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PATENT LAW AND REGENERATIVE MEDICINE: A CONSIDERATION OF THE CURRENT LAW AND PUBLIC POLICY CONCERNS REGARDING UPSTREAM PATENTS

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INTRODUCTION

This article focuses on patentability issues concerning biotechnology, with specific emphasis on the status of patent law as it applies to regenerative medicine. The purpose of the article is to consider whether the United States' protection of patents covering gene sequences and human embryonic stem cells is consistent with traditional patentability standards of patent law. In addition, the article provides an analysis of the impact and potential consequences of providing broad patent protection over what are, essentially, the building blocks of human life and essential keys to the progress of biotechnology.

Part I provides a brief overview of biotechnology in general. This section notes the impressive advances that are currently developing and the exciting opportunities and growth the field of biotechnology promises. Furthermore, Part I introduces the somewhat controversial and recently upheld Wisconsin Alumni Research Foundation ("WARF") patents which broadly cover the creation and use of embryonic stem cells.[1] This section briefly reflects on the

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[1] These controversial patents which have been embroiled in controversy for over two years include Patent 6,200,806, widely known as the "stem cell patent," which claims a method of "isolating a . . . human embryonic stem cell line," as well as the "purified preparation of . . . human embryonic stem cells." Amy Rachel Davis, *Patented Embryonic Stem Cells: The Quintessential "Essential Facility"?*, 94 GEO. L.J. 205, 207 (2005).

potentially adverse goals of the biotechnology industry: the societal goal of providing optimal and holistic healthcare and open sharing of knowledge versus the fiscal goal of investing in important research for commercial gain and protecting that commercial interest. Simply put, patents ensure that the inventor is granted a limited monopoly. After the monopoly period runs, other players in the market will be able to enter and utilize the technology to benefit society; patent owners can also recoup their investments in technology through licensing their patented inventions and processes to others in the field. However, the broad granting of upstream patents can result in prohibitive costs and prevent small biotechnology companies from entering the field, thereby potentially hindering the advance and availability of important inventions benefiting society.

Part II analyzes the law regarding patents granted for living organisms and their building blocks like genes and stem cells. The analysis begins with an explanation of *Diamond v. Chakrabarty*, the first case to recognize that under 35 U.S.C. § 101[2] living organisms are indeed patentable.[3] Part II continues with a synopsis of the history of patent law regarding controversial gene patents—patents that seek to protect human DNA sequences responsible for forming proteins and other necessary building blocks of human life. Finally, Part II applies the United States Patent and Trademark Office's treatment of gene patents to the future of patents like those held by WARF regarding human stem cells, the very tools regenerative medicine currently utilizes to attempt relative medical miracles.

Part III considers the policy arguments against the issuance of broad patent protection with regard to genes and regenerative medicine. Additionally, this section outlines legislative attempts to regulate the issuance of upstream patents for inventions that are inherently part of human life, as well as several recommended approaches set forth by scholars to address biotechnology patents. Furthermore, Part III discusses the benefits and shortcomings of the advocated reforms and looks to the future of patent law as it affects the progress of the science of biotechnology and its potential benefits for society.

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[2] "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement therefor, may obtain a patent therefore, subject to the conditions and requirements of this title." 35 U.S.C. § 101 (2000).

[3] Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980).

I. THE PROGRESS, PROMISE, AND POTENTIAL PITFALLS OF BIOTECHNOLOGY

Advances in the field of biotechnology seek to revolutionize humans' ability to treat diseases and conditions in ways that years ago would have seemed impossible fantasies of science fiction. Today biotechnology is a multi-billion-dollar industry that has the potential to improve human life in significant ways.[4] From regenerating human tissue like fingers, or muscle tissue, to cultivating entire organs to be transplanted into humans, regenerative medicine promises just a few of the exciting developments in the field of biotechnology that await society.[5] Dr. Steven Badylak of the University of Pittsburgh's McGowan Institute of Regenerative Medicine has reported using a powder made from pig bladders to "tell" the body to start the process of tissue re-growth of a human finger.[6] Perhaps even more impressive, Dr. Atala who is the head of the Wake Forest Institute of Regenerative Medicine has successfully grown tissues and organs, including human bladders cultivated in a lab from patients' own cells, which were then successfully transplanted into those patients.[7] Other efforts in the regenerative medicine field include clinical trials that attempt to grow new arteries to supply the heart with blood by injecting a patient's stem cells into her heart, an experiment that, if successful, would substantially limit the need for actual open-heart surgery.[8]

In addition, advances in gene therapy and the mapping of the human genome have led to a multitude of medical and technological

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[4] *See*, *e.g.*, Press Release, Wake Forest University Baptist Medical Center, *Wake Forest Baptist's Selection to Co-Lead Regenerative Medicine Project Will Increase Activity at Piedmont Triad Research Park*, (Apr. 17, 2008), http://www.wfubmc.edu/news/newsprintfriendly.htm?ArticleID=2349. Tens of millions of dollars have been invested in research projects like Wake Forest University Baptist Medical Center's project for regenerative medicine. *Id.* Eighty-five million dollars in federal funds has been provided by the Armed Forces Institute for Regenerative Medicine ("AFIRM"). *Id.* These funds will supplement close to the two hundred million dollars raised by Wake Forest's consortium of partners who have pledged funds for regenerative medicine projects in the region. *Id.*

[5] Wyatt Andrews, *Medicine's Cutting Edge: Re-Growing Organs*, Mar. 23, 2008, CBS News, http://www.cbsnews.com/stories/2008/03/22/sunday/printable3960219.shtml.

[6] *Id.* The McGowan Institute has also recently patented technology for providing a platform for bone and tooth engineering and repair applications and in gene delivery. U.S. Patent No. 7,247,288 (filed Jul. 24, 2007).

[7] Press Release, Wake Forest University Baptist Medical Center, *Wake Forest Physician Reports First Human Recipients of Laboratory-Grown Organs*, (Apr. 3, 2006), http://www1.wfubmc.edu/News/NewsARticle.htm?ArticleID=1821.

[8] *See* Andrews, *supra* note 5.

advances that have significantly benefited society. Through the successful efforts of the Human Genome Project to identify the sequence of the human genome, scientists are now capable of identifying all human genes by their DNA sequence.[9] This capability creates a number of "opportunities for genetic intervention that include medical therapy (gene therapy), diagnostic screening for diseases (genetic testing), and large-scale production of medically-relevant purified proteins."[10]

In order to facilitate and stimulate research and development in the field of biotechnology, the U.S. Patent and Trademark Office has been quite liberal in its consideration of broad patents in the field of biotechnology. Faced with the pressure of attracting biotechnology investment to advance the domestic biotechnology industry, patent protection has increased, arguably at the expense of moral and ethical considerations and possibly to the disadvantage of progress in the field.[11] Patents have been awarded to protect necessary tools for the development and progress of biotechnology like gene sequences and human embryonic stem cells. As a result, downstream technologies may be prohibited from entering the market due to upstream patent holders setting up 'tollbooths' of high bargaining costs and licensing fees which arguably slow the pace of innovation.[12]

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[9] Laurie L. Hill, *The Race to Patent the Genome: Free Riders, Hold Ups, and the Future of Medical Breakthroughs*, 11 TEX. INTELL. PROP. L.J. 221, 226 (2003).

[10] *Id.* Gene therapy consists of replacing a malfunctioning gene with a functional gene. *Id.* This process enables scientists and researchers to explore new avenues for treating diseases that were once thought to be untreatable or intractable. *Id.* Genetic testing enables screening of individuals for genetic predispositions to specific diseases. *Id.* at 228. This field helps predict future risks, permit early intervention, and design patient-specific therapies. *Id.* Finally, purified protein production creates a stockpile of biologically functional proteins that can be used to treat disease and other disorders. *Id.*

[11] *See, e.g.*, Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698, 698 (1998) (warning of "the tragedy of the anticommons" where "a proliferation of intellectual property rights upstream may be stifling life-saving innovations further downstream in the course of research and product development"). A counterpoint to this argument is the reality that encouraging patent filing ensures the full disclosure that is required for patentability. Without patents in this field, those who would have only held a limited monopoly through a patent for a set period of time might keep their discovery undisclosed through the use of trade secret protection. This could potentially have a devastating effect on the free dissemination of research and discovery in the field of biotechnology; one that would rival the tragedy of the anticommons that Professors Heller and Eisenberg describe.

[12] Gregory C. Ellis, *Emerging Biotechnologies Demand Defeat of Proposed Legislation That Attempts to Ban Gene Patents*, 15 RICH. J.L. & TECH. 1, 18 (2008) (citing Linda J. Demaine & Aaron Xavier Fellmeth, *Reinventing the Double Helix: A*

The recent decision to uphold the WARF patents, covering three broad patents relating to embryonic stem cell research, potentially creates one such tollbooth.[13] These patents "broadly cover the preparation of embryonic stem cells, which are the basic material from which virtually all organs, cells and other body tissues are formed."[14] According to Tom Still, president of the Wisconsin Technology Council, the Patent Office's decision "secures the WARF intellectual property and secures WARF's place as a must-visit stop for people interested in stem cell technology."[15]

Adding to the controversy of these patents, Geron Corporation, a leader in the development of human embryonic stem cell-based therapeutics, holds an exclusive licensing agreement under these patents "to develop and commercialize therapies based on the three types of cells derived from human embryonic stem cells: neural cells, cardiomyocytes and pancreatic islet cells."[16] Though WARF has "adopted a policy of making [embryonic stem cells] widely available to non-profit researchers and granting non-exclusive licenses to firms pursuing commercial development of [embryonic stem cells]," Geron's exclusive contract to the three types of stem cells mentioned creates a potential dilemma for the advance of research requiring embryonic stem cells.[17] Geron has merely indicated that it will entertain licensing offers from commercial researchers, and its position as a large corporate entity might afford it the opportunity to refrain from licensing its cells, "forfeiting millions of dollars in royalties . . . [but] holding out for billions of dollars in profits . . . [once the company] finds its first groundbreaking cure."[18]

The implications of granting patents over such critical research tools are a major concern and the resulting public policy considerations are further developed in Part III. First, Part II will explore the statutory hurdles found in 35 U.S.C. §§ 101, 102, and 103,

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Novel and Nonobvious Reconceptualization of the Biotechnology Patent, 55 STAN. L. REV. 303, 418 (2002)).

[13] These include U.S. Patent No. 5,843,780 (filed Jan. 18, 1996), U.S. Patent No. 6,200,806 (filed Jun.26, 1998), and U.S. Patent No. 7,029,913 (filed Oct. 18, 2001).

[14] Kathleen Gallagher, *U.S. Office Upholds Embryonic Stem Cell Patents*, MILWAUKEE JOURNAL SENTINEL, June 27 2008, at D1, *available at* http://www.jsonline.com/business/29551579.html.

[15] *Id.*

[16] Press Release, *U.S. Patent Office Upholds Key Human Embryonic Stem Cell Patent*, Feb. 28, 2008, REUTERS, http://www.reuters.com/article/pressRelease/idUS144413+28-Feb-2008+BW20080228 (last visited Dec. 17, 2008).

[17] Davis, *supra* note 1, at 210 n.21.

[18] *Id.* at 210. Admittedly, this would amount to a significant gamble on the part of Geron; however, the possibility remains that a company could at least theoretically use their patent in such a way.

and their application with regard to gene patents, embryonic stem cells and the future of biotechnology and regenerative medicine.

II. THE PATENTABILITY, UTILITY, AND NON-OBVIOUSNESS OF REGENERATIVE MEDICINE THROUGH THE LENS OF GENE PATENTS

The United States Constitution grants Congress the power "[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."[19] The underlying purpose of the Patent Clause is to promote a balance between encouraging innovation and avoiding stifling competition by awarding monopolies. In achieving this end, the current federal law permits patents to provide for monopolies for a limited time of about twenty-years. In return, a patentee is required to specifically describe the invention, and the manner and process for making and using the invention "in such full, clear, concise, and exact terms as to enable any person skilled in the art" to make and use the claimed invention.[20]

A. 35 U.S. § 101—"PATENTABLE SUBJECT MATTER" AND "USEFULNESS" STANDARDS AS APPLIED TO GENE PATENTS AND REGENERATIVE MEDICINE

Once a claimed patent fulfills the requirements of specificity and exactness required by 35 U.S.C. § 112, it must overcome the hurdles of §§ 101, 102, and 103. The first hurdle, 35 U.S.C. § 101, describes what qualifies as patentable statutory subject matter under the statute. The statute states that: "[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title."[21] Generally, three areas do not qualify as patentable: (1) natural laws, (2) phenomena of nature, and (3) abstract principles (i.e., algorithms).[22] Thus, the question regarding the patentability of

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[19] U.S. CONST. art. I, § 8, cl. 8.

[20] 35 U.S.C. § 112 (2006). It should be noted that in addition to meeting the statutory hurdles of §§ 101, 102 and 103, those seeking a patent must also satisfy the requirements of the "enablement doctrine" codified in § 112. It is this principle of patent law that provides for the full disclosure that is the consideration for granting a limited monopoly in the first place.

[21] 35 U.S.C. § 101 (2006).

[22] *See* Parker v. Flook, 437 U.S. 584 (1977); Gottschalk v. Benson, 409 U.S. 63 (1972).

regenerative medicine is dependent upon whether patenting something like stem cells or genes, which occur in nature, are un-patentable phenomena of nature.

In a landmark case, *Diamond v. Chakrabarty*, the Supreme Court considered whether a human-made, genetically-engineered bacterium capable of breaking down crude oil, a property which is not possessed by any naturally-occurring bacteria, is patentable under § 101.[23] Originally, the patent examiner's rejection of the patent applicant's claims was affirmed by the Patent Office Board of Appeals on the ground that living things are not patentable subject matter under § 101.[24] The Court of Customs and Patent Appeals reversed, concluding that the fact that microorganisms are alive lacks legal significance.[25] The Supreme Court affirmed, holding that a live, human-made microorganism is patentable and that it constitutes a "manufacture" or "composition of matter" under the statute.[26]

In reaching its decision, the Court took note of the legislative history regarding the 1930 Plant Patent Act.[27] The Court noted that Congress "recognized that the relevant distinction was not between living and inanimate things, but between products of nature, whether living or not, and human-made inventions." Thus, the Court found that respondent's microorganism, though living, was the result of human ingenuity and research.[28]

Furthermore, the Court rejected The Commissioner of Patents' argument that microorganisms could not qualify as patentable subject matter until Congress expressly authorized such protection.[29] The Commissioner warned that the legislative process was best equipped

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[23] *See* Diamond v. Chakrabarty, 447 U.S. 303, 305 (1980).

[24] *Id.* at 306. The patent examiner rejected the claims for bacteria, stating (1) that microorganisms are "products of nature," and (2) that as living things they are not patentable subject matter under 35 U.S.C. § 101. *Id.* The Patent Office Board of Appeals relied on the legislative history of the 1930 Plant Act in affirming the rejection of the patent examiner. *Id.* The Board concluded that the bacteria were not "products of nature" because they were not naturally occurring, but nonetheless concluded that § 101 was not intended to cover living things. *Id.* at n.3.

[25] *Id.*

[26] *Id.* at 309-10 (stating that "[r]espondent's micro-organism plainly qualifies as patentable subject matter. His claim is not to a hitherto unknown natural phenomenon, but to a nonnaturally occurring manufacture or composition of matter—a product of human ingenuity 'having a distinctive name, character [and] use.'") (citation omitted).

[27] *Id.* at 311. The Court explained that, prior to 1930, two factors were relevant in excluding plants from patent protection: (1) the belief that plants were products of nature and (2) that plants were thought not amenable to written description. *Id.* at 311-12.

[28] *Id*. at 313.

[29] *Id.* at 314.

to weigh the competing economic, social and scientific considerations regarding "whether living organisms produced by genetic engineering should receive patent protection."[30] However, the Court rejected these arguments and the foreboding warnings of the implications of granting patent protection to such genetic research, finding it was the legislature's job to consider the policy, while the Court's job is the narrow task of determining what Congress meant by the words Congress used in the statute.[31] Thus, the Court interpreted the statutory language to protect respondent's invention and advised that Congress was free to amend § 101 to exclude from patent protection organisms produced by genetic engineering as it saw fit.[32]

Congress did no such thing and because of the judicial acceptance, demonstrated by the *Chakrabarty* case, a number of patents relating to biotechnology, including gene patents, and most recently, patents for developing human embryonic stem cells, have been found to be valid. Critics of gene patents have asserted that genes are "products of nature" and, therefore, are not patentable, echoing the original criticisms against the patent issued in *Chakrabarty*.[33] Today, despite these criticisms, the relaxed standard of *Chakrabarty* has extended from genetically modified microorganisms to the U.S. Patent and Trademark Office's ("USTPO") recognition of purified DNA sequences as patentable subject matter.[34]

In 2001, the USTPO published a revised version of guidelines for office personnel in their review of patent applications for compliance with the "utility" requirements of 35 U.S.C. § 101.[35] This revision was published in response to numerous comments urging that genes are discoveries rather than inventions, thereby suggesting that patents should not be issued for genes.[36] The USTPO looked to the Patent Clause and the relevant statute in determining that "an inventor's discovery of a gene can be the basis for a patent on the genetic composition isolated from its natural state and processed through purifying steps that separate the gene from other molecules naturally associated with it."[37] In response to concerns that genes are not a new composition of matter because they exist in nature, the

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[30] *Id* at 314. The Petitioner further points to the grave risks that may be generated by research endeavors such as respondent's. *Id.* at 316.
[31] *Id*. at 318.
[32] *Id.* According to the Court's interpretation of the statutory language, "Congress intended statutory subject matter to include anything under the sun that is made by man." *Id.* at 309 (citation omitted).
[33] Ellis, *supra*, note 12, at 12.
[34] *See* Utility Examination Guidelines, 66 Fed. Reg. 1092, 1095 (Jan. 5, 2001).
[35] *Id.* at 1092.
[36] *Id.* at 1093.
[37] *Id.*

USPTO observed that "synthetic DNA preparations are eligible for patents because their purified state is different from the naturally occurring compound."[38] This reaffirmed principles set out in legislative history and judicial precedent, upholding the granting of patents to chemical compounds, hormones, and other naturally occurring phenomena that did not occur in an isolated form in nature.[39] This principle can be applied to the WARF patents for embryonic stem cells since the patents cover all purified preparations of isolated stem cells matching the patents' descriptions, making these inventions patentable statutory subject matter under § 101.[40]

Despite being found to be patentable under § 101, the claimed invention must also satisfy the "utility" requirement of the statute. Prior to the issuance of the revised Guidelines it was relatively unclear what degree of disclosure was necessary to satisfy the utility requirement, and further, how broad disclosure affected previously unconsidered applications.[41]

For example, in 1992, Dr. Craig Ventner applied for gene patents covering expressed sequence tags, short segments of DNA that represent portions of expressed genes that could be useful in mapping which DNA sequences are protein-coding genes.[42] Though Ventner eventually applied for patents for these sequences citing their utility to diagnose genetic disorders, the USPTO denied his applications, implying that "simply finding a gene sequence without an established utility does not merit patent protection."[43]

The issue of undiscovered uses for genes not disclosed in gene patents raises an even larger and more complex issue.[44] In 1995, the Human Genome Sciences ("HGS") filed an application for a gene known as HDGNR10, citing generic claims that the gene was useful

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[38] *Id.*

[39] *See*, *e.g.*, Parke-Davis & Co. v. H.K. Mulford Co., 189 F. 95, 103 (S.D.N.Y. 1911) (holding that adrenaline removed from the gland in which it was found was patentable where it became a new thing commercially and therapeutically); *In re* Bergstrom, 427 F.2d 1394, 1397 (CCPA 1970) (holding purified compounds that do not exist in nature in pure form are patentable). *See also* Amgen, Inc. v. Chugai Pharm. Co., Ltd., 927 F.2d 1200, 1206 (1991). *Amgen* established the "human intervention" standard that the U.S. Court of Appeals observes in upholding the patentability of human DNA sequences in their purified and isolated form. Donna M. Gitter, *International Conflicts Over Patenting Human DNA Sequences In the United States and the European Union: An Argument For Compulsory Licensing and a Fair-Use Exemption*, 76 N.Y.U. L. REV. 1623, 1642 (2001) (citing *Amgen*, 927 F.2d 1200 (1991)).

[40] Davis, *supra* note 1, at 219.

[41] Ellis, *supra* note 12, at 16-22.

[42] *Id.* at 17 (citation omitted).

[43] *Id.* (citation omitted).

[44] *Id.* at 18.

for "'identifying [receptor] antagonists and agonists.'"[45] Unbeknownst to HGS and discovered just a year later by the National Institutes of Health ("NIH") was the fact "that the protein encoded by the gene, named CCR5 by the NIH scientists, was . . . a receptor essential for HIV infection."[46] Thus, despite being unaware of the true utility of its patent, HGS ultimately enjoys the exclusive right to license and patent the CCR5 protein to companies attempting to develop an HIV vaccine, based merely on its generic and broadly stated patent.[47]

In addressing these issues, the USPTO added in its revisions regarding gene patents that "[when] the inventor also discloses how to use the purified gene isolated from its natural state, the application satisfies the 'utility' requirement."[48] In disclosing "how to use" the claimed gene sequence, the patentee must meet three utility criteria: the utility must be specific, substantial and credible.[49]

While the USTPO guidelines are not law, *In re Fisher*, a 2005 Federal Circuit decision, affirms the heightened utility guidelines.[50] *In re Fisher* concerned a claimed invention relating to five purified nucleic acid sequences and protein fragments in maize plants.[51] Like Ventner's failed patent claim discussed above, Fisher's claimed sequences were also expressed sequence tags or "ESTs."[52] The patent examiner rejected claim one for lack of utility under § 101, finding that the disclosed uses were "not supported by a specific and substantial utility." In reviewing the examiner's decision, the Board focused on two claimed utilities: "(1) use for identification of polymorphisms; and (2) use as probes or as a source for primers."[53] The Board concluded that the use of ESTs to isolate nucleic acid molecules of other plants and organisms which had no known utility is not a substantial utility.[54] The Board also held that the claimed sequence must provide some sort of teaching regarding how to use the data relating to gene expression observed using the ESTs.[55]

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[45] *Id.* at 18. *See also* U.S. Patent No. 6,025,154 (filed June 6, 1995).
[46] Ellis, *supra* note 12, at 18.
[47] *Id.*
[48] Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (Jan. 5, 2001).
[49] *Id.* at 1092.
[50] Ellis, *supra* note 12, at 22.
[51] *In re* Fisher, 421 F.3d 1365, 1367 (2005).
[52] *Id.*
[53] *Id.* at 1368.
[54] *Id.* at 1369.
[55] *Id.*

In explaining its reasoning, the Board relied on the Supreme Court's decision in *Brenner v. Manson* in which the Court rejected a process for making a compound with no known use.[56]

The Court of Customs and Patent Appeals, in considering the Board's rejection of the patent, held that a patent application must contain disclosure which establishes a specific and substantial utility for the claimed invention.[57] Recognizing that the Supreme Court has not defined what the terms "specific" and "substantial" mean per se, the court explained that "substantial utility" has been used by the courts interchangeably with the labels "practical utility" and "real world" utility.[58] The court observed that these terms mean that one skilled in the art can use the claimed discovery in a manner that provides some "'*immediate benefit to the public*.'"[59] The court reasoned that this means that "an application must show that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research."[60]

In considering the WARF Patent No. 6,200,806, covering primate embryonic stem cells, the utility function is clearly and concisely stated and, as stated, provides immediate benefits to society.[61] Specifically, the patent covering these human embryonic stem cells cites uses, such as "generating transgenic non-human primates for models of specific human genetic diseases," as well as usage in "[t]issue transplantation."[62] Thus, because the isolated and purified human stem cell does not occur naturally in its isolated form, and because the stated uses in the patent are specific and provide immediate benefit to the public, the WARF stem cell patent adequately satisfies the first prong of the three-hurdle analysis.

B. 35 U.S.C. §§ 102 AND 103—"NOVELTY" AND "NON-OBVIOUSNESS" STANDARDS AS APPLIED TO GENE PATENTS AND REGENERATIVE MEDICINE

[56] *Id.* ("Just as the process in *Brenner* lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the specification does not disclose how to use SEQ ID NO: 1-5 specific gene expression data." (citing Brenner v. Manson, No. 58, slip op. at 22 (U.S. March 21, 1966))).
[57] *In re* Fisher, 421 F.3d 1365, 1371 (2005).
[58] *Id.*
[59] *Id.* (citing Nelson v. Bowler, 626 F.2d 853, 856 (C.C.P.A. 1980)).
[60] *Id.*
[61] U.S. Patent No. 6,200,806 (filed June 26, 1998) (issued Mar. 13, 2001).
[62] *Id.* at col. 6 ll. 4-5, 14.

After establishing under Title 35 of the United States Code (i.e. the Patent Act) that an invention is indeed patentable, statutory subject matter and that the invention has substantial utility in that it has immediate public benefit, one seeking a patent must next overcome the statutory hurdles set forth in 35 U.S.C. §§ 102 and 103. These provisions consider whether an invention seeking patent protection is "novel" and "non-obvious" respectively.[63] The Federal Circuit Court of Appeals considered these requirements in detail in the gene patent discussion set forth in *Amgen, Inc. v. Chugai Pharmaceutical, Co.,* in 2001.[64]

Amgen involved Erythropoietin (EPO),[65] a protein that stimulates the production of red blood cells.[66] EPO is commonly used as a therapeutic agent in the treatment of anemias or blood disorders stemming from low or defective bone marrow production of red blood cells.[67] Prior to the inventions claimed in this case, EPO was appropriated through the purification of urine from individuals exhibiting high EPO levels.[68] The new technology claimed in *Amgen* was a technique for producing EPO using "recombinant DNA technology in which EPO is produced from cell cultures into which genetically-engineered vectors containing the EPO gene have been introduced."[69] The litigation in *Amgen* centered on two patents granted by the United States Patent and Trademark Office, U.S. Patent 4,677,195 entitled "Method for Purification of Erythropoietin and Erythropoietin Compositions," issued June 30, 1987, and U.S. Patent 4,703,008 entitled "DNA Sequences Encoding Erythropoietin," issued October 27, 1987.[70]

Chugai claimed that their Dr. Fritsch "was first to conceive a probing strategy of using two sets of fully-degenerate cDNA probes of two different regions of the EPO gene to screen a g[enomic] DNA library, which was the strategy which the district court found eventually resulted in the successful identification and isolation of the EPO gene."[71] Chugai further alleged that because Frisch conceived of the strategy in 1981 and "was diligent until he reduced the invention in May of 1984," he should be considered a § 102(g) prior inventor over

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[63] 35 U.S.C. §§ 102-03 (2008).
[64] Amgen, Inc. v. Chugai Pharm., Co.,927 F.2d 1200, 1205-09 (Fed. Cir. 1991).
[65] EPO is the performance enhancer American cyclist Lance Armstrong was accused of using in the Tour de France.
[66] *Amgen*, 927 F.2d at 1203.
[67] *Id.*
[68] *Id.*
[69] *Id.*
[70] *Id.*
[71] *Id.* at 1205.

Amgen's Dr. Lin "who reduced the invention to practice in September of 1983."[72]

To satisfy the "novelty" standard for obtaining a patent, the patentee must establish that the invention is in fact new and not "prior art." Section 102(g)(2) of Title 35 provides in part that:

> A person is entitled to a patent unless—
> (g)(2) before such person's invention thereof, the invention was made . . . by another who had not abandoned, suppressed, or concealed it. In determining priority of invention under this subsection, there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.[73]

In *Amgen*, the court found that the pertinent subject matter was "the novel *purified and isolated* sequence which codes for EPO, and neither Fritsch nor Lin knew the structure or physical characteristics of it and had a viable method of obtaining that subject matter until it was actually obtained and characterized."[74] For Fritsch's work to be considered prior art, his conception had to be "sufficiently specific that one skilled in the relevant art would succeed in cloning the EPO gene."[75] In determining that Fritsch's conception did not constitute prior art, the court reasoned that "conception of a generalized approach for screening a DNA library that might be used to identify and clone the EPO of then unknown constitution is not conception of a 'purified and isolated DNA sequence' encoding human EPO."[76] According to the *Amgen* court's reading of § 102, in order to claim that a purified and isolated gene, human embryonic stem cell, or protein is indeed novel and not precluded from patent protection under prior art, the conception must not have been reduced to an isolated, purified and useable form through human intervention. Thus, despite the fact that several institutions and companies may have conceived of a strategy for isolating embryonic stem cells, WARF's actual success in reducing that conception to a tangible form makes it novel under § 102.

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[72] *Id.* at 1205-06.
[73] 35 U.S.C. § 102(g)(2) (2006).
[74] *Amgen*, 927 F.2d at 1206 (emphasis added).
[75] *Id.* at 1207.
[76] *Id*. at 1209.

In addition, the court in *Amgen* considered the alleged obviousness of the inventions claimed by Amgen.[77] The test for obviousness under 35 U.S.C. § 103 is "whether the prior art would have suggested to [a person] of ordinary skill in the art" that a particular method "should be carried out and would have a reasonable expectation of success, viewed in light of the prior art."[78]

The district court found that as of 1983, no prior art references suggested the probing strategy employed by Chugai and Amgen would be likely to succeed in isolating the human EPO gene.[79] The court found that the procedures were "obvious to try," but lacked any reasonable expectation of success.[80] The Court of Appeals found that the district court applied the proper analysis in determining that the claims asserted by Amgen were not invalid due to obviousness under § 103.[81]

Some critics in the public and non-profit sectors contend that "with the advent of automated sequencing machines, 'virtually any monkey' can generate numerous unidentified gene sequences," and call for heightened standards in the USTPO's granting of gene patents.[82] These criticisms are seemingly dismissed by the court's holding that while procedures may be "obvious to try," they must in addition have a "reasonable expectation of success." Therefore, as long as a sought gene has not been identified, reduced and purified, it seems that the first claimed process to successfully extract that particular gene will qualify for patent protection in the future, despite the use of methods that are arguably obvious to try.

Thus, the WARF patents protecting the isolation and purification of human embryonic stem cells, viewed according to the courts' treatment of other biotechnology patents such as gene patents, would likely be found to be valid under the statutory analysis of 35

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[77] *Id.* at 1207.
[78] *Id.*
[79] *Id.*
[80] *Id* at 1208. (citing *In re* O'Farrell, 853 F.2d 894, 903-04 (Fed. Cir. 1988). The court in *O'Farrel* held that:

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

O'Farrel 853 F.2d at 903-04 (citations omitted).
[81] *Amgen*, 927 F.2d at 1209.
[82] Gitter, *supra* note 39 at 1673.

U.S.C. §§ 101, 102, 103 and 112. Close to one-hundred years of legislative history and judicial precedent has established that patents will be issued for novel and non-obvious creations that are the product of human ingenuity. Indeed, the Supreme Court observed in *Chakrabarty* that Congress intended that "anything under the sun made by man" would constitute patentable, statutory subject matter.[83] Thus, where something occurs in nature, but does not exist in a purified and isolated state, the human intervention of extracting and reducing that product to a useable form is a discovery worthy of patent protection.

III. CRITICISMS, PUBLIC POLICY AND LEGAL SOLUTIONS REGARDING THE ISSUANCE OF UPSTREAM BIOTECHNOLOGY PATENTS

Perhaps the most poignant policy consideration against the issuance of broad biotechnology patents is the notion of the "tragedy of the anticommons" as articulated by Professors Michael A. Heller and Rebecca S. Eisenberg.[84] Under this theory, "[e]ach upstream patent allows its owner to set up a tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation."[85] In biotechnology, scenarios can exist where, for example, drug developers are required to pay several separate entities and arrange licensing agreements of many interrelated genes in order to produce just one drug or treatment.[86] The danger inherent in this scenario is compounded by other concerns such as foreseeability, as discussed above, with regard to the HGS patent issued for the receptor gene that was later found to be an entry point in humans for the HIV infection.[87] When patents are broadly granted for essential tools of discovery and progress in the field of biotechnology, the danger for stifling innovation and progress due to high bargaining costs, exclusive licensing agreements, and licensing fees is very real.

As a proliferation of patents has been broadly and liberally issued in the field of biotechnology concerning many of these basic tools, and the warned against "tollbooths" have emerged, critics and scholars alike have grappled with how to deal with biotechnology

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[83] *Chakrabarty*, 447 U.S. at 309 (citing S. Rep. No. 1979, 82d Cong., 2d Sess., 5 (1952); H.R. Rep. No. 1923, 82d Cong., 2d Sess., 6 (1952)).
[84] Gitter, *supra* note 39 at 1669 (citing Heller, *supra* note 11 at 698).
[85] *Id.*
[86] *Id.* (citation omitted).
[87] *Id.*; s*ee supra* note 45.

patents.[88] One approach to solving the problems surrounding broad biotechnology is through legislative action limiting the protection available for such patents. Indeed, the Supreme Court in *Chakrabarty* took notice of the fact that public policy considerations regarding the implications of granting biotechnology patents were not the domain of the courts, but were the responsibility of the legislature.[89] One such attempt by the legislature to curb the patent protection afforded to biotechnology tools like gene patents has been introduced by Congressmen Xavier Becerra and Dave Weldon, known as the Genomic Research Accessibility Act ("GRAA").[90]

The GRAA calls broadly for the banning of patent eligibility for all nucleotide sequences as well as their functions and occurrences.[91] At least one scholar warns that this bill is "unnecessary and would have ruinous effects on health care . . ." and recommends that a bill similar to the Genomic Research and Diagnostic Accessibility Act of 2002 ("GRDAA"), which allows for infringement exemptions for noncommercial research and diagnostic testing, would be more appropriate.[92] In his article explaining the likely detrimental effects of the GRAA, Gregory C. Ellis asserts that gene patents do not restrain basic or biomedical research.[93] In support of his thesis, Ellis cites studies that found that although access to research materials may be restricted at times "the patent status of the requested material had no significant effect" on why those materials were restricted.[94] Ellis goes on to note that only one percent of researchers questioned in the study "stated that their research was delayed as a result of another party's patent."[95]

Ellis also points out the legitimate concern that legislation banning such patents could have the effect of preventing recent advances in biotechnology from ever materializing.[96] Without patents,

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[88] *See*, *e.g.*, Ellis, *supra* note 12; Gitter, *supra* note 39. *See also* Michael John Gulliford, *Much Ado About Gene Patents: The Role of Foreseeability*, 34 SETON HALL L. REV. 711 (2004); Lori B. Andrews & Jordan Paradise, *Gene Patents: The Need for Bioethics Scrutiny and Legal Change*, 5 YALE J. HEALTH POL'Y, L. & ETHICS 403 (2005).

[89] *See* Chakrabarty, 447 U.S. at 305 (1980).

[90] Ellis, *supra* note 12, at 4.

[91] *Id.* (citing Genomic Research Accessibility Act, H.R. 977, 110th Cong. § 2(a) (1st Sess. 2007) ("Notwithstanding any other provision of law, no patent may be obtained for a nucleotide sequence, or its functions or correlations, or the naturally occurring products it specifies.")).

[92] Ellis, *supra* note 12, at 62, 63.

[93] *Id.* at 26.

[94] *Id.* at 14 (quoting John P. Walsh et al., *View from the Bench: Patents and Material Transfers*, 309 SCI. 2002, 2002 (2005).

[95] *Id.*

[96] *Id.* at 31.

biotechnology companies might choose to rely on trade secrets.[97] In the event robust patent protection is not afforded to biomedical companies, the use of trade secrets could greatly reduce the "instances of innovative advancement for all biotechnologies requiring substantial investment costs."[98] Indeed, "[b]iotechnology industrialists strenuously defend the patentability of genes and resist industry-specific intervention by Congress."[99] Proponents of biotechnology patent protection assert its limited duration is important for the dissemination of genomic research.[100] Without protection, research might remain undisclosed under the protection of trade secrets, never to be shared and disseminated for the public benefit.

While it seems an outright legislative ban on issuing biotechnology patents is largely unnecessary and possibly unwise, scholars have suggested a number of other legal alternatives for addressing issues inherent in biotechnology patents and achieving the balance sought by the Patent Clause, such as a shorter patent term.[101] This would accelerate the time when genes or other valuable research tools are dedicated to the public domain.[102] In addition, this would reduce the duration of royalty payments and licensing negotiations,[103] which would have the effect of reducing the "tragedy of the anticommons" discussed above. Critics of this view argue that shortening the patent term available for biotechnology would act as a disincentive for invention and innovation.[104]

Another approach would be for Congress to enact a compulsory licensing scheme that would "ensure that, in return for a fair sum, researchers would have access to the DNA sequence data [or other essential research tools] they require for further experimentation."[105] This might lead to companies maintaining less bargaining power over particular licensing agreements and enable smaller biotechnology firms to enter the market and seek to find new and useful inventions based on the research tools which, under today's scheme, might be prohibitively expensive.

One final unique approach considers the WARF stem cell patents specifically and cleverly suggests that the essential facilities doctrine might be a way to ensure the availability of necessary tools in

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[97] *Id.*
[98] *Id.*
[99] Hill, *supra* note 9 at 240.
[100] *Id.* at 239-40.
[101] *Id.* at 251.
[102] *Id.*
[103] *Id.*
[104] *Id.*
[105] Gitter, *supra* note 39 at 1679.

biotechnology while retaining the continued patent protection afforded to such inventions.[106] In an article written by Amy Rachel Davis for the Georgetown Law Journal, Davis articulates the dilemma presented by a patent granted for stem cells that holds true for gene patents as well: "Unlike a patent claiming a particular reclining chair or a specific formula of cough medicine (either of which could be 'invented around' by a company able to devise a different reclining mechanism or an alternate cough elixir), embryonic stem cells are unique combinations of matter with no possible substitutes."[107] Davis also points out stem cells' status as a necessary input for downstream products rather than a marketable product.[108]

In describing her solution to the issues presented by broad biotechnology patents being granted for such essential inputs for downstream products such as embryonic stem cells, Davis explains the essential facilities doctrine, a doctrine rooted in the Supreme Court's antitrust jurisprudence.[109] The essential facilities doctrine is traced by most scholars to the Supreme Court decision in *United States v. Terminal Railroad Association*.[110] In that case, the Court held that it was a violation of antitrust law to "create a corporation consisting of every terminal company with rights to the only existing railroad bridge into or out of St. Louis."[111] The Court reasoned that holding otherwise would prevent any other company from entering the city without using the facilities entirely owned by the terminal company.[112]

In analogizing the embryonic stem cell patents with the antitrust violation present in *Terminal Railroad*, Davis points to five reasons embryonic stem cells should be considered an essential facility: (1) embryonic stem cells are an essential input that is controlled by a monopolist, namely WARF; (2) the input cannot be duplicated, which is a "literal inability" with regard to the WARF stem cells whose patent covers all such cells, no matter what method is used to derive them; (3) access to the input could be denied, which could be realized if Geron were to act on its exclusive license and decide not to license the stem cells to other researchers and competing companies;

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[106] Davis, *supra* note 1, at 209.
[107] *Id.* at 211.
[108] *Id.* Scientists anticipate that such downstream products could include the use of stem cells as "'universal donor cells' that could serve as 'the raw material for new liver cells . . . or new spinal cord cells' . . . ." *Id.* at 212.
[109] *Id.* at 222. Though never expressly embraced by the Supreme Court, this doctrine is traced back to 1912 when the Supreme Court decided *United States v. Terminal Railroad Association*, 224 U.S. 383, 397 (1912).
[110] *Id.*
[111] *Id.*
[112] *Id.* at 223 (citing United States v. Terminal R.R. Ass'n., 224 U.S. 383, 397 (1912)).

(4) providing access to the input would be economically feasible for the entity controlling it, satisfied by the fact that licensing the stem cells for others to use would in no way impede WARF or Geron's use of the cells in their own research; and (5) a distinct downstream market exists.[113] Under this analysis, it seems that the essential facilities doctrine could protect future medical research from one company attempting to assert a monopoly over essential biomedical tools such as embryonic stem cells or particular genes.

CONCLUSION

In conclusion, the United States Patent and Trademark Office's treatment of biotechnology patents and its liberal issuance of broad patents over essential upstream research tools such as gene patents and human embryonic stem cells raises serious questions about the patentability, utility, novelty, and non-obviousness requirements of 35 U.S.C §§ 101, 102 and 103, as well as important public policy concerns. The purpose of the Patent Clause of the United States Constitution is to promote the progress of the Arts and Sciences by granting patents for a limited time to inventors. This clause demonstrates a delicate balance between the encouraging innovation for the public benefit and stifling competition by awarding limited monopolies to compensate the inventors.

The recent debate over whether gene patents or patents claiming a process for isolating human embryonic stem cells are indeed patentable has been viewed in favor of promoting industry and encouraging innovation through the issuance of robust and broad patent protection. Though these tools occur in nature, they do not occur naturally in their purified and isolated forms without human intervention. Where the claims specifically state the function of the invention seeking patent protection, the patent will likely be found to be patentable under § 101. In addition, while methods exist for isolating DNA sequences, cells and proteins, these methods do not necessarily lead to a reasonable expectation of success in deriving a particular gene, protein or cell type. Furthermore, until that particular product is isolated and the concept of isolating the gene is reduced to a marketable form for the public benefit, a process for reducing the concept to a marketable form will be found to be novel under § 102. Despite the fact that a process for deriving an isolated and purified form of a product may be obvious to try, there must also be a reasonable expectation of success in order to be prevented under § 103 scrutiny.

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[113] *Id.* at 232-39.

The tragedy of the anticommons presents a challenge that suggests that awarding too many rights to exclude others might lead to a reduction in progress and innovation. Under this theory, broad upstream patents establish tollbooths that slow progress and innovation by increasing costs, thereby limiting downstream product development. Despite efforts, the legislature has been unable to effectively address the problems inherent in the issuance of broad biotechnology patents. However, a number of alternative solutions, including a shortened patent period, compulsory licensing, and application of the essential facilities doctrine, might have the potential to successfully and appropriately balance public policy with commercial interests. For now, upstream biotechnology patents will continue to be awarded in order to encourage investment and progress in the field. It is hoped that these broad patent rights will not be abused and act as a deterrent for future innovation, but rather will be exploited fairly, in a way that benefits society and rewards innovators for their investment.