish bacteriologist Alexander Fleming discovered penicillin, it was not until Andrew Moyer, an employee of the U.S. Department of Agriculture, patented it that U.S. pharmaceutical firms manufactured this life-saving drug on a large scale.[236]

Bioethicists also emphasize that intellectual property rights in human DNA should not be equated with ownership of an individual person's genes.[237] Rather, the patentholder has rights in isolated and purified genetic material.[238] Moreover, patent rights in other human body parts are generally accepted in our society. According to David Resnik, a bioethicist at East Carolina University in North Carolina,

> A human gene patent would be analogous to a patent for making or manipulating other kinds of human body parts, such as hair, bones, or hearts. . . . If the patenting of technologies for transplanting, growing, analyzing or modifying bone marrow is morally acceptable, then [so is] the patenting of human genetic technologies.[239]

Such ethical and moral arguments in support of intellectual property rights in human DNA sequences are unlikely to persuade the opposition. Yet, while that opposition remains strongly committed to its cause, it is unlikely to succeed in bringing about a complete ban on DNA sequence patents in either the United States or the E.U. for two reasons. First, antipatenting forces are underfunded and poorly organized as compared to the biotech lobby.[240] Second, as stated earlier, courts and patent offices in both the United States and the E.U. are under pressure to adopt a liberal attitude toward the grant of patents in order to attract foreign direct investment.[241] Failure to do so leads domestic biotech firms to depart to other locales.[242] And while opposition to human DNA sequence patents is more vigorous in the E.U. than in the United States, as demonstrated by current challenges

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does when a patent is granted is stimulate others to invent around it, to improve upon it, to find a different way to do the same thing . . . .").

236 James Meek, Who Owns the Genome?: Patenting Our Genes, Guardian (London), June 26, 2000, Supp. (The Story of Life) at 8.

237 The EPO recognized this idea in the *Relaxin* case, stating that "[i]t cannot be overemphasized that patents covering DNA encoding human H2-relaxin, or any other human gene, do not confer on their proprietors any rights whatever to individual human beings." Hormone Relaxin, 1995 O.J. E.P.O. 388, 402 (Opp. Div.).

238 See Reynolds, supra note 177, at 184. See supra notes 130-138 and accompanying text for a discussion of the isolation and purification of human DNA sequences.

239 Reynolds, supra note 177, at 184.

240 See Martin Bobrow & Sandy Thomas, Patents in a Genetic Age, 409 Nature 763, 764 (2001) (noting that commercial interests are well represented before patent offices and, in United States, "industrial lobbies have been influential in Congress and the Senate in maintaining what is essentially a pro-patent, liberal policy-framework for biotechnology").

241 See supra notes 84-85 and accompanying text.

242 See supra note 220 and accompanying text.

to the new Biotechnology Directive,[243] the granting of patents for human DNA sequences likely will continue there as well.

Clearly, moral and ethical dilemmas such as these do not lend themselves to resolution through legislative and judicial pronouncements.[244] Patents on fully sequenced human DNA will surely remain anathema to their most steadfast opponents. The debate becomes more complex as it relates to patenting DNA of *unknown* function, such as homologous DNA sequences.[245] Even those who generally favor DNA patenting protest that such a DNA sequence does not satisfy the utility criterion and therefore should remain unpatentable until researchers have fully characterized its function.

III
DO HUMAN DNA SEQUENCES SATISFY THE UTILITY CRITERION OF PATENTABILITY UNDER U.S. AND E.U. LAW?

The debate over the patent awarded to HGS for the CCR5 receptor gene also raises the issue of the utility, or function, of an invention. Although HGS freely admits that it did not know the gene's role in the HIV virus at the time it filed its patent application, the company nonetheless can command royalties from others who pursue any future research involving the gene, including with respect to its role in HIV.[246] HGS's ability to block others from using the CCR5 gene arises ineluctably from current gene-hunting methods. When inventors first began obtaining gene patents in the 1970s and 1980s, they unfailingly were able to meet the utility criterion because they often started with a known protein and "reverse-engineered" their way back to the encoding gene.[247] Beginning with the inception of the Human Genome Project,[248] however, some researchers decided to pursue a

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243 See supra notes 221-30 and accompanying text.

244 See Michael E. Sellers, Patenting Nonnaturally Occurring, Man-Made Life: A Practical Look at the Economic, Environmental, and Ethical Challenges Facing Animal Patents, 47 Ark. L. Rev. 269, 290-91 & n.144 (1994) (explaining that it is "unlikely that legislative or judicial line-drawing on [animal patenting] will substantially affect a particular person's beliefs").

245 See supra notes 10-13 and accompanying text.

246 See supra note 12 and accompanying text.

247 Enserink, supra note 11, at 1196. Traditionally, scientists identified genes by first focusing on a disease they wanted to cure. Then they isolated the protein underlying the disease. Next, using the amino acid structure of the protein, they deduced the genetic code sequences producing the protein. Finally, through rigorous experimentation and, quite often, luck, scientists would locate the gene of interest on its chromosome and extract it. Herman, supra note 207; see also Reid G. Adler, Genome Research: Fulfilling the Public's Expectations for Knowledge and Commercialization, 257 Science 908, 908 (1992) (discussing reverse-engineering process).

248 See supra note 16.

sequence-based approach to locating genes.[249] Using this approach, HGS was able to deduce the receptor function of the CCR5 receptor gene simply by comparing the gene with other genes of similar sequence, known as homologous genes.[250] Not until about six months later did other groups of scientists identify the several receptors that HIV uses to slip into the gene, and by that time HGS already had filed its patent claim.[251] Presently, HGS has agreements with pharmaceutical partners that allow those partners to use the gene in AIDS drug development, and HGS itself plans to develop antibody-based therapies to treat HIV infection.[252]

In a recent revision to its utility examination guidelines, the PTO has announced its intention to continue granting patents for homologous DNA sequences.[253] In the E.U. as well, homologous DNA sequences likely are patentable under the Biotechnology Directive. Scholars and researchers the world over, primarily those in the public sector and nonprofit communities, fear that a proliferation of such patents will impede future research. They warn that, forced to negotiate a complex web of licensing arrangements and confronted with prohibitive royalty fees, scientists will be dissuaded from conducting further experimentation. Conversely, international biotech firms demand increased patent protection that they claim is necessary to safeguard their investments. This gives rise to a conflict that transcends national borders, and the lack of coordination between U.S. and E.U. policies threatens international scientific collaboration.

A. The Patentability of Homologous Gene Sequences in View of the Utility Requirement Under U.S. Law

Under the Patent Act,[254] an invention must be useful to qualify for patent protection.[255] This requirement reflects the notion that patent law is based upon contract law: In return for patent protection, an inventor offers valuable consideration by disclosing a useful technological advance to the public.[256] In general, an invention will meet the

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249 Adler, supra note 247, at 908; see also supra note 37 regarding the sequencing techniques of Celera and the HGP.

250 See supra notes 10-11 and accompanying text.

251 See supra note 12 and accompanying text.

252 Marshall, supra note 4.

253 See infra notes 275-77 and accompanying text.

254 See supra note 87 and accompanying text.

255 35 U.S.C. § 101 (1994).

256 See, e.g., Bonito Boats, Inc. v. Thunder Craft Boats, Inc., 489 U.S. 141, 150-51 (1989) ("The federal patent system thus embodies a carefully crafted bargain for encouraging the creation and disclosure of new, useful and nonobvious advances in technology and design

utility standard if it actually works to achieve at least one of its stated purposes.[257]

In addition to meeting the general utility standard, a patent application claiming chemical processes and compounds, such as a gene patent, must meet a heightened utility standard, called "practical utility," that was established by the Supreme Court in the 1966 case *Brenner v. Manson*.[258] In *Manson*, the Court held that, in order to satisfy the utility requirement, a chemical invention must be useful for something other than chemical or pharmaceutical research.[259]

The applicant in *Manson* sought a patent for a process for synthesizing a certain class of steroids.[260] Although the applicant presented evidence that the products of the applicant's process were homologues[261] of a steroid known to be effective in treating tumors in mice, the PTO denied a patent on the grounds of lack of utility.[262] On appeal, however, the Court of Customs and Patent Appeals[263] held that the invention possessed utility.[264] The Supreme Court reversed, with its famous declaration that "a patent is not a hunting license."[265] According to the Court, an invention is not patentable unless it demonstrates "substantial" utility, meaning that "specific benefit exists in currently available form."[266] The Court reasoned that issuing broad patents that offer no clear benefits threatens to create "a monopoly of knowledge" that "may confer power to block off whole areas of scien-

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in return for the exclusive right to practice the invention for a period of years."); see also Machin, supra note 88, at 424-25 (exploring contract rationale of utility requirement).

257 See 1 Chisum, supra note 1, § 4.01, at 4-2 to 4-2.1, 4-42 (2000 & Supp.). Thus, after it has been isolated and purified, a full gene sequence is patentable once it has been characterized, meaning that the gene's function, i.e., the protein for which it codes and the role of that protein, is known. See, e.g., Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501 (Fed. Cir. 1997) (upholding patent grant for DNA sequence coding for human insulin growth factor-I, growth-promoting protein that mediates effects of human growth hormone); Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1206 (Fed. Cir. 1991) (upholding patent on purified and isolated gene sequence encoding human erythropoietin).

258 383 U.S. 519 (1966).

259 Id. at 535-36.

260 Id. at 520-21.

261 The *Manson* Court defined a homologue as one member of "a family of chemically related compounds, the composition of which varies from member to member by CH_2 (one atom of carbon and two atoms of hydrogen). . . . Chemists knowing the properties of one member of a series would in general know what to expect in adjacent members." Id. at 522 n.3 (quoting Application of Henze, 181 F.2d 196, 200-01 (1950)).

262 Id. at 521.

263 The Court of Customs and Patent Appeals (C.C.P.A.) is the predecessor to the Court of Appeals for the Federal Circuit. See Rai, supra note 14.

264 *Manson*, 383 U.S. at 522.

265 Id. at 536.

266 Id. at 534-35.

tific development, without compensating benefit to the public."[267] This warning articulated by the *Manson* Court fuels those opposed to patents on partial gene sequences of unknown function, who contend that such patents will serve only to foreclose future research on human DNA sequences.

The courts initially embraced and extended the *Manson* holding in two companion cases, *In re Kirk*[268] and *In re Joly*.[269] In the former case, the Court of Customs and Patent Appeals held that chemical products that were useful only as intermediates in the production of other chemicals without known utilities were not patentable due to lack of utility.[270] In the latter, the court ruled that chemical processes for generating the chemical intermediates for products without known utilities were similarly unpatentable.[271]

Manson represents prevailing law, as the Supreme Court has not considered practical utility since that decision, nor has Congress enacted legislation superseding the *Manson* Court's holding with respect to utility. Pursuant to *Manson*, one would expect the PTO to deny patent protection to homologous DNA sequences such as the CCR5 receptor gene, since the inventor asserts only a "theoretical," not a definite, gene function.[272] However, beginning in the 1990s, the PTO and the Federal Circuit have backed away from the practical utility standard articulated in *Manson*,[273] demonstrating greater willingness to recognize the patentability of human DNA sequences.[274]

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267 Id. at 534.

268 376 F.2d 936 (C.C.P.A. 1967).

269 376 F.2d 906 (C.C.P.A. 1967).

270 *In re Kirk*, 376 F.2d at 945.

271 *In re Joly*, 376 F.2d at 908-09.

272 See Enserink, supra note 11, at 1197.

273 Adler argues that *Manson* was intended to be a narrow decision in any event, because the patent applicant did not assert any utility and relied entirely on speculation. See Adler, supra note 247, at 911. This view is supported by Judge Rich's lengthy dissent in *In re Kirk*, which argues vociferously against extending the *Manson* holding beyond the facts of that case. See *In re Kirk*, 376 F.2d at 947-66 (Rich, J., dissenting).

274 See Rai, supra note 14, at 106-09 (describing PTO and Federal Circuit liberalization of utility requirement); Machin, supra note 88, at 429 (same). For example, in 1995 the PTO announced new guidelines relating to ESTs, see supra note 207, that lowered the utility threshold. See Patent and Trademark Office Utility Examination Guidelines, 60 Fed. Reg. 36,263, 36,264 (July 14, 1995) (asserting that rejection for lack of utility is inappropriate if applicant makes assertion of utility that would be credible to person of ordinary skill in field or if invention has well-established utility). The PTO also announced in 1997 that it would grant patents on ESTs, based on the recognition that their utility lay in "their potential use as probes to detect the expression of the corresponding gene." US Patents on ESTs 'to be Permitted', 385 Nature 670, 671 (1997). Then, in November 1998, Incyte announced that, in the previous month, the PTO had awarded it the first patent for an EST. Tony Reichhardt, Patent on Gene Fragments Sends Researchers a Mixed Message, 396 Nature 499, 499 (1998). It should be noted, however, that there was some debate

While the PTO did implement, in January 2001, a heightened utility standard for patent examiners,[275] the new guidelines nonetheless presume the utility of a claimed homologous DNA sequence unless the PTO satisfies its considerable burden to rebut this presumption.[276] According to the PTO Utility Examination Guidelines,

> when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion. A "rigorous correlation" need not be shown in order to establish practical utility; "reasonable correlation" is sufficient.[277]

The PTO's director of biotechnology has asserted that such searches have become "very well established and very well accepted in the academic community."[278] Moreover, the new PTO Guidelines confirm the existing legal principle that "[a] patent on a composition gives *exclusive* rights to the composition for a limited time, even if the inventor disclosed only a single use for the composition."[279] Thus, when a company such as HGS deduces one function of a gene, as in the case of the CCR5 receptor gene, it can preclude other researchers from obtaining any patents relating to other functions of the same gene. As of May 2000, companies like HGS and Incyte had filed thousands of

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as to whether Incyte's invention was actually an EST, since the company's claim encompassed a full-length gene and highly characterized fragments, as opposed to mere fragments of unknown function. Id.; see also Holman & Munzer, supra note 5, at 770-71 (noting that Incyte patent claims for EST actually specified utility, unlike most such applications).

275 See Patent and Trademark Office Utility Examination Guidelines, 66 Fed. Reg. 1092, 1098 (Jan. 5, 2001) (requiring patent application for purified and isolated gene to demonstrate specific, substantial and credible utility). According to John Doll, the PTO's director of biotechnology, the revised guidelines represent a "significant change" with respect to ESTs, which "will have a difficult time" meeting the utility requirement. Enserink, supra note 11, at 1197. Under the revised guidelines, the PTO may begin to reject the millions of EST patent applications claiming unspecific utility, such as potential use in forensic science or in locating genes on a chromosome. See id.

276 Patent and Trademark Office Utility Examination Guidelines, 66 Fed. Reg. at 1096. But see Smaglik, supra note 4, at 322 (suggesting that PTO might have denied HGS's patent application for CCR5 receptor gene under revised PTO guidelines).

277 Patent and Trademark Office Utility Examination Guidelines, 66 Fed. Reg. at 1096 (internal quotation omitted).

278 Enserink, supra note 11, at 1197.

279 Patent and Trademark Office Utility Examination Guidelines, 66 Fed. Reg. at 1095. U.S. law, however, does allow an inventor who develops a new use of a patented compound to get a process patent for that new use, notwithstanding that the DNA is itself patented. See id.

patent applications based on DNA sequence similarity. The PTO already has awarded hundreds of them.[280]

B. *The Patentability of Homologous Gene Sequences in View of the Utility Requirement Under E.U. Law*

Europe, like the United States, recently has strengthened its industrial applicability, or utility,[281] standard with respect to biotech patents. Under the EPC, European patent examiners and courts traditionally applied the utility requirement rather liberally as compared to their U.S. counterparts. Article 52 of the EPC provides that a claimed invention has to be susceptible of industrial application in order to be patentable,[282] and Article 57 further explains that "[a]n invention shall be considered as susceptible of industrial application if it can be made or used in any kind of industry, including agriculture."[283] Thus, a claimed invention satisfies the industrial applicability requirement if the "subject matter of the invention can be *manufactured or used* in any kind of industry."[284] Unlike U.S. law, the EPC requirement "does not signify that, in order to be patentable, an invention must represent a technical progress, nor that it should have any useful effect."[285] In this respect, the EPC, and the corresponding national laws that have been amended in conformance with it, are in conflict with the Biotechnology Directive, which establishes for human DNA sequences a heightened utility standard akin to the U.S. utility criterion.[286]

The Biotechnology Directive provides in Article 5(3) that "[t]he industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application."[287] While this language appears simply to reiterate EPC Article 57, scholars have questioned why the framers expressly restated the industrial-application requirement in the Biotechnology Directive.[288] Examination of Recitals 23 and 24 of the Biotechnology Directive makes abundantly clear that

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280 Boyce & Coghlan, supra note 4, at 15.

281 These two terms will be used interchangeably with respect to E.U. patent practice. See supra note 146.

282 See supra note 145 and accompanying text.

283 EPC, supra note 141, art. 57, at 273.

284 Andreas Oser, Patenting (Partial) Gene Sequences Taking Particular Account of the EST Issue, 30 Int'l Rev. Indus. Prop. & Copyright L. 1, 8 (1999). In the United States, *Manson* established that usefulness for research is not sufficient to satisfy the utility criterion. See supra text accompanying note 259.

285 Sterckx, supra note 191, at 11.

286 See Oser, supra note 284, at 8-9.

287 Biotechnology Directive, supra note 142, art. 5.3, at 18.

288 Professor Bostyn, puzzled by the "unclear meaning" of Article 5(3) of the Biotechnology Directive, queries:

the Directive requires patent applications for human DNA sequences to meet a higher standard of industrial application. Recital 23 declares that "a mere DNA sequence without indication of a function does not contain any technical information and is therefore not a patentable invention."[289] Furthermore, Recital 24 requires that

> in order to comply with the industrial application criterion it is necessary in cases where a sequence or partial sequence of a gene is used to produce a protein or part of a protein, to specify which protein or part of a protein is produced or what function it performs[.][290]

Nevertheless, as in the United States, no patent protection is available to researchers who subsequently discover different functions for genetic information that already has been patented by a previous inventor.[291]

C. The Tragedy of the Commons: Public Policy Arguments in the United States and the E.U. Against Patenting Human DNA Sequences of Unknown Function

While both the United States and E.U. recently have strengthened their respective utility criteria for human DNA sequences, many scholars and researchers, particularly in the public sector, contend that current utility standards remain too lax. In their view, genetic patents based purely on homology, such as the CCR5 receptor gene, will hinder future biotechnological research, and, most especially, international collaboration. According to Maria Freire, director of the Office of Technology Transfer at NIH, "[I]n 3 or 5 years, people can come and say: 'Hey, you can't be working on that gene. That's mine,' . . . [t]hat's a very scary proposition."[292] Likewise, University of Penn-

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> Was it merely the intention of the drafters to emphasise the industrial applicability criterion which must be fulfilled for any invention? If this was the case, adding this subsection was superfluous and could as well be left aside. Or was it the intention of the drafters to limit the scope of protection of this type of inventions to the application mentioned in the patent application[?]

Bostyn, supra note 223, at 7; see also Oser, supra note 284, at 7-8 (observing that Article 5(3) of Directive likely is intended to heighten utility requirement for human DNA sequence patents).

289 Biotechnology Directive, supra note 142, ¶ 23, at 15.

290 Id., ¶ 24, at 15.

291 See Region Watch, Instrument Bus. Outlook, Sept. 15, 2000, available at 2000 WL 15416037 [hereinafter Region Watch]. However, the Biotechnology Directive does provide for the situation where DNA sequences claimed by inventors overlap each other partially. According to Recital 25 of the Biotechnology Directive, "for the purposes of interpreting rights conferred by a patent, when sequences overlap only in parts which are not essential to the invention, each sequence will be considered as an independent sequence in patent law terms." Biotechnology Directive, supra note 142, ¶ 25, at 15.

292 Enserink, supra note 11, at 1196-97.

sylvania bioethicist Jon Merz warns that patents such as those on the CCR5 receptor gene could prove a disincentive for scientists who do not hold the rights, whose "'research would be immediately taxed if it was ever fruitful.'"[293] Thus, patentholders would "have little incentive to continue to a full characterization of the gene product—but could claim the rights to the results of other researchers who later did this."[294] According to Merz, this scenario is likely to "'tie up the development of therapeutics based on the gene.'"[295] This problem is exacerbated when it involves researchers from different nations in competition with one another to attract biotechnology investment. As one biotechnology lawyer stated with regard to partial gene sequences of unknown function: "'What if the gene turns out to be linked to another gene that the French have licensed? . . . I'm not going to invest a million dollars with that kind of uncertainty.'"[296]

Those who contend that homologous DNA sequences fail to satisfy the utility criterion emphasize that it is extremely difficult to make an accurate prediction of the biological function of a protein solely on the basis of the similarity of its sequence to another one.[297] At the time the current PTO utility guidelines[298] were proposed in December

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293 Boyce & Coghlan, supra note 4, at 15 (quoting Jon Merz).

294 Dickson, supra note 11, at 3. Some critics of such broad rights use the term "submarine patent" to refer to "a broad early claim" that remains quietly submerged at the PTO "only to surface when another inventor's work gives it commercial significance." Regalado, supra note 41, at 51. As described by one commentator,

> [a]n inventor . . . files an application with broad claims . . . and then files a series of continuing applications to keep the patent submerged in the patent office; then, one day, someone innocently decides to use the yet to be patented idea, and after they begin production, the inventor surfaces the application through its issuance, and demands the payment of royalties, lest a lawsuit will be filed for infringement.

Steve Blount, The Use of Delaying Tactics to Obtain Submarine Patents and Amend Around a Patent That a Competitor Has Designed Around, 81 J. Pat. & Trademark Off. Soc'y 11, 13 (1999); see also Renewed Fight over Gene Patent Policy, 276 Science 187, 187 (1997) (referring to submarine patents in context of ESTs).

295 Boyce & Coghlan, supra note 4, at 15 (quoting Jon Merz). Nonprofit researchers also fear that biotech companies that possess patent rights to a human gene will exploit that monopoly in detrimental ways. For example, instead of granting others a license to conduct further research, such a biotech firm might instead "'promote genetic tests which are still in many ways experimental.'" Krimsky, supra note 14, at 27 (quoting Jon Merz). Moreover, the profit motive might lead the patent owner to conduct genetic tests without providing the proper genetic counseling. See Naysmith, supra note 186 (describing reaction of British NHS to Rosgen's announcement that it had obtained exclusive U.K. license to screen for breast cancer). For a discussion of the Rosgen license, see supra notes 195-203 and accompanying text.

296 Christopher Anderson, US Patent Application Stirs Up Gene Hunters, 353 Nature 485, 486 (1991).

297 See Dickson, supra note 11, at 3 (stating argument that "a difference in a single base pair in a DNA sequence can have important functional implications").

298 See supra notes 275-77 and accompanying text.

1999, then-NIH director Harold Varmus, along with Francis Collins, director of the HGP, wrote to the PTO Commissioner that they were "very concerned with the PTO's apparent willingness" to grant claims based on "theoretical" functions, arguing that while databases may help researchers develop hypotheses about a gene's function, these databases do not furnish determinative proof of such function, much less give researchers new ideas for pharmaceutical products.[299]

Professors Heller and Eisenberg have dubbed this dilemma "the tragedy of the anticommons," explaining it as follows:

> Thirty years ago in *Science*, Garrett Hardin introduced the metaphor 'tragedy of the commons' to help explain overpopulation, air pollution, and species extinction. People often overuse resources they own in common because they have no incentive to conserve. . . . Although the metaphor highlights the cost of overuse when governments allow too many people to use a scarce resource, it overlooks the possibility of underuse when governments give too many people rights to exclude others. Privatization can solve one tragedy but cause another.[300]

The tragedy, as articulated by Professors Heller and Eisenberg, is that "[a] proliferation of intellectual property rights upstream may be stifling life-saving innovations further downstream in the course of research and product development."[301] This is because "[e]ach upstream patent allows its owner to set up another tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation."[302] Because the commercial products of genetic research often require the use of several gene fragments, each of which may be patented by a different person or entity, the licensing arrangements that must be obtained in order to develop those products could prove prohibitively expensive.[303] For example, Dr. William Haseltine of HGS has remarked that researchers who create inventions involving the CCR5 receptor gene could obtain separate patents which complement the HGS patent, resulting in a scenario where drug developers would have to pay several entities in order to produce one drug.[304] The NIH, along with many publicly

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299 Enserink, supra note 11, at 1197 (internal quotation marks omitted).

300 Michael A. Heller & Rebecca S. Eisenberg, Can Patents Deter Innovation? The Anticommons in Biomedical Research, 280 Science 698, 698 (1998) (citations omitted).

301 Id.

302 Id. at 699.

303 Id.

304 Smaglik, supra note 4, at 322. One example of a compound that eventually might merit a complementary patent is a small CCR5-binding molecule that Schering-Plough Corporation is in the process of developing. However, Schering-Plough maintains that it may not be subject to HGS's intellectual property rights because it commenced work on the compound before the PTO approved HGS's patent application. Id.

funded scientists, objects to this scenario and therefore opposes even the stricter new PTO guidelines, arguing that "no DNA patent should be granted unless researchers know a gene's full sequence and have figured out what protein it produces and what that protein does in the cell."[305]

E.U. researchers are in accord with their U.S. colleagues, as demonstrated by a joint article authored by the President of the U.S. National Academy of Sciences and the President of the Royal Society of London, who admonish that

> [t]hose who would patent DNA sequences without real knowledge of their utility are staking claims not only to what little they know at present, but also to everything that might later be discovered about the genes and proteins associated with the sequence. They are, in effect, laying claim to a function that is not yet known or a use that does not yet exist. This may be in current shareholders' interests. But it does not serve society well.[306]

Like their counterparts in the United States, E.U. researchers in the nonprofit and public sectors fear that patents on human DNA sequences of unknown function will stifle basic genomics research and competition for pharmaceutical innovation. In Germany, for example, two prominent leaders of research organizations urged Wolf-Michael Catenhusen, the German science ministry's secretary of state for research, to interpret the EPC and the Biotechnology Directive so as to preclude patents that cover "all possible applications of a particular gene sequence."[307] They insist, in the alternative, that patents should be restricted to identified functions, lest the owner of a patent on a gene sequence block the commercialization of any newly discovered function of this sequence, or else demand a licensing fee.[308]

The German government has responded to the arguments of its research community by drafting legislation that appears to "defy the spirit, if not the letter," of the Biotechnology Directive.[309] Under the proposed legislation, an inventor could patent a DNA sequence only

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305 Enserink, supra note 11, at 1196.

306 Bruce Alberts & Sir Aaron Klug, The Human Genome Itself Must Be Freely Available to All Humankind, 404 Nature 325, 325 (2000). This statement echoed an earlier one by the Human Genome Organization (HUGO), the predecessor of the HGP, which declared in 1995 that "HUGO is worried that the patenting of partial and uncharacterized cDNA sequences will reward those who make routine discoveries but penalize those who determine biological function or application. Such an outcome would impede the development of diagnostics and therapeutics, which is clearly not in the public interest." Reynolds, supra note 177, at 184.

307 Schiermeier, supra note 10, at 111.

308 Id.

309 Ralph Atkins & Timm Krägenow, Germany Imposes Extra Gene Patent Limits, Fin. Times (London), Aug. 11, 2000, at 6.

after specifying a detailed function. Moreover, if subsequent researchers later determined that the DNA segment was involved in other illnesses, the original patentholder would not be entitled to royalties on diagnostics and therapeutics related to those other maladies.[310] According to the German education and science minister, the proposed legislation is intended to "make sure innovation is not obstructed and researchers have legal security."[311]

D. Industry Arguments in the United States and the E.U. Supporting Patent Protection for Homologous DNA Sequences

In response to the public-sector and nonprofit researchers who oppose patenting homologous DNA sequences on the grounds of utility, many private biotechnology firms tout the scientific accuracy of such gene-searching methods. PTO biotechnology director John Doll states that "[s]cientifically, it's very well established and very well accepted in the academic community" to search sequence databases for homologous genes, and Incyte's general counsel emphasizes that "[e]verybody uses these techniques and they are virtually 100% correct."[312]

Biotech industry leaders also emphasize that strong patent protection ensures both investment in, and dissemination of, research. First, they contend that, absent strong intellectual property protection, pharmaceutical firms would not risk large sums on developing and marketing gene-based drugs.[313] In particular, patent protection permits small firms to raise sufficient venture capital to conduct research and development.[314] Moreover, absent patent protection, biotech firms would protect their research as a trade secret rather than sharing it with others.[315] Certainly, the absence of adequate patent protection can spur biotech firms to relocate.[316] Finally, private industry also em-

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310 Id.

311 Id.

312 Enserink, supra note 11, at 1197. Interestingly, assertions that the detection of homologous sequences is commonly accepted and routine can detract from claims of nonobviousness. See infra note 329 and accompanying text.

313 See Doll, supra note 139, at 690; see also Enserink, supra note 11, at 1196; Heller & Eisenberg, supra note 300, at 698 ("Patents and other forms of intellectual property protection for upstream discoveries may fortify incentives to undertake risky research projects and could result in more equitable distribution of profits across all stages of R&D.").

314 Doll, supra note 139, at 690. In contrast, French public-sector researchers financed their human genome map through annual telethons. Clive Cookson, A Spur for the Gene Hunters, Fin. Times (London), Dec. 20, 1993, at 12.

315 See Doll, supra note 139, at 690 (explaining that "strong U.S. patent system is critical" to dissemination of DNA sequence information); see also supra note 235.

316 See supra note 220 and accompanying text.

phasizes that competition is beneficial for the public sector, because it expedites the rate of discovery. For example, there is no question that the HGP accelerated its pace to compete with Celera in the race to decode the human genome.[317]

Even within the biotech industry, however, opinion is divided as to the wisdom of patenting DNA sequences of unknown function. For example, Dr. Robert I. Levy of American Home Products[318] calls the gene-patenting situation a "minefield," citing the difficulty of ascertaining who owns the rights to which genetic sequences and tools, as well as the high royalty fees, which can total twelve percent to fourteen percent of the cost of a drug.[319] Increasingly, those firms that focus on the development of end products as opposed to upstream research (e.g., large pharmaceutical manufacturers) seek to facilitate access to basic genomic information. For example, Merck & Co. has put into the public domain the results of an EST identification project it sponsored at Washington University.[320] According to Professor Rai, "Merck hopes to take advantage of the efforts of those who will use the results to do fundamental research," believing that "its own comparative advantage lies in using the fundamental research of others to do downstream work directed towards the formulation of particular drugs."[321] Similarly, several pharmaceutical companies have formed a consortium dedicated to identifying and publicizing information about all the single nucleotide polymorphisms (SNPs)[322] in the human genome.[323] According to Arthur Holden, chief executive of the consortium, putting the information in the public domain, and

317 See Wade, supra note 24 (noting that HGP was halfway through its fifteen-year program to sequence human genome by 2005 when Celera commenced its efforts, and that HGP consequently accelerated its schedule); see generally Preston, supra note 16 (profiling Celera's Craig Venter and his role in competition to decode human genome).

318 American Home Products, a publicly traded company based in New Jersey, is engaged in the manufacture and marketing of health products, including pharmaceuticals and medical supplies. American Home Products Corp., LEXIS, News Library, Hoover's Company Profile Database File.

319 Pollack, supra note 178.

320 Rai, supra note 14, at 134; see also Washington University-Merck Human EST Project, at http://genome.wustl.edu/est/esthmpg.html (last modified Sept. 17, 2001).

321 Rai, supra note 14, at 134. According to Professor Dronamraju, another possible explanation of Merck's strategy is that the company plans "to undermine the value of investments already made by its commercial competitors. Such a strategy would force Incyte, HGS and their collaborators to seek patent rights to protect their investments. Merck may be betting that those patent rights will be scarce." Krishna R. Dronamraju, Biological and Social Issues in Biotechnology Sharing 112-13 (1998).

322 Single nucleotide polymorphisms (SNPs) are the genomic differences between individuals and are studied to help determine susceptibility to disease. Pollack, supra note 178.

323 Rai, supra note 14, at 134. Professor Rai notes, however, that this collaboration was not possible until the Wellcome Trust, see supra note 16, agreed to provide approximately half of the consortium's funding. Rai, supra note 14, at 134.

thereby precluding patenting of the SNPs, will "'ensure we have the basic alphabet.'"[324]

Ultimately, the only way to determine the precise parameters of patentability for human DNA sequences of unknown function is to test such patents in the courts. The PTO reportedly is preparing a test case whereby it will agree to grant a patent on such a sequence with full knowledge that the patent will be challenged by a third party.[325]

IV

DO HUMAN DNA SEQUENCES SATISFY THE NONOBVIOUSNESS CRITERION OF PATENTABILITY UNDER U.S. AND E.U. LAW?

The debate as to whether human DNA sequences can satisfy the final major criterion of patentability—nonobviousness, or inventive step[326]—parallels the debate over utility.[327] The policy reason for the nonobviousness requirement is that most technological advances occur incrementally. Awarding patents to obvious inventions would impede innovation by imposing potentially prohibitive licensing fees on subsequent inventors who seek to improve upon these existing inventions.[328] Many researchers in the public and nonprofit communities contend that, with the advent of automated sequencing machines, "virtually any monkey" can generate numerous unidentified gene sequences,[329] and therefore they oppose on the grounds of nonobviousness patents such as the one granted to HGS for the CCR5 receptor gene.

Homologous gene sequences have thus far received patent protection in the United States and the E.U. As gene-sequencing techniques become increasingly routine, however, it grows ever harder to satisfy the nonobviousness criterion.[330] Once again, this issue pits public-sector and nonprofit researchers the world over against international biotech firms, giving rise to a conflict that transcends national

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[324] Pollack, supra note 178 (quoting Arthur Holden).

[325] Enserink, supra note 11, at 1197.

[326] The United States term "nonobviousness" is expressed in the E.U. as "involving an inventive step." See supra note 146.

[327] See supra Part III.

[328] See Ducor, supra note 95, at 16-17.

[329] Roberts, supra note 137, at 184 (quoting James Watson, former director of HGP).

[330] See, e.g., Adler, supra note 247, at 911 ("[R]apid scientific advances first expand and then somewhat contract the boundaries of patentable subject matter as revelatory laboratory techniques quickly become technologically and legally mundane."); Eisenberg, supra note 90, at 730 ("Since the obviousness of an invention is measured against the background of human knowledge at the time the invention is made, this requirement is increasingly difficult to pass as scientific knowledge advances in a field.").

borders. Ultimately, coordination of U.S. and E.U. policies is necessary to preserve international scientific collaboration.

A. *U.S. Legislative and Judicial Application of the Nonobviousness Criterion to Human DNA Sequences of Unknown Function*

The U.S. Patent Act precludes patent protection for an obvious invention, providing that a patent will not be granted if the "differences between the subject matter sought to be patented and the prior art[331] are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains."[332] In 1966, the Supreme Court established that the following factors are relevant in determining nonobviousness: the scope and content of the prior art, the differences between the prior art and the invention, and the level of ordinary skill in the pertinent art.[333] In 1988, the Federal Circuit further clarified the operative test for obviousness in *In re O'Farrell*.[334] The patent applicant claimed a method for producing proteins in bacteria by using a new plasmid.[335] In finding the invention obvious, the court held:

> Obviousness does not require absolute predictability of success. Indeed, for many inventions that seem quite obvious, there is no absolute predictability of success until the invention is reduced to practice. There is always at least a possibility of unexpected results, that would then provide an objective basis for showing that the invention, although apparently obvious, was in law nonobvious. For obviousness under § 103, all that is required is a reasonable expectation of success.[336]

With respect to human DNA sequences, the Federal Circuit applied this "reasonable expectation of success" standard in *Amgen*, the 1991 landmark case establishing that human DNA sequences constitute patentable subject matter if they are "purified and isolated" from the human body.[337] In defending itself against Amgen's allegations of

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331 See supra note 18 for a definition of "prior art."

332 35 U.S.C. § 103(a) (1994).

333 Graham v. John Deere Co., 383 U.S. 1, 17 (1966). The *Graham* Court also suggested that secondary indications of obviousness, "such as commercial success, long felt but unresolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented," id. at 17-18, and subsequent cases hold that secondary considerations of this sort must be taken into account. See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1380 (Fed. Cir. 1986).

334 853 F.2d 894 (Fed. Cir. 1988).

335 See supra note 112 for a definition of the term "plasmid."

336 *O'Farrell*, 853 F.2d at 903-04 (citations omitted).

337 See supra notes 125-35 and accompanying text for a discussion of *Amgen*.

patent infringement, the defendant asserted, inter alia, that Amgen's patent was invalid under 35 U.S.C. § 103 due to obviousness.[338] Although the Federal Circuit found that it was "obvious to try" to obtain the DNA sequence of erythropoietin following probing methods available at the time, it affirmed the trial court's holding that such probing methods did not enable the inventor to do so with a "reasonable expectation of success."[339] In other words, the applicant had used a nonobvious improvement to the prior art method to find the DNA sequence. As a result, the DNA was found nonobvious, and the patent valid.[340]

In 1995, the Federal Circuit interpretation of the nonobviousness doctrine in *In re Deuel*[341] significantly strengthened patent rights in human gene sequences. In *Deuel*, the Federal Circuit held that with respect to a patent claim for a DNA sequence, the obviousness determination must focus on a DNA molecule as a chemical compound,[342] rather than on the obviousness of the method used to isolate the DNA molecule. In other words, a DNA sequence will be adjudged obvious only if it is structurally similar to previous chemical products, not simply because the method used to isolate the DNA molecule is itself obvious.[343] Scholars have criticized *Deuel* for mistakenly applying to DNA sequences an obviousness standard that is better suited to chemical compounds, thereby permitting patents on DNA sequences of unknown or speculative function obtained through routine, automated methods.[344] Nonetheless, *Deuel* still represents prevailing law, and under this standard, homologous gene sequences likely are deserving of patent protection notwithstanding the automated gene-sequencing techniques used to locate them.[345]

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338 Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1204 (Fed. Cir. 1991).

339 Id. at 1208-09.

340 Id. at 1209.

341 51 F.3d 1552 (Fed. Cir. 1995).

342 See supra note 129 and accompanying text.

343 *Deuel*, 51 F.3d at 1558-59.

344 See, e.g., Philippe Ducor, The Federal Circuit and *In re Deuel*: Does § 103 Apply to Naturally Occurring DNA?, 77 J. Pat. & Trademark Off. Soc'y 871, 888-90 (1995); Arti Rai, Addressing the Patent Gold Rush: The Role of Deference to PTO Patent Denials, 2 Wash. U. J.L. & Pol'y 199, 205-06 (2000).

345 Of course, a homologous DNA sequence may be considered prima facie obvious simply due to its similarity to a known DNA sequence. In such a case, the burden of showing nonobviousness shifts to the patent applicant, who can meet the burden by showing that the claimed compound has unexpected properties that constitute an improvement over prior art. Murray, supra note 186, at 244.

B. *European Application of the Nonobviousness Criterion to Human DNA Sequences of Unknown Function*

The European criterion of nonobviousness hews rather closely to the U.S. standard. Article 56 of the EPC provides that "[a]n invention shall be considered as involving an inventive step if, having regard to the state of the art, it is not obvious to a person skilled in the art."[346] Similarly, in 1988, the same year that the Federal Circuit set forth the "reasonable expectation of success" standard in *O'Farrell*,[347] the EPO Technical Board of Appeal appeared to adopt, at least in dicta, a similar test in *Monsanto/Milk Production*, which involved the patentability of a method for increasing the milk production of a cow.[348] The EPO held:

> The necessity of experimentally confirming a reasonably expected result does not render an invention unobvious. Absolute predictability, especially in the field of biologically active chemical compounds, is rather exceptional, but inventions relating to such compounds and their administration to living organisms may nevertheless be obvious. However, if such administration were to lead to unexpected results, which is not the case here, this might provide a basis for demonstrating unobviousness.[349]

With respect to the patentability of DNA sequences in particular, the EPO, like the PTO and courts, considers DNA sequences analogous to chemical compounds.[350] In *Biogen/Alpha-Interferon II*,[351] a 1991 case dealing with the patentability of DNA sequences encoding alpha-interferon, an issue similar to that examined in *Deuel*,[352] the EPO Board of Appeals articulated a rather lenient standard for nonobviousness of human DNA sequences in light of the state of the art. The EPO concluded that:

> [H]aving regard to the fact that the area of genetic engineering here under consideration was relatively new at the relevant date, having further regard to the uncertainty at that date about facts influencing the success of the attempted recombinant-DNA techniques, and to the absence of a well-established general level of knowledge in this

346 EPC, supra note 141, art. 56, at 273.

347 See supra notes 334-36 and accompanying text.

348 T249/88, [1996] E.P.O.R. 29, 30 (Technical Bd. App. 1989).

349 Id. at 35.

350 See, e.g., Biogen/Recombinant DNA, T301/87, [1990] E.P.O.R. 190, 207-11 (Technical Bd. App. 1989) (assessing inventive-step criterion for human DNA sequence as for chemical compound); Dr. Hans-Rainer Jaenichen, The European Patent Office's Case Law on the Patentability of Biotechnology Inventions 243 (1997) (noting that EPO treats DNA like chemical compound when assessing patentability).

351 T500/91, [1995] E.P.O.R. 69 (Technical Bd. App. 1992).

352 See supra notes 341-45 and accompanying text.

> particular technical area, the present successful technical application of recombinant-DNA techniques . . . involves an inventive step.[353]

While this decision represents the EPO's approach during the last several years,[354] European scholars and policymakers increasingly emphasize that the European patent criterion of inventive step "might soon become impossible to satisfy for any [human DNA] sequence," as sequencing becomes an increasingly "routine and obvious operation."[355] Thus, in the E.U. as in the United States, public-sector and nonprofit researchers contest the patentability of human DNA located through automated sequencing, arguing that the very ease with which researchers sequence DNA militates against a finding of nonobviousness.

C. Public Policy Arguments Surrounding the Nonobviousness Criterion

According to many public-sector and nonprofit researchers, automated gene sequencing is a "'dumb, repetitive task'"[356] which requires little investment of time or money.[357] They argue that the usual rationale for patent protection, that it encourages costly research and development, is not apposite since corporations need not invest millions of dollars to sequence genes.[358] Rather, they advocate strict application of the nonobviousness criterion, which will stimulate research by precluding inventors from too easily obtaining monopolies that would stifle further innovation.[359]

On the other hand, advocates of broad patent protection contend that the method by which an invention is made is not determinative of nonobviousness. According to the former Director of the Office of

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353 *Biogen/Alpha-Interferon II*, [1995] E.P.O.R. at 81.

354 See Jaenichen, supra note 350, at 248 (noting in 1997 that *Biogen/Alpha-Interferon II* decision "is a good example of the current approach in the assessment of inventive step in DNA sequences").

355 Bostyn, supra note 223, at 5 n.21; see also Frequently Asked Questions, supra note 34 ("The rapid advancement of the technology and our understanding in this area has indeed made the isolation and manufacture of genes more straightforward.").

356 Roberts, supra note 137, at 184 (quoting unnamed critic of sequencing process).

357 See D. Benjamin Borson, The Human Genome Projects: Patenting Human Genes and Biotechnology. Is the Human Genome Patentable?, 35 IDEA 461, 483 (1995) (discussing ease of sequencing ESTs); Holman & Munzer, supra note 5, at 776 ("In the time it takes to characterize completely one full-length gene," a company "could identify thousands" of partial DNA sequences).

358 This argument overlooks the expense of purchasing costly sequencing machines. See Preston, supra note 16, at 66, 68 (describing Celera's vast rooms full of sequencing machines costing $300,000 each).

359 See supra notes 328-29 and accompanying text. This argument is similar to that advanced with respect to the utility criterion. See supra Part III.

Technology Transfer at the NIH, who was speaking at that time about ESTs, "[p]atenting is not a value judgment about the elegance of an invention's underlying discovery, and the standards for patentability differ from the criteria applied to publication in peer-reviewed journals."[360] According to Professor Merges, "'[y]ou don't require a flash of genius to get a patent.' . . . 'It can be a step-by-step working out of an obvious idea. Although it may be obvious to try, it may not be obvious you are going to succeed . . . .'"[361] Moreover, the biotech industry insists that broad patent protection is necessary to encourage innovation in this field.[362]

V

A Proposed Solution to the Debate Over Patenting Human DNA Sequences

As described above, the debate over patents on human DNA sequences galvanizes many groups that oppose biotech patents. Those opposed to DNA sequence patents per se contend that such patents are immoral and unethical and therefore fail to satisfy the patentable subject matter/novelty criterion of patentability. This group, comprised of human rights activists, religious adherents, and some members of the medical community, is unlikely to be appeased by any legislative or judicial action short of a complete ban on DNA sequence patenting. Although their position garners more support in the E.U. than in the United States,[363] it is unlikely, after nearly two decades of recognizing intellectual property rights in human DNA, that either the United States or the E.U. will reverse this policy completely.[364]

Another group, comprised of public- and nonprofit-sector researchers the world over, generally favors DNA sequence patents so long as the utility and nonobviousness standards are satisfied. They contend that excessively lenient application of these criteria hamper biotech research, particularly international scientific collaboration, by permitting patentholders with only a vague notion of a sequence's function to demand exorbitant royalty fees from later researchers. In response, international biotech firms assert that broad patent protection is necessary to stimulate costly biotech research and development. Thus arises a conflict that transcends international borders.

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360 Adler, supra note 247, at 911.

361 Herman, supra note 207 (quoting Professor Merges).

362 See supra notes 233-36 and accompanying text.

363 See supra Part II.D.

364 See supra note 84 and accompanying text.

Recently, both the United States and the E.U. have sought to resolve this issue by continuing to provide patent protection for human DNA sequences while simultaneously imposing a heightened utility requirement.[365] While these measures are a step in the right direction, they are incomplete, because researchers worldwide still decry even the revised utility criteria as too weak, especially in situations involving automated sequencing of homologous DNA.

Therefore, Congress ought to enact a compulsory-licensing statute, coupled with an experimental-use exemption. This system would ensure that, in return for a fair sum, researchers would have access to the DNA sequence data they require for further experimentation. In addition, public- and nonprofit-sector scientists could conduct research free of charge so long as it were directed toward noncommercial ends. This approach promises to lessen much of the international tension surrounding human DNA sequence patents.

A. The Need for Congressional Enactment of Compulsory-Licensing Legislation With Respect to Patented DNA Sequences

Congress should enact a compulsory-licensing system, which would require an owner of patent rights in a DNA sequence to license that sequence to any and all scientists pursuing commercial research[366] related to that sequence in return for a reasonable licensing fee. The licensing fee would not be established by the individual licensor, but would instead depend on the commercial value of the product developed as a result of the research. Thus, potential licensees would not be dissuaded from making an initial investment to pursue research, because the amount of the royalty payment would be tied to the success of the product they develop. This system is also fair to the licensor, who would receive adequate compensation from licensees who achieve financial success through their use of the patented sequence.

There is some support in recent empirical literature for the theory that licensing and cross-licensing of intellectual property rights could arise naturally in the biotech industry, without the need for government intervention.[367] Professor Merges gives the example of copy-

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365 The PTO revised its Examination Guidelines, while the E.U. enacted the Biotechnology Directive. See supra notes 275, 286-90 and accompanying text.

366 Scientists pursuing noncommercial research would be subject to the experimental-use exemption described infra in Part V.B.

367 See generally Robert P. Merges, Contracting into Liability Rules: Intellectual Property Rights and Collective Rights Organizations, 84 Cal. L. Rev. 1293 (1996) (arguing against statutory compulsory-licensing on grounds that, left to their own devices, "repeat

right collectives that have evolved in the music industry to facilitate licensing transactions so that broadcasters and other producers readily may obtain permission to use numerous copyrighted works held by different owners.[368] Another example is the computer industry, where personal computer manufacturers have arranged to share hundreds of patents held by many different inventors.[369] Thus, one might expect biotech patentholders, who are indeed mutually dependent upon one another's inventions, freely to grant licenses to one another and to develop institutions to reduce transaction costs of bundling multiple licenses. One commentator points out that patentholders welcome subsequent research and willingly grant licenses already, on the theory that this ultimately will enhance the value of their patents.[370] Incyte, for example, encourages such research, since each of the company's patents becomes more valuable to the extent that scientists find additional uses for its genetic material.[371]

Many scholars indicate, however, that widespread licensing will not be achieved without government intervention because of the numerous disincentives that discourage such sharing. First, a patentee might refuse to license an invention in order to assemble a comprehensive patent portfolio that effectively would preclude others from working with competing technologies. Second, a patentee might attempt to preclude others from inventing around the patent, since the development of a noninfringing substitute would hurt the original patent's market value. Third, in the interest of gaining scientific renown and future intellectual property rights, a patentee might prefer to block the entry of others into the field.[372] This is particularly true in the balkanized biotech industry. According to Professors Heller and

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players" in industries dependent upon intellectual property rights successfully negotiate licensing agreements without government intervention).

368 See id. at 1328-40. However, it must be noted that firms are often reluctant to form patent pools for fear of antitrust litigation. See Heller & Eisenberg, supra note 300, at 700 (

> Although antitrust law may be less hostile to patent pools today than it was in 1975 when a consent decree dismantled the aircraft patent pool, the antitrust climate changes from one administration to the next. Even a remote prospect of facing treble damages and an injunction may give firms pause about entering into such agreements.

(citations omitted)).

369 Regalado, supra note 41, at 53.

370 Pollack, supra note 178.

371 Laurent Belsie, Progress or Peril, Christian Sci. Monitor, Aug. 19, 1999, at 15, 18. Naturally, this arrangement does not circumvent the problem of exorbitant licensing fees. Therefore, Congress should set a scale of fees based upon the commercial value of the invention at issue.

372 See Rebecca S. Eisenberg, Proprietary Rights and the Norms of Science in Biotechnology Research, 97 Yale L.J. 177, 217-18 (1987) (noting that "patentee might wish to

Eisenberg, "[b]ecause patents matter more to the pharmaceutical and biotechnology industries than to other industries, firms in these industries may be less willing to participate in patent pools that undermine the gains from exclusivity."[373] What is more, "the lack of substitutes for certain biomedical discoveries (such as patented genes or receptors) may increase the leverage of some patentholders, thereby aggravating holdout problems."[374] As stated forcefully by Iain Cockburn, an economist at Boston University:

> The nature of the biotech industry is the potential cause of some problems. There are a lot of small, hungry companies out there whose only asset is intellectual property. It's less likely that broad cross-licensing agreements can happen. If you have too many people owning small, overlapping slices of the same pie, there could be a breakdown.[375]

The automobile and aviation industries furnish apt examples of analogous situations from a century ago. During the first decades of these industries, broad patents led to a welter of antitrust and patent litigation. Ultimately, government intervention helped to create patent pools that cross-licensed everything and divided up the royalties.[376] Moreover, even if biotech companies do license their intellectual property, there is a high likelihood that these firms will set royalty fees so high as to discourage subsequent firms from undertaking the daunting risks of biotech research and development.[377] This is especially true because patentholders tend to overestimate the value of their patents.[378]

Any compulsory-licensing proposal likely would meet vigorous opposition on the part of the biotech industry, which would gain strength from the traditional antipathy in U.S. law toward any incursions on a patentholder's monopoly.[379] Nonetheless, there is some

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preserve exclusivity in subsequent research in order to maximize future claims to priority of discovery for purposes of both intellectual property and scientific credit").

373 Heller & Eisenberg, supra note 300, at 700.

374 Id.

375 Regalado, supra note 41, at 53.

376 See Seth Shulman, Toward Sharing the Genome, Tech. Rev., Sept.-Oct. 2000, at 67.

377 See supra notes 234-35 and accompanying text.

378 As noted by Professors Heller and Eisenberg:

> People consistently overestimate the likelihood that very low probability events of high salience will occur. . . . [I]f each owner overestimates the likelihood that her patent will be the key, then each will demand more than the probabilistic value, the upstream owners collectively will demand more than the aggregate value of their inputs, the downstream user will decline the offers, and the new drug will not be developed.

Heller & Eisenberg, supra note 300, at 701.

379 See Cornish, supra note 142, at 291 (noting "[t]he hostility of the United States to the very idea of compulsory patent licensing"); Ducor, supra note 95, at 157 (citing "a tradi-

precedent under U.S. law for derogations of patent rights in the public interest. For example, the Bayh-Dole Act permits the federal government to require a federally funded patentee to grant licenses under its patent to third-party applicants where the party holding title to the patent has failed to achieve sufficient practical application of the invention[380] or where "action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees."[381] The Atomic Energy Act authorizes the federal government to grant a nonexclusive license to an applicant in a case where a patent is "affected with the public interest" because of "primary importance in the production or utilization of special nuclear material or atomic energy."[382] Similarly, the Clean Air Act authorizes federal district courts to order licensing of air pollution prevention and control patents "on such reasonable terms and conditions as the court, after hearing, may determine," where unavailability of such licenses might result in "substantial lessening of competition or tendency to create a monopoly . . . ."[383] In the nonpatent context, the Plant Variety Protection Act[384] permits the government to compel a plant breeder to license a novel plant variety to others at a reasonable royalty if necessary to ensure an adequate supply of fiber, food, or feed, when the owner is unwilling or unable to meet public demand at a reasonable price.[385] As with research relating to energy production, clean air, and the cultivation of food, innovation relating to human DNA sequences is essential for the public welfare and must be facilitated via compulsory-licensing provisions.

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tional reluctance of American legal tradition toward compulsory licenses"); see also Dawson Chem. Co. v. Rohm & Haas Co., 448 U.S. 176, 215 & n.21 (1980) (describing compulsory licensing as "a rarity" in the U.S. patent system and noting that Congress considered but ultimately rejected inclusion of compulsory licensing in Patent Act).

380 35 U.S.C. § 203(1)(a) (1994).

381 § 203(1)(b). Although the federal government has enjoyed this "march-in" right since 1980, the government never actually has exercised it. Janice M. Mueller, No "Dilettante Affair": Rethinking the Experimental Use Exception to Patent Infringement for Biomedical Research Tools, 76 Wash. L. Rev. 1, 51 n.253 (2001). In light of the heightened fear of bioterrorism in the United States after the terror attacks of September 11, 2001 and the subsequent mailings of anthrax-tainted letters, there is increased attention paid to the possibility of compulsory licensing in the United States. See Shankar le Dantam & Terence Chea, Drug Firm Plays Defense in Anthrax Scare; For Now, U.S. Declines to Suspend Bayer's Patent and Authorize Generic Cipro, Wash. Post, Oct. 21, 2001, at A4; see also Amy Harmon & Robert Pear, A Nation Challenged: The Treatment; Canada Overrides Patent for Cipro to Treat Anthrax, N.Y. Times, Oct. 19, 2001, at A1.

382 42 U.S.C. § 2183 (1994).

383 § 7608.

384 7 U.S.C. § 2402 (1994 & Supp. IV 1998). This Act recognizes ownership rights in plant varieties.

385 § 2404.

The compulsory-licensing system proposed here would require a later scientist to give written notice to, but not to request the consent of, the patentholder before beginning research, in return for a reasonable after-the-fact royalty.[386] By eliminating pre-use license negotiations and up-front payments while still protecting a patentee's rights to a reasonable royalty, this compulsory-licensing system will foster innovation. However, it will be necessary to amend the Trade-Related Aspects of Intellectual Property Rights (TRIPS),[387] which was negotiated as part of the General Agreement on Tariffs and Trade (GATT),[388] to which the United States and all the E.U. member states are signatories. According to TRIPS Article 31(b), a compulsory license can be granted only if "prior to such use, the proposed user has made efforts to obtain authorization from the right holder on reasonable commercial terms and conditions and that such efforts have not been successful within a reasonable period of time."[389] European nations, which traditionally have facilitated compulsory licensing when the person applying for it is the owner or licensee of a dependent invention,[390] would willingly agree to amend Article 31(b), which was included at the insistence of the United States.[391]

Compulsory licensing of human DNA sequences represents a workable compromise, taking into account the importance of patent rights for stimulating costly genetic research while simultaneously recognizing that future scientists must be assured of the opportunity to conduct further experimentation on the sequences in return for a reasonable royalty based on the market value of any subsequent invention. Moreover, an international compulsory-licensing system that

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386 Professor Mueller, who has advocated an "intent to use" declaration in the context of compulsory licensing for research tools, states that such a declaration serves as notice to a patentee that it must police its patent rights. She also suggests that the law require the later researcher to provide additional written notice if it intends to market any product using the patented invention. Finally, she proposes the imposition of treble damages for any violation of the foregoing notice provisions. Mueller, supra note 381, at 58-59.

387 General Agreement on Tariffs and Trade—Multilateral Trade Negotiations (The Uruguay Round): Agreement on Trade-Related Aspects of Intellectual Property Rights, Including Trade in Counterfeit Goods, Dec. 15, 1993, 33 I.L.M. 81 (1994) [hereinafter TRIPS].

388 General Agreement on Tariffs and Trade: Multilateral Trade Negotiations Final Act Embodying the Results of the Uruguay Round of Trade Negotiations, Apr. 15, 1994, 33 I.L.M. 1125 (1994).

389 TRIPS, supra note 387, art. 31(b), at 95.

390 F.K. Beier & R. Moufang, Patentability of Human Genes and Living Organisms: Principles of a Possible International Understanding, in Patenting of Human Genes and Living Organisms, supra note 168, at 205, 217.

391 According to Professor Cornish, "[t]he hostility of the United States to the very idea of compulsory patent licensing finds determined expression in these provisions [of TRIPS Article 31]." Cornish, supra note 142, at 291.

harmonizes U.S. and E.U. patent law addresses the fears expressed by scientists worldwide that the current race to patent DNA sequences imperils international scientific collaboration.

B. The Importance of Congressional Codification of an Experimental-Use Exemption for Noncommercial Research on Human DNA Sequences

In addition to implementing a compulsory-licensing system for human DNA sequences, which would preserve incentives for private investment in research and development, Congress also should codify an experimental-use exemption for public-sector researchers at the federal level[392] and nonprofit researchers.[393] These scientists would be permitted to pursue research on patented DNA sequences for noncommercial purposes,[394] free of any licensing fee and without facing

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392 Public-sector researchers at the state level are immune from patent infringement liability under the federal patent laws. College Sav. Bank v. Florida Prepaid Postsecondary Educ. Expense Bd., 527 U.S. 666, 691 (1999). For a discussion of the problems arising from this decision, see Mueller, supra note 381, at 54. However, the only derogation of a patent's exclusivity currently available to federal government researchers is legislation permitting the federal government to use any patented invention so long as just compensation is paid if infringement is proved. See 28 U.S.C. § 1498 (1994 & Supp. V 2000). A codified experimental-use exemption is necessary to establish clearly the right of federal public sector researchers to use patented inventions for further experimentation.

393 Some scholars and practitioners suggest that the experimental-use exemption should not be limited to academic and nonprofit researchers, but extended to the for-profit sector as well. See generally Mueller, supra note 381; see also Experimental Use After *Roche v. Bolar*, ABA Section of Patent, Trademark & Copyright Law, 1988 Committee Reports, Proposed Resolution 101-4, at 25-28 (1988) ("RESOLVED, that the Section of Patent, Trademark & Copyright Law favors in principle an exemption from infringement for experimental or research use, not limited to pharmaceutical products, whether or not such use is conducted by a commercial organization."). They rely on case law suggesting that commercial entities successfully can invoke the experimental-use exemption so long as their activities are not directed toward earning a profit, but are instead intended to determine whether a patented invention is commercially useful before seeking a license for that particular technology. See, e.g., Dugan v. Lear Avia, Inc., 55 F. Supp. 223, 229 (S.D.N.Y. 1944), aff'd, 156 F.2d 29, 33 (2d Cir. 1946); Akro Agate Co. v. Master Marble Co., 18 F. Supp. 305, 333 (N.D. W. Va. 1937); Albright v. Celluloid Harness-Trimming Co., 1 F. Cas. 320, 323 (C.C.N.J. 1877) (No. 147). However, judicial precedent makes clear that the experimental-use exemption is "truly narrow," Roche Products, Inc. v. Bolar Pharmaceutical Co., 733 F.2d 858, 863 (Fed. Cir. 1984) (holding that defense does not permit "unlicensed experiments conducted with a view to the adaptation of the patented invention to the experimentor's business," as opposed to experiments conducted "for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry"), and rarely shelters the activities of a private for-profit entity. Thus, I propose that the initial codification of the experimental-use exemption apply only to the public and nonprofit sectors, so as to avoid stirring strong opposition by the biotech lobby and also to test the effectiveness of this exemption on a limited basis.

394 I advocate an experimental-use exemption for research on patented DNA sequences, but not for research using patented DNA sequences as mere tools to conduct experiments unrelated to the gene sequence itself. In the former instance, the experimental-use exemp-

liability in an infringement action. Essentially, the experimental-use exemption permits, under certain circumstances, a limited royalty-free compulsory license.

At first glance, it might seem as if a statutory experimental-use exemption is unnecessary in the field of human DNA sequence patents. One could argue that even without such an exemption, holders of patents on human DNA sequences would choose not to enforce their exclusive rights against public-sector or nonprofit researchers. For example, Celera has stated that academic researchers can use its sequence data free of charge,[395] and HGS is negotiating with the British NHS to permit the latter to continue its breast cancer screening notwithstanding HGS's patent rights in the CCR5 receptor gene.[396] Thus, one might surmise that biotech companies seek to generate good will, and to avoid negative publicity, by making their data available to nonprofit researchers.[397] Moreover, case law has already established an experimental-use exemption where the infringer's use is for entirely noncommercial purposes.[398]

Congressional action is necessary, however, to clarify the experimental-use exemption. First, although Celera and HGS have on occasion waived their rights to collect licensing fees from certain public-sector and academic researchers, such allowances are purely discretionary on the part of the patentholders, and therefore provide neither

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tion should apply because the researcher's goal, increasing knowledge about the sequence itself, is consonant with the interests of the public and the scientific community. Without an experimental-use defense, further innovation on the sequence might halt until expiration of the patent. However, use of a DNA sequence as a mere research tool should not fall within the experimental-use exemption because it would deprive the patentee of the right to licensing fees without actually contributing to understanding of the sequence. The NIH Working Group on Biomedical Research Tools supports this distinction, contending that

> [r]esearchers are ordinary consumers of patented research tools, and if these consumers were exempt from infringement liability, the patentholder would have nowhere else to turn to collect patent royalties. An excessively broad research exemption could eliminate incentives for private firms to develop and disseminate new research tools, which could on balance do more harm than good to the research enterprise.

Report of the National Institutes of Health (NIH) Working Group on Research Tools, Presented to the Advisory Committee to the Director June 4, 1998, app.D, at http://www.nih.gov/news/researchtools/appendd.htm (visited Apr. 24, 2001); see also Eisenberg, supra note 372, at 224-25 (rejecting notion of experimental-use exemption for research tools); Ronald D. Hantman, Experimental Use as an Exception to Patent Infringement, 67 J. Pat. & Trademark Off. Soc'y 617, 639-40 (1985) (same).

395 See supra note 37.

396 See supra note 202 and accompanying text.

397 More cynically, others might suggest that these firms hope to benefit at some later point from such research. See supra notes 370-71 and accompanying text.

398 See supra note 393 (citing cases).

a model for future arrangements nor the legal certainty necessary to foster invention. Other patentholders instead might offer such licenses only for a fee beyond the budget of the typical public-sector or nonprofit institution. Second, some patentholders might be unwilling to offer licenses at all, fearing that subsequent researchers will invent around the patented invention, decreasing its market value. Third, even if a patentholder did not object to the use of its invention by nonprofit researchers and offered it for a nominal fee, the need to contact patentholders and obtain licenses to use their inventions in research could add significantly to the transaction costs facing researchers.[399] What is more, although courts have recognized the experimental-use exemption,[400] the Court of Appeals for the Federal Circuit has characterized it as "truly narrow,"[401] implying that "legislative action is necessary in order to clarify" the parameters of this ambiguous doctrine.[402]

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399 See Eisenberg, supra note 90, at 743 (citing reasons in support of experimental-use exemption in U.S. patent law).

400 For thorough analyses of the case law interpreting the experimental-use doctrine, see generally 5 Chisum, supra note 1, § 16.03[1]; Hantman, supra note 394; Ned A. Israelsen, Making, Using and Selling Without Infringing: An Examination of 35 U.S.C. Section 271(e) and the Experimental Use Exception to Patent Infringement, 16 Am. Intell. Prop. L. Ass'n Q. J. 457 (1988-1989).

401 Roche Products, Inc. v. Bolar, 733 F.2d 858, 863 (Fed. Cir. 1984) (denying experimental-use defense to generic-drug manufacturer who performed clinical tests of patented drug prior to expiration of patent, for purpose of marketing generic version of drug upon expiration of patent, since "that inquiry has definite, cognizable and not insubstantial commercial purposes"). Although the specific holding of *Roche* was overruled legislatively by the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended at 35 U.S.C. § 271 (1994))—which permits a limited amount of testing by generic drug manufacturers prior to the expiration of a patent on a drug product in order to prepare for commercial activity after the patent expires—the *Roche* court's holding regarding experimental use is still valid. See Deuterium Corp. v. United States, 14 U.S.P.Q.2d 1636, 1643 n.14 (Cl. Ct. 1990) (noting that "[a]lthough [Congress, by enacting Section 271 (e)(1),] changed that narrow application of the doctrine affecting reporting requirements for federal drug laws, Congress did not disturb the Federal Circuit's enunciation of the parameters of the experimental use exception").

402 Eisenberg, supra note 90, at 742. Professor Eisenberg explains the difficulties in determining the parameters of the experimental-use exemption as follows:

> Since experimental use becomes an issue only in infringement actions, judicial pronouncements on its reach address situations where patentees have found a defendant's activities sufficiently annoying to be worth the trouble of pursuing a lawsuit. This factor has undoubtedly skewed the universe of experimental use decisions toward cases that implicate commercial interests. Within this universe, the experimental use defense is frequently raised and rarely sustained.

Eisenberg, supra note 372, at 220; see also 5 Chisum, supra note 1, § 16.03[1][b], at 16-103 (noting that "[r]elatively few decisions actually excused the making and use of patented products or processes on the basis of experimental or nonprofit purpose").

A patent experimental-use exemption would parallel the "fair use" defense to infringement available in copyright law, which does not require the later user to contact the owner of the intellectual property under certain circumstances.[403] A longstanding equitable defense to copyright infringement,[404] the fair-use doctrine eventually was codified in the 1976 Copyright Act.[405] The Act, rather than defining fair use, sets forth several examples of the types of uses often considered to be "fair," including "criticism, comment, news reporting, teaching . . ., scholarship, or research,"[406] as well as factors that courts may consider in evaluating this question.[407] Essentially, fair use in copyright law turns on the degree to which the infringer "has added substantial value to the original work and 'transformed' it in some way."[408] Such an exemption is appropriate for biotechnology research, especially research relating to homologous DNA sequences, since later inventors often contribute significant information about a particular sequence's function, thereby transforming scientists' understanding of that sequence.

Although some theories in the scholarly literature seem to support the notion that the copyright fair-use doctrine is inapplicable to the patent law context, these theories do not withstand scrutiny. First, the traditional view maintains that patent law must provide a greater incentive structure, by ensuring the monopoly rights of patentees, than copyright law, since inventors must be encouraged to engage in costly research and development in inventions whereas artists do not require as much inducement to create their works.[409] However, when

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403 The Supreme Court has defined fair use as "a privilege in others than the owner of a copyright to use the copyrighted material in a reasonable manner without his consent." Harper & Row, Publishers, Inc. v. Nation Enter., 471 U.S. 539, 549 (1985) (quoting H. Ball, The Law of Copyright and Literary Property 260 (1944)).

404 The fair-use doctrine existed at U.S. common law approximately one hundred thirty-five years before its codification in the 1976 Copyright Act. See Lydia Pallas Loren, Redefining the Market Failure Approach to Fair Use in an Era of Copyright Permission Systems, 5 J. Intell. Prop. L. 1, 15-22 (1997) (describing development of fair-use doctrine in United States).

405 Act of Oct. 18, 1976, Pub. L. 94-553, 90 Stat 2546 (codified as amended at 17 U.S.C. § 107 (1994)).

406 Id.

407 These factors include, but are not limited to: (1) the purpose and character of the use, including its commercial nature; (2) the nature of the copyrighted work; (3) the proportion that was "taken"; and (4) the economic impact of the "taking." Id.

408 Maureen A. O'Rourke, Toward a Doctrine of Fair Use in Patent Law, 100 Colum. L. Rev. 1177, 1191 (2000); see also Campbell v. Acuff-Rose Music, Inc., 510 U.S. 569, 579 (1994) (stating that "the more transformative the new work, the less will be the significance of other factors, like commercialism, that may weigh against a finding of fair use").

409 See, e.g., Dan L. Burk, Patenting Speech, 79 Tex. L. Rev. 99, 153 (2000) (noting that high costs associated with research and development of patented technology require legal system to furnish strong incentives for such pursuits).

one considers the ease with which present-day researchers can identify human DNA sequences through the use of automated sequencing machines, the idea that holders of patents on human DNA sequences invariably require unlimited patent protection becomes significantly less compelling.

Second, some claim that patented inventions simply do not raise the First Amendment issues implicated by copyrighted materials, seemingly reducing the need for an experimental-use defense to patent infringement.[410] Yet just as the copyright fair-use doctrine promotes the laudable social goal of vigorous debate, so too would codification of an experimental-use exemption in patent law foster dissemination of genetic information that would ultimately enhance human health.[411] Indeed, other intellectual property statutes incorporate provisions akin to an experimental-use exemption in order to promote research in areas far less important than human health. For example, the Plant Variety Protection Act provides that "[t]he use and reproduction of a protected variety for plant breeding or other bona fide research shall not constitute an infringement of the protection provided under this Chapter."[412] Similarly, the Semiconductor Chip Protection Act of 1984[413] exempts from infringement liability the reproduction of a protected work "solely for the purpose of teaching, analyzing, or evaluating the concepts or techniques" embodied therein or the creation of an original work incorporating the results of such analysis or evaluation.[414]

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410 For example, one of the purposes of the copyright fair-use doctrine is to permit criticism of and comment upon a given artistic work, thereby fostering discourse on important social issues. See supra text accompanying note 406; see also Dan L. Burk, Software as Speech, 8 Seton Hall Const. L.J. 683, 690-91 (1998) (criticizing traditional notion that no fair-use doctrine is necessary in patent law context, which notion is based on assumption that inventions, unlike artistic works, supposedly raise no First Amendment issues).

411 Indeed, patent law already recognizes the importance of this goal, through the reverse doctrine of equivalents. Under this doctrine, courts may excuse a patent infringement when the infringer is a radical improver whose "[infringing] device is so far changed in principle from a patented article that it performs the same or a similar function in a substantially different way, but nevertheless falls within the literal words of the claim." Graver Tank & Mfg. Co, Inc. v. Linde Air. Prods. Co., 339 U.S. 605, 608-09 (1950). By sheltering the radical improver, the reverse doctrine of equivalents increases the likelihood that the public will benefit from substantial improvements. Moreover, Congress has enacted tailored provisions to address specific situations in which the public interest demands some weakening of the patent rights. For example, as mentioned previously, Section 271(e) of the Patent Act, see supra note 401, allows certain infringements when they constitute a step in obtaining Federal Drug Administration approval for a new drug. The Patent Act also limits the ability of patentees to recover damages for infringements that occur when treating a patient. See 35 U.S.C. § 287(c)(1) (Supp. V 2000).

412 7 U.S.C. § 2544 (1994).

413 17 U.S.C. § 906(a) (1994).

414 Id.

Finally, with respect to biotechnology in particular, some have argued that the natural blurring between basic and applied science may not lend itself to an experimental-use exemption. Increasingly, private companies not only fund many projects in university research centers, but also collaborate with university scientists, who often form their own small firms to pursue commercial interests in their biotech research.[415] However, the compulsory-licensing provision proposed above[416] addresses this issue, since products made for profit will be covered thereunder.

Statutory codification of an experimental-use exemption not only will allay concerns about DNA sequence patents raised within the United States by public sector and nonprofit researchers, but will also help ease tensions between the United States and the E.U. member states. Many E.U. nations already except from liability for patent infringement "acts done for experimental purposes relating to the subject-matter of the patented invention."[417] What is more, TRIPS[418] has been interpreted to permit an experimental-use exemption for patent law. Specifically, TRIPS Article 30 provides that:

> Members may provide limited exceptions to the exclusive rights conferred by a patent, provided that such exceptions do not unreasonably conflict with a normal exploitation of the patent and do not unreasonably prejudice the legitimate interests of the patent owner, taking account of the legitimate interests of third parties.[419]

Although the meaning of this provision is unclear, at least one scholar has suggested that based on legislative history and comparative law, it is likely that TRIPS Article 30 was intended to allow exceptions for

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415 See supra note 14.

416 See supra Part V.A.

417 Gen'l Secretariate of the Council of the Eur. Communities, Records of the Luxembourg Conference on the Community Patent 1973, art.31(b), at 302; see also William R. Cornish, Experimental Use of Patented Inventions in European Community States, 29 Int'l Rev. Indus. Prop. & Copyright L. 735, 735-36 (1998) (noting nearly identical wording of experimental-use exemption in Belgian, Danish, Finnish, French, German, Greek, Irish, Italian, Spanish, Swedish, and United Kingdom patent laws). European case law further supports the proposition that the experimental-use exemption can be used by commercial entities. See id. at 735-37 (noting that in Europe, experimental-use doctrine may, under certain circumstances, apply in commercial as well as noncommercial context); Wolfgang von Meibom & Dr. Johann Pitz, Experimental Use and Compulsory License Under German Patent Law, Pat. World, June-July 1997, at 27, 29 (noting that Federal Supreme Court of Germany has interpreted this provision to absolve from liability certain clinical trials of patented pharmaceutical, although trials were conducted for purpose of finding new applications for that pharmaceutical, and that Court also indicated that exemption would be available even if unlicensed use resulted in accused infringer filing patent application on results of its research). However, I have confined my proposed experimental-use exemption to the nonprofit and public sectors.

418 See supra note 387 and accompanying text.

419 TRIPS, supra note 387, art. 30, at 95.

infringements conducted for (1) private, noncommercial purposes, (2) research, (3) experimentation for testing or improvement, and (4) educational purposes.[420]

TRIPS Article 8 also permits member countries to "adopt measures necessary to protect public health and nutrition, and to promote the public interest in sectors of vital importance to their socio-economic and technological development" as well as "measures . . . to prevent the abuse of intellectual property rights by right holders."[421] According to Professor O'Rourke, TRIPS Article 8 "states a strong international norm in favor of allowing socially beneficial infringements to occur,"[422] and public-sector and nonprofit research into the human genome surely falls within this category. She also points out that the language of TRIPS Article 30 is similar to that of TRIPS Article 13, which deals with exceptions to copyright rights. TRIPS Article 13 provides that "[m]embers shall confine limitations or exceptions to exclusive rights to certain special cases which do not conflict with a normal exploitation of the work and do not unreasonably prejudice the legitimate interests of the right holder."[423] The United States contends that its copyright fair use doctrine is permissible under Article 13, though some other countries question that position.[424] Thus, according to Professor O'Rourke, "[t]o the extent that Article 30 parallels Article 13, this suggests that some type of patent fair use is not only permissible but also expected under TRIPS."[425]

CONCLUSION

The legal and policy issues raised by the patenting of human DNA sequences have become quite controversial within the United States and also have affected U.S.-E.U. relations. Having determined that such sequences meet the criteria of patentability, neither the

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420 See Carlos M. Correa, Patent Rights, in Intellectual Property and International Trade: The TRIPS Agreement 189, 208 (Carlos M. Correa & Abdulqawi A. Yusuf eds., 1998) (interpreting provision "based on comparative law and other proposals," including draft Treaty Supplementing Paris Convention, and stating other contexts in which infringement would likely be excused).

421 TRIPS, supra note 387, art. 8, at 87.

422 O'Rourke, supra note 408, at 1202.

423 TRIPS, supra note 387, art. 13, at 88.

424 See Tyler G. Newby, What's Fair Here Is Not Fair Everywhere: Does the American Fair Use Doctrine Violate International Copyright Law?, 51 Stan. L. Rev. 1633, 1648-62 (1999) (describing U.S. position, which E.U. has called into question, that U.S. fair-use doctrine complies with TRIPS Article 13).

425 O'Rourke, supra note 408, at 1202; see also Michael Blakeney, Trade Related Aspects of Intellectual Property Rights: A Concise Guide to the TRIPS Agreement 87 (1996) ("Article 30 will except the use of patented products or processes under a compulsory license or solely for the purpose of scientific research and experiment.").

United States nor the E.U. is likely to reverse this policy in light of the importance of biotech investment to their economies. In crafting effective patent protection for human DNA sequences, U.S. policymakers must weigh the arguments advanced by researchers in the public and nonprofit sectors as well as those expressed by biotech industry leaders. The former warn that excessively broad patent protection for human DNA sequences threatens to stifle the very innovation it was meant to promote, while the latter maintain that strong patent protection is necessary to stimulate biotech research and development. This debate replicates itself on a meta-international scale, pitting international bodies such as the HGP against multinational biotech companies, and the tension heightens as U.S. biotech firms increasingly seek patent protection in Europe in order to recoup the significant costs associated with biotechnological research.

In order to address the domestic and international conflicts surrounding patents on human DNA sequences, Congress ought to enact a compulsory-licensing statute and an experimental-use exemption. A compulsory-licensing scheme, with fees set on a sliding scale depending upon the commercial value of the invention, would ensure royalties for inventors while allowing further research on the patented DNA sequences. In addition, an experimental-use exemption would promote innovation by protecting from infringement liability public-sector and nonprofit scientists engaged in noncommercial research. Because the E.U. member states already recognize the compulsory-licensing and experimental-use doctrines, this proposal would effectively harmonize U.S. and E.U. law. Thus, legislation to this effect would stimulate research while simultaneously promoting harmonious international relations.