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**The Biotechnology Balancing Act: Patents for
Gene Fragments, and Licensing the
“Useful Arts”**

by

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THE BIOTECHNOLOGY BALANCING ACT: PATENTS FOR GENE FRAGMENTS, AND LICENSING THE “USEFUL ARTS”

*by Byron V. Olsen**

“Today, the only wealth there is in the world is the wealth that
comes from the human mind.”¹

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¹ Linda Marsa, *Whose Ideas Are They Anyway: Intellectual Property in the Information Age*, OMNI, December 22, 1995, at 36 (quoting Bruce A. Lehman, United States Commissioner of Patents and Trademarks).

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I. INTRODUCTION

The Human Genome Project, originally designed in 1988 to be a 15-year \$3 billion dollar research effort,² was launched by the United States with the goal of mapping the entire human genetic blueprint—the human genome.³ This effort was believed by many in the field to promise the availability of a treasure trove of scientific knowledge.⁴ Knowledge that could be used by researchers to investigate not only the causes of genetic diseases, but to understand, on a much more expansive and detailed level, the nature of the human genetic composition and inheritance. With this as the promised pot of gold, many other countries have joined the United States in its trip across the genetic rainbow.⁵ These countries have joined the effort to map the location and function of all human genes, partially for the scientific allure and partly to get in on the ground floor of 21st century science.⁶ While the Project's successful conclusion suggests a tremendous increase in knowledge, it is also important to point out that this increased knowledge has within it a very lucrative commercial potential; lucrative because the mapping of the human genome also represents the unlocking of our chemical composition⁷ which will bring a clearer understanding of how our cellular processes work. With

² See D'Arcy Jenish, *A Patent on Life; Scientists Seek Legal Rights to Genes*, MACLEAN'S, Aug. 31, 1992, at 38. See generally Robert M. Cook-Deegan, *Origins of the Human Genome Project*, 5 RISK: HEALTH, SAFETY & ENVT. 97 (1994) (providing background on the Human Genome Project); Bernadine Healy, *Special Report on Gene Patenting*, 327 NEW ENG. J. MED. 664 (1992) (reporting that the Human Genome Project was undertaken by the National Institutes of Health to "accelerate gene discovery by systematically sequencing all 24 unique human chromosomes").

³ See U.S. DEPT. OF HEALTH AND HUMAN SERVS. & U.S. DEPT. OF ENERGY, UNDERSTANDING OUR GENETIC INHERITANCE - THE U.S. HUMAN GENOME PROJECT: THE FIRST FIVE YEARS, FY 1991-1995 (1990).

⁴ See *Drug Research: SmithKline Leads Genetics Race*, Health Line, November 27, 1995 [hereinafter *Drug Research*]; S. OLSON, BIOTECHNOLOGY: AN INDUSTRY COMES OF AGE (1986).

⁵ See Victor Chase, *Genome Project Faces Scientific, Business Hurdles*, 37 R & D 24 (1995); Jenish, *supra* note 2, at 38.

⁶ See Jenish, *supra* note 2, at 38.

⁷ See J. Leslie Glick, *The Industrial Impact of the Biological Revolution in Technology and the Future* 364 (Albert H. Teich ed., 5th ed. 1990). See generally Barbara Looney, *Should Genes Be Patented? The Gene Patenting Controversy: Legal, Ethical, and Policy Foundations of an International Agreement*, 26 LAW AND POLY IN INT'L BUS. 231, 231 (1994) (asserting that the "[m]apping of the entire genome is one of the goals of the Human Genome Project, a worldwide effort seeking greater understanding of the genetic basis of life.").

this knowledge, new diagnostic tools will be developed, new answers on how to end genetic diseases will be found, new gene products will be discovered that can be turned into highly useful therapeutics and the mechanisms of cellular processes will be better understood.⁸ All of these things have potentially far reaching applications, and if ownership of this information is possible, then the potential value of biotechnology patents becomes obvious.

Existing judicial precedent suggests that living organisms and their individual genes are patentable.⁹ However, the extension of this economic protection to gene fragments is problematic. In the recent past, the National Institutes of Health (NIH) attempted to patent not the full sequence of genes, but partial fragments of those genes.¹⁰ Though the Patent and Trademark Office rejected these initial NIH applications,¹¹ many within the biotechnology industry are feverishly trying to file their own patents on the fragments of partially sequenced genes.¹² This effort, and the money behind it, is most assuredly done with an eye on the commercial potential that some gene products or new biotechnology have.¹³

It is the goal of this paper to discuss the commercial applications of the information garnered by the Human Genome Project, focusing primarily on the intellectual property or patent law aspects of this accumulating knowledge. Also of concern is the

⁸ See U.S. CONGRESS, OFFICE OF TECHNOLOGY ASSESSMENT, *MAPPING OUR GENES - THE GENOME PROJECTS: HOW VAST, HOW FAST?* 46 (1988) [hereinafter *MAPPING OUR GENES*].

⁹ See *Diamond v. Chakrabarty*, 447 U.S. 303 (1980) (a live, human-made microorganism is patentable); *Yoder Brothers, Inc. v. California-Florida Plant Corp.*, 537 F.2d 1347 (5th Cir. 1976) (plants are patentable); *Merck & Co. v. Olin Mathieson Chemical Corp.*, 253 F.2d 156 (4th Cir. 1958) (organically derived vitamins patentable); *Ex parte Allen*, 2 U.S.P.Q.2d (BNA) 1425 (PTO Bd. of Patent Appeals and Interferences 1987) (synthetically grown oysters patentable).

¹⁰ See Paul H. Ginsburg, *The NIH cDNA Patent Application and Technology Transfer Issues*, 4 No. 7 J. PROPRIETARY RTS. 18 (1992); Daniel L. McKay, *Patent Law and Human Genome Research at the Crossroads: The Need for Congressional Action*, 10 SANTA CLARA COMPUTER & HIGH TECH. L.J. 465, 466 (1994).

¹¹ See Christopher Anderson, *Genome Project Goes Commercial: NIH to Appeal Patent Decision*, 259 SCI. 300 (1993); Leslie Roberts, *NIH Gene Patents, Round Two*, 255 SCI. 912 (1992).

¹² See John Carey, *The Gene Kings*, BUSINESS WK., May 8, 1995, at 72; Craig D. Rose, *Race is on to Stake Claims to Our DNA: San Diego's Sequana Among Pioneer Firms in Fertile New Field*, SAN DIEGO UNION-TRIBUNE, Sept. 11, 1994, at A1.

¹³ See Gene Bylinsky, *Genetics: The Money Rush is On*, FORTUNE, May 30, 1994, at 94.

potential use of this knowledge by academia or others through licensing agreements with "owners" of this information.

II. BIOTECHNOLOGY

Biotechnology is a broad term that refers to the biological processes and recently developed technologies that actually harness the abilities of organisms, or their component parts, for the benefit of science, commerce, and/or individuals.¹⁴ Though focusing on the manipulation of either the cells of multicellular organisms, or of single-celled microorganisms for some desired end, this term encompasses such diverse disciplines as molecular genetics, x-ray crystallography, antibiotic production, and fermentation technologies.¹⁵ Through the use of biotechnology techniques, scientists have sought to study the biological systems of these creatures not only as an end in itself, but also as a way to better understand more complex living systems.¹⁶ This use of microorganisms for the benefit of humanity is not a new idea. For thousands of years, mankind has used microbiota for the manufacture of our food and drink.¹⁷ Today this use has matured into the use of microorganisms for the production of medicines, antibiotics, hormones, and vitamins, among other products.¹⁸

A. *The Beginnings of Biotechnology*

To understand the beginnings of modern biotechnology it is necessary to understand the allure of studying the nature of heredity and reproduction. For millennia the puzzle of how traits present in animals, plants, or people were passed onto future generations was without an answer.¹⁹ It was only after the invention of glass lenses capable of magnifying microscopic cells that the fundamental nature of genetic inheritance, and the existence of living cells, could be grasped.²⁰

¹⁴ See U.S. DEP'T. OF COMMERCE, U.S. INDUSTRIAL OUTLOOK '92: BUSINESS FORECASTS FOR 350 INDUSTRIES 17-1 (1992) [hereinafter INDUSTRIAL OUTLOOK].

¹⁵ See *id.*

¹⁶ See MAPPING OUR GENES, *supra* note 8, at 46; Looney, *supra* note 7, at 231.

¹⁷ See ANDREW GOUDIE, THE HUMAN IMPACT ON THE NATURAL ENVIRONMENT 15-20 (4th ed. 1994).

¹⁸ See INDUSTRIAL OUTLOOK, *supra* note 14, at 17-1.

¹⁹ See DAVID T. SUZUKI ET AL., AN INTRODUCTION TO GENETIC ANALYSIS 11-13 (3rd. ed. 1986); HELENA CURTIS, BIOLOGY 237-40 (4th ed. 1983).

²⁰ See JAMES D. WATSON ET AL., MOLECULAR BIOLOGY OF THE GENE 3-4 (4th ed. 1988).

Even with microscopes, it was up to the monk Gregor Mendel and his famous pea plants to show that heritable traits, later to be linked to the expression of one or more genes, were not the result of a "blending" of parental characteristics but were the result of isolated factors (e.g. genes) that segregated into progeny in a generally random, but mathematically straightforward, pattern.²¹

The beginnings of modern genetics technology came in the 1970s with the arrival of recombinant DNA technology, which essentially allows a researcher to remove a gene from one creature and to insert it or "clone" it into another, where it will be expressed, along with the DNA of its host.²² This selective manipulation of one or more genes in a variety of heavily studied hosts²³ has provided the techniques that allowed for the explosive growth of knowledge within the realm of biotechnology and later for the commercial development and exploitation of this field.²⁴

1. Scientific Techniques

The development of new technologies in the last twenty-five years has provided scientists, both in commerce and in academia, with the ability to alter microbiota with unprecedented precision and relative ease.²⁵ In effect, these critical technologies, usually seen to be under the banner of "genetic engineering" or "molecular genetics," have given scientists the power to harness the capabilities of organisms to aid in pure research,²⁶ to mimic disease etiology,²⁷ or to produce some useful gene product in massive quantities.²⁸ With each passing year, the technology provides ever more precise and powerful techniques to reveal the secrets of

²¹ See *id.* at 10-12; CURTIS, *supra* note 19, at 239.

²² See, e.g., Stanley N. Cohen et al., *Construction of Biologically Functional Bacterial Plasmids In Vitro*, 70 PROC. NAT'L ACAD. SCI. 3240, 3240 (1973).

²³ See *id.*

²⁴ See Yusing Ko, Note, *An Economic Analysis of Biotechnology Patent Protection*, 102 YALE L.J. 777, 783-86 (1992).

²⁵ See generally McKay, *supra* note 10, at 467-74 (providing scientific background of recent advances in genetic research).

²⁶ See generally SUZUKI, *supra* note 19, at 301-23.

²⁷ See Roger Highfield, *Mouse Will Aid War on Fibrosis*, THE DAILY TELEGRAPH (London), Aug. 1, 1995, at 05; *DNX Develops New Mouse Model to Advance Heart Disease Research*, PR Newswire, May 23, 1995; Harry M. Georgiou & Thomas E. Mandel, *Induction of Insulinitis in Athymic Nude Mice: The Effect of NOD Thymus and Pancreas Transplantation*, DIABETES, Jan. 1995, at 49.

²⁸ See Richard Lipkin, *Artificial Spider Silk*, SCIENCE NEWS, Mar. 9, 1996, at 152.

living systems and their component parts.²⁹ These techniques are then quickly adapted by biotech commercial interests to aid in their exploitation of nature's genomic bounty. Thus, the "maturation" of biotechnology is in truth the product of the increased availability and power of those techniques developed for the study of microorganisms.

Though the discussion centering on genetic engineering envisions the manipulation of living organisms, what is most often being manipulated to reach the desired end is a given organism's genetic information.³⁰ This is the information that allows organisms to pass on their individual traits, as well as the information which allows all the life processes from birth to death to proceed.³¹ All organisms as we know them pass on this extensive bundle of information through precisely coded nucleic acids,³² and for the most part through single or multiple molecules of deoxyribonucleic acid (DNA), known as chromosomes.³³ It is generally DNA that is manipulated, through the techniques of biotechnology, to serve human ends.³⁴ The functional unit of inheritance is a precisely coded segment of DNA called a gene.³⁵ This gene generally encodes the production of one functional protein³⁶ molecule that is itself built of a variable number of a specifically arranged amino acids. The resulting sequence then folds into a generally

²⁹ See D.J. WEATHERALL, *THE NEW GENETICS AND CLINICAL PRACTICE* 1-3 (2nd. ed. 1985).

³⁰ See generally SUZUKI, *supra* note 19, at 301-22.

³¹ See *id.* at 3.

³² See generally CURTIS, *supra* note 19, at 278-93.

³³ The DNA molecule is actually two strands of sugar residues.

³⁴ Of particular importance to the corporations devoted to the commercial application of biotechnology is recombinant DNA technology. This technology makes it possible to transfer specific genetic messages from the genetic complement of one organism to the genetic complement of another. Once accomplished, and with the aid of other procedures designed to stimulate the second organism to express the inserted genetic message, large quantities of the desired gene or gene product(s) can be produced for harvest from the expressing organism or for the beneficial effect the receiving organism is to realize from the inserted gene. Examples of such products are human growth hormone, interferon, or disease resistant crops. See INDUSTRIAL OUTLOOK, *supra* note 14, at 17-1 - 17-2.

³⁵ See SUZUKI, *supra* note 19, at 1-4 (stating that a gene is a unit of heredity in the chromosome which performs a specific function, such as coding for an RNA molecule or a polypeptide (e.g. protein)); see also CURTIS, *supra* note 19, at 1095.

³⁶ See CURTIS, *supra* note 19, at 1104 (stating that a protein is a "complex organic compound composed of one or more polypeptide chains, each made up of many . . . amino acids linked together" in a specific sequence through covalent bonds).

specific three-dimensional form³⁷ which provides for the biologic and/or enzymatic activity of the protein encoded by the gene.³⁸ By changing, altering, or modifying the genetic code of an organism, in even a minor way, that organism can be made to produce a variety of products, or be used to study how a given change effects cellular processes.³⁹

So complex is every human gene that geneticists often spend years identifying its chromosomal location, protein product, or function in a given system.⁴⁰ And it is estimated that, with the exception of red blood cells, which in mammals carry no genomic DNA, every cell of the human body contains well over 50,000 and as many as 100,000 genes.⁴¹ To date, very few of those genes comprising the human genetic complement, or genome, have been studied in any depth.⁴² It is thought that with an understanding of the physical composition and layout of the human genome, courtesy of the Human Genome Project, will come a better perspective not only on how to treat those genetic diseases which afflict us,⁴³ but the prospect that in the race to understand our own makeup, there will be considerable opportunity to use this knowledge for the development of commercially invaluable therapeutic agents.⁴⁴

2. Science on the Fast Track

Today genes are commonly identified by two different methods: genetic sequencing and cDNA sequencing. Genetic sequencing technology relies on isolating large genetic fragments, perhaps entire chromosomes, that are then cut through the action of a variety of restriction endonucleases into much shorter fragments, that may or may not contain a full gene transcript.⁴⁵ These frag-

³⁷ See *id.* at 66-71.

³⁸ See generally *id.* at 166-81 (explaining that an enzyme is a globular protein molecule that accelerates a specific chemical reaction).

³⁹ See generally SUZUKI, *supra* note 19, at 296-328.

⁴⁰ See generally *id.*

⁴¹ This approximation is derived from chromosome banding experiments which indicate the presence of expressed genes through the differential behavior of expressed and non-expressed regions of the chromosomes themselves. See MAPPING OUR GENES, *supra* note 8, at 33.

⁴² See Carey, *supra* note 12, at 72 (stating that the function of more than one-half of the discovered human gene sequences remains unknown).

⁴³ See David N. Leff, *Gene-Hunters' Free for All On Web*, BIOWORLD TODAY, December 22, 1995.

⁴⁴ See *Drug Research*, *supra* note 4.

⁴⁵ A restriction endonuclease is an enzyme that will cut the DNA double helix in a specific pattern, based on that nucleic acid sequence of the DNA itself.

ments are thereafter specifically isolated through agarose gel electrophoresis⁴⁶ and sequenced,⁴⁷ altogether a process which reveals the precise nucleic acid sequence of that genomic fragment. The overall sequence of this still relatively large genetic fragment, the genomic DNA, is itself determined by finding overlapping sequences⁴⁸ of the restriction endonuclease cleaved into smaller fragments and piecing those fragments together in their most likely order,⁴⁹ a process which sometimes requires the use of specially developed software containing algorithms designed to make this piecing-together process easier. From this description it should be clear that this process, while fairly precise and amenable to some automation, is relatively slow, especially when used to decipher or sequence extremely large stretches of DNA,⁵⁰ as is the case with the 3 billion base pair-long human genome.⁵¹

The other technique used to sequence DNA is cDNA sequencing, or copy DNA sequencing. This process starts with a fundamentally different perception of what the sequencing target is when compared to the traditional genomic sequencing already described. The key to the speed of cDNA method is the realization that the genetic code of all known organisms does not provide for the translation of DNA-encoded genes directly into a protein product.⁵² Instead, the information leading to a single gene's eventual product, the expressed protein, must first be transcribed from DNA into ribonucleic acid⁵³ (RNA), which is itself later translated into the end protein. The intermediate molecule, termed messen-

Therefore the cuts can be consistently replicated within a species, but the generated fragments vary species by species. See CURTIS, *supra* note 19, at 319-20, 1105.

⁴⁶ This process is simply loading the generated fragments into a preformed gel, to which an electric current is applied. Due to the negatively electrically charged nature of DNA the molecular fragments will move within the gel from the anode towards the cathode (negative to positive) at a rate dependent upon their size. This method can separate fragments very similar in size and charge. See WATSON, *supra* note 20, at 102-03.

⁴⁷ To sequence is to use chemical processes to break down a DNA fragment in a way that will allow researchers to determine the exact order of nucleic acids. See generally JOHN McMURRY, ORGANIC CHEMISTRY 1123-31 (1984).

⁴⁸ See generally *id.*

⁴⁹ See THE HUMAN GENOME PROJECT: DECIPHERING THE BLUEPRINT OF HEREDITY 157-58 (Necia G. Cooper ed. 1994).

⁵⁰ See Healy, *supra* note 2, at 664.

⁵¹ See BRUCE ALBERTS ET AL., MOLECULAR BIOLOGY OF THE CELL 483-84 (2nd ed. 1989). The 3 billion base pair figure represents a single set (i.e. haploid) of genes. Normal human cells have two full sets of genes (i.e. diploid). See *id.*

⁵² See generally *id.* at 201-08.

⁵³ See generally *id.* at 201-10.

ger RNA or mRNA because it carries the information for a specific protein within its sequence, is itself translated⁵⁴ into the building blocks of protein and amino acids,⁵⁵ by the protein factories of the cell, the ribosomes.⁵⁶ Just as the DNA carries its information through its specific sequence of nucleic acids, proteins gain their sequence and form, and thereby their function, through the sequential arrangement of their amino acids.⁵⁷ The protein product is the derivative of the genetic code that biotech companies are interested in due to the possibility of commercial application.⁵⁸ In any case, mRNA represents the nucleic acid expression of a given gene without any intervening sequences, or introns,⁵⁹ so prevalent in the DNA of humans and other mammalian creatures. Techniques exist which allow for the quick isolation of mRNA molecules. Once this has been accomplished, the most important step of cDNA sequencing quickly follows.

The central dogma in genetics is that the movement of information from DNA to RNA to protein is a one way street. That is, there is no way for information stored at the protein or RNA level to make its way back into DNA.⁶⁰ While this is for the most part true, the genetic material of some viruses⁶¹ contain a certain enzyme called reverse transcriptase.⁶² Like its name implies, this particular protein allows for the transcription of mRNA back into DNA. The reaction catalyzed by reverse transcriptase takes RNA, in our case mRNA free of the introns already mentioned, and turns it into a copy of the original DNA present in the chromosome of a given creature.⁶³ This cDNA can then be sequenced using the

⁵⁴ See generally *id.* at 210-19.

⁵⁵ See generally *id.* at 100-10.

⁵⁶ See generally *id.* at 210-17.

⁵⁷ See generally ALBERTS, *supra* note 51, at 118-31.

⁵⁸ See Carey, *supra* note 12, at 72.

⁵⁹ An intron is a segment of DNA that is present in the chromosome, but is removed enzymatically before translation of the gene into protein. See ALBERTS, *supra* note 51, at 102, 602-04. These portions of the genetic complement, present in higher animals and plants, are not thought to have any known function (i.e., "junk DNA"), but perhaps may be useful in positioning genes three-dimensionally, and therefore involved in controlling the expression of genes.

⁶⁰ See WATSON, *supra* note 20, at 81-82.

⁶¹ A submicroscopic, noncellular particle composed of a nucleic acid core and a protein coat. It is parasitic, and therefore can only reproduce in a host. See CURTIS, *supra* note 19, at 1109.

⁶² See WATSON, *supra* note 20, at 91, 610-11.

⁶³ The mRNA molecule represents the complete expressed message of a given gene, and is fully processed in the nucleus after transcription. See WATSON, *supra* note 20, at 89-91.

methods already described, and will yield the precise expressed sequence of a given gene.⁶⁴ Once the sequence of a gene is known, it is relatively easy for the location of that gene on a given chromosome to be determined.

With the known sequence of at least a portion of the gene in hand, techniques exist which allow scientists to create a probe of a complementary sequence to be synthesized.⁶⁵ This probe is simply a small sequence, usually 15 to 25 nucleic acids long, that will specifically hybridize⁶⁶ with a portion of the sequence of the larger gene of interest.⁶⁷ A radioactive or fluorescent tag is attached to the probe which allows researchers to identify where in the genome, and on which chromosome, the gene is located. This method is precise and relatively quick, and as indicated allows for mapping of the genes within the chromosomes to be completed. One drawback to this, however, is that the overall sequence of the chromosome is *not* determined.⁶⁸ That is, the nucleic acid sequence of the introns must be found through other methods, as must the upstream and downstream portions of the chromosome.⁶⁹ Often, regions not expressed by genes have a great deal to do with the actual expression of a given gene in a specific organism.⁷⁰ These regions, generally flanking a given gene, are not determined by the cDNA method.⁷¹

It is apparent that the method of choice for those wanting to sequence the entire human genome, generally academics, is likely to be the genomic sequencing method which determines the full sequence of a given chromosome, coding or non-coding.⁷² The method favored by those seeking a particular gene or generally looking only for expressed segments, generally commercial interests, is the cDNA approach. In addition, the cDNA approach offers a great deal more speed in the determination of genetic sequences.

Adding to the allure of the cDNA method for commercial interests is the fact that much of the procedure can be automated, as

⁶⁴ See *id.*

⁶⁵ See generally ALBERTS, *supra* note 51, at 260-71.

⁶⁶ See *id.* at 262.

⁶⁷ See *id.* at 262-63.

⁶⁸ See generally *id.* at 262-70.

⁶⁹ See *id.* at 262-65.

⁷⁰ See generally ALBERTS, *supra* note 51, at 201-07.

⁷¹ See generally *id.* at 201-07, 262-71.

⁷² If this method is not used, then the "map" would not be complete.

Dr. Craig Venter has shown.⁷³ Tired of the relatively slow pace of complete gene sequencing, Venter set out to successfully develop a fast and highly automated method of identifying gene locations and a portion of their sequences.⁷⁴ He accomplished this by using the general cDNA model but modified it through a highly automated process.⁷⁵ As of March 1993, the entire Human Genome Project, comprising many teams of researchers working in several countries, had only sequenced 2,600 genes.⁷⁶ With Dr. Venter's method, his lab had, by itself, identified up to 2,000 genes a month.⁷⁷ And when Dr. Venter left the NIH, and helped to set up Human Genome Sciences Inc. (HGS), his lab there was finding 300 to 400 genes per day.⁷⁸

B. *The Genetic Goldrush*

Like the fevered pace of gold miners staking their claim in search of the "mother lode,"⁷⁹ patent applications for gene or gene fragments may overwhelm an already backlogged PTO.⁸⁰ Researchers and corporations staking out their "claims" in gene fragments have not blinked in the face of the NIH's failure to pursue its own claims in the face of PTO rejection.⁸¹ Because of the commercial success of recent gene products as therapeutics,⁸² many of these high tech prospectors fail to see the possible futility

⁷³ See Eliot Marshal, *The Company that Genome Researchers Love to Hate*, 266 SCI. 1800 (1994).

⁷⁴ See *id.*

⁷⁵ See *id.*

⁷⁶ See Michael Waldholz, *Huntington's Disease Gene is Found at Last*, WALL ST. J., Mar. 24, 1993, at B1.

⁷⁷ See Gina Kolata, *Biologist's Speedy Gene Method Scares Peers but Gains Backer*, N.Y. TIMES, July 28, 1992, at C2.

⁷⁸ See Jerry E. Bishop, *Human Genome Sciences Sees Gold in Trove of Genes*, WALL ST. J., Mar. 18, 1994, at B4.

⁷⁹ In this context "mother lode" refers to a gene product which can be used to generate a highly valuable medicinal agent.

⁸⁰ See McKay, *supra* note 10, at 494.

⁸¹ The reasons for the rejection of the NIH's gene fragments by the PTO might be framed in the technical aspects of 35 U.S.C. (i.e., the federal patent statute), but the decision by the leadership of the NIH not to appeal this rejection is primarily one of perceived public policy combined with a personnel shift at the leadership level of the NIH. While failure to pursue an appeal of the rejection for public policy reasons may inhibit government action, it has apparently offered no reason for hesitancy on the part of biotechnology corporations in the throes of "gene fever."

⁸² See Matthew Erramouspe, Comment, *Staking Patent Claims on the Human Blueprint: Rewards and Rent-Dissipating Races*, 43 UCLA L. REV. 961, 962-63 (1996)

of much of their effort.⁸³ Similar to the experience of many of those making the long and arduous trek to the gold fields of the Yukon or mid-nineteenth century California, many of the current researchers, and the institutions behind them, are likely to lose money in torrents rather than strike it rich while mining the human genome for useful therapeutics.⁸⁴ This will be especially true if many of the researchers in the public domain are successful in their efforts to make as much human genome information as possible a part of the public domain⁸⁵ before patent protection can be garnered.⁸⁶

The current pace of research investigating the mapping and functional aspects of genes has all the earmarks of "gold fever," an ailment that affected many in the gold strikes already mentioned. In the face of failure at the PTO,⁸⁷ and scientific derision,⁸⁸ companies have simply continued to deluge the PTO with patent applications regarding genes and gene fragments.⁸⁹ Using the methods made famous by Dr. Craig Venter, many have filed applications for ownership of a piece of the human genome for which neither function, nor a full protein copy has been determined.⁹⁰ The tools are in place to identify genes as such, but both the effort to fully sequence them and the careful experimentation required to yield the precious knowledge of function are glaringly absent. Some claim that the sequences for which they seek ownership are useful as "tag" sequences or genetic markers.⁹¹ This generally

⁸³ See generally *id.* at 976-79 (discussing the "rent dissipation theory" in the context of patent law).

⁸⁴ See generally Mark F. Grady & Jay I. Alexander, *Patent Law and Rent Dissipation*, 78 VA. L. REV. 305, 312-20 (1992) (comparing, by analogy, the invention/patenting and prospecting systems).

⁸⁵ Once information becomes a part of the public domain, that is, already within the pool of knowledge held by the public, it is no longer patentable. This is because the purpose of the patent laws is to foster the development of scientific invention and creativity in the useful arts by giving rewards to inventors—traditionally in the form of the exclusivity and ownership of a patent. Once this knowledge falls into the public trough, no reward need be given. See 35 U.S.C. § 102 (a) (1994).

⁸⁶ See Marshal, *supra* note 73, at 1800.

⁸⁷ See Leslie Roberts, *Top HHS Lawyer Seeks to Block NIH: What the Patent Office Report Says*, 258 SCI. 209 (1992).

⁸⁸ See Marshal, *supra* note 73, at 1800.

⁸⁹ See Bylinsky, *supra* note 13, at 94; Carey, *supra* note 12, at 72.

⁹⁰ See Rose, *supra* note 12, at A1.

⁹¹ See Rebecca S. Eisenberg, *Genes, Patents, and Product Development*, 257 SCI. 903 (1992); Roberts, *supra* note 11, at 912.

masks the true intention: to lay claim to the unknown gene product which that small mapped sequence represents.⁹²

If the biotech prospectors are successful in claiming ownership of one or more of those genes which can be used to produce a cure or medicine capable of treating genetic afflictions, or diseases generally, they then stand to make very high profits in their race to extract the secrets of the human genome.⁹³

1. Characterizing the Genes

The process of characterizing a gene is that of identifying the behavior, function and sequence of the gene.⁹⁴ That is, not only is the physical sequence of its nucleic acids determined, but its molecular weight is approximated and its protein product is identified and/or isolated.⁹⁵ These determinations are in addition to determining its function and genetic effect within the genome where it is native.⁹⁶ The methods used to divine this knowledge vary, but often involve isolating the gene and cloning it into another living system, typically bacteria, for study.⁹⁷

It is important to mention that although each cell of a creature generally has within it all of that organism's genes, not every cell type will express all of those genes. Gene expression varies by cell type,⁹⁸ the condition of the cells,⁹⁹ and perhaps the stage of their life cycle.¹⁰⁰ Within the context of this article, that means that different cell types, or cells raised in different conditions, will express different genes.¹⁰¹ For those seeking gene fragment patents, this means that when attempting to collect different gene fragments, scientists must work with a variety of cell types and cell culture conditions.¹⁰² This is all done in order to maximize the number of different mRNA's (i.e., expressed genes) retrieved.

⁹² See McKay, *supra* note 10, at 486-88; see also Thomas Kiley, *Patents on Random Complementary DNA Fragments?*, 257 Sci. 915 (1992).

⁹³ See *Drug Research*, *supra* note 4.

⁹⁴ See generally ALBERTS, *supra* note 51, at 188-96.

⁹⁵ See generally *id.* at 190-96.

⁹⁶ See generally *id.* at 190-96, 570-87.

⁹⁷ See generally *id.* at 180-95.

⁹⁸ Cells, though they contain within their genetic complement all of the genes of an organism, vary in their expression of those proteins. That is, skin cells do not express an identical set of proteins with neural cells. See generally *id.* at 595-602.

⁹⁹ See generally ALBERTS, *supra* note 51, at 595-602.

¹⁰⁰ See generally *id.* at 750-80.

¹⁰¹ See generally *id.*

¹⁰² See generally *id.* at 740-55.

2. The Commercial Importance of Biotechnology

Through the techniques already described, biotechnology is finding applications in a wide variety of fields with a large and growing number of lucrative commercial uses.¹⁰³ However, precise determinations of the effect of biotechnology on the economy is difficult mainly because many of the firms employing the techniques developed through biotech research are not "obviously" part of the biotechnology industry. In fact, many of the firms may be classified as belonging to very different economic sectors.¹⁰⁴ The federal government estimated that, in 1992, over 1,200 firms nationwide were extensively engaged in this technology.¹⁰⁵ This census of biotechnology firms ranges from those pursuing R&D, to those supplying raw materials.¹⁰⁶ Almost half of these firms are small and relatively new corporations, start-ups, that tend to be very sensitive to the economics of patent protection and availability.¹⁰⁷ Though small, these companies are known to provide jobs for over 45,000 people.¹⁰⁸

Another measure of this industry is accomplished by classifying the end products and services that have been supplied largely through the use of biotechnology. This list includes over 2,800 each of drugs, diagnostic tools, and other biotech products (serums, vaccines, and cell culture stocks of microorganisms).¹⁰⁹

The government estimated that, by 1992, biotechnology sales reached the \$3 billion mark, a track record that indicates steady growth.¹¹⁰ The reason for this consistent and spectacular growth in sales may be that the therapeutics developed are often the only source of treatment for a given affliction, which leads to extremely healthy prices for the delivered goods. This is typically in conjunction with, and reliant upon, patent protection for the therapeutics delivered, thereby limiting or eliminating competition for a significant period.¹¹¹

¹⁰³ See INDUSTRIAL OUTLOOK, *supra* note 14, at 17-1.

¹⁰⁴ See *id.* In fact the federal government does not consider "biotechnology" an industry of its own. This is reflected in the failure of the government to include those companies extensively using biotechnology in the production of their goods or services.

¹⁰⁵ See *id.* at 17-2.

¹⁰⁶ See *id.*

¹⁰⁷ See *id.*

¹⁰⁸ See INDUSTRIAL OUTLOOK, *supra* note 14, at 17-2.

¹⁰⁹ See *id.*

¹¹⁰ See *id.*

¹¹¹ See *SmithKline Beecham Chief Says Patents Vital to New Cures*, PR Newswire, Sept. 14, 1995.

While it is likely that the economic importance of biotechnology will continue to grow, the future commercial success of biotechnology will depend on a number of factors. A vast amount of research, both basic and applied, remains to be completed before even the fundamental functions of many microorganisms and their genes are understood.¹¹² This must be done in an effort to develop new therapeutics or new approaches to disease treatment. The ability to attract the necessary capital is also a difficult problem, since the time that elapses between the initiation of basic research and the approval of an applied product or process can be incredibly lengthy and draining.¹¹³ Within that time frame, there is a growing backlog of patent applications in the Patent and Trademark Office (PTO), which is known for the inconsistencies of its approvals.¹¹⁴

III. PATENTABILITY

A. Basic Patent Law

According to Black's Law Dictionary, the definition of a patent is "[a] grant of right to exclude others from making, using or selling one's invention and includes [the] right to license others to make, use or sell it."¹¹⁵ This grant of right, in effect a monopoly on the invention, is effective for only a limited duration, for which the Constitution gave no specified length.¹¹⁶ Thus, the actual duration was left for Congress to manipulate as it saw fit. Through recent changes, the statutory duration is twenty years from the date of application.¹¹⁷ This is the end product of a balancing act between public policy and individual monopoly power,¹¹⁸ with the understanding that by giving inventors personal rewards for their efforts, which are embodied in the patent given to them, society and the "useful Arts" will be fostered.¹¹⁹

¹¹² See Carey, *supra* note 12, at 72.

¹¹³ See Chase, *supra* note 5, at 24.

¹¹⁴ See INDUSTRIAL OUTLOOK, *supra* note 14, at 17-5. See, e.g., John Carey, *Untangling the Legal Strands of DNA*, BUS. WK., May 22, 1995, at 42.

¹¹⁵ BLACKS LAW DICTIONARY 1125 (6th ed. 1990).

¹¹⁶ U.S. CONST. art. I, § 8, cl. 8.

¹¹⁷ See 35 U.S.C. §154 (1994).

¹¹⁸ See Richard Hofstadter, *What Happened to the Antitrust Movement*, in THE BUSINESS ESTABLISHMENT 113 (Earl F. Cheit ed. 1964). See, e.g., U.S. v. Aluminum Co. of America, 148 F.2d 416 (2d Cir. 1945) (asserting that "a patentee may not use his patent as a sanction for extending his monopoly beyond its terms").

¹¹⁹ See ARNOLD PLANT, *The Economic Theory Concerning Patents for Inventions*, in SELECTED ECONOMIC ESSAYS AND ADDRESSES 35 (1974).

The PTO actually issues more than one type of patent. There are utility patents, design patents, and plant patents.¹²⁰ Genes and gene fragments most usually fit in the utility patent framework. Utility patents cover machines, industrial processes, compositions of matter, and manufactured articles.¹²¹ These patents also cover patents relating to both a particular process and a straightforward patent on a given product. As would be expected from the name, the process patent holder controls the use of his patent and must receive royalties for the use of it. The process patent holder cannot, however, expect royalties from someone who uses an alternative process to get to the same product. Alternatively, a product patentee has rights in the product no matter how it is derived.¹²² For the most part, gene fragment patent applications fall into the product patent category.

By definition plant patents cover plants and their modification. It is important to note that it is possible to get patent protection for modification of plant cells similar to that given for bacteria.¹²³

Design patents provide protection for the design of different objects, usually of little relevance in the biotechnology arena.

1. Purpose

With the power to use tools to change our environment comes the understanding that some individuals will create something novel, unique, and useful. This creation is not directly the product of generations of tool users, it is a truly new addition to our store of knowledge. As a society, we know that some of these creations are beneficial to us. Such being the case, we have come to the conclusion that it is in our benefit to promise and thereafter deliver incentives to these individuals to reward their creativity. Since, as a society, we have decided that the ownership of property is proper, limited ownership of ideas or intellectual property follows (if not logically, then for the sake of expediency) the public policy of stimulating creativity for the public good.¹²⁴ This is the basis for the issuance and ownership of patents and other intangi-

¹²⁰ See Thomas G. Field, Jr., *Brief Survey of Intellectual Property*, 31 IDEA 85, 91-92 (1990).

¹²¹ See *id.*

¹²² See *In re Pilkington*, 411 F.2d 1345 (C.C.P.A. 1969) (patenting improved plate glass).

¹²³ See *Ex parte Hibberd*, 227 U.S.P.Q. (BNA) 443, 444 (PTO Bd. of Patent Appeals and Interferences 1985).

¹²⁴ See Michael S. Greenfield, *Recombinant DNA Technology: A Science Struggling with the Patent Law*, 44 STAN. L. REV. 1051, 1057-58 (1992).

ble property.¹²⁵ This is also what the genetic entrepreneur seeks—ownership of a portion of the human genetic complement. With it, they will have a tool with which to control the access to, and rents for, its therapeutic, commercial, and/or scientific value.¹²⁶

The roots of American intellectual property protection are old ones, enshrined in the Constitution itself. Article I, § 8, cl. 8, of the Constitution instructs us that the purpose of patents is to “[p]romote 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.”¹²⁷ Though the system has been changed several times since its Constitutional creation, it remains largely intact today, and arguably one of the reasons for the eminence of the United States in the value of its intellectual property.¹²⁸ Inherent in its basic mode of award, the brief monopoly, is the concept that inventors will be given the time to exploit their creation. They need not fear more financially powerful competitors, for theirs is the power to exclude all others from making, using, or selling the patented concept.¹²⁹ This includes the right to exclude even innocent infringers who have developed the technology entirely on their own.¹³⁰

2. Requirements

Pursuant to its Constitutional authority, Congress has created several statutory provisions dealing with patents. While some argue that discoveries within the life sciences should have their own intellectual property category, or alternatively are not be patentable at all, currently all applications dealing with biotechnology are measured by the same federal statutory provisions all other would-be inventions are. To receive the brief monopoly that is a patent, the inventor must demonstrate that the invention (1) falls within the class of those things patentable, (2) demonstrates

¹²⁵ See ADAM SMITH, *THE WEALTH OF NATIONS* 189 (James E. Thorold Rogers ed., 2nd ed. 1880); JEREMY BENTHAM, *A Manual of Political Economy*, in *THE WORKS OF JEREMY BENTHAM* 71 (John Bowring ed. 1962); *Atlantic Works v. Brady*, 107 U.S. 192, 200 (1882).

¹²⁶ See Carey, *supra* note 12, at 72.

¹²⁷ U.S. CONST. art. 1, § 8, cl. 8.

¹²⁸ See Tara G. Giunta & Lily H. Shang, *Ownership of Information in a Global Economy*, 27 *GEO. WASH. J. INT'L L. & ECON.* 327, 328-29 (1994).

¹²⁹ See REPORT OF THE PRESIDENT'S COMMISSION ON THE PATENT SYSTEM 1-3 (1966).

¹³⁰ See generally 35 U.S.C. §281 (1994) (discussing remedies for patent infringements).

some utility, (3) is non-obvious to an ordinary practitioner in the relevant field, (4) is novel, and (5) is adequately disclosed.¹³¹

If the prospective patentee can meet all of these requirements, then a United States patent should be issued. The inventor, thereafter, has a right to exploit the technology disclosed, and/or to prevent all others from using this technology.

a. Patentability, § 101

Section 101 of the Patent Act broadly defines patentable subject matter as "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof."¹³² Existing case law and statutes clearly indicate that the products and processes elucidated through biotechnology techniques can be patented.¹³³ The commercial rewards that patentability promises are critical to the maintenance of the biotechnology industry, without which, the future of the industry may be compromised.¹³⁴

The only true judicial obstacle to the patenting of biotechnology products and processes was the "products of nature" doctrine. This view, best articulated in *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, holds that products of nature cannot be patented, since nothing novel was ever created.¹³⁵ More recently, however, the Court has steadily moved away from this position barring biotechnology patents. In the landmark *Diamond v. Chakrabarty*¹³⁶ case, the Court, in a 5-4 decision, held that microorganisms modified by Man were patentable. Thereafter, a steady series of case law has developed supporting the view that biotechnology inventions are properly the subject of patent protection.¹³⁷

¹³¹ See 35 U.S.C. §§101-104 (1994).

¹³² See 35 U.S.C. § 101 (1994).

¹³³ See *Diamond v. Chakrabarty*, 447 U.S. 303 (1980) (holding that a live, human-made microorganism is patentable).

¹³⁴ See Michael Waldholz & Hilary Stout, *A New Debate Rages Over the Patenting of Gene Discoveries*, WALL ST. J., Apr. 17, 1992, at B1.

¹³⁵ See *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948) (holding that a patent for bacteria was invalid because "patents cannot issue for the discovery of the phenomena of nature" and because the qualities of the bacteria were "manifestations of laws of nature, free to all men and reserved exclusively to none").

¹³⁶ 447 U.S. 303 (1980).

¹³⁷ See *Ex parte Hibberd*, 227 U.S.P.Q. at 443 (granting a patent on plants and seeds); *Ex parte Allen*, 2 U.S.P.Q.2d (BNA) 1425 (PTA Bd. of Patent Appeals & Interferences 1987) (holding that synthetically grown oysters were patentable); see also, *In re Bergy*, 596 F.2d 952 (C.C.P.A. 1979), cert. granted, 444 U.S. 924 (1979), vacated as moot, 444 U.S. 1028 (1980) (holding that processes, one of the

b. Utility, § 101

Because the utility standard has long been considered a de minimis one,¹³⁸ it is seldom a real bar to the issue of a given patent. All that is required is a showing that the claimed invention has some practical, if attenuated, application or use.¹³⁹ Further, there is no requirement for the utility of the new product or process to be superior to any existing or established products or processes.¹⁴⁰ Within the realm of biotechnology, it is to be expected that a patent sought probably relates to some inherent biologic function, but a use must still be demonstrated for the patent to be issued.¹⁴¹ In the context of this article, the gene fragments for which patent protection is sought would seem to have at least the modest utility of serving as chromosomal markers, or gene probes, to aid in the mapping of the human genome.¹⁴²

c. Non-Obviousness, § 103

Section 103 of the Patent Act lays out the parameters of non-obviousness when it states that:

A patent may not be obtained . . . , if the differences between the subject matter sought to be patented and the prior art 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 [relevant] art.¹⁴³

The standard enunciated by section 103 is a blanket one that applies, as do all of the statutory standards described herein, to

categories of subject matter specified in § 101, are uniformly and consistently considered to be statutory subject matter "notwithstanding the employment therein of living organisms and their life processes").

¹³⁸ See, e.g., *Ex parte Drulard*, 223 U.S.P.Q. (BNA) 364 (PTO Bd. of Patent Appeals & Interferences 1983) (holding patentable a portable lightning rod which, even though potentially unsafe, was sufficiently useful to satisfy 35 U.S.C. § 100's utility standard).

¹³⁹ See 35 U.S.C. §101 (1994).

¹⁴⁰ See 1 DONALD S. CHISUM, PATENTS § 4.01 (1996).

¹⁴¹ See *Brenner v. Manson*, 383 U.S. 519 (1966) (upholding a PTO rejection of a specific steroid because the applicant had not demonstrated any practical use or function). In *Brenner*, the Court was reluctant to overturn the PTO's rejection of the patent because to do so without the demonstration of a function could "block off whole areas of scientific development." *Id.* at 534.

¹⁴² See *Roberts*, *supra* note 11, at 912. Many would dispute this in asserting that the gene fragments are just that, fragments with no known function. Without this function and true utility, patentability cannot be established. See Lynn E. Barber, *Biotechnology Inventions: What is Patentable?*, BT CATALYST, May 1, 1994.

¹⁴³ 35 U.S.C. § 103 (1994).

all patents with no changes made for the technical peculiarities of biotechnology or the nature of the subject matter, organic or otherwise.¹⁴⁴

Courts are directed to consider, besides the differences between the "new" and already existing technology, secondary factors such as commercial success, the need for the invention, and the failure of others to develop the technology previously.¹⁴⁵ These factors are used as indicia of the non-obvious nature of the new technology. For example, if the invention has great commercial success, it could be inferable that had it been an obvious improvement, someone would have already developed it. If the analysis of the newly claimed invention and the pre-existing technology leads to the conclusion that one of ordinary skill in the relevant field would have developed the technology, or that such an improvement would have been obvious to such a person, then the improvement is considered obvious and patent protection is not available.¹⁴⁶

Regarding biotechnology, the methods used to achieve a given end are often rejected by the PTO examiners because these methods are analogous to the methods of other researchers or are obvious from methods previously described in the journal art.¹⁴⁷

d. Novelty, § 102

As is well known, a patent issues only for some "new" creation or invention.¹⁴⁸ If the element of novelty does not exist in a given creation, then the proper subject matter of a patent is also absent. Section 102 requires that the invention cannot be in the hands of others, nor can it have been disclosed to the public domain prior to the application of the patent.¹⁴⁹ In essence, this requirement mandates that the *quid pro quo* for the limited monopoly of a patent is the development or revelation of something that is truly new. The demand for absolute secrecy prior to filing the patent application has been softened in the United States by allowing a patent to issue as long as the public disclosure, typically scientific

¹⁴⁴ See MICHAEL A. EPSTEIN, MODERN INTELLECTUAL PROPERTY § 11.02[A][4](1995).

¹⁴⁵ See *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966); see also Richard L. Robbins, Note, *Subtests of "Non-Obviousness": A Nontechnical Approach to Patent Validity*, 112 U. PA. L. REV. 1169 (1964).

¹⁴⁶ See *Graham*, 383 U.S. at 17.

¹⁴⁷ See Barber, *supra* note 142.

¹⁴⁸ See 35 U.S.C. § 102 (1994).

¹⁴⁹ See R.S. CRESPI, PATENTS: A BASIC GUIDE TO PATENTING IN BIOTECHNOLOGY 62 (1988).

publication, is followed by the filing of a patent application within a year.¹⁵⁰

e. Disclosure, § 112

Section 112 of the Patent Act requires an enabling disclosure before an invention is patentable.¹⁵¹ This disclosure must be sufficient to allow one skilled in the art to practice the invention.¹⁵² This public disclosure, and eventual entrance of the knowledge into the public domain, as already mentioned, is the *quid pro quo* that society requires of inventors in exchange for the reward of a temporary monopoly, and was one of the grounds upon which the NIH's patent applications for gene fragments was rejected.¹⁵³

B. Patenting Organisms

Should "human-made" life be patentable or otherwise amenable to ownership and protection in a market economy? Although the more correct term would be "human-modified" life,¹⁵⁴ this question has arisen as a consequence of modern genetics technology, and the unprecedented powers of precisely directed manipulation which it offers.¹⁵⁵ For example, the prospect of genetically

¹⁵⁰ See *id.* at 123.

¹⁵¹ See 35 U.S.C. § 112 (1994). This enablement requirement is necessary so that the information which is protected by the patent can be practiced by the public, as a part of the public domain, after the patent expires. This requirement is distinct from the "best mode" requirement also present in section 112. The enablement requirement calls for an objective description of the invention, capable of "teaching" it; while the "best mode" is a subject measure of how to practice that invention, and is very difficult to police. See also *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1986).

¹⁵² See 35 U.S.C. § 112 (1994).

¹⁵³ The problem was one of providing an adequate enabling disclosure. See Roberts, *supra* note 87, at 210. It seems that problems of this sort would be easily resolved if industry were given the certainty that patents for gene fragments would issue, if they met other statutory requirements.

¹⁵⁴ Modified in that humans are taking pre-existing organisms and manipulating them to express genes that they normally would not. To properly "create" an object it would seem that it should be made out of whole cloth, or at least something that functions or exists in an entirely new way- the vast majority of genes present within genetically altered organisms function as they have for millennia. See Ned Hettinger, *Patenting Life: Biotechnology, Intellectual Property, and Environmental Ethics*, 22 B.C. ENVTL. AFF. L. REV. 267, 279-83 (1995).

¹⁵⁵ Some possibilities that are presented by the advent of genetics technology include age-separated clones as children, cadavers as embryo donors, immunosuppressed animals as "incubators" for human organs, microorganisms as factories for any organic chemical or hormone that someone desires to produce, gene therapy for real or *perceived* deficiencies in any organ system or trait,

manipulating animals to recreate human disease systems is an old tool in contemporary research.¹⁵⁶ And the recognition of patent rights in these animals has grown apace.¹⁵⁷ In short, the answer to the question posed is one we have already heard. The province of our patent laws has long since recognized the ownership of ideas, and more recently, this ownership has been extended to living things.¹⁵⁸

With the advent of modern biotechnology we accelerate what we have done for millennia - the development of new and better tools. Today these tools can be organic and/or animate in nature,¹⁵⁹ but in essence the same human creativity and ingenuity which gave life to all of the previous generations of tools has also made these new organic tools, or vectors, possible.¹⁶⁰ This then puts the validity of these patents on the same theoretical plane with the manipulation of non-living matter. Thus, it is as logical to issue patents for work on the truly novel and beneficial creations derived from the life sciences, as it is to issue patents for inventions in the areas of computer science or metallurgy.¹⁶¹ If this answer is troubling, then the concept of ownership itself must be examined, not the

selective abortion based on the likely genetic predisposition of a fetus to any of a number of criteria. For a discussion of these possibilities and their accompanying issues see Michael D. Davis, *The Patenting of Products of Nature*, 21 RUTGERS COMPUTER & TECH. L.J. 293 (1995); Byron V. Olsen, Note, *Rust in the Laboratory: When Science is Censored*, 58 ALB. L. REV. 299, 318-21 (1994); Rebecca S. Eisenberg, *Genetics and the Law: Patenting the Human Genome*, 39 EMORY L.J. 721 (1990); Eric W. Gutttag, *The Patentability of Microorganisms: Statutory Subject Matter and Other Living Things*, 13 U. RICH. L. REV. 247 (1979); Philip L. Bereano, *Body and Soul: The Price of Bio-Tech — Who Owns What Rights to Which Parts of Living Organisms?*, THE SEATTLE TIMES, Aug. 20, 1995, at B7; Mike McKee, *The Patent That Time Forgot*, THE RECORDER, June 26, 1995.

¹⁵⁶ See *DNX Develops New Mouse Model to Advance Heart Disease Research*, PR Newswire, May 23, 1995.

¹⁵⁷ See Edmund L. Andrews, *US Resumes Granting Patents on Genetically Altered Animals*, N.Y. TIMES, Feb. 3, 1993, at A1.

¹⁵⁸ In 1987 the Board of Patent Appeals and Interferences held that genetically altered (polyploid) oysters were patentable subject matter. See *Ex parte Allen*, 2 U.S.P.Q.2d at 1425. On April 12, 1988, the Patent and Trademark Office issued its first animal patent. This patent was for a mouse genetically altered to recreate a human disease condition which would lead to cancer. See also U.S. Patent No. 4,736,866.

¹⁵⁹ See Highfield, *supra* note 27, at 5.

¹⁶⁰ See *Diamond*, 444 U.S. at 1028; *In re Bergy*, 596 F.2d at 952. But cf. Ronald Cole-Turner, *Religion and Gene Patenting*, 270 SCIENCE 52 (1995) (discussing the disagreement that some religious, including Christian, denominations have with the notion of patenting life or living systems).

¹⁶¹ But see Hettinger, *supra* note 154, at 304 (arguing that "[o]rganism and gene patents should be resisted not because technology should be resisted, but

peripheral questions of ownership or exploitation of a certain class of material, land, or creatures.

Humanity does not, as yet, have the power to create any conscious or coherent life forms from inert materials; this power remains in the hands of the metaphysical. However, researchers in the biologic sciences do have the training and power to significantly alter or modify existing organic systems. But we must admit that in truth this is no different from what We have done for ages. Humankind has long cultivated specific varieties of plants or domesticated certain animals, always with an eye towards making the strain or breed more beneficial for Us and Our interests.¹⁶² The break with the past provided by biotechnology, so alarming to some, does not come from the nature of the activity, just its speed. The tools now available are simply more powerful, more swift, and are available for the manipulation of all life as we know it, not simply a narrow class of domesticated forms.¹⁶³

1. Case Law Landmarks

A single vote majority in the *Diamond v. Chakrabarty*¹⁶⁴ decision upheld the idea that human altered life is patentable. Since this decision, considerable advancement has been made in the biological sciences, to the point that a mouse as well as several other living things have been granted patents using the same rationale.¹⁶⁵

rather because these bio patents are a morally dangerous and inappropriate way of thinking about and encouraging biotechnology.”)

¹⁶² See Reid G. Adler, *Controlling the Applications of Biotechnology: A Critical Analysis of the Proposed Moratorium on Animal Patenting*, 1 HARV. J.L. & TECH. 1, 20 n.126 (1988).

¹⁶³ What is important in the debate over the patentability of human-modified life is not that technology changes our lives and our understanding of how the world works, but that the things which make us uniquely human and more than a collection of cells or chemical reactions are preserved and celebrated.

¹⁶⁴ See *Diamond*, 447 U.S. at 303 (holding in favor of a patent on a microorganism genetically designed to consume oil). See also *In re Bergy*, 596 F.2d at 952; Lisa J. Raines, *The Mouse that Roared: Patent Protection for Genetically Engineered Animals Makes Legal, Moral, and Economic Sense*, ISSUES SCI. & TECH., Summer 1988, at 64, 65-66.

¹⁶⁵ See *Ex parte Hibberd*, 227 U.S.P.Q. at 443 (granting a patent on plants and seeds); *Ex parte Allen*, 2 U.S.P.Q.2d at 1425 (holding that synthetically grown oysters could be patented); see also *In re Bergy*, 596 F.2d at 952 (holding that processes, one of the categories of subject matter specified in § 101, are uniformly and consistently considered to be statutory subject matter “notwithstanding the employment therein of living organisms and their life processes”).

Recent cases reflect not only the occasional difficulty that courts sometimes have with the technical aspects of gene patents but more importantly, the overall trend which supports the patentability of living organisms generally, and genes in particular. Moreover, this trend has specific resonance within the context of this article, since the recognition that the courts have extended has only come with the disclosure of a complete genetic sequence. That is, these cases demonstrate that courts respect the patentability of genes only when those genes are fully disclosed, as demonstrated through the provision of their full DNA sequence.

In *Amgen, Inc. v. Chugai Pharmaceutical Co.*,¹⁶⁶ the court provided patent protection for the genomic sequence of a valuable blood protein erythropoietin - a protein which acts by stimulating the growth of red blood cells. Validity in *Amgen* was found through the patentee's provision of the full DNA sequence of the protein.¹⁶⁷ This position was strengthened in *Ex Parte Maizel*,¹⁶⁸ where the tribunal found *unpatentable* an application that did not provide a full DNA sequence for a specific sequence of amino acids.¹⁶⁹ Other cases have followed this same pattern of granting patents for gene products, but only where the full DNA sequence is laid out in the claims of the patent.¹⁷⁰

2. Genes and Gene Fragments

As discussed *supra*, the Patent and Trademark Office and the federal courts have recognized the patentability of genes. Since the *Chakrabarty* decision in 1980, well over 5,000 United States patents have issued related to human or animal genes.¹⁷¹ Some of the better known and more recent examples of this practice

¹⁶⁶ *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200 (Fed. Cir. 1991).

¹⁶⁷ *See id.* at 1206-07.

¹⁶⁸ 27 U.S.P.Q.2d (BNA) 1662 (PTO Bd. of Patent Appeals and Interferences 1992).

¹⁶⁹ *See id.* at 1665.

¹⁷⁰ *See In Re Bell*, 991 F.2d 781, 783 (Fed. Cir. 1993) (declaring the validity of a patent issued to an applicant who provided a full DNA sequence and holding that a fully sequenced gene is not *prima facie* obvious merely because the amino acid sequence of its coded protein is known); *Fiers v. Revel*, 984 F.2d 1164 (Fed. Cir. 1993) (awarding, in an interference proceeding between three foreign patent applicants, the patent for an interferon molecule to the applicant who had provided the full DNA sequence).

¹⁷¹ *See Jenish, supra* note 2, at 36.

include genes controlling diabetes,¹⁷² tuberculosis,¹⁷³ colon cancer,¹⁷⁴ or genes helpful in detecting leukemia,¹⁷⁵ or breast cancer.¹⁷⁶ Though the value of genetic information, in a scientific sense, is due to the physiological and genetic activity of that gene in a living system, the potential rewards for the commercial use of the genes cited above is obvious and constitutes the primary reason why the race to patent the genome is on.

What has recently thrown the biotechnology patent field into turmoil, however, was the attempt by the NIH to patent gene fragments before the functional nature of their gene products or even their full DNA sequence was known.¹⁷⁷ The NIH filed an application to patent 351 cDNA gene sequences or gene fragments in June of 1991.¹⁷⁸ In February of 1992, the NIH added another application for patents on over 2,400 more gene fragments.¹⁷⁹ With the sheer number of fragments claimed by the NIH and the possibility that the NIH could swiftly repeat this action with more fragment patents,¹⁸⁰ the whole of the biotechnology industry was forced to take notice.¹⁸¹ This activity was a significant departure from customary scientific and patent practice. Typically scientists and the biotech industry have waited to patent genes or their products until the gene had been fully characterized or sequenced.¹⁸² Corporations and individual researchers are under-

¹⁷² See U.S. Patent No. 5,324,641 (claiming genetic sequences for insulin precursors).

¹⁷³ See U.S. Patent No. 5,370,998 (claiming a DNA sequence that can be used in screening for tuberculosis).

¹⁷⁴ See U.S. Patent No. 5,362,623 (claiming a gene that if mutated can cause cancerous tumors in several organs, including the colon).

¹⁷⁵ See U.S. Patent No. 5,397,696 (claiming a human T-cell line with an infecting virus, thought to be useful in developing screening techniques for T-cell leukemia).

¹⁷⁶ See Eliot Marshal, *A Showdown Over Gene Fragments (Commercial Control of Genetic Data)*, 266 SCI. 208 (1994) (stating that the gene isolated is called BRCA1 (breast cancer antigen 1) and will help scientists devise genetic probes to identify not only its presence in its normal form, but also in its defective form which seems to lead to breast cancer). Myriad Genetics, Inc. and the University of Utah have applied for a patent. *Id.*

¹⁷⁷ See *id.*

¹⁷⁸ See Pamela A. Docherty, Comment, *The Human Genome: A Patenting Dilemma*, 26 AKRON L. REV. 525, 525 (1993).

¹⁷⁹ McKay, *supra* note 10, at 476.

¹⁸⁰ See *id.* at 474-77.

¹⁸¹ See Leslie Roberts, *Genome Patent Fight Erupts*, 254 SCI. 184 (1991); Christopher Anderson, *NIH Drops Bid for Gene Patents*, 263 SCI. 909 (1994).

¹⁸² See generally Rebecca S. Eisenberg, *Proprietary Rights and the Norms of Science in Biotechnology Research*, 97 YALE L.J. 177, 186 (1987) (observing that patent law "restricts the patentability of basic research discoveries through the

standably fearful that waiting to fully characterize, or at least fully sequence, genes or gene products could mean the loss of patent protection and their financial investments. They have and continue to mimic the actions of the NIH by filing or preparing to file patent applications for their own massive libraries of gene fragments.¹⁸³

C. *Gene Fragments: The Case for Patentability*

Perhaps the principal argument for the patentability of these gene fragments is that, with patent protection, there would be sufficient financial incentive for biotech corporations, and their supporters in the venture capital field, to invest the money and resources needed to develop the therapeutics that are locked within the human genome.¹⁸⁴ The possibilities for the cure of different types of cancer, heart disease or other afflictions lends tremendous support to the view that if the patent laws currently do not support the patentability of these fragments, the patent laws should change to reflect the societal need for this technology and/or the special nature of biotechnology.¹⁸⁵ This view holds that the prizes to be gained are potentially so socially valuable that society itself should provide every incentive to the corporations who can make these life saving therapeutics a reality.

Another, but related, argument for the patentability of genes generally, and gene fragments specifically, is the commercial need for this protection.¹⁸⁶ In many cases the availability of patent protection for corporations engaging in biotechnology R&D is essential to their survival.¹⁸⁷ Today the biotechnology industry is growing, but is still in its infancy.¹⁸⁸ Because it generally takes so much investment to develop and get approval for a new therapeutic, the companies within the field are still economically vulnerable.¹⁸⁹ If the fringes of patent protection were deemed to include

requirement that a patent applicant make a disclosure demonstrating that the invention is 'operable and capable of use' before a patent will issue").

¹⁸³ See McKay, *supra* note 10, at 477.

¹⁸⁴ See *Drug Research*, *supra* note 4.

¹⁸⁵ See *Patents: Senate Subcommittee Hearing Focuses on Rejection of NIH Gene Patent Requests*, Daily Rep. for Executives (BNA), at 186-89 (Sept. 24, 1992); Christopher Anderson, *A New Model for Gene Patents?*, 260 SCI. 23 (1993).

¹⁸⁶ See Hilary Stout, *U.S. Pursuit of Gene Patents Riles Industry*, WALL ST. J., Feb. 13, 1992, at B1.

¹⁸⁷ See Barber, *supra* note 142.

¹⁸⁸ See INDUSTRIAL OUTLOOK, *supra* note 14, at 17-2 - 17-3.

¹⁸⁹ See CONGRESS OF THE UNITED STATES, OFFICE OF TECHNOLOGY ASSESSMENT, *BIOTECHNOLOGY IN A GLOBAL ECONOMY* 6 (1991); Dan L. Burk,

gene fragments, quickly unlocking the human genome to biotech prospecting, it is likely that the industry itself would see the increased investment and improved security that the ownership of such patents would generally provide.¹⁹⁰

Besides the argument for enhanced industry security, allowing patent protection would stimulate this and related business sectors by creating jobs and contributing to a positive balance of trade that the United States generally enjoys within the intellectual property marketplace.¹⁹¹

Any unfair advantage or excessive profits taken by the biotech industry is simply the price that must be paid. If the government wants to temper this potential robber baron activity it should not fail to pursue its own patents, as the NIH has done, but pursue its own patents.¹⁹² These patents would provide the government with a tool of leverage over the biotechnology companies with regard to their eventual market pricing and behavior.¹⁹³ Or, the government could simply allow the patents and later set a price ceiling.

D. Gene Fragments: The Case Against Patentability

It is possible that some therapeutic agents may reach those who need them faster by way of making special provisions for the biotechnology industry and the patentability of gene fragments. However, it must also be pointed out that by allowing the patentability of gene fragments under current patent laws, the PTO could be forced to later invalidate more important applications, such as those revealing a gene's full sequence and/or functional nature, as obvious due to the presence of these prior "fragment patents."¹⁹⁴ Moreover, the fact is that patents for gene fragments could lead to the dilemma where multiple research teams, each with a partial gene sequence, could receive a patent for segments of the same gene.¹⁹⁵ While this is not a problem with regard to the utility of

Biotechnology and Patent Law: Fitting Innovation to the Procrustean Bed, 17 RUTGERS COMPUTER & TECH. L.J. 1, 22-23 (1991).

¹⁹⁰ See Burk, *supra* note 189, at 22-23.

¹⁹¹ See INDUSTRIAL OUTLOOK, *supra* note 14 at 17-3.

¹⁹² See McKay, *supra* note 10, at 476-477.

¹⁹³ See Stout, *supra* note 186, at B1.

¹⁹⁴ Simply stated, patents on application for gene fragments.

¹⁹⁵ By the possession of patents on separate fragments of a gene, and not that gene's full sequence, there is the possibility of conflict in the form of patent interference litigation, over ownership if the different parties have claimed different portions of the same underlying gene. The chance of this occurring is made more possible if the investigators are looking in the same chromosomal

these separate fragments as chromosomal markers or probes,¹⁹⁶ it could cause some high anxiety if these two fragments turned out to be portions of the same expressed gene. The first conflict would be between the patent holders to determine which one controlled access to the gene product, and second, if both were determined to have control over their given fragment of the gene, researchers or corporations would likely have to negotiate with both patent holders in order to utilize the protein product of the underlying gene. And it is possible that this could have the effect of preventing useful research simply because of the cost of negotiating a second license.¹⁹⁷ The resulting drag on research could have the downstream effect of actually slowing down research and the arrival of needed therapeutics.¹⁹⁸

1. Science at Too High a Price

The arguments above generally relate to the positive aspects the commercial exploitation of the human genome would bring, but they generally do not address the concerns that critics of patenting gene fragments bring forward. Among these is the need to foster the development of the scientific arts.

As a society it is generally in our interest to stimulate research. But by providing patent protection and private ownership for portions of the human genome, and thereby the right to collect rents on use, we run the risk of inflating the price of basic or applied research to the point that it is too costly for academics and some corporations to use.¹⁹⁹ In a world where government money for basic research is consistently declining,²⁰⁰ and many biotechnology firms exist on the margins, this increase in costs not only runs counter to the principles underlying the patent laws, preventing

region for a gene that is believed to contain one or more potentially valuable commercial application(s).

¹⁹⁶ The separate fragments, and the patents on them, would not interfere with each other in the context of markers, simply because while they might be a part of the same underlying gene, their role as markers or probes would remain unaffected, since in this context they are in actuality separate sequences that are simply located closely together.

¹⁹⁷ See McKay, *supra* note 10, at 493-94.

¹⁹⁸ See *NIH Gene Patent Application is Debated at Forum on Human Genome*, 44 PAT., TRADEMARK & COPYRIGHT J. (BNA) 73, 75 (1992) (statement of attorney of Michael Roth: "[i]nstead of paving the road to further advances, . . . NIH has erected a tollbooth along the way by filing for a patent.").

¹⁹⁹ See Eisenberg, *supra* note 155, at 741-42.

²⁰⁰ See Olsen, *supra* note 155, at 313, tbl. I.

widespread use of improvements, but could act as a restraint on the rate of scientific progress.²⁰¹

2. Scientific Collaboration

Within the confines of academia, the concept of collaboration is an old one.²⁰² However, the possibility of private ownership of segments of the human genome, and the potential value thereof, could send a chill through the scientific research community.²⁰³ Though this suggestion is rather a broad one, the international and collaborative character of the Human Genome Project²⁰⁴ itself lends credence to the view that if fragment patents are seen to be legitimate, then labs around the world could turn from treating the Project as a collaborative effort for the social good, into a race in which he who has the most patents wins. This attitude is potentially detrimental to the concept of collaboration in general and could lead to increased secrecy between laboratories, even in the labs of public research institutions,²⁰⁵ thereby preventing the free flow and full disclosure of information, confounding the public policy justifications for patent protection, and needed scientific collaboration.²⁰⁶

3. Current PTO Standards

The most basic case against the patentability of gene fragments is the application of current statutory requirements. The PTO rejected the NIH patent applications for genetic fragments under more than one statutory ground.²⁰⁷ Though, as already discussed *supra*, fragment patents constitute patentable subject matter and most likely meet the necessary threshold of utility, their problems

²⁰¹ See WARD S. BOWMAN, JR., *PATENT AND ANTITRUST LAW: A LEGAL AND ECONOMIC APPRAISAL* 26 (1973).

²⁰² See Eisenberg, *supra* note 182, at 181-82.

²⁰³ See McKay, *supra* note 10, at 477-78.

²⁰⁴ See MAPPING OUR GENES, *supra* note 8, at 8.

²⁰⁵ See Bernice Wuethrich, *All Rights Reserved: How the Gene-Patenting Race is Affecting Science*, SCI. NEWS, Sept. 4, 1993, at 154.

²⁰⁶ See *id.*; see also BOWMAN, *supra* note 201, at passim (discussing, throughout, the conflicts and compatibilities of patent and antitrust law).

²⁰⁷ See Hilary Stout, *Gene-Fragment Patent Request Is Turned Down*, WALL ST. J., Sept. 23, 1992, at B1. This is not to say that the NIH's applications would have been denied had they been appealed, but that their initial rejection should, at the least, provide a healthy amount of caution for those investing time and resources into an effort to generate and garner patent protection for their gene fragments.

lie with successfully enduring the scrutiny of both the requirement for non-obviousness and the novelty standard.

First the PTO indicated that in light of prior art, the fragments themselves were obvious.²⁰⁸ The importance of this prior art is difficult to overstate in the discussion as to whether the gene fragments that many corporations are seeking to patent can, in fact, be patented. If the procedures used by the average researcher are identical to those used by these companies to find and classify their cDNA clones, it may prove impossible to patent *any* gene fragments in the future, since the process by which the gene fragments are generated, sequences varying as they may, would be obvious.²⁰⁹ Additionally, once a full gene is found the obvious next step is to sequence it using established procedures and to try and identify the protein product of the gene. Thus, it is possible that this protein itself, or the process used to find it, would itself be unpatentable as obvious under existing technology.²¹⁰ Moreover these techniques represent not only established procedures in many molecular biology labs, but have long been published in the relevant journal art, affecting both obviousness and novelty concerns.²¹¹ In addition, the use of gene fragments, essentially small sequences of cDNA, as probes or genetic markers, is not a novel concept.²¹²

Two interesting caveats are important to note here. It is possible that if the human genome is claimed through the generation of a torrent of fragments, later discoveries of truly unknown genes may be unpatentable for obviousness. That is, the simple use of "known" gene fragments in conjunction with reverse transcriptase PCR techniques, or other newer sequencing tricks, could bar patentability even though a future researcher might be providing a

²⁰⁸ See *id.*

²⁰⁹ The typical procedure involved is the use of the enzyme reverse transcriptase to create a cDNA clone from a messenger RNA molecule (mRNA). The mRNA represents an active or expressed gene, typically without any introns or intervening sequences. The use of mRNA and reverse transcriptase can then be used to generate a large pool of cDNA's. Then the use of various techniques to capture these cDNA's and determine a portion of their sequence for use as probes, or markers, or as gene fragments is subject to a host of already obvious procedures. See WATSON, *supra* note 20, at 260-70.

²¹⁰ See McKay, *supra* note 10, at 485.

²¹¹ See AMERICAN SOCIETY OF HUMAN GENETICS, POSITION PAPER ON PATENTING OF EXPRESSED SEQUENCE TAGS 2 (1992) [hereinafter AMERICAN SOCIETY].

²¹² See SUZUKI, *supra* note 19, at 79-81.

new protein with a previously unknown function.²¹³ More to the point, some of the gene sequences which the NIH sought to patent had within them stretches that had already entered into the public domain through prior publication.²¹⁴ This obviously destroyed their novelty.

From a statutory perspective these factors indicate that not only may future patent applications for gene fragments be rejected as obvious, they may also be denied through similar reasoning for lack of novelty. After all, as more and more cDNA fragments make their way into the public domain via journal publications, it will become more and more difficult to prove that a given application demonstrates the required non-obviousness, or that a given sequence is novel.²¹⁵

With the current existence of a severe backlog on patent applications at the PTO,²¹⁶ there exists another, very simple, reason to deny the patentability of gene fragments- the PTO simply cannot handle the volume. As researchers and corporations race to locate as many gene fragments (*e.g.* cDNA's) as possible, there is the possibility that the PTO will be overwhelmed by a tsunami of applications for gene fragment patents.²¹⁷ One need only conjure up the example of Venter's solitary NIH lab locating 2,000 gene fragments each month to understand that it is possible that there could be, literally, tens of thousands of applications dropped on the PTO in short order.²¹⁸ And though there is "only" an outer limit of 100,000 human genes, the availability of thousands of different gene fragment patents from the genes of a multitude of other organisms demonstrates the point that the four or five year wait seen as recently as 1990, could be considerably extended.²¹⁹ This outcome is itself inhibitory of scientific progress and since patent protection now begins from the date of application, this deluge could adversely affect the intellectual property rights, and

²¹³ See *id.* at 80.

²¹⁴ See Stout, *supra* note 207, at B1. In addition, other organizations have taken the public position that the short cDNA sequences that Dr. Venter and the NIH have sought to patent are obvious in light of the fact that the techniques used to generate these fragments are already within widespread use in the scientific community. See also AMERICAN SOCIETY, *supra* note 211, at **.

²¹⁵ See McKay, *supra* note 10, at 482-84.

²¹⁶ See Eisenberg, *supra* note 155, at 741-42.

²¹⁷ See Anderson, *supra* note 11, at 301.

²¹⁸ See Deborah Shapley, *Gene Genie: A Look at One Scientist's Potentially Revolutionary Effect on Genetic-Related Business*, FIN. TIMES (London), June 14, 1994, at 17.

²¹⁹ See Eisenberg, *supra* note 155, at 742; Wuethrich, *supra* note 205, at 155.

therefore the economic stability, of those seeking patent protection simply by slowing down the PTO.²²⁰

Alternatively, if gene fragments were determined to be unpatentable, then the route to patent protection for genes or their products would have to at least travel through the full sequencing of the gene. This would have the beneficial effect of limiting patent applications, not to small fragments of every human gene expressed, but only to those which actually had some real potential for therapeutic or commercial use. Consequently, the PTO would be able to do its job and give patent applicants a chance to have their patents issue in a reasonable time.

IV. THE LICENSING OF GENE FRAGMENTS

The holder of a patent for a gene or gene product is actually the owner of a bit of genetic information concerning the chemical composition of that gene. Anyone wanting to use this information, or the product it encodes, must then negotiate an assignment or licensing arrangement with the patent holder.²²¹ While the purchase of an assignment transfers substantially all the right inherent in the patent to the assignee, this is not true of a license.²²² The purchase of a license, exclusive or non-exclusive, does not transfer ownership of the patent to the licensee, it merely allows that licensee to practice the patent while being immune from suit by the patent owner.²²³ Without this privilege, the monopoly power of the patentee would allow him to exclude all others from the practice of the invention.²²⁴

Because the issue of gene fragment patentability has not been resolved, it is not surprising to suggest that the best course to take when involved in negotiations over the licensing of gene fragments is one in full contemplation of their tenuous patentability. Because the NIH did not pursue the rejection of their fragment applications, we do not know if the fragments are, in fact, unpatentable. And while the analysis above indicates that these fragment applications are unlikely to issue, that outcome is not certain. In fact, many corporations are investing quite a bit of time and money proceeding on the assumption that gene frag-

²²⁰ See Rose, *supra* note 12, at A-1.

²²¹ Any unauthorized use of a patent is illegal infringement, and is actionable.

²²² See *Waterman v. MacKenzie*, 138 U.S. 252, 255 (1891).

²²³ See HARRY R. MAYERS & BRIAN G. BRUNSVOLD, *DRAFTING PATENT LICENSE AGREEMENTS* 29-33 (3rd. ed. 1991).

²²⁴ See *id.* at 217-19.

ments are patentable.²²⁵ Given the broad readings that patent cases from *Chakrabarty* to *Amgen* have received from the courts, it is possible that existing jurisprudence, which would likely deny patentability, could be brushed aside to aid both the delivery of therapeutic agents and the biotechnology industry.

The best course for all concerned is to act cautiously. Perhaps the most instructive course is to look at *Aronson v. Quick Point Pencil Co.*²²⁶ In that case, the participants anticipated the invalidity of the patent, or its denial, and planned for royalty arrangements accordingly. Because the royalty arrangement negotiated reflected that situation, some assurance was made with regard to the longterm relationship between the parties. Given the uncertain climate, and the NIH's failure to appeal the denial of its gene fragment patent applications, this provision for a certain level of royalties should a patent issue, and another level if it does not, is the best approach for both potential licensors and licensees.²²⁷ Licensing of intellectual property is an important consideration in biotechnology because the individual discoverer of a new product or process often does not have the desire or the wherewithal to fully develop or market the idea enclosed within the patent.²²⁸ Licensing allows the patent holder to generate royalties while the licensee is free to develop and deliver the product.

²²⁵ See Erramouspe, *supra* note 82, at 962-63.

²²⁶ 440 U.S. 257 (1979); see also *Boggild v. Kenner Products*, 776 F.2d 1315 (6th Cir. 1985) (holding that "the terms of a licensing agreement calling for royalty payments beyond the life of the patent are unenforceable where the parties enter the agreement with clear expectations that a valid patent will issue").

²²⁷ That said, it is clear that the two parties negotiating the transfer of unpatented proprietary information (i.e. gene fragments) certainly do have different interests to maintain, and likely, different strategies to follow. The strategy potentially of value to the putative patent holder is to license the technology in light of the probable denial of patentability with regard to the royalties. That is, to structure the license in such a way that acknowledges the difficulty in obtaining the patent, and its possible invalidity, and thereafter set the royalty rates accordingly- a higher rate, or maintenance of an initial rate if the patent issues, and a lower rate in the event that the patent does not issue.

The strategy of value for the potential licensee is to license the technology at a given rate, assuming it will be patented, and with no other language. If the patent does not issue or is held invalid through other proceedings, the licensee has no more royalties to pay, even if the licensee initiated those proceedings (i.e. patent invalidity proceedings).

²²⁸ See generally Ronald Rosenberg, *Taking Gene Therapy to the Market*, BOSTON GLOBE, Jan. 22, 1995, at 80, (discussing how biotechnology firms are now providing research to larger pharmaceutical companies).

V. FUTURE CHANGES

A. *International Implications*

The growing importance of intellectual property in the world market is hard to overstate. This is clearly demonstrated through the remarks of Bruce A. Lehman, United States Commissioner of Patents and Trademarks, when he said, "Property has always been the essence of capitalism. The only difference is property is changing from tangible to intangible. Today, the only wealth there is in the world is the wealth that comes from the human mind."²²⁹ The conception that the wealth of nations will, in the future, originate primarily from human ingenuity and control of information, as opposed to wealth in raw materials, is one gaining in acceptance.²³⁰ With regard to biotechnology and genetic information, however, there exist several hurdles between acceptance of patentability in the United States and similar acceptance in the world community.²³¹

1. The European Union

While there is little to suggest that Japan has difficulties in pursuing the patentability of genes,²³² the same is not true within the European Union (EU).²³³ As one of our biggest trading partners and chief competitors in the biomedical research field,²³⁴ Western Europe currently has an internal debate ongoing about biotechnology patentability issues.²³⁵ Similar in many respects to debate within the United States about the ethics of biotechnology, European reservations about patentability issues have a strong element of ethical outrage to them.²³⁶ These ethical concerns

²²⁹ Marsa, *supra* note 1, at 36.

²³⁰ See Giunta & Shang, *supra* note 128, at 327 (discussing how the economy of the world is becoming more dependent on informational goods).

²³¹ See Looney, *supra* note 7, at 232 (discussing that while the United States has attempted to patent gene sequences, France has chosen not to do so).

²³² See Joan O.C. Hamilton, *Measuring Biotech by Patents is Patently Absurd*, BUS. WK., Apr. 22, 1996, at 47; Dennis Normile, *Consortia to Boost Efforts to Develop Genome Industry*, 270 SCI. 1432 (1995); Stephen H. Dunphy, *The Newsletter*, SEATTLE TIMES, Apr. 5, 1996, at D1.

²³³ See Convention on the Grant of European Patents, Oct. 5, 1973, art. 53(a)-(b).

²³⁴ The United States, through its massive investment in biomedical research, leads the world in this field. See INDUSTRIAL OUTLOOK, *supra* note 14, at 17-3.

²³⁵ See generally *id.* at 17-5 (commenting that the United States government is attempting to "harmonize" patent procedures with those of Europe).

²³⁶ See Looney, *supra* note 7, at 231 (discussing several ethical questions concerning genetic technology).

originate from what is seen as the race to own the universal heritage of Mankind.²³⁷ It is important to note, however, that the practical outcome of these public policy statements is limited. Importantly, they have not inhibited the move towards the patentability of organisms, and perhaps gene fragments, within the EU.²³⁸ Though some of these criticisms have found voice within European policy directives,²³⁹ and that debate will continue for sometime, it is doubtful that the trend towards the acceptance of intellectual property protection for genes will be halted.²⁴⁰ Recent examples of patent protection being extended to living organisms and other products of biotechnology indicate that although many have difficulty with the allowance, there will be protection for biotechnology corporations when they seek patent protection for their discoveries in the EU.²⁴¹ Regarding gene fragments, it seems as if in the EU the issue of gene fragment patentability is not as separable from gene patenting overall.²⁴² Therefore once gene patenting is more clearly available in Europe, it is likely that some protection for gene fragments would follow quickly thereafter, even if this is not the case in the United States.²⁴³

2. Genetic Colonialism

Within the international community some have decried the efforts of American researchers or corporations to gather genetic sequences from the four corners of the world.²⁴⁴ The reason for this criticism is not in the collection of the genetic information *per se*, but rather in the attempt to make it proprietary or patentable.

²³⁷ See Hubert Curien, *The Human Genome Project and Patents*, 254 *SCI.* 1710 (1991).

²³⁸ See Looney, *supra* note 7, at 231-34.

²³⁹ See *id.* at 231-32.

²⁴⁰ See *id.* at 240-43 (discussing how patenting is a reward for human efforts).

²⁴¹ See *id.* at 245-47.

²⁴² See *id.* at 265-66.

²⁴³ See Looney, *supra* note 7, at 265-66.

²⁴⁴ See Eliot Marshal, *The Company that Genome Researchers Love to Hate: Human Genome Sciences Inc.*, 266 *SCI.* 1800 (1994); Marsa, *supra* note 1, at 36.

ble.²⁴⁵ These practices have been dubbed "genetic colonialism,"²⁴⁶ and are akin to the Western exploitation of the raw materials, seen all too often in lesser developed countries (LDC's).²⁴⁷ Many other cultures see the approval of patents on portions of the genetic code as improper in and of itself,²⁴⁸ but even more so when Western researchers present in LDC's take genetic sequences from local inhabitants or other sources and turn them into potentially valuable patents, with no concern either for the values of the individuals used, or the approval of the governments involved.²⁴⁹ It is uncertain what the outcome of this new exploitation will be,²⁵⁰ but it is unlikely that the sources of these novel genetic sequences, namely the people living in the LDC's of the sequences' origin, will ever benefit financially or medicinally for their contribution to the West's pharmacies.²⁵¹

B. Proposals for Legislative Change in the United States

As technology pushes back the frontiers of what is possible, society must decide what it will allow. In the discussion above the focus has been on the availability of patent protection for discoveries and developments within the arena of biotechnology. That discussion has referenced the current statutory structure for patents generally, as well as the trends in the judicial interpretation of these statutes. The current reading of what is required for biotechnology patents in the areas of organisms and genes indicates both tolerance for these patents and a broad reading of the Patent

²⁴⁵ See Charles J. Hanley, *Are Patents Business as Usual Even in Biology*, THE COMMERCIAL APPEAL (Memphis, Tennessee), Apr. 21, 1996, at 11A. After all, if the lesser developed countries were assured of access to the therapeutics that might result, independent of their economic ability to pay the resulting premium prices, it is very unlikely that any protest would be voiced. Alternatively, patenting and use of these genetic resources in the West without any remuneration to those from whom they were taken is the essence of colonialism.

²⁴⁶ See Charles J. Hanley, *A Case of Good Research or "Genetic Colonialism?"*, L.A. TIMES, Apr. 21, 1996, at A1.

²⁴⁷ See Hope Shand, *Agbio and Third World Development*, BIO/TECHNOLOGY, Mar. 1993, at S13.

²⁴⁸ See BBV Foundation, INTERNATIONAL WORKSHOP ON THE HUMAN GENOME PROJECT: LEGAL ASPECTS - *Bilbao Declaration* para. 10, adopted May 26, 1993; Philip L. Bereano, *Patent Nonsense — Patent Pending: The Race to Own DNA*, SEATTLE TIMES, Aug. 27, 1995, at B5; Curien, *supra* note 237, at 1710.

²⁴⁹ See Bereano, *supra* note 248, at B5; see also, Hettinger, *supra* note 154, at 287-288 nn. 107 & 109.

²⁵⁰ See Bereano, *supra* note 248, at B5.

²⁵¹ See Hettinger, *supra* note 154, at 287-288 n. 109.

Act.²⁵² Ultimately, however, control of the proper boundaries of patentability lies with Congress, as the elected representatives of our society. It is important that Congress address a number of concerns in this industry so that there can at least be certainty not only for those concerned about realizing patent protection for their creativity, but also for those concerned about limiting ownership rights in the patrimony of all Mankind.

Among the issues that Congress should resolve regarding gene patents is the artificial tollbooth that thousands of patents on various segments of the human genome would create for basic research.²⁵³ The prospect of forcing scientists to pay a toll for fundamental research, in an era of declining expenditure on research, is a very unpleasant one. The public interest is generally served by allowing scientists full access to current technology. Therefore Congress should consider an exemption from patent infringement when the art taught by the patent is used solely for experimentation.²⁵⁴ This would not deprive patent holders from commercially exploiting their invention, and would support the public interest in furthering research.²⁵⁵

By definition, gene fragments and patents relating to them do not include full DNA sequences of the gene. Those seeking patent applications for fragments are claiming that the utility of the fragments lies in their use as markers or probes.²⁵⁶ To allow patents on these gene fragments, for anything other than *as* probes or markers, could be to unnecessarily prevent patents on the full sequences later.²⁵⁷ Thus legislation limiting the protection of the gene fragment patents to the use of that fragment as a marker or probe would be appropriate.²⁵⁸ This would prevent corporations or other filers from realizing a monopoly on a full gene product when they only know a fragment of its sequence, giving incentive to further research.

²⁵² See *Diamond v. Chakrabarty*, 447 U.S. 303 (1980); *In re Bell*, 991 F.2d 781 (Fed. Cir. 1993).

²⁵³ See McKay, *supra* note 10, at 493.

²⁵⁴ See Eisenberg, *supra* note 182, at 217-22.

²⁵⁵ See Eisenberg, *supra* note 155, at 741-43.

²⁵⁶ See David N. Leff, *Gene-Hunters' Free For All on Web, Whitehead Institute Unveils World's First Complete Map of Human Genome*, 6 *BIOWORLD TODAY*, Dec. 22, 1995; Roberts, *supra* note 11, at 912.

²⁵⁷ See McKay, *supra* note 10, at 493.

²⁵⁸ See Christopher Anderson, *A New Model for Gene Patents?*, 260 *SCIENCE* 23 (1993). See, e.g., Ko, *supra* note 24, at 796-804.

Alternatively, Congress should make the decision that the patentability of genes is appropriate and in the interests of our society because it is likely that the patentability of such fragments will hasten the delivery of life-saving medicines or treatments. If this delivery, with its attendant problems discussed *supra*, is deemed a social good, then Congress should amend the Patent Act to either create a new biotechnology specific provision, or act to lower the hurdles to passing the obviousness and novelty requirements of current regulations. As already seen, gene fragment patentability is doubtful precisely because of obviousness and novelty concerns within existing statute provisions.

C. *The Speed of Technological Progress*

It is possible that the dilemma faced by those seeking to patent gene fragments will soon be moot. The speed of change and development within the biotechnology community is a startling one, and the development of an alternate procedure for determining the chromosomal location, sequence, and function of a human gene is highly possible. Dr. Venter's automation certainly accelerated the identification of human genes.²⁵⁹ It did not, however, allow any measurable insight into the functions of those genes, or their potential scientific or commercial application. Despite this potentially significant problem with patentability, the gene-hunters seeking commercial control of their discoveries feel that if they can claim enough DNA segments they can expect to refine a treasure trove of genetic products. However, progress in biotechnology is rapid and it is possible that the development of a new process will emerge that will allow a quick process of identifying full genes and their functions, thereby by-passing the current dilemma.²⁶⁰

VI. CONCLUSION

In balancing societal interests for the patentability of genes the most relevant issue is the knowing manipulation of living systems. It is this new power of controlled and precise change, tied to the creativity of an inventor, that makes the manipulation of living matter the proper subject of patent protection.

²⁵⁹ See Marshal, *supra* note 73, at 1800; see also Chase, *supra* note 5, at 24.

²⁶⁰ See Carey, *supra* note 114, at 42.

Living systems, from bacteria,²⁶¹ to tomatoes,²⁶² to mice²⁶³ have been redesigned in a way to perform some known task or function, or to mass produce some gene product. Without an understanding of the precise change made or the actual function of the discovery, there is no invention or creation from the mind of Man which has been crafted. Instead, a recapitulation of Nature's own structure is only partially described. For this reason, patents for gene fragments should not issue. Not only do these applications fail under existing statutory provisions, but to allow them would greatly complicate the burden on the PTO, and perhaps impede progress within the useful arts as well.

The control of living systems now available through the development of biotechnology is both an expansion of what can be patented and a limit on what should be. Controlled manipulation of the sequence of a gene or genes is necessary for an inventor to actually know what he or she has developed and helps justify the patentability of organisms or genes. Limits are drawn when this basic knowledge is absent.

Perhaps a genetic gold rush is imminent, but right now the technology responsible for the quick determination and accumulation of gene fragments is insufficient to provide patent protection. For this reason, the actions of the biotechnology corporations are premature and attempts to license this technology should proceed with caution.

²⁶¹ See *Diamond v. Chakraborty*, 447 U.S. 303, 307-10 (1980).

²⁶² See *Union of Concerned Scientists, FDA Approves the Calgene Tomato, No Labeling Required*, THE GENE EXCHANGE, June 1994, at 1.

²⁶³ See U.S. Patent No. 4,736,866; see also SHELDON KRIMSKY, BIOTECHNICS AND SOCIETY: THE RISE OF INDUSTRIAL GENETICS 44-46 (1991).