

DNA AS PATENTABLE SUBJECT MATTER AND A NARROW FRAMEWORK FOR ADDRESSING THE PERCEIVED PROBLEMS CAUSED BY GENE PATENTS

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ABSTRACT

Concerns about the alleged harmful effects of gene patents—including hindered research and innovation and impeded patient access to high-quality genetic diagnostic tests—have resulted in overreactions from the public and throughout the legal profession. These overreactions are exemplified by Association for Molecular Pathology v. U.S. Patent and Trademark Office, a 2010 case in the Southern District of New York that held that isolated DNA is unpatentable subject matter under 35 U.S.C. § 101. The problem with these responses is that they fail to adequately consider the role that gene patents and patents on similar biomolecules play in facilitating investment in the costly and risky developmental processes required to transform the underlying inventions into marketable products. Accordingly, a more precisely refined solution is advisable. This Note proposes a narrowly tailored set of solutions to address the concerns about gene patents without destroying the incentives for companies to create and commercialize inventions derived from these and similar patents.

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INTRODUCTION

Gene patents¹ have always been controversial. Some commentators object to gene patents on the ground that genes and the human genome are “the common heritage and inheritance of mankind.”² Others object to gene patents because of ethical considerations, arguing that gene patents restrict patient access to genetic diagnostic tests developed using patented genes.³ Still others object to gene patents on the ground that they potentially impede foundational research rather than stimulate innovation.⁴

These collective concerns have engendered overreactions exemplified by a 2010 case in the Southern District of New York, *Association for Molecular Pathology v. U.S. Patent and Trademark Office (Myriad I)*,⁵ which held that “[b]ecause . . . isolated DNA is not markedly different from native DNA as it exists in nature, it constitutes unpatentable subject matter under 35 U.S.C. § 101.”⁶ Similarly, the U.S. government has taken a position against the patentability of isolated DNA, at least in the context of a genomic DNA sequence.⁷ Other responses, though less extreme, have still been excessive. For example, a 2010 report on the impact of gene patents by the Secretary’s Advisory Committee on Genetics, Health, and Society (SACGHS) for the Department of Health and Human

1. For the purposes of this Note, gene patents are “patent claims to isolated nucleic acid molecules whose sequences correspond to human genes, intergenic DNA (DNA located between genes), or mutations that occur in the human body.” SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, U.S. DEP’T OF HEALTH & HUMAN SERVS., GENE PATENTS AND LICENSING PRACTICES AND THEIR IMPACT ON PATIENT ACCESS TO GENETIC TESTS 15 (2010).

2. Linda J. Demaine & Aaron Xavier Fellmeth, *Reinventing the Double Helix: A Novel and Nonobvious Reconceptualization of the Biotechnology Patent*, 55 STAN. L. REV. 303, 442–45 (2002).

3. See SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 1, at 38–45 (addressing the effects of gene patents on access to genetic testing).

4. See generally Kate Murashige, *Patents and Research—An Uneasy Alliance*, 77 ACAD. MED. 1329 (2002) (evaluating the claim that patents such as gene patents inhibit scientific progress).

5. *Ass’n for Molecular Pathology v. U.S. Patent & Trademark Office (Myriad I)*, 702 F. Supp. 2d 181 (S.D.N.Y. 2010), *rev’d in part*, 653 F.3d 1329 (Fed. Cir. 2011). For clarity and readability, this Note uses “Myriad I” to refer to this district court opinion and “Myriad II” to refer to the Federal Circuit opinion in the same case, *Ass’n for Molecular Pathology v. U.S. Patent & Trademark Office (Myriad II)*, 653 F.3d 1329 (Fed. Cir. 2011).

6. *Myriad I*, 702 F. Supp. 2d at 232.

7. Brief for the United States as Amicus Curiae in Support of Neither Party at 18, *Myriad II*, 653 F.3d 1329 (No. 2010-1406) (concluding that “isolated but otherwise unaltered genomic DNA is not patent-eligible subject matter under 35 U.S.C. § 101”).

Services⁸ suggests the creation of broad exemptions from liability for anyone who infringes gene patents “while making, using, ordering, offering for sale, or selling a genetic test for patient care purposes” or while “us[ing] patent-protected genes in the pursuit of research.”⁹

The problem with these responses is that they fail to adequately consider the role that gene patents and patents on similar biomolecules play in facilitating investment in the costly, lengthy, and risky developmental processes required to transform the underlying biological discoveries and inventions into marketable products.¹⁰ Because the patent system provides the incentive for translating basic research into marketable products in this context, a more precisely refined solution is advisable.¹¹

Part I of this Note provides background information on the underlying biology of genes and the appeal of gene patents, summarizes the objectives and patentability requirements of the U.S. patent system, explains how those requirements have been applied to gene patents, and discusses the alleged problems created by gene patents. Part II describes and critiques two noteworthy responses to those problems: the *Myriad* case—including the response of the U.S. government to that case—and the SACGHS gene-patent report. Finally, Part III proposes a narrowly tailored set of solutions to address the concerns about patients and innovation without destroying the incentives required to create and commercialize inventions derived from gene patents.

I. PATENT LAW AND GENE PATENTS

A. *Genes and Their Appeal as Patentable Subject Matter*

1. *The Biology of Genes.* Genetic information flows from deoxyribonucleic acid (DNA) to ribonucleic acid (RNA) to proteins.¹² Though the nucleotide subunits of DNA encode basic biological

8. SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 1.

9. *Id.* at 94–95.

10. See Wolrad Prinz zu Waldeck und Pyrmont, *Research Tool Patents After Integra v. Merck—Have They Reached a Safe Harbor?*, 14 MICH. TELECOMM. & TECH. L. REV. 367, 372 (2008) (“Under [the incentive to invest] theory, the patent system . . . facilitates investment into costly and risky development processes that are necessary to transform a ‘mere’ invention into a marketable product.”).

11. See *infra* notes 184–91 and accompanying text.

12. BRUCE ALBERTS, ALEXANDER JOHNSON, JULIAN LEWIS, MARTIN RAFF, KEITH ROBERTS & PETER WALTER, *MOLECULAR BIOLOGY OF THE CELL* 331 (5th ed. 2008).

information through “a four-letter alphabet that spells out biological messages,”¹³ proteins are the primary molecules responsible for putting that information into action.¹⁴

Genes, the “functional units of heredity” within a cell,¹⁵ are the portions of DNA that correspond to a protein or a related set of protein variants.¹⁶ Cells use—or express—the instructions encoded in genes to produce proteins in two steps.¹⁷ In the first step—transcription—the cell copies the gene from the DNA to an intermediary called RNA.¹⁸ After the cell processes the RNA,¹⁹ the information in the RNA is used in a second step—translation—to generate the end-product protein.²⁰ Through this process, cells can “synthesize and accumulate different sets of RNA and protein molecules” according to need.²¹

2. *The Appeal of Gene Patents.* Although genes as they exist within human bodies are not patentable,²² genes that are isolated, purified, and modified are attractive as patentable subject matter for several reasons.²³ For example, gene patents are useful for developing genetic diagnostic tests.²⁴ Because genes are ultimately informational templates for the proteins that carry out most of the functions within the cell,²⁵ gene mutations²⁶ can produce adverse outcomes such as

13. *Id.* at 199.

14. *Id.* at 6. Proteins perform most of the cell’s functions, including “direct[ing] the vast majority of chemical processes in the cell,” as well as “maintaining structures, generating movements, [and] sensing signals.” *Id.*

15. *Id.* at 204.

16. *Id.* at 7.

17. *Id.* at 4.

18. *Id.*

19. *See, e.g., infra* text accompanying note 142.

20. ALBERTS ET AL., *supra* note 12, at 4.

21. *Id.* at 411.

22. Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (Jan. 5, 2001) (internal guidelines) (“A patent on a gene covers the isolated and purified gene but does not cover the gene as it occurs in nature. Thus, the concern that a person whose body ‘includes’ a patented gene could infringe the patent is misfounded.”).

23. *See* Best Practices for the Licensing of Genomic Inventions, 70 Fed. Reg. 18,413, 18,414 (Apr. 11, 2005) (notice) (“Much of the value associated with the commercial use of these technologies involves nucleic acid-based diagnostics, potential gene therapy applications, and the development of new DNA and RNA-based therapeutics.”).

24. *See* SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 1, at 20–35 (discussing the effects of gene patents in promoting the development of genetic diagnostic tests).

25. *See supra* note 16 and accompanying text.

disease.²⁷ Consequently, genetic testing can provide information about the predisposition of a particular person to develop a particular disease and the likely responsiveness of a person to a particular type of therapy.²⁸

Gene patents are also attractive because of the potential to use isolated, purified, and modified genes in the development of novel drugs. Three examples of categories of drugs that can be developed using gene patents are recombinant-protein therapeutics,²⁹ gene-therapy drugs,³⁰ and RNA interference (RNAi) therapeutics.³¹ Recombinant-protein therapeutics—proteins derived from a selected recombinant gene³²—are useful for treating diseases when the increased presence of a particular protein would have a beneficial effect for the patient.³³ The concept behind gene therapy is similar: “a

26. Mutations include deletions, inversions, translocations, and substitutions of an incorrect nucleotide for a correct nucleotide within a DNA sequence. ALBERTS ET AL., *supra* note 12, at 555.

27. See, e.g., Douglas Hanahan & Robert A. Weinberg, *The Hallmarks of Cancer*, 100 CELL 57, 57 (2000) (explaining that cancer development involves “mutations that produce oncogenes with dominant gain of function and tumor suppressor genes with recessive loss of function”).

28. See, e.g., Eileen M. Kane, *Patent-Mediated Standards in Genetic Testing*, 2008 UTAH L. REV. 835, 837 (“Genetic testing can serve a number of objectives: predictive testing of an asymptomatic individual whose family history suggests an inherited risk of a particular disease, diagnostic testing of a symptomatic individual to confirm the presence of genetic correlates to a specific disease, and genetic testing of diagnosed individuals to optimize drug therapy in pharmacogenomic applications.”).

29. See generally Florian M. Wurm, *Production of Recombinant Protein Therapeutics in Cultivated Mammalian Cells*, 22 NATURE BIOTECHNOLOGY 1393 (2004) (discussing the diversity of manufacturing approaches that are capable of producing therapeutic proteins from recombinant mammalian cells).

30. See generally Roland W. Herzog, Ou Cao & Arun Srivastava, *Two Decades of Clinical Gene Therapy—Success Is Finally Mounting*, 9 DISCOVERY MED. 105 (2010) (discussing recent progress in human gene therapy).

31. See generally David Bumcrot, Muthiah Manoharan, Victor Koteliensky & Dinah W.Y. Sah, *RNAi Therapeutics: A Potential New Class of Pharmaceutical Drugs*, 2 NATURE CHEMICAL BIOLOGY 711 (2006) (discussing the molecular mechanics of RNAi, studies of RNAi administration in animal models of human disease, and clinical trials of RNAi therapeutic candidates).

32. Recombinant DNA is “produced by splicing together two or more DNA fragments.” ALBERTS ET AL., *supra* note 12, at 533. Recombinant DNA technology is useful for modifying a particular gene or for dramatically increasing expression of a particular gene to produce large amounts of a given protein. See *id.* at 514 (“Using . . . recombinant DNA methods . . . , any gene can be modified to produce its protein with a special recognition tag attached to it, so as to make subsequent purification of the protein . . . simple and rapid.”).

33. One example is Activase, a recombinant tissue plasminogen activator developed by Genentech Inc. for treating heart attacks. *Activase*, GENENTECH, <http://www.gene.com/gene/products/information/cardiovascular/activase/insert.jsp> (last visited Nov. 9, 2011).

functional copy of [a] defective gene is introduced [into the patient's body] to replace the missing function" caused by a defect or mutation in the native gene.³⁴ RNAi therapeutics, however, use only small fragments of a gene and exploit a natural regulatory mechanism within the cell to degrade RNAs encoded by a particular gene, thereby decreasing the amount of the corresponding protein that is produced.³⁵ This type of therapeutic is effective for treating diseases driven by the presence of a particular pathological protein.³⁶

B. Objectives of Patent Law and the Patentability Requirements

The foundation of the U.S. patent system is Article I, Section 8, Clause 8 of the Constitution, which 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."³⁷ This clause and the federal patent laws Congress has enacted pursuant to it envision the stimulation of innovation through the creation of a delicately constructed balance³⁸: in exchange for a time-limited,³⁹ exclusive right to make, use, or sell an invention,⁴⁰ an inventor provides a disclosure to the public that is sufficient to enable a person of ordinary skill in the relevant field to make and use the claimed invention.⁴¹

34. Herzog et al., *supra* note 30, at 105. There have been over one thousand gene-therapy clinical trials. Michael L. Edelstein, Mohammad R. Abedi & Jo Wixon, *Gene Therapy Clinical Trials Worldwide to 2007—An Update*, 9 J. GENE MED. 833, 833 (2007).

35. Bumcrot et al., *supra* note 31, at 711.

36. One example is ALN-RSV01, an RNAi therapeutic in Phase II clinical trials. ALN-RSV01 silences a gene required for the replication of respiratory syncytial virus. *RSV Infection*, ALNYLAM PHARM., <http://alnylam.com/Programs-and-Pipeline/Partner-Programs/index.php> (last visited Nov. 9, 2011).

37. U.S. CONST. art. I, § 8, cl. 8.

38. *See Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 63 (1998) ("[T]he patent system represents a carefully crafted bargain that encourages both the creation and the public disclosure of new and useful advances in technology, in return for an exclusive monopoly for a limited period of time. The balance between the interest in motivating innovation and enlightenment by rewarding invention with patent protection on the one hand, and the interest in avoiding monopolies that unnecessarily stifle competition on the other, has been a feature of the federal patent laws since their inception.").

39. The term of protection for utility patents is twenty years from the effective filing date of the patent application. 35 U.S.C. § 154(a)(2) (2006).

40. *See id.* § 154(a)(1) ("Every patent shall contain a . . . grant to the patentee . . . of the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States or importing the invention into the United States . . .").

41. *Id.* § 112 ("The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to

To be eligible for this limited monopoly, a claimed invention must meet several requirements. The invention must first be patentable subject matter, defined by statute to include “any new . . . process, machine, manufacture, or composition of matter, or any new . . . improvement thereof.”⁴² As the Supreme Court has recognized, this broad language reflects Congress’s intent that, under the Patent Act of 1952,⁴³ patentable subject matter should “include anything under the sun that is made by man.”⁴⁴ The scope of patentable subject matter is not without limits, however, as the Court has held that “laws of nature, physical phenomena, and abstract ideas”⁴⁵ are not patentable because “[s]uch discoveries are ‘manifestations of . . . nature, free to all men and reserved exclusively to none.’”⁴⁶

Even if a claimed invention reaches the threshold of patent eligibility, it is still not patentable unless it is useful,⁴⁷ novel,⁴⁸ and nonobvious.⁴⁹ Under Supreme Court precedent, an invention is considered useful if it has “substantial utility” and can provide an identifiable “specific benefit” in its current form.⁵⁰ An invention has substantial utility if it “has a significant and presently available

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same . . .”).

42. *Id.* § 101.

43. Patent Act of 1952, Pub. L. No. 82-593, 66 Stat. 797 (codified as amended at 35 U.S.C.).

44. *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980) (quoting S. REP. NO. 82-1979, at 5 (1952); H.R. REP. NO. 82-1923, at 6 (1952)).

45. *Id.* (providing “a new mineral discovered in the earth” and “the law of gravity” as examples of unpatentable subject matter).

46. *Id.* (quoting *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948)).

47. 35 U.S.C. § 101 (“Whoever 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 therefor . . .”) (emphasis added).

48. *Id.* § 102 (setting forth the novelty bars to patentability). Section 102’s requirements will change slightly when the Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) (to be codified in scattered sections of 15, 28, 35, 42, and 51 U.S.C.), goes into effect. For a summary of the changes, see Howard Skaist & Ted Karr, *Guest Post—Defining Prior Art Under the Leahy-Smith AIA*, PATENTLY-O (Sept. 13, 2011, 7:24 PM), <http://www.patentlyo.com/patent/2011/09/guest-post-defining-prior-art-under-the-leahy-smith-aia.html>.

49. 35 U.S.C. § 103.

50. See *Brenner v. Manson*, 383 U.S. 519, 534–36 (1966) (noting that “a patent is not a hunting license” but rather is “compensation for [the] successful conclusion” of a search for something useful).

benefit to the public”⁵¹ and an invention provides a specific benefit if it has “a use which is not so vague as to be meaningless.”⁵²

An invention is novel if it has not been previously disclosed.⁵³ Relevant considerations listed by statute include whether the invention was “known or used by others in this country,”⁵⁴ “patented or described in a printed publication in this or a foreign country,”⁵⁵ “described in [a published] application for patent [or patent granted on an application] . . . by another filed in the United States,”⁵⁶ or “made in this country by another inventor who ha[s] not abandoned, suppressed, or concealed it.”⁵⁷ The U.S. Court of Appeals for the Federal Circuit has held that novelty does not exist if “each and every element [of the claimed invention] is found, either expressly or inherently described, in a single prior art reference.”⁵⁸

Even if an invention is novel, it may still be unpatentable if it fails to satisfy the nonobviousness requirement. Obviousness bars patentability in cases in which “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 art to which said subject matter pertains.”⁵⁹ Several factors are relevant in determining whether an invention is obvious, including whether there was “some motivation or suggestion to combine” or modify relevant prior art references to create the claimed invention,⁶⁰ whether the

51. *In re Fisher*, 421 F.3d 1365, 1371 (Fed. Cir. 2005) (noting that substantial utility requires that an invention have real-world value in its current form rather than after further research).

52. *Id.* (observing that to satisfy the specific-utility requirement, the claimed invention must “provide a well-defined and particular benefit to the public”).

53. 35 U.S.C. § 102(a), (e), (g).

54. *Id.* § 102(a).

55. *Id.*

56. *Id.* § 102(e).

57. *Id.* § 102(g)(2).

58. *Verdegaal Bros., Inc. v. Union Oil Co.*, 814 F.2d 628, 631 (Fed. Cir. 1987). Prior art includes any reference or information made available to the public before the date of a patent applicant’s invention. See ROBERT PATRICK MERGES & JOHN FITZGERALD DUFFY, *PATENT LAW AND POLICY: CASES AND MATERIALS* 360 (4th ed. 2007) (“Any reference having an effective date before the critical date is considered part of the prior art and may be used against the applicant.” (emphasis omitted)).

59. 35 U.S.C. § 103(a).

60. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 407 (2007) (quoting *Al-Site Corp. v. VSI Int’l, Inc.*, 174 F.3d 1308, 1323–24 (Fed. Cir. 1999) (internal quotation mark omitted)) (noting that motivation can be found “in the prior art, the nature of the problem, or the knowledge of a person having ordinary skill in the art”).

“combination was obvious to try,”⁶¹ and whether there was a reasonable expectation of success.⁶² Moreover, “secondary considerations,” such as “commercial success, long felt but unsolved needs, [and the] failure of others,” weigh against finding obviousness.⁶³

C. Application of the Patentability Requirements to Gene Patents

1. Gene Patents and the Patentable-Subject-Matter Requirement.

One attack on gene-patent validity is that genes are not patentable subject matter because they are products of nature.⁶⁴ The Supreme Court has found products to be patentable when they have “markedly different characteristics from any found in nature.”⁶⁵ In other words, a product produced from natural raw materials must “possess[] a new or distinctive form, quality, or property” to be patentable.⁶⁶

In *Diamond v. Chakrabarty*,⁶⁷ the Supreme Court considered a patent for a “human-made, genetically engineered bacterium . . . capable of breaking down multiple components of crude oil,” a property “possessed by no naturally occurring bacteria.”⁶⁸ The Court held that the bacterium was patent eligible because, unlike “a new mineral discovered in the earth or a new plant found in the wild,”⁶⁹ the bacterium was “not . . . a hitherto unknown natural phenomenon, but . . . a nonnaturally occurring manufacture or composition of matter—a product of human ingenuity ‘having a distinctive name, character [and] use.’”⁷⁰

61. *Id.* at 421.

62. *See In re Merck & Co.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986) (“Obviousness does not require absolute predictability. Only a reasonable expectation that the beneficial result will be achieved is necessary to show obviousness.” (citation omitted)).

63. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

64. *See Myriad I*, 702 F. Supp. 2d 181, 220–32 (S.D.N.Y. 2010) (surveying the legal precedent and concluding that the DNA in the claim at issue was essentially a product of nature), *rev'd in part*, 653 F.3d 1329 (Fed. Cir. 2011).

65. *Diamond v. Chakrabarty*, 447 U.S. 303, 310 (1980).

66. *Am. Fruit Growers, Inc. v. Brogdex Co.*, 283 U.S. 1, 11 (1931).

67. *Diamond v. Chakrabarty*, 447 U.S. 303 (1980).

68. *Id.* at 305.

69. *Id.* at 309.

70. *Id.* at 309–10 (alteration in original) (quoting *Hartranft v. Wiegmann*, 121 U.S. 609, 615 (1887)). Other cases support the idea that products are patentable when sufficiently distinguishable from corresponding natural products. *See, e.g., In re Kratz*, 592 F.2d 1169, 1175 (C.C.P.A. 1979) (holding that a substance purified from strawberries to produce strawberry flavor is patentable subject matter).

By contrast, in *Funk Brothers Seed Co. v. Kalo Inoculant Co.*,⁷¹ the claimed invention, a mixture of root-nodule bacteria that aids plants in fixing nitrogen, was held unpatentable.⁷² Though the discovery was useful because it overcame the mutually inhibitive effects of the bacteria,⁷³ the Court held that it was not patentable subject matter because it was “no more than the discovery of some of the handiwork of nature.”⁷⁴

Until 2011, neither the Supreme Court nor the Federal Circuit had directly addressed the issue of whether isolated DNA is patentable subject matter under 35 U.S.C. § 101⁷⁵ and courts seemed generally to assume that DNA was patentable subject matter.⁷⁶ This assumption was consistent with the long-held position of the U.S. Patent and Trademark Office:

An isolated and purified DNA molecule that has the same sequence as a naturally occurring gene is eligible for a patent because (1) an excised gene is eligible for a patent as a composition of matter or as an article of manufacture because that DNA molecule does not occur in that isolated form in nature, or (2) synthetic DNA preparations are eligible for patents because their purified state is different from the naturally occurring compound.⁷⁷

71. *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948). The issue in *Funk Bros.* might better be viewed as one of obviousness rather than of patentable subject matter. *See Myriad II*, 653 F.3d 1329, 1351 (Fed. Cir. 2011) (noting that the Supreme Court has “cast[] this case decided on obviousness in terms of § 101”).

72. *Funk Bros.*, 333 U.S. at 132.

73. *Id.* at 129–30.

74. *Id.* at 131 (“No species acquires a different use. The combination of species produces no new bacteria, no change in the six species of bacteria, and no enlargement of the range of their utility. Each species has the same effect it always had. . . . They serve the ends nature originally provided and act quite independently of any effort of the patentee.”). Other cases support the idea that products are not patentable if they have the same characteristics as corresponding natural products. *See, e.g., Am. Fruit Growers, Inc. v. Brogdex Co.*, 283 U.S. 1, 11–12 (1931) (holding that an orange impregnated with borax to prevent blue-mold decay was unpatentable because “[t]here [was] no change in the name, appearance, or general character of the fruit”).

75. *See Intervet Inc. v. Merial Ltd.*, 617 F.3d 1282, 1293 (Fed. Cir. 2010) (Dyk, J., concurring in part and dissenting in part) (“Neither the Supreme Court nor this court has directly decided the issue of the patentability of isolated DNA molecules.”).

76. *See, e.g., Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1204, 1219 (Fed. Cir. 1991) (holding that a claim to “[a] purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin” was valid).

77. Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (Jan. 5, 2001) (internal guidelines). The U.S. government’s amicus brief took a position inconsistent with this statement in the *Myriad* case, *see supra* note 7 and accompanying text, but the U.S. Patent and Trademark

This status quo, however, was called into question by the district court's holding in *Myriad I* that isolated DNA is an unpatentable product of nature because the unaltered information-encoding function of DNA is also central to the utility of DNA in its isolated form.⁷⁸ Although the Federal Circuit reversed this holding on appeal,⁷⁹ the case has not been finally resolved by the courts.⁸⁰

2. *Gene Patents and the Utility Requirement.* Another area in which courts have strictly construed the patentability requirements to limit the availability of gene patents is the utility requirement. In 2005, the Federal Circuit addressed the utility requirement for DNA patents in *In re Fisher*.⁸¹ The claims at issue in *Fisher* involved purified nucleic-acid-sequence fragments known as “expressed sequence tags” (ESTs).⁸² The claimed ESTs corresponded with fragments of specific genes, but the patentee knew neither the precise structure nor the functions of those genes.⁸³ The court first held that the ESTs failed to satisfy the substantial-utility requirement, noting that they “act as no more than research intermediates that may help scientists to isolate the particular underlying . . . genes and conduct further

Office appears to disagree with the brief's position, see Dan Vorhaus & John Conley, *Swine Soar Higher in Myriad Thanks to US Government's Amicus Brief*, GENOMICS L. REP. (Nov. 1, 2010), <http://www.genomicslawreport.com/index.php/2010/11/01/swine-soar-higher-in-myriad-thanks-to-us-governments-amicus-brief> (noting that the brief was contrary to the longstanding position of the U.S. Patent and Trademark Office and that the absence of visible support for the brief from Patent Office lawyers may indicate that the Patent Office opposed its filing, consistent with its preference for maintaining the status quo).

78. *Myriad I*, 702 F. Supp. 2d 181, 185, 227–32 (S.D.N.Y. 2010) (“DNA’s existence in an ‘isolated’ form alters neither this fundamental quality of DNA as it exists in the body nor the information it encodes.”), *rev’d in part*, 653 F.3d 1329 (Fed. Cir. 2011); see also *infra* Part II.A.1.

79. *Myriad II*, 653 F.3d 1329, 1334 (Fed. Cir. 2011). Although the Federal Circuit reversed the district court, its rationale for doing so cast doubt on the patentability of other natural products. See *infra* notes 192–201 and accompanying text.

80. See Mary Beth Tung, *Myriad: Isolated DNA Claims from “Ball Bats in Trees,” and “Kidneys” to “Magic Microscopes,”* IPWATCHDOG (Sept. 25, 2011, 8:00 AM), <http://ipwatchdog.com/2011/09/25/myriad-isolated-dna-claims> (“The ACLU requested reconsideration of the decision by the same panel based on assertions that Judge Lourie’s explanation of covalent bonds resulting in a distinct DNA molecule was an error because neither side had presented the argument. The ACLU Petition was denied on September 13, 2011, and *Myriad’s* Petition was denied on September 16. Since an en banc rehearing was not requested it has been waived. It appears that cert. by the Supreme Court is the only option for both parties at this point.”).

81. *In re Fisher*, 421 F.3d 1365 (Fed. Cir. 2005).

82. *Id.* at 1367 (“An EST is a short nucleotide sequence that represents a fragment [of the nucleotide sequence encoding a protein].”).

83. *Id.* at 1368.

experimentation on those genes.”⁸⁴ The court then held that the ESTs did not satisfy the specific-utility requirement, as “[a]ny EST transcribed from any gene . . . has the potential to perform any one of the alleged uses.”⁸⁵ Thus, the court concluded that for this type of DNA sequence to meet the utility standard, it must “correlate to an underlying gene of known function.”⁸⁶

3. *Gene Patents and the Obviousness Requirement.* Courts have also been imposing more stringent nonobviousness standards for gene patents.⁸⁷ For example, the Federal Circuit held in *In re Kubin*⁸⁸ that the gene patent at issue was obvious because “the prior art [taught the] protein of interest, a motivation to isolate the gene coding for that protein, and illustrative instructions . . . for cloning this gene.”⁸⁹ Thus, the court appeared to cabin the permissibility of gene patents to situations in which “the improvement is more than the predictable use of prior art elements according to their established functions.”⁹⁰ Ultimately, these changes in the utility and nonobviousness standards, as well as the more robust written-description requirement that has developed,⁹¹ have restricted the availability of gene patents.

D. *Alleged Problems Created by Gene Patents*

Approximately 20 percent of human genes are allegedly patented.⁹² This staggering estimate, combined with the restrictive

84. *Id.* at 1373.

85. *Id.* at 1374; *cf. In re Kirk*, 376 F.2d 936, 941 (C.C.P.A. 1967) (holding that “the nebulous expressions ‘biological activity’ [and] ‘biological properties’” do not satisfy the utility requirement).

86. *In re Fisher*, 421 F.3d at 1374.

87. Nonobviousness became a bigger hurdle when the Supreme Court held in 2007 that the attribute of being “[o]bvious to try” can demonstrate an invention’s obviousness “[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007) (first alteration in original) (quoting *Teleflex, Inc. v. KSR Int’l Co.*, 119 F. App’x 282, 289 (Fed. Cir. 2005), *rev’d*, 550 U.S. 398 (2007)) (internal quotation marks omitted).

88. *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009).

89. *Id.* at 1360.

90. *KSR*, 550 U.S. at 417.

91. *See, e.g., Centocor Ortho Biotech, Inc. v. Abbott Labs., Inc.*, 636 F.3d 1341, 1349–53 (Fed. Cir. 2011) (applying a strengthened written-description requirement under 35 U.S.C. § 112 (2006) to invalidate patent claims to antibodies).

92. Kyle Jensen & Fiona Murray, *Intellectual Property Landscape of the Human Genome*, 310 *SCIENCE* 239, 239 (2005) (“[N]early 20% of human genes are explicitly claimed as U.S. IP. This represents 4382 of the 23,688 of genes in the NCBI’s gene database at the time of

licensing that often accompanies gene patents,⁹³ has caused concern. Aside from general uneasiness about patenting human DNA,⁹⁴ concerns exist about hindering access to medical treatments, diminishing the quality of patient care, and stifling research and innovation.⁹⁵ Although some of these concerns may be warranted, the data cited in their support are far from clear,⁹⁶ and patents may not be the primary underlying problem.⁹⁷

1. *Diminishing Patient Access.* One concern about gene patents is that they may hinder timely, equitable access to medical treatments or tests.⁹⁸ The limited monopolies granted by gene patents, combined with exclusive licensing, create a lack of competition that has the potential to hinder access to products falling within the scope of the patents.⁹⁹ The example of genetic diagnostic tests is illustrative.

Gene patents limit the number of providers of genetic diagnostic tests.¹⁰⁰ Clinical laboratories that are capable of offering particular tests may be forced to stop offering or developing those tests because of patents.¹⁰¹ In the rare circumstance in which a patent holder

writing . . .”). *But see* Christopher M. Holman, Will Gene Patents Impede Whole Genome Sequencing?: Deconstructing the Myth That 20% of the Human Genome Is Patented 2, 13 (July 25, 2011) (unpublished manuscript), available at <http://ssrn.com/abstract=1894715> (noting that Professor Fiona Murray and then-doctoral candidate Kyle Jensen examined whether genes were mentioned in patent claims rather than whether they were actually claimed and further noting that many of the patents in their study have since expired).

93. See Best Practices for the Licensing of Genomic Inventions, 70 Fed. Reg. 18,413, 18,415 (Apr. 11, 2005) (notice) (responding to purportedly restrictive licensing practices by suggesting a more limited use of exclusive licensing with genomic inventions).

94. See *supra* note 2 and accompanying text.

95. See generally SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 1 (examining the effects of gene patents on access to genetic testing and research and innovation).

96. See *infra* Part I.D.1–3.

97. For example, health-insurance issues are a major underlying factor. See *infra* notes 103–04 and accompanying text.

98. See *supra* note 3 and accompanying text.

99. See SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 1, at 38–39 (discussing a case study suggesting that patents and exclusive licenses can result in higher prices for some genetic tests).

100. See *id.* at 39 (finding that “the patenting and licensing of genetic tests has limited the ability of clinical laboratories to offer genetic testing”).

101. See Mildred K. Cho, Samantha Illangasekare, Meredith A. Weaver, Debra G.B. Leonard & Jon F. Merz, *Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services*, 5 J. MOLECULAR DIAGNOSTICS 3, 3 (2003) (surveying clinical-laboratory directors and finding that 25 percent had stopped performing clinical genetic tests and 53 percent had decided not to develop new clinical genetic tests because of patents or licenses).

enforces its patent without filling the resulting void, patient access can be negatively affected.¹⁰²

Increased costs may also diminish patient access. This is particularly the case when increased costs are borne directly by patients, such as when the sole test provider does not accept a particular type of insurance¹⁰³ or when a patient's insurance does not cover the test.¹⁰⁴ Patients and insurance providers might also directly shoulder the burden of increased costs if the costs of obtaining a particular test increase due to the lack of competition created by the presence of a sole test provider.¹⁰⁵ This latter concern, however, may be exaggerated. For example, prices for genetic tests based on exclusively licensed patents are often similar to prices for tests based on nonexclusively licensed patents.¹⁰⁶

102. *E.g.*, Misha Angrist, Subhashini Chandrasekharan, Christopher Heaney & Robert Cook-Deegan, *Impact of Patents and Licensing Practices on Access to Genetic Testing for Long QT Syndrome*, 12 *GENETICS MED.* S111, S111 (2010) (finding that the enforcement of gene patents before the development of a commercial test led at least one of two previous providers of genetic testing for long QT syndrome (LQTS) to cease testing, a decision that “probably had a small but tangible negative effect on patient access to genetic testing for LQTS between 2002 and 2004”). Nevertheless, restrictions on who can offer a genetic diagnostic test do not necessarily lead to decreased patient accessibility. *See* Christopher M. Holman, *Gene Patents Under Fire: Weighing the Costs and Benefits* 22 (Nov. 16, 2010) (unpublished manuscript), available at <http://ssrn.com/abstract=1710150> (discussing how Myriad, as a sole provider, had more incentive to invest “substantially in facilitating insurance reimbursement and in promoting awareness of BRCA testing,” which would likely result in increased accessibility).

103. *E.g.*, *Ordering & Billing*, ATHENA DIAGNOSTICS, <http://www.athenadiagnostics.com/content/ordering> (last visited Nov. 9, 2011) (“Athena Diagnostics is not a participating provider in any Medicaid program . . .”). *But see* Matt Jones, *Myriad, ACLU Case Hits Higher Court*, GENOMEWEB (Apr. 5, 2011), <http://www.genomeweb.com/dxpgx/myriad-aclu-case-hits-higher-court> (“[Myriad] . . . said that insurance currently covers 90 percent of BRCA testing and that an average co-pay for the test is approximately \$100. [Myriad] also said it provides financial assistance programs for patients who are uninsured or have high deductibles or limited incomes.”).

104. Karen P. Mann, *Gene Patents: Perspectives from the Clinical Laboratory*, 14 *MOLECULAR DIAGNOSIS & THERAPY* 137, 139 (2010) (providing an example of a case in which insurance did not cover testing for Charcot-Marie-Tooth disease, leaving the patient with a \$10,000 bill).

105. *See* Angrist et al., *supra* note 102, at S113 (finding that “a competitive presence could have accelerated the [LQTS] test to market and lowered the cost”).

106. *See* Robert Cook-Deegan, Christopher DeRienzo, Julia Carbone, Subhashini Chandrasekharan, Christopher Heaney & Christopher Conover, *Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Inherited Susceptibility to Cancer: Comparing Breast and Ovarian Cancers with Colon Cancers*, 12 *GENETICS MED.* S15, S15 (2010) (finding that “[p]rices for *BRCA1* and 2 testing do not reflect an obvious price premium attributable to exclusive patent rights compared with colorectal cancer testing,” for which the relevant patents are nonexclusively licensed).

Alternatively, clinical laboratories may bear the increased costs and then pass them along to patients and insurance providers. For example, costs could increase when a laboratory is forced to send multiple samples to different sole test providers.¹⁰⁷ Similarly, a laboratory's expenses related to staying informed about which genes are patented, which are licensed, and how they are licensed could increase costs.¹⁰⁸

2. Diminishing Quality of Patient Care. Another concern is that the allowance of gene patents may cause the quality of medical treatments to diminish.¹⁰⁹ Again, this phenomenon is illustrated by the example of genetic diagnostic tests.

When only one test provider exists, second opinions are not available, even to confirm an ambiguous result.¹¹⁰ This fact is particularly concerning because major medical decisions—such as whether to have a mastectomy—can hinge on the interpretation of genetic test results.¹¹¹

Product quality and reliability may also decrease if gene patents prevent competitors from providing comparative standards. A principal method of assessing the performance of genetic diagnostic tests is comparison among several test providers. Because different providers develop different methods and technologies, the comparison and subsequent improvement of tests ultimately allows providers to increase sensitivity, specificity, and reproducibility.¹¹² Thus, without any competing peers to provide the incentive to improve available genetic diagnostic tests, optimal performance may not be achieved.¹¹³ Without gene patents, however, some current

107. Mann, *supra* note 104, at 139.

108. SEC'Y'S ADVISORY COMM. ON GENETICS, HEALTH & SOC'Y, *supra* note 1, at 41; see also Mann, *supra* note 104, at 138 (discussing the challenges of determining the patent and licensing landscape).

109. SEC'Y'S ADVISORY COMM. ON GENETICS, HEALTH & SOC'Y, *supra* note 1, at 46–48.

110. Mann, *supra* note 104, at 139. Although confirmatory tests could be performed by the sole test provider, this arrangement is not as desirable, particularly if that sole provider has a deficiency in its test.

111. SEC'Y'S ADVISORY COMM. ON GENETICS, HEALTH & SOC'Y, *supra* note 1, at 44; see also *infra* notes 220–21 and accompanying text.

112. Mann, *supra* note 104, at 139.

113. See, e.g., Steve Benowitz, *French Challenge to BRCA1 Patent Underlies European Discontent*, 94 J. NAT'L CANCER INST. 80, 80–81 (2002) (noting that geneticist Dr. Dominique Stoppa-Lyonnet claimed that Myriad's test "misse[d] some 10% to 20% of the expected BRCA1 mutations").

genetic diagnostic tests may have never been developed and, even if they had been developed, they likely would not have been as extensively marketed and used.¹¹⁴

Gene patenting may also cause healthcare to become more fragmented and inefficient. Exclusivity prevents all the tests that a patient needs from being provided in one central location. Requiring patient samples to be sent to multiple locations for testing increases turnaround time¹¹⁵ and makes interpreting test results more difficult because tests obtained from several different locations must be interpreted together as a relevant group.¹¹⁶ Moreover, sending samples to multiple test providers increases the risk of having insufficient samples, and additional sample collection may not be feasible if treatment has already started.¹¹⁷

3. *Impeding Research and Innovation.* The final alleged problem created by gene patents is interference with research and innovation.¹¹⁸ The primary concern in this area is the theory of the “anticommons effect,” which posits that “a resource is prone to underuse . . . when multiple owners each have a right to exclude others from a scarce resource and no one has an effective privilege of use.”¹¹⁹ According to this theory, the large number of gene patents and gene-patent owners¹²⁰ will create a “patent thicket” that will stifle further innovation.¹²¹ The argument is that by “draw[ing] no distinction between downstream inventions that lead directly to commercial products and fundamental research discoveries that

114. See Holman, *supra* note 102, at 22 (discussing how Myriad, as a sole provider, had more incentive to invest “substantially in facilitating insurance reimbursement and in promoting awareness of BRCA testing,” which would likely result in increased accessibility); *infra* notes 184–86 and accompanying text.

115. Mann, *supra* note 104, at 138.

116. *Id.* at 138–39.

117. *Id.* at 138.

118. See *supra* note 4 and accompanying text.

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

120. See Jensen & Murray, *supra* note 92, at 239 (finding that “[t]he 4270 [gene] patents [that existed at the time were] owned by 1156 different assignees”).

121. See Carl Shapiro, *Navigating the Patent Thicket: Cross Licenses, Patent Pools, and Standard Setting*, 1 INNOVATION POL’Y & ECON. 119, 120 (2000) (describing how a “patent thicket” can stifle innovation because it is “a dense web of overlapping intellectual property rights that a company must hack its way through in order to actually commercialize new technology”).

broadly enable further scientific investigation,” research and innovation will be hindered.¹²²

In general, however, the empirical data regarding the effects of biotechnology patents on research and innovation are equivocal or show insubstantial effects.¹²³ Although inhibitory effects have been documented in the context of clinical laboratories providing genetic diagnostic tests¹²⁴—a context in which laboratories are presumably engaged not just in research and innovation, but also in competition with the patent holders—the available data generally fail to demonstrate the effects that would be expected to attend a classic anticommons problem.¹²⁵ For example, in a survey of 381 academic scientists, only 1 percent reported experiencing modifications or delays due to the existence of third-party patents, and none of the scientists reported being stopped by such patents.¹²⁶ This effect may

122. See Arti K. Rai & Rebecca S. Eisenberg, *Bayh-Dole Reform and the Progress of Biomedicine*, 66 LAW & CONTEMP. PROBS. 289, 289–91 (2003) (explaining how allowing universities to patent foundational biomedical discoveries may hinder the private innovation that the patent system was designed to encourage).

123. See John M. Conley, *Gene Patents and the Product of Nature Doctrine*, 84 CHI.-KENT L. REV. 109, 131 (2009) (“The empirical evidence for the effect of biotechnology patents on research is mixed.”); Demaine & Fellmeth, *supra* note 2, at 414 (“There has been no conclusive empirical study to support one or the other viewpoint.”).

124. See Timothy Caulfield, *Evidence and Anecdotes: An Analysis of Human Gene Patenting Controversies*, 24 NATURE BIOTECHNOLOGY 1091, 1092 (2006) (noting that, generally, “the effects predicted by the anticommons problem are not borne out in the available data,” but recognizing that “[o]ne important exception is in the area of gene patents that cover a diagnostic test”); *supra* note 101 and accompanying text.

125. Caulfield, *supra* note 124, at 1092; John P. Walsh, Charlene Cho & Wesley M. Cohen, *View from the Bench: Patents and Material Transfers*, 309 SCIENCE 2002, 2002–03 (2005) (finding “little empirical basis for claims that restricted access to IP is currently impeding biomedical research”); see also Christie Rizk, *The Big Fight*, GENOMEWEB (July 1, 2011), <http://www.genomeweb.com/big-fight> (drawing attention to the infringing research permitted by Myriad that has led to thousands of articles on Myriad’s patented genes and suggesting that if an infringing researcher were to find an important, novel mutation, “not only would [Myriad] not enforce the patent, it would most likely pay for the research”). Available gene-patent-litigation data also suggest that no anticommons problem exists. See Christopher M. Holman, *Trends in Human Gene Patent Litigation*, 322 SCIENCE 198, 198–99 (2008) (“Human gene patent litigation invariably has involved an alleged infringer engaged in substantial commercial activities focused specifically on the single gene that is the subject of the asserted patent, the antithesis of a patent thicket scenario.”). But see Fiona Murray & Scott Stern, *Do Formal Intellectual Property Rights Hinder Free Flow of Scientific Knowledge? An Empirical Test of the Anti-Commons Hypothesis*, 63 J. ECON. BEHAV. & ORG. 648, 648 (2007) (finding a modest anticommons effect in a study of patent-paper pairs and the effect of issuance of a patent on the citation rate to the corresponding paper).

126. Walsh, *supra* note 125, at 2002. Even if researchers were forced to change course because of patents, that result might not necessarily decrease social welfare. See John P. Walsh, Wesley M. Cohen & Charlene Cho, *Where Excludability Matters: Material Versus Intellectual*

be so minimal because researchers often ignore third-party patents¹²⁷ and because patent holders typically choose not to enforce their patents against infringing researchers.¹²⁸ Thus, although it is unclear what effect gene patents have on research and innovation, the situation is not nearly as grim as predicted by the theory of the anticommons.

II. CRITIQUE OF RECENT DEVELOPMENTS

The perceived problems caused by gene patents have triggered numerous passionate responses.¹²⁹ Among those responses are two noteworthy developments: *Myriad I* and the SACGHS report on gene patents, neither of which properly addressed the competing concerns implicated by gene patents. The *Myriad I* holding would have caused unintended, far-reaching consequences because it was based on an improper application of the law and ignored important policy considerations.¹³⁰ Similarly, the SACGHS recommendations for infringement exemptions are hasty, overly broad, and unwise given the uncertainty in the regulatory framework for genetic diagnostic tests.¹³¹

A. Critique of the *Myriad Case*

The progression of the *Myriad* case has resulted in several proposed frameworks for the patentability of DNA, ranging from the

Property in Academic Biomedical Research, 36 RES. POL'Y 1184, 1200 (2007) (“[I]f such redirection reduces duplicative research, the social welfare loss may be minimal. There may even be a net welfare gain if redirection increases the variety of projects pursued.” (citations omitted)).

127. See Zhen Lei, Rakhi Juneja & Brian D. Wright, *Patents Versus Patenting: Implications of Intellectual Property Protection for Biological Research*, 27 NATURE BIOTECHNOLOGY 36, 39 (2009) (remarking that academic agricultural-biology “[s]cientists by and large pay no attention to the patent status of their research tools because they rightly view themselves as judgment-proof due to their lack of personal resources”).

128. See Rebecca S. Eisenberg, *Noncompliance, Nonenforcement, Nonproblem? Rethinking the Anticommons in Biomedical Research*, 45 HOUS. L. REV. 1059, 1062 (2008) (“With patents, the burden of inertia is on the property owner to identify infringers and to enforce the patent against them. When owners face high costs of detection and enforcement, it is unlikely that they will bother to pursue claims of relatively low value (such as claims against noncommercial academic researchers).” (footnote omitted)); *supra* note 125.

129. See *supra* notes 5–9 and accompanying text. For a study on the negative media response to the *Myriad* case, see Timothy Caulfield, Tania Bubela & C.J. Murdoch, *Myriad and the Mass Media: The Covering of a Gene Patent Controversy*, 9 GENETICS MED. 850 (2007).

130. See *infra* Part II.A.2.

131. See *infra* Part II.B.

holding in *Myriad I* that isolated DNA is unpatentable subject matter¹³² to its reversal on appeal in *Myriad II* based on the reasoning that isolated DNA has a distinctive chemical structure.¹³³ None of these frameworks, however, are ideal.

1. *Progression of the Case and Its Various Proposed Frameworks for DNA Patentability.* The *Myriad* case has had several twists and turns. In April 2010, Judge Robert Sweet from the Southern District of New York dropped a bombshell in *Myriad I*, holding in part that isolated human genes were unpatentable subject matter.¹³⁴ The DNA sequences at issue in the case were the *BRCA1* and *BRCA2* genes, the mutations of which correlate with increased risks of developing breast cancer and ovarian cancer.¹³⁵

Interpreting the patentable-subject-matter standard to require that an invention must be markedly different from a product of nature to be patentable, the district court concluded that isolated DNA is not markedly different from native DNA because of the dual nature of DNA: it is not only a chemical molecule but also a carrier of information.¹³⁶ The court noted that through this information-carrying capacity, DNA “serves as the physical embodiment of laws of nature,” and that because this capacity is what also gives isolated DNA its utility, isolated DNA sequences are “unpatentable products of nature.”¹³⁷ Ultimately, the court’s rationale was that the “purification of native DNA does not alter its essential characteristic—its nucleotide sequence—that is defined by nature and central to both its biological function within the cell and its utility as a research tool in the lab.”¹³⁸

When the appeal reached the Federal Circuit, the U.S. government took a seemingly less extreme position in its amicus brief by drawing a distinction between isolated genomic DNA and

132. *Myriad I*, 702 F. Supp. 2d 181, 227–32 (S.D.N.Y. 2010), *rev’d in part*, 653 F.3d 1329 (Fed. Cir. 2011).

133. *Myriad II*, 653 F.3d 1329, 1353 (Fed. Cir. 2011).

134. *Myriad I*, 702 F. Supp. 2d at 227–32.

135. *Id.* at 203 (“Women with [*BRCA1*] and *BRCA2* mutations face up to an 85% cumulative risk of breast cancer, as well as up to a 50% cumulative risk of ovarian cancer.”).

136. *Id.* at 228.

137. *Id.* at 228–29.

138. *Id.* at 231.

complementary DNA (cDNA).¹³⁹ Understanding this distinction requires an understanding of the process underlying the conversion of genes to the proteins they encode. Within genomic DNA, most genes consist of coding sequences called exons—which provide the blueprint for the protein encoded by the gene—and noncoding sequences called introns—which are not necessary for the creation of the protein.¹⁴⁰ Although both exons and introns are initially transcribed into RNA, introns are removed from the RNA before it is translated into the end-product protein.¹⁴¹ This processed version of the RNA can be used as a template to artificially create cDNA—a non-naturally occurring form and sequence of DNA that contains the exons of a gene but not the noncoding introns.¹⁴² Because of this distinction, the government reasoned that genomic DNA is a product of nature, whether isolated or not,¹⁴³ whereas cDNA is a human-made invention.¹⁴⁴ The government thus concluded that cDNA should be patentable, whereas isolated genomic DNA should not.¹⁴⁵

The Federal Circuit, however, rejected both *Myriad I*'s holding and the position taken by the U.S. government in its amicus brief. It instead held that isolated DNA is patentable subject matter “[b]ecause isolated DNAs, not just cDNAs, have a markedly different chemical structure compared to native DNAs.”¹⁴⁶ The court emphasized that isolated DNA can be generated only by synthesizing it in a laboratory or by chemically cleaving a piece of genomic DNA from the chromosome on which it naturally resides.¹⁴⁷ Neither process is mere purification; both create a new molecule with “a distinctive chemical identity.”¹⁴⁸

139. Brief for the United States as Amicus Curiae in Support of Neither Party, *supra* note 7, at 37.

140. ALBERTS ET AL., *supra* note 12, at 347.

141. *Id.*

142. *See id.* at 544 (explaining that genes usually consist of coding and noncoding sequences and claiming that the most important advantage of cDNA is that it instead consists of an uninterrupted coding sequence).

143. Brief for the United States as Amicus Curiae in Support of Neither Party, *supra* note 7, at 17–27.

144. *Id.* at 14–17.

145. *Id.* at 37.

146. *Myriad II*, 653 F.3d 1329, 1353 (Fed. Cir. 2011).

147. *Id.* at 1351–52.

148. *Id.* at 1352.

2. *Analysis of Myriad's Various Proposed Frameworks for DNA Patentability.* The three positions that arose during the *Myriad* case—the *Myriad I* holding, the U.S. government's position, and the *Myriad II* holding—all have flaws or raise important unanswered questions.

The court's holding in *Myriad I*—that isolated DNA is unpatentable because it is most importantly a carrier of information¹⁴⁹—ignored important ways in which isolated DNA is markedly different from native DNA in both structure and utility.¹⁵⁰ Native DNA within a cell exists in the form of chromosomes, which are “enormously long linear DNA molecule[s] associated with proteins that fold and pack the fine DNA thread into a more compact structure.”¹⁵¹ Within these chromosomes are linear arrangements of genes surrounded by a much greater amount of non-gene-encoding DNA.¹⁵² Isolated DNA differs from genomic DNA in that it is free from surrounding chromosomal proteins and is not covalently bonded to surrounding chromosomal DNA, thereby representing a new molecule with “a distinctive chemical identity.”¹⁵³ The structural differences between cDNA and native genomic DNA are even greater. Unlike isolated genomic DNA, cDNA has a unique, non-naturally occurring DNA sequence.¹⁵⁴

These structural differences, created through human intervention, cause an “enlargement of the range of . . . utility”¹⁵⁵ for isolated DNA, as compared to the range of utility for native DNA. Gene-based diagnostic and therapeutic applications, for example,

149. *Myriad I*, 702 F. Supp. 2d 181, 227–32 (S.D.N.Y. 2010), *rev'd in part*, 653 F.3d 1329 (Fed. Cir. 2011).

150. The majority opinion in *Myriad II* stated that arguments regarding utility were not appropriate for patentable-subject-matter inquiries. *See Myriad II*, 653 F.3d at 1353 (“[I]t is the distinctive nature of DNA molecules as isolated compositions of matter that determines their patent eligibility rather than their physiological use or benefit.”). Judge Moore's concurring opinion used enlargement in the range of utility as evidence in the patentable-subject-matter inquiry. *Id.* at 1363–67 (Moore, J., concurring in part).

151. ALBERTS ET AL., *supra* note 12, at 202 (“The complex of DNA and protein is called chromatin In addition to the proteins involved in packaging the DNA, chromosomes are also associated with many proteins and RNA molecules required for the processes of gene expression, DNA replication, and DNA repair.” (emphasis omitted)).

152. *Id.* at 218.

153. *Myriad II*, 653 F.3d at 1351; *accord id.* at 1361–63 (Moore, J., concurring in part) (providing details on the different physical and chemical characteristics of isolated DNA).

154. *Id.* at 1364 (Moore, J., concurring in part). Although cDNA sequences do occur naturally in RNA, “DNA has a different chemical structure than RNA, including a different base . . . and sugar units.” *Id.*

155. *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 131 (1948).

often require use of shorter, isolated DNA sequences.¹⁵⁶ Moreover, isolated genes can be separated from their regulatory sequences, “which are responsible for ensuring that the gene is turned on or off at the proper time, expressed at the appropriate level, and only in the proper type of cell.”¹⁵⁷ By separating a gene from its regulatory sequences, researchers can combine the isolated gene with new regulatory sequences,¹⁵⁸ thereby allowing manipulation of when, where, and at what level the gene is expressed.¹⁵⁹ The ability to manipulate gene expression in this manner facilitates the use of isolated DNA for recombinant-protein therapeutics¹⁶⁰ and gene therapy.¹⁶¹

There are even more advantages to using the uninterrupted coding sequence of cDNA instead of isolated genomic DNA. For example, neither bacterial nor yeast cells will remove introns from RNA produced by a human gene that has been introduced into those cells.¹⁶² This fact is important because bacteria and yeast have characteristics that make the production of recombinant proteins in

156. For example, diagnostic tests are often “based on the sequence-specific binding of short complementary DNA probes . . . to DNA samples from patients in order to detect mutations.” W. Gregory Feero, Alan E. Gutmacher & Francis S. Collins, *Genomic Medicine—An Updated Primer*, 362 *NEW ENG. J. MED.* 2001, 2006 (2010).

157. ALBERTS ET AL., *supra* note 12, at 206.

158. *See supra* note 32.

159. *See, e.g.*, Carolina Roa-Rodríguez, *Promoters Used To Regulate Gene Expression*, PATENT LENS, 2–3 (Apr. 11, 2007, 4:10 PM), http://www.cambia.org/daisy/promoters/3141/version/default/part/AttachmentData/data/patentlens_techlandscape_promoters.pdf (describing different types of regulatory DNA sequences called promoters and discussing how they can be used to control the expression of a gene).

160. In the production of recombinant-protein therapeutics, regulatory sequences that drive high amounts of expression of the isolated gene are desired. *See* Wurm, *supra* note 29, at 1393 (explaining how, once the vectors containing the isolated gene are transferred into cells, “individual clones are evaluated for recombinant protein expression, with the highest producers being retained for further cultivation and analysis”). Moreover, the ability to splice the isolated gene together with DNA encoding selectable markers enables the selection of cells expressing the highest levels of a recombinant gene. *See* ALBERTS ET AL., *supra* note 12, at 514 (noting the utility of attaching special recognition tags to DNA).

161. For example, it is often desirable in gene therapy to use tissue-specific promoters to direct expression of the gene to a particular type of tissue within the body. *See, e.g.*, B. Wang, J. Li, F.H. Fu, C. Chen, X. Zhu, L. Zhou, X. Jiang & X. Xiao, *Construction and Analysis of Compact Muscle-Specific Promoters for AAV Vectors*, 15 *GENE THERAPY* 1489, 1489 (2008) (noting that, in the context of gene therapy for muscular dystrophy, “the use of muscle-specific promoters is highly desirable” because nonspecific promoters that cause “widespread targeted gene expression” can “result in overall toxicity and/or the initiation of a host immune response against tissues expressing the transgene or gene vector”).

162. *Id.*

bulk technically feasible.¹⁶³ Consequently, they are often used to produce recombinant-protein therapeutics from isolated DNA.¹⁶⁴

As these examples demonstrate, although the information-bearing capacity of DNA is one characteristic that enables isolated DNA to be used in genetic diagnostic tests and biologic drugs, it is not the sole important characteristic. Other characteristics that are not present in native DNA are equally important; whether it is cDNA without intron sequences or simply DNA separated from other chromosomal DNA and proteins, isolated DNA has been materially changed through human intervention, not so that it is more effective than native DNA, but so that it can be used for applications for which native DNA cannot.¹⁶⁵ Thus, isolated DNA is unlike the claimed invention in *Funk Brothers*, which consisted merely of a mixture of naturally-occurring bacteria performing the same functions they performed in nature.¹⁶⁶ Rather, like the bacteria in *Chakrabarty*—which, although still bacteria, had been altered to enable their use in breaking down crude oil¹⁶⁷—isolated DNA is still DNA, but it has been altered through human intervention to enable its use in therapeutics and diagnostics. Isolated DNA is, therefore, a “nonnaturally occurring manufacture or composition of matter . . . ‘having a distinctive . . . character [and] use,’”¹⁶⁸ and should be patentable subject matter.

This conclusion is consistent with Congress’s intent that patentable subject matter be construed broadly enough to “include anything under the sun that is made by man.”¹⁶⁹ Likewise, the Supreme Court has recognized only narrow exceptions to patent-

163. Neus Ferrer-Miralles, Joan Domingo-Espín, José Luis Corchero, Esther Vázquez & Antonio Villaverde, *Microbial Factories for Recombinant Pharmaceuticals*, MICROBIAL CELL FACTORIES, Mar. 24, 2009, at 1, 3.

164. *See id.* at 2 (“Among the 151 protein-based recombinant pharmaceuticals licensed up to January 2009 by the FDA and EMEA, 45 (29.8%) are obtained in [bacteria], 28 (18.5%) in [yeast], . . . and 59 (39%) in mammalian cells.”). *But see* Wurm, *supra* note 29, at 1393 (“Today about 60–70% of all recombinant protein pharmaceuticals are produced in mammalian cells.”).

165. *See supra* notes 150–64 and accompanying text.

166. *See* Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 131 (1948) (“Each of the species of root-nodule bacteria contained in the package infects the same group of leguminous plants which it always infected. No species acquires a different use.”).

167. *Diamond v. Chakrabarty*, 447 U.S. 303, 305 (1980).

168. *Id.* at 309–10 (alteration in original) (quoting *Hartranft v. Wiegmann*, 121 U.S. 609, 615 (1887)).

169. *Id.* at 309 (quoting S. REP. NO. 82-1979, at 5 (1952); H.R. REP. NO. 82-1923, at 6 (1952)) (internal quotation marks omitted).

eligible subject matter—“laws of nature, physical phenomena, and abstract ideas”¹⁷⁰—because “[t]he § 101 patent-eligibility inquiry is only a threshold test.”¹⁷¹ To hold that something is not patent eligible because it is a product of nature creates a slippery slope, for “[n]early everything . . . directly or tangentially involves a product of nature.”¹⁷² As such, the utility, novelty, obviousness, and written-description requirements “provide finer, more appropriate filters for separating truly inventive additions to human knowledge from unpatentable matter.”¹⁷³

Policy factors also weigh in favor of upholding the patentability of isolated DNA. It is generally not disputed that the biotechnology industry is particularly dependent on patent protection.¹⁷⁴ The reason for this dependence is that the development of therapeutics in the biotechnology industry is a lengthy, costly, and risky endeavor.¹⁷⁵ The average time required to bring a therapeutic to market—including drug discovery, preclinical testing, clinical trials, and Food and Drug Administration (FDA) review—is fifteen years.¹⁷⁶ In addition to being time-intensive, the process is also accompanied by high expenses, with various estimates ranging from \$500 million to \$2 billion.¹⁷⁷ For

170. *Id.*

171. *Bilski v. Kappos*, 130 S. Ct. 3218, 3225 (2010).

172. Brief of Amici Curiae Rosetta Genomics, Ltd. et al. in Support of Defendants-Appellants, Supporting Reversal at 33, *Myriad II*, 653 F.3d 1329 (Fed. Cir. 2011) (No. 2010-1406); *see also* *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 135 (1948) (Frankfurter, J., concurring) (“Everything that happens may be deemed ‘the work of nature,’ and any patentable composite exemplifies in its properties ‘the laws of nature.’ Arguments drawn from such terms for ascertaining patentability could fairly be employed to challenge almost every patent.”).

173. Brief for the Appellants at 50, *Myriad II*, 653 F.3d 1329 (No. 2010-1406). Importantly, the patentability requirements of §§ 102, 103, and 112 are being applied more stringently. *See supra* Part I.C.2–3.

174. *See, e.g.*, Robert J. Paradiso & Lisa K. Schroeder, *District Court Holds Myriad’s Gene Patents Invalid*, 18 METROPOLITAN CORP. COUNS. 25, 25 (2010) (“Because the development of biotechnology and pharmaceuticals can be time intensive, unpredictable, and expensive, life sciences innovators need the mechanisms provided by the patent system to recoup their investments and ensure a steady revenue stream for further research and development.”).

175. *See supra* note 10 and accompanying text.

176. U.S. GOV’T ACCOUNTABILITY OFFICE, GAO-07-49, NEW DRUG DEVELOPMENT: SCIENCE, BUSINESS, REGULATORY, AND INTELLECTUAL PROPERTY ISSUES CITED AS HAMPERING DRUG DEVELOPMENT EFFORTS 6 (2006).

177. *See* Christopher P. Adams & Van V. Brantner, *Estimating the Cost of New Drug Development: Is It Really \$802 Million?*, 25 HEALTH AFF. 420, 427 (2006) (“[F]or one large pharmaceutical firm, the expected cost of developing a drug is \$521 million, while for another large firm, it is \$2,119 million.”); Joseph A. DiMasi & Henry G. Grabowski, *The Cost of Biopharmaceutical R&D: Is Biotech Different?*, 28 MANAGERIAL & DECISION ECON. 469, 475

drugs derived from biological products like DNA, the costs tend to be even higher.¹⁷⁸ These costs result not only from the extensive development process but also from the unpredictability inherent in biological innovation: for every compound that is brought to market as a drug, there are approximately ten-thousand failed attempts.¹⁷⁹ As a consequence, costs include both “the research and development that led to the product” and “the scores of failed experiments that did not result in a commercial product but may have ultimately led to the patented invention.”¹⁸⁰

Commentators have argued that patents are not always necessary to stimulate biotechnology researchers to invent because they have many other incentives, particularly when it comes to identifying genes associated with different diseases.¹⁸¹ This argument is premised on the fact that “[n]early all disease genes are identified not by private industry, but by researchers working at non-profit institutions.”¹⁸² As such, those academic or nonprofit researchers might be driven by a desire to help patients or to advance understanding, a desire to enhance their reputations by receiving credit for priority of discovery, or a desire to enhance their careers by being able to secure research funding based on past scientific achievement and to compete more effectively for faculty positions and other jobs.¹⁸³

(2007) (finding that the “[t]otal capitalized cost per approved molecule for biopharmaceuticals is . . . \$1241 million” in 2005 dollars); Steven M. Paul, Daniel S. Mytelka, Christopher T. Dunwiddie, Charles C. Persinger, Bernard H. Munos, Stacy R. Lindborg & Aaron L. Schacht, *How To Improve R&D Productivity: The Pharmaceutical Industry’s Grand Challenge*, 9 NATURE REVIEWS DRUG DISCOVERY 203, 204 (2010) (“[T]he average cost for [pharmaceutical] companies to bring [a new molecular entity] to market is now estimated to be approximately \$1.8 billion.”).

178. Henry Grabowski, *Follow-On Biologics: Data Exclusivity and the Balance Between Innovation and Competition*, 7 NATURE REVIEWS DRUG DISCOVERY 479, 482 (2008) (“Biologics also have higher discovery and preclinical expenditures and longer mean clinical development times. It was also found that the development of biologics involve [*sic*] higher development costs associated with process engineering and manufacturing than is true for chemical drugs. This reflects the need to resolve novel manufacturing challenges at the R&D stage.”). Biologics are essentially “complex molecules produced from cultures of living cells.” *Id.* at 481.

179. U.S. GOV’T ACCOUNTABILITY OFFICE, *supra* note 176, at 1.

180. Larry A. Roberts, *Myriad: How Did Public Policy Weigh In?*, INTELL. PROP. STRATEGIST, May 2010, at 1, 5.

181. See SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 1, at 20 (noting researchers’ desire to advance understanding and help patients).

182. *Id.* at 22.

183. *Id.* at 20–22.

This argument, however, ignores a more important function of the patent system in the context of biotechnology and gene patents: providing the incentive to invest in the development and commercialization of biotechnology and gene-patent-derived inventions.¹⁸⁴ The premise underlying this theory is that, in some contexts, “the patent system is not so much needed to stimulate inventive activity; rather, it facilitates investment into costly and risky development processes that are necessary to transform a ‘mere’ invention into a marketable product.”¹⁸⁵ The development of the genetic diagnostic tests at issue in *Myriad* reflects this theory: “While university scientists received substantial grants from the National Institutes of Health, Myriad was largely financed by private venture capital totaling at least \$22 [million].”¹⁸⁶ These private capital investments are often required for small biotechnology companies to survive because these companies generally have considerable research and development expenses but may not yet have a marketable product.¹⁸⁷ Without patents, the ability to attract this necessary private investment would be greatly diminished¹⁸⁸ and many biotechnology companies would no longer survive.¹⁸⁹ This effect in

184. See Prinz zu Waldeck und Pyrmont, *supra* note 10, at 372 (“The ‘incentive to invest’ theory focuses on a patent’s function to induce investment for the development and commercialization of inventions.”). See generally Edmund W. Kitch, *The Nature and Function of the Patent System*, 20 J.L. & ECON. 265 (1977) (discussing the “prospect” function of patents). For example, from 1994 to 2005, Myriad lost money because it “spent \$500 million not just on research and development of its BRACAnalysis test, but also on educating patients, marketing the test, educating physicians as to its use and necessity, and working with insurance companies to cover the cost of testing.” Rizk, *supra* note 125.

185. Prinz zu Waldeck und Pyrmont, *supra* note 10, at 372. In the biotechnology industry, this function is particularly important because “a patent on a promising compound or technology can attract capital for product development.” *Id.*

186. Roberts, *supra* note 180, at 5.

187. See, e.g., Subhashini Chandrasekharan, Sapna Kumar, Cory M. Valley & Arti Rai, *Proprietary Science, Open Science, and the Role of Patent Disclosure: The Case of Zinc-Finger Proteins*, 27 NATURE BIOTECHNOLOGY 140, 141 (2009) (discussing the example of Sangamo Biosciences and noting that “a dominant patent position facilitates Sangamo’s ability to attract private capital,” which is necessary “[g]iven Sangamo’s considerable R&D expenses and lack of marketable products”).

188. See Roberts, *supra* note 180, at 5 (“[I]f a patent applicant cannot enjoy its period of exclusivity to recoup its R&D costs and make a profit for its investors, from where will future financing of biotechnology come?”).

189. See Iain M. Cockburn, *The Changing Structure of the Pharmaceutical Industry*, 23 HEALTH AFF. 10, 15 (2004) (“Without patent rights in inventions in areas such as isolation and purification of proteins, DNA sequences, monoclonal antibodies, knockout and transgenic organisms, gene expression systems, and so on (or at least the prospect of obtaining and enforcing them), many biotech companies would never have been founded.”). One example of a

turn could lead to stagnation in product development because small biotechnology companies play an important role in bridging the gap between basic scientific discoveries and the development of marketable products based on those discoveries;¹⁹⁰ in essence, they serve a critical role as “specialist suppliers of leading-edge technology to downstream firms” that have the resources to bring that technology to market.¹⁹¹

Unintended consequences could also result from the more moderate position of the U.S. government that cDNA is patentable because “such molecules do not occur in nature, either in isolation or as contiguous sequences contained within longer natural molecules,” whereas genomic DNA is unpatentable because it does occur in nature in such forms.¹⁹² For example, it is unclear how other natural products such as proteins would continue to be patentable: unlike cDNAs, proteins exist in nature.¹⁹³ Similarly, although *Myriad II* is the most gene-patent friendly of the frameworks for DNA patentability considered in *Myriad*, it also appears to cast some doubt on the patentability of other natural products by emphasizing that isolated DNA is patentable because it is “manipulated chemically” to create a “distinct chemical entity” and is, therefore, more than simply “purified DNA.”¹⁹⁴

One example of a situation in which these positions could have detrimental effects is antibiotic development. Some commentators

drug that has needed to rely on gene-patent protection is Epogen—recombinant erythropoietin. Holman, *supra* note 102, at 23.

190. See Cockburn, *supra* note 189. This critical gap has been called the “valley of death.” See Arti K. Rai, Jerome H. Reichman, Paul F. Uhler & Colin Crossman, *Pathways Across the Valley of Death: Novel Intellectual Property Strategies for Accelerated Drug Discovery*, 8 YALE J. HEALTH POL’Y L. & ETHICS 1, 4 (2008) (“[O]ne of the most serious pitfalls involves the difficulty of moving across the so-called ‘valley of death’ that separates upstream research on promising genes, proteins, and biological pathways from downstream drug candidates.”). Especially in the case of biological macromolecules, small biotechnology companies have had success in bridging this gap. *Id.* at 5 n.12.

191. Cockburn, *supra* note 189, at 15.

192. Brief for the United States as Amicus Curiae in Support of Neither Party, *supra* note 7, at 15.

193. See *supra* Part I.A.1.

194. *Myriad II*, 653 F.3d 1329, 1352 (Fed. Cir. 2011); see also Christopher M. Holman, *AMP v. PTO Casts Doubt on Patent Eligibility of “Purified” (as Opposed to “Isolated”) Biomolecules*, HOLMAN’S BIOTECH IP BLOG (Aug. 1, 2011, 9:51 AM), <http://holmansbiotechblog.blogspot.com/2011/08/amp-v-ptocasts-doubt-on-patent.html> (“[I]t seems that . . . [the Federal Circuit’s] decision suggests that a purified natural product is patent ineligible unless it has distinctions in chemical structure sufficient to render it ‘markedly different’ from its naturally occurring counterpart.” (quoting *Myriad II*, 653 F.3d at 1352)).

have expressed concern that at the same time resistance to antibiotics is increasing, development of new antibiotics is decreasing.¹⁹⁵ Part of the reason underlying this decrease is that antibiotic development has become a low priority for biotechnology companies due to the relatively low return on their investment.¹⁹⁶ Given this reality, the protection and incentives provided by patents could be critical for the development of new antibiotics.¹⁹⁷ There are two general pathways to develop antibiotics: “isolation of natural products with antibiotic activity and preparation of synthetic antibiotics.”¹⁹⁸ The former pathway, “the discovery of natural product antibiotics from bacterial sources,”¹⁹⁹ has been the subject of increasing interest. This method of development, however, could be hampered by the U.S. government’s position, and perhaps by the court’s rationale in *Myriad II*, because it is unclear how or whether natural-product antibiotics would continue to be patentable.²⁰⁰ This potential deterrent could exacerbate the existing lack of incentive to develop antibiotics.²⁰¹

In summary, the holding of *Myriad I* and the position taken by the U.S. government in its amicus brief both fail to consider adequately the investment-backed expectations of the biotechnology industry²⁰² and the fact that there are “many drugs currently on the

195. See generally Martin L. Katz, Lisa V. Mueller, Mark Polyakov & Steven F. Weinstock, *Where Have All the Antibiotic Patents Gone?*, 24 NATURE BIOTECHNOLOGY 1529 (2006) (discussing the slowdown in antibiotic development and noting that it is crucial to continue developing new antibiotics in light of increasing antibiotic resistance).

196. See *id.* at 1530 (comparing the return on investment from antibiotic drugs with the return on investment from nonantibiotic drugs).

197. See *id.* at 1531 (suggesting that two incentives that could be provided to companies engaged in antibiotic research are “extending market exclusivity for antibiotics (especially when second uses are discovered) and providing longer patent term extensions to compensate for longer and costlier developments of antibiotics as compared to chronically used drugs”).

198. Jon Clardy, Michael A. Fischbach & Christopher T. Walsh, *New Antibiotics from Bacterial Natural Products*, 24 NATURE BIOTECHNOLOGY 1541, 1541 (2006).

199. *Id.*

200. It should be noted that “virtually every newly discovered antibiotic since 1929 has been patented,” including “erythromycin, vancomycin, rifamycin, clarithromycin, ciprofloxacin and azithromycin.” Katz, *supra* note 195, at 1529.

201. Narrower patents, such as patents directed to uses of the newly discovered antibiotics, could still be obtained. Process patents, however, are not as desirable as product patents on the DNA or protein. Some of the disadvantages include “(1) the difficulty of detecting infringement[and] (2) the defects in infringement doctrines.” MERGES & DUFFY, *supra* note 58, at 388–91.

202. See Brief of Amici Curiae Rosetta Genomics, Ltd. et al. in Support of Defendants-Appellants, Supporting Reversal, *supra* note 172, at 29 (“[A]n adverse decision here could negatively impact thousands of existing patents. For example, a search conducted on September

market that simply would not exist without such patents” and the incentives they provide.²⁰³ Although the Federal Circuit corrected these problems temporarily in *Myriad II*, its rationale unfortunately cast doubt on the patentability of other natural products.²⁰⁴ And, no matter how the Federal Circuit’s rationale and holding are ultimately interpreted, the case has yet to be finally resolved by the courts.²⁰⁵

B. Critique of the SACGHS Report on Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Diagnostic Tests

Another proposed solution to the alleged problems created by gene patents is a 2010 SACGHS report that recommends two statutory changes: (1) “an exemption from liability for anyone who infringes a patent on a gene while making, using, ordering, offering for sale, or selling a genetic test for patient care purposes,”²⁰⁶ and (2) “an exemption from patent infringement liability for those who use patent-protected genes in the pursuit of research.”²⁰⁷ Although these proposed exemptions attempt to address the perceived problems created by gene patents, their broad language threatens to undermine the entire gene-patent system. As one commentator notes, “Patient care and research are broad, nebulous categories that, if interpreted generously, could cover every reasonably likely use for many patent-protected genes and related tests.”²⁰⁸ Additionally, as this Section demonstrates, because of the faulty reasoning behind the SACGHS recommendations, the proposed statutory exemptions are both unwise and difficult to define.

1. *Exemption for Patient-Care Purposes.* In suggesting the creation of a patient-care exemption, the SACGHS relies on its belief that gene “patents do not appear to be necessary to stimulate

22, 2010, on the USPTO website for U.S. issued patents filed within the last 17 years . . . having claims [directed to isolated or purified nucleic acids] brought up 23,710 patents alone.”).

203. Gregory C. Ellis, *Emerging Biotechnologies Demand Defeat of Proposed Legislation That Attempts To Ban Gene Patents*, 15 RICH. J.L. & TECH., no. 1, 2008, at 1, 24–25, <http://jolt.richmond.edu/v15i1/article1.pdf>; see also *supra* notes 22–36 and accompanying text.

204. See *supra* notes 192–201 and accompanying text.

205. See *supra* note 80.

206. SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 1, at 94.

207. *Id.* at 95.

208. Dan Vorhaus, *SACGHS Gene Patent Recommendations Still Controversial*, GENOMICS L. REP. (Feb. 8, 2010), <http://www.genomicslawreport.com/index.php/2010/02/08/sacghs-gene-patent-recommendations-still-controversial>.

research and genetic test development,” in part because “development costs are minimal” for genetic diagnostic tests.²⁰⁹ Though existing development costs may be minimal for some types of tests, those costs may change because the FDA has taken steps to increase regulation of diagnostic tests.²¹⁰

There are currently two main categories of genetic diagnostic tests: test kits—or in vitro diagnostic tests—and laboratory-developed tests (LDTs).²¹¹ The first category, test kits, can be manufactured for distribution in interstate commerce²¹² and are regulated as medical devices by the FDA under the Federal Food, Drug, and Cosmetic Act.²¹³ To ensure safety and efficacy, the FDA takes a data-driven approach and requires test-kit manufacturers to “provide data supporting any analytical and clinical claims related to the use and/or effectiveness of a product.”²¹⁴ LDTs, on the other hand, can be used only in the test developer’s laboratory²¹⁵ and are generally regulated by the Centers for Medicare & Medicaid Services under the Clinical Laboratory Improvement Amendments of 1988 (CLIA).²¹⁶ Unlike the rigorous regulatory approach taken by the FDA for test kits, “CLIA takes a process-oriented approach that focuses on factors such as credentials of laboratory personnel and laboratory testing procedures.”²¹⁷ Consequently, the cost of developing LDTs is modest compared to the cost of developing test kits.²¹⁸

209. SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 1, at 90.

210. *See* Oversight of Laboratory Developed Tests, 75 Fed. Reg. 34,463, 34,463 (June 17, 2010) (notice of public meeting and request for comments) (soliciting comments on proposals to increase the regulation of laboratory-developed tests (LDTs)).

211. SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, U.S. DEP’T OF HEALTH & HUMAN SERVS., U.S. SYSTEM OF OVERSIGHT OF GENETIC TESTING: A RESPONSE TO THE CHARGE OF THE SECRETARY OF HEALTH AND HUMAN SERVICES 3, 21 (2008).

212. *Id.* at 3.

213. Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301–399 (2006); *see also* SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 1, at 34 (discussing the FDA’s regulation of test kits).

214. SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 211, at 29.

215. *Id.* at 3.

216. Clinical Laboratory Improvement Amendments of 1988, Pub. L. No. 100-578, 102 Stat. 2903 (codified at 42 U.S.C. § 263a (2006)).

217. SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 211, at 30.

218. SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 1, at 34. The SACGHS calculates that “the cost of developing a laboratory-developed genetic test that relies on gene sequencing as opposed to probe hybridization to detect a single mutation is, on average, between \$8,000 and \$10,000.” *Id.* The cost for gaining approval of a test kit is significantly higher. *See, e.g.,* Roberts, *supra* note 180, at 5 (noting that development of the genetic diagnostic tests at issue in *Myriad* was financed by \$22 million in private venture capital); Frost & Sullivan,

Commentators, however, have increasingly called for the FDA to exert greater regulatory control over all genetic diagnostic tests, including LDTs.²¹⁹ The rationale is that “diagnostic tests are playing an increasingly important role in clinical decisionmaking and disease management”²²⁰ and, thus, that significant consequences could result if the tests are inaccurate:

False positive results can lead to unnecessary confirmatory testing, unnecessary treatment that can be invasive or have harmful side effects, and/or unnecessary psychological trauma False negative results can lead to a delay in establishing the correct diagnosis, failure to start or continue needed treatment, false security that may prevent timely follow-up and retesting, and contribute to the potential spread of infectious agents to others.²²¹

In response, the FDA announced its intention to make regulatory changes in the genetic-testing industry.²²²

The upshot of the FDA’s new position will likely be a more expensive process for developing genetic diagnostic tests, particularly LDTs.²²³ The FDA appears to believe that a risk-based regulatory

Opportunities and Growth Strategies for the APAC IVD Industry, SLIDESHARE, 16, <http://www.slideshare.net/FrostandSullivan/diagnostic-world-asia-apac-ivd-outlook-2010> (last visited Nov. 9, 2011) (calculating the average diagnostic-development cost to be approximately \$40 million).

219. See, e.g., SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 211, at 8 (concluding that to ensure proper oversight of clinical validity, the “FDA should address all laboratory tests in a manner that takes advantage of its current experience in evaluating laboratory tests”).

220. Oversight of Laboratory Developed Tests, 75 Fed. Reg. 34,463, 34,463 (June 17, 2010) (notice of public meeting and request for comments).

221. CTR. FOR BIOLOGICS EVALUATION & RESEARCH, U.S. DEP’T OF HEALTH & HUMAN SERVS., GUIDANCE FOR INDUSTRY AND FDA STAFF: IN VITRO DIAGNOSTIC (IVD) DEVICE STUDIES—FREQUENTLY ASKED QUESTIONS 10 (2010), available at <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071230.pdf>. The potential for inaccuracy and inconsistency is demonstrated by a study comparing diagnostic tests for thirteen diseases from two different test providers. This study found that “only two-thirds of relative risk predictions qualitatively agree between [the providers] when averaged across [the] five [tested] individuals.” Pauline C. Ng, Sarah S. Murray, Samuel Levy & J. Craig Venter, *An Agenda for Personalized Medicine*, 461 NATURE 724, 724 (2009).

222. See Oversight of Laboratory Developed Tests, 75 Fed. Reg. at 34,464 (“[T]he agency believes it is time to reconsider its policy of enforcement discretion over LDTs. The public must be assured that the tests used in the provision of health care, whether developed by a laboratory or other manufacturer, are safe and effective.”).

223. See Letter from Daryl Pritchard, Dir., Research Programs Advocacy, Biotechnology Indus. Org., to Div. of Dockets Mgmt., Food & Drug Admin. 3 (Aug. 15, 2010) (on file with the *Duke Law Journal*) (“This shift from the current system, under which FDA has exercised enforcement discretion with respect to LDTs while laboratories have continued to be regulated under CLIA, will have an impact on the cost of development and ongoing compliance . . .”).

framework is appropriate.²²⁴ Although it is unclear what such a framework would entail, a comparison to the medical-device framework used for test kits²²⁵ suggests that it would likely be costly.²²⁶ Consequently, arguments for more stringent patenting standards or exemptions in the context of genetic diagnostic tests may soon no longer be valid insofar as those arguments are premised on the idea that LDTs are “inexpensively designed, developed, and validated” because they “do not undergo FDA clearance.”²²⁷

The SACGHS claims that, notwithstanding the FDA’s position and the more extensive regulatory framework that could result from it, exclusive rights will not be necessary for the development of genetic diagnostic tests.²²⁸ In support of its position, the SACGHS cites a case study on genetic testing for cystic fibrosis that shows that multiple parties have developed test kits with nonexclusive licenses.²²⁹ Because test kits are subject to FDA approval, the SACGHS believes that this study suggests that exclusive rights are unnecessary.²³⁰ Nevertheless, many others disagree and believe that without exclusive rights, there will usually be insufficient incentive to develop genetic

224. See Oversight of Laboratory Developed Tests, 75 Fed. Reg. at 34,464 (“At this time, FDA believes that a risk-based application of oversight to LDTs is the appropriate approach to achieve the desired public health goals . . .”). But see Sharon Goswami & Dan Vorhaus, *News Roundup: Biotech Funding and LDT Regulation*, GENOMICS L. REP. (May 5, 2011), <http://www.genomicslawreport.com/index.php/2011/05/05/news-roundup-biotech-funding-and-ldt-regulation> (providing examples of alternative approaches being considered).

225. See Allain Andry & Dan Vorhaus, *The Business Effects of Regulatory Uncertainty in Genetic Testing*, GENOMICS L. REP. (Aug. 31, 2010), <http://www.genomicslawreport.com/index.php/2010/08/31/the-business-effects-of-regulatory-uncertainty-in-genetic-testing> (“The most common category of medical device is a medium-risk . . . device . . . which . . . [i]n the case of [IVD] devices . . . requires, among other things, (i) considering whether there is a ‘predicate device’ on which a 510(k) application could be based, (ii) generating both analytical and clinical data to support an FDA application and (iii) preparing to manufacture the devices and operate laboratories under compliance and inspection regimes that are likely to be more demanding than the currently-applicable CLIA compliance requirements.”).

226. See *supra* note 218.

227. See R.D. Klein, *Legal Developments and Practical Implications of Gene Patenting on Targeted Drug Discovery and Development*, 87 CLINICAL PHARMACOLOGY & THERAPEUTICS 633, 633 (2010) (discussing the higher costs of developing therapeutics for market as opposed to genetic tests).

228. SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 1, at 35.

229. *Id.* at 34–35 (citing Subhashini Chandrasekharan, Christopher Heaney, Tamara James, Chris Conover & Robert Cook-Deegan, *Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Cystic Fibrosis*, 12 GENETICS MED. S194 (2010)).

230. *Id.* at 34.

diagnostic tests.²³¹ In view of the notable effects of exclusive licensing in other contexts,²³² it is likely that exclusive rights provide a critical economic incentive in the context of genetic diagnostic tests as well.

2. *Exemption for Research Purposes.* Although the SACGHS recommends an exemption for the use of patent-protected genes in the pursuit of research, it does not provide details on how such research would be defined. In failing to do so, the SACGHS consequently fails to establish clearly the limits of the exemption.²³³ Although several types of statutory research exemptions have been suggested elsewhere, each proposal has drawn a different line between exempt and nonexempt research.²³⁴ For example, some proposed research exemptions focus on differentiating between commercial and noncommercial research, exempting only the latter.²³⁵

231. See, e.g., Best Practices for the Licensing of Genomic Inventions, 70 Fed. Reg. 18,413, 18,414 (Apr. 11, 2005) (notice) (“Practical realization of [benefits arising from biomedical innovation] depends on the ability and willingness of private sector partners to develop and commercialize new technologies For potential preventive, diagnostic, and therapeutic products, the interest of the private sector in commercializing new technologies often depends on the existence of patent protection”). Even the American Medical Association has recognized the important role of patents in the development of genetic test kits subject to FDA approval. See Brief of Amici Curiae American Medical Association et al. in Support of Respondents at 13, *Bilski v. Kappos*, 130 S. Ct. 3218 (2010) (No. 08-964) (“[P]atents can enhance the provision of high-quality and cost-effective medical care. The financial incentive offered by patents supports the expensive and uncertain research required to identify, test, and gain approval for products such as new pharmaceuticals, medical devices, and *diagnostic testing kits*. In this respect, the patent system has served patients and the medical profession well.” (emphasis added)).

232. Exclusive licensing has played an important role in other contexts such as the Bayh-Dole Act, Pub. L. No. 96-517, 94 Stat. 3015 (1980) (codified as amended at 35 U.S.C. §§ 200–212 (2006)). The Bayh-Dole Act has stimulated the commercialization of government-funded scientific breakthroughs in part by allowing federal contractors to grant exclusive licenses for patented inventions whose research and development has been funded by the government. See BAYHDOLE25, INC., THE BAYH-DOLE ACT AT 25, at 13, 20 (2006), available at http://bayhdolecentral.com/BayhDole25_WhitePaper.pdf (explaining that before the Bayh-Dole Act—which “granted federal contractors the authority to grant exclusive patent licenses”—“rights belong[ed] to everyone, [so] no one had sufficient incentive to bring innovations to market”).

233. See SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 1, at 95–96 (discussing the suggested exemption at only a broad level).

234. Although there is a common-law research exemption, it is too narrow for this context. See *Madey v. Duke Univ.*, 307 F.3d 1351, 1362 (Fed. Cir. 2002) (“[S]o long as the act is in furtherance of the alleged infringer’s legitimate business and is not solely for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry, the act does not qualify for the very narrow and strictly limited experimental use defense.”).

235. See Rebecca S. Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use*, 56 U. CHI. L. REV. 1017, 1034–35 (1989) (discussing a previously proposed

The idea behind this type of exemption is that the patent holder's interest will not be harmed if the patented invention is used merely for noncommercial research.²³⁶ Others advocate for exemptions for research *on* a patented invention but not *with* a patented invention.²³⁷ Arguably, this type of exemption would be beneficial in the context of genetic testing because it would allow “[r]esearch and development to make testing more comprehensive, more accurate or less expensive,” thereby improving testing quality.²³⁸

One could also argue, however, that a *de jure* exemption for research is unnecessary because a *de facto* exemption already exists.²³⁹ Myriad has maintained that it never enforces its patents against researchers or against test providers offering services or forms of tests that Myriad does not offer.²⁴⁰ In addition, researchers tend to ignore third-party patents.²⁴¹ But some commentators note that, even if these statements are true, “Myriad [has] never publicly stated its *de facto* research use exemption policy” and the resulting “[a]mbiguity may itself stifle basic or clinical research as researchers either avoid the work altogether or are wary of publicly reporting results.”²⁴² Moreover, there is no guarantee that Myriad's peer companies have equivalent policies.²⁴³ Given these concerns, a statutory research exemption could be more effective than reliance on a *de facto* exemption through corporate policies.

experimental-use exemption that “refines the no-harm standard by drawing a distinction between commercial and noncommercial research”).

236. *Id.* at 1034.

237. COMM. ON INTELLECTUAL PROP. RIGHTS IN GENOMIC & PROTEIN RESEARCH & INNOVATION, NAT'L RESEARCH COUNCIL OF THE NAT'L ACADS., REAPING THE BENEFITS OF GENOMIC AND PROTEOMIC RESEARCH: INTELLECTUAL PROPERTY RIGHTS, INNOVATION, AND PUBLIC HEALTH 14 (2006), available at http://www.nap.edu/catalog.php?record_id=11487. Research *on* a patented invention minimally includes research to discover the validity and scope of the patent, the characteristics and advantages of the invention, novel methods of making and using the patented invention, and improvements or alternatives to the patented invention. *Id.*

238. Robert Cook-Deegan, Subhashini Chandrasekharan & Misha Angrist, *The Dangers of Diagnostic Monopolies*, 485 NATURE 405, 406 (2009).

239. See Eisenberg, *supra* note 235, at 1034 (“Ironically, a no-harm limitation would seem to confine the defense to situations in which it is unnecessary, since patent holders are unlikely to bring infringement actions unless they feel harmed by the defendants' conduct.”).

240. Cook-Deegan et al., *supra* note 106, at S28.

241. See *supra* note 127 and accompanying text.

242. Cook-Deegan et al., *supra* note 106, at S28 (emphasis omitted).

243. But see generally Christopher M. Holman, *Trends in Human Gene Patent Litigation*, 322 SCIENCE 198 (2008) (“Human gene patent litigation invariably has involved an alleged infringer engaged in *substantial commercial activities* focused specifically on the single gene that is the subject of the asserted patent . . .” (emphasis added)).

The difficulty of conceiving a suitable demarcation between exempt and nonexempt research, however, weighs more heavily against creating a research exemption. Demarcations that have been proposed thus far are not only ambiguous,²⁴⁴ but their policy rationales are also unconvincing in some circumstances. For example, the rationale behind the seemingly clear distinction between commercial and noncommercial research—that noncommercial research does not harm a patent holder’s interests—breaks down when the market for a patented invention is for its use as a research tool, in which case exempting research users would potentially destroy the market for the patented invention.²⁴⁵

The rationale behind the distinction between research *with* and research *on* also breaks down in some situations. If research *on* a patented invention were exempt, a patent holder’s interests would initially seem to be protected because researchers would have to acquire a license from the patent holder before marketing subsequent improvements that fall within the patent’s scope.²⁴⁶ Such research, however, might also result in a noninfringing substitute for the patented technology, which, if commercially exploited, would undermine the patent holder’s ability to earn an adequate return on his investment.²⁴⁷

Ultimately, these and other proposed lines between exempt and nonexempt research are nebulous and difficult to define. More importantly, data suggest that a de facto research exemption already exists: researchers tend to ignore patents,²⁴⁸ and patent holders tend

244. See, e.g., Holman, *supra* note 102, at 25 (“[W]ith the increasing level of involvement and collaboration between for-profit companies and universities, the line between basic and commercial research is blurring.”).

245. See Eisenberg, *supra* note 235, at 1035 (“[F]or inventions with significant markets among researchers, such as patented laboratory techniques and other research tools, exempting even purely academic researchers from the patent monopoly could deprive patent holders of a portion of the monopoly profits they might otherwise expect to earn and thereby reduce incentives to make and disclose such inventions in the future.” (footnote omitted)).

246. See *id.* at 1076 (“[I]f a subsequent researcher develops an improvement that falls within the scope of the claims of the earlier patent, the financial interests of the patent holder may be adequately protected by allowing enforcement of the patent after the research is completed when the improvement is ready for commercial exploitation.”).

247. See *id.* (“[I]f the subsequent researcher is able to develop a substitute technology that does not infringe the patent claims, denying the patent holder a remedy for the research use could prevent the patent holder from earning an adequate return on the initial investment in developing the earlier patented invention.”).

248. See *supra* note 127 and accompanying text.

not to enforce their patents against researchers.²⁴⁹ Given the line-drawing problems and the evidence suggesting that research has not been substantially hindered, any slight benefits created by a statutory research exemption are not enough to justify establishing such an exemption.

III. A NARROWLY TAILORED SOLUTION

Although it is debatable whether the concerns underlying gene patents are sufficiently well founded to warrant a response by Congress or the courts, the *Myriad I* holding and the exemptions recommended by the SACGHS go too far. *Myriad I*, by broadly holding that isolated DNA is not patentable subject matter,²⁵⁰ ignored both the reality that isolated DNA has important characteristics that make it vitally different from native DNA²⁵¹ and the importance of gene patents in the biotechnology industry.²⁵² Moreover, the fact that courts are rightly beginning to enforce the utility and nonobviousness standards more strictly in the context of gene patents makes *Myriad I*'s drastic response inadvisable and unnecessary.²⁵³ The SACGHS recommendations for patient-care and research exemptions are not much better. These recommendations would eliminate important development incentives for genetic diagnostic tests by removing protections for what are often the only envisioned uses for a patent-protected gene²⁵⁴ and would not give enough consideration to the increased costs and burdens that might develop under a new FDA regulatory framework for genetic diagnostic tests.²⁵⁵ Ultimately, neither the *Myriad I* solution nor the SACGHS solution is an appropriate response to the unique problems posed by gene patents. And although *Myriad II* largely corrected the problems that would have been created by *Myriad I*,²⁵⁶ it did not consider whether the inconclusive data underlying the alleged problems created by gene

249. See *supra* note 128 and accompanying text.

250. See *supra* note 78 and accompanying text.

251. See *supra* Part II.A.

252. See *supra* Part II.A.2.

253. See *supra* Part I.C.2–3.

254. See *supra* note 208 and accompanying text.

255. See *supra* Part II.B.1.

256. See *supra* notes 146–48 and accompanying text. *But see supra* notes 192–201 and accompanying text.

patents might eventually warrant a more precise response than the *Myriad I* holding.²⁵⁷

The narrowly tailored approach proposed by this Note would better address the unique challenges created by gene patents without adversely affecting the incentives for the development of therapeutics and diagnostics resulting from DNA-based innovations. This approach consists of two prongs: (1) addressing patient-access and standard-of-care concerns by gathering more information to determine whether future exemptions for confirmatory diagnostic testing or whole-genome sequencing might be warranted and (2) addressing research and innovation concerns by increasing transparency in genetic diagnostic testing, gene patents, and licensing.

A. *Addressing the Alleged Problems of Patient Access and Standard of Care*

The SACGHS recommendation of a broad exemption for gene-patent infringement for patient-care purposes mirrors a preexisting exemption for the performance of patented medical procedures by medical practitioners.²⁵⁸ Although this broad exemption is ill conceived in the context of gene patents,²⁵⁹ narrower exemptions have also been proposed in which otherwise-infringing activity would be exempted only in specific patient-care circumstances.²⁶⁰ As Congress has recognized, however, more information is needed before

257. See *Myriad II*, 653 F.3d 1329, 1355 (Fed. Cir. 2011) (“If the law is to be changed . . . the decision must come not from the courts, but from Congress.”).

258. See 35 U.S.C. § 287(c)(1) (2006) (“With respect to a medical practitioner’s performance of a medical activity that constitutes an infringement . . . the [remedy] provisions . . . shall not apply against the medical practitioner or against a related health care entity with respect to such medical activity.”). “[M]edical activity” does not encompass “(i) the use of a patented machine, manufacture, or composition of matter in violation of such patent, (ii) the practice of a patented use of a composition of matter in violation of such patent, or (iii) the practice of a process in violation of a biotechnology patent,” *id.* § 287(c)(2), thereby precluding application to genetic diagnostic tests.

259. See *supra* Part II.B.1.

260. See Cook-Deegan et al., *supra* note 238, at 406 (proposing that “[p]atient rights should trump patent rights” when “[p]erforming a test in a form that [the exclusive rights holder] does not offer,” “[t]esting in a territory where the company does not offer a test but has exclusive rights,” or “[g]etting second opinions or verification testing”); Geertrui Van Overwalle, *Turning Patent Swords into Shares*, 330 SCIENCE 1630, 1630 (2010) (recommending an exemption “restricted to clinicians using their own ‘homemade’ gene-based tests”).

considering any new exemptions.²⁶¹ Depending on what is shown by that information, two possible exemptions could prove to be beneficial: (1) a limited exemption for providing second opinions and (2) a limited exemption for whole-genome sequencing.

1. *Exemption for Second Opinions.* If properly limited, the first type of exemption—an exemption for second opinions—would address the concern that patients do not have access to important second opinions, but would not deprive patent holders of their investment-backed expectations.²⁶² The SACGHS argues that a limited exemption like this would not be effective “because there would be little incentive, and many disincentives, for a laboratory to develop and maintain a test simply to provide second opinions or verification requests.”²⁶³ But this argument is contradicted by statements in the same report regarding the ease of developing these tests.²⁶⁴ Nevertheless, the concern is valid, as costs will likely increase if the FDA expands its regulation of genetic diagnostic tests.²⁶⁵ These costs, however, could be kept in check if the FDA adopted a lower threshold for the approval of confirmatory tests, which is possible if it follows through on its apparent plan to adopt a risk-based approach.²⁶⁶ For such an exemption to provide the intended benefits, however, the

261. See Leahy-Smith America Invents Act, Pub. L. No. 112-29, § 27(b), 125 Stat. 284, 338 (2011) (mandating a study on, among other things, the need for independent, second-opinion genetic diagnostic tests and the effect such an exemption would have on rights holders).

262. See John Conley & Dan Vorhaus, *House Introduces Patent Reform Proposal To Permit Second Opinions in Genetic Diagnostic Testing*, GENOMICS L. REP. (June 15, 2011), <http://www.genomicslawreport.com/index.php/2011/06/15/house-introduces-patent-reform-proposal-to-permit-second-opinions-in-genetic-diagnostic-testing> (providing an analysis of a proposed but ultimately unenacted portion of an amendment to the House version of the Leahy-Smith America Invents Act). The proposed amendment would have limited the exemption in several ways. It would have, for example, permitted genetic diagnostic testing for the sole purpose of confirming another test provider’s results only under circumstances in which confirmation is not already available from another provider under a patent license. *Id.* In addition, the proposed amendment would have ensured that the patent holder or licensee would be the first option for future retesting conducted to monitor medical status, and it would have put the burden on the infringer to prove the applicability of the exemption. *Id.* With limitations such as these and others like them, patent holders would not be deprived of any of the expected benefits of their patents: the only exempt tests would be those second-opinion tests that the patent holders themselves could not provide. *Id.*

263. SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 1, at 48.

264. *E.g., id.* at 34 (“The costs of developing these laboratory-developed tests appear to be relatively modest.”).

265. See *supra* Part II.B.1.

266. See *supra* note 224 and accompanying text.

hurdle of regulatory approval would have to be low enough that potential confirmatory-test providers would be encouraged to develop tests that are not merely exact replicas of the initial test, thus providing more robust and effective confirmatory tests.

2. *Exemption for Whole-Genome Sequencing.* The second type of potentially beneficial exemption would address a problem that may be looming on the horizon: whole-genome sequencing.²⁶⁷ Though it is far from clear whether whole-genome sequencing will infringe the thousands of gene patents that already exist,²⁶⁸ this is one area in which the threat of a detrimental holdup due to a patent thicket is real.²⁶⁹ If gene patents are shown to erect an insurmountable barrier to whole-genome sequencing as it becomes more commercially viable,²⁷⁰ a narrow exemption could be created for whole-genome-sequencing diagnostic tests. Under such an exemption, infringers could be allowed to offer whole-genome-sequencing tests under the condition that they provide notice and pay a percentage of their profits to gene-patent rights holders.²⁷¹

Several practical difficulties would arise in applying such an exemption. One difficulty would be determining what percentage of

267. See *Myriad II*, 653 F.3d 1329, 1373 (Fed. Cir. 2011) (Bryson, J., concurring in part and dissenting in part) (“[T]he court’s decision will likely have broad consequences, such as preempting methods for whole-genome sequencing”); SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 1, at 58–59 (noting that “affordable clinical whole-genome sequencing is on the horizon” and expressing concern that “a [gene] patent thicket could delay or prevent [its] development”).

268. See Dan Vorhaus & John Conley, *Whole-Genome Sequencing and Gene Patents Coexist (for Now)*, GENOMICS L. REP. (Aug. 11, 2009), <http://www.genomicslawreport.com/index.php/2009/08/11/whole-genome-sequencing-and-gene-patents-coexist-for-now> (concluding that “[t]he answer is not entirely clear”).

269. SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 1, at 58–59. Though it would also theoretically be possible to solve the whole-genome-sequencing problem with judicially imposed compulsory licenses under *eBay Inc. v. MercExchange, L.L.C.*, 547 U.S. 388 (2006), the awards—when multiplied by hundreds or thousands of different patent holders—would likely become cost prohibitive.

270. See, e.g., Matthew Dublin, *Researchers Demonstrate Feasibility of Whole-Genome Sequencing in the Clinic*, GENOMEWEB (Apr. 2011), <http://www.genomeweb.com/sequencing/researchers-demonstrate-feasibility-whole-genome-sequencing-clinic> (“The [research] team successfully sequenced tumor and normal cells from a male patient with pancreatic cancer, making him the first patient at the Mayo Clinic to undergo whole-genome sequencing. . . . [This study] also demonstrated that whole-genome sequencing can be utilized in the clinic in a timely fashion.”).

271. Cf. 17 U.S.C. § 115 (2006) (creating compulsory licensing for the making and distributing of phonorecords of copyrighted, nondramatic musical works that have been publicly distributed).

profits the compulsory license should require. Because of the potentially large number of gene patents that would need to be licensed, the percentage would have to be small enough that whole-genome sequencing would still be commercially feasible.²⁷² Moreover, it would be prohibitively expensive to insist that whole-genome-sequencing providers search for the thousands of patents that they might be infringing and then serve notice to each patent holder.²⁷³ To minimize this problem, a central collecting agency could be created, and the burden could lie with patent holders to prove their entitlement to a share of the license fees.²⁷⁴

Ultimately, these exemptions may be unnecessary. It is unclear how often second-opinion options are unavailable or how often confirmatory diagnostic testing is used even when such tests do exist. Similarly, it is unclear whether gene patents will be infringed when whole-genome sequencing becomes commercially viable. But before any new exemptions are considered, these issues must be resolved.

B. Addressing the Alleged Problem of Hindered Research and Innovation

A unique problem with gene patents is that they cover not only commercial therapeutic and diagnostic products but also research tools.²⁷⁵ Because gene patents do not draw a distinction between these two categories, one concern is that they might impede research and innovation.²⁷⁶ One way of addressing this concern would be to make isolated DNA unpatentable, thereby pushing patents downstream so that they encompass only specific uses or applications of DNA.²⁷⁷ This

272. See Sam Kean, *The Human Genome (Patent) Project*, 331 *SCIENCE* 530, 531 (2011) (discussing the problem of “royalty stacking” in this context by noting that “[i]f 50 companies each want 2% of net profits, that’s not a good business model”).

273. See *id.* at 530 (estimating that for a set of approximately one hundred genes relevant to cancer, “[i]nvestigating all the relevant patent claims (issued and pending) for possible infringement would cost at least \$35 million”).

274. See *id.* at 531 (“One solution could involve an independent clearinghouse to manage intellectual property, which could reduce the cost of compliance by providing a single place to find patents and licenses.”).

275. See *supra* notes 118–22 and accompanying text.

276. See *supra* notes 118–22 and accompanying text.

277. See Helen M. Berman & Rochelle C. Dreyfuss, *Reflections on the Science and Law of Structural Biology, Genomics, and Drug Development*, 53 *UCLA L. REV.* 871, 902 (2006) (“One approach, recently enacted in Germany for genomic patents, is to limit the patentee to the use recited in the patent—that is, to use the *utility* requirement as the measure of *scope*. For example, if the patentee claims that the sequence can be used to diagnose a susceptibility to Condition X, then the patent covers only diagnosis of X.”).

solution, however, is not ideal.²⁷⁸ Given the uncertainty inherent in biotechnology research and development, and given the risk involved in the time-intensive and costly process of translating basic research into marketable products, patent protection needs to be secured at a stage early enough to make the required private investment feasible.²⁷⁹ In the context of genes, this early stage may come before it is even known whether the highest-value use would be in diagnostics, protein therapeutics, RNAi therapeutics, or elsewhere.²⁸⁰ Consequently, this solution, like the research exemptions discussed in Part II,²⁸¹ is not advisable, particularly given the uncertainty about whether gene patents are in fact significantly hindering research and innovation.²⁸²

Research and innovation could still be bolstered, however, by increased transparency in genetic diagnostic testing, gene patents, and licensing. The SACGHS, in a report on the oversight of genetic testing, recommends “a mandatory, publicly available, Web-based registry” that would include all laboratory tests.²⁸³ The database would contain “data elements associated with analytical validity, clinical validity, clinical utility, and accessibility.”²⁸⁴

This concept could be even more beneficial if expanded. For example, the database could contain information on all human-gene patents—not just the already-available information on the scope and length of time of patent protection and patent-holder identity, but

278. See *supra* note 201. This type of change might also be superfluous because, as the prior art grows, more patent applicants will likely find it necessary to make narrower claims directed to specific uses. See Berman & Dreyfuss, *supra* note 277, at 903 (“[I]t may be that most patentees would not be able to claim products, and would instead be limited by the novelty and nonobviousness requirements to patents on specific processes.”).

279. See *supra* note 179 and accompanying text; see also Berman & Dreyfuss, *supra* note 277, at 903 (“[N]arrowing patent scope could set a precedent that will make investors wary . . .”).

280. See Donald Zuhn, *BIO Comes Out Swinging Against SACGHS Report—Updated*, PAT. DOCS (Feb. 4, 2010), <http://www.patentdocs.org/2010/02/bio-comes-out-swinging-against-sacghs-report.html> (discussing how “when [HGS] first identified the [*bliss*] gene, it did not know whether its value would lie in diagnostics, as a target to generate small molecule therapeutics, in its encoded protein, or in antibodies directed to that protein” and how the development of the lupus drug that ultimately resulted from the discovery required expenditures of “some \$2 billion on a number of programs, the majority of which failed after reaching the clinic or which never made it out of the lab”).

281. See *supra* Part II.B.2.

282. See *supra* notes 123–28 and accompanying text.

283. SEC’Y’S ADVISORY COMM. ON GENETICS, HEALTH & SOC’Y, *supra* note 211, at 8.

284. *Id.*

also information on whether the patent has been licensed and to whom, whether that license is exclusive or nonexclusive, and what the scope of the field of use is for that license.²⁸⁵ Some commentators have even suggested that license terms be made publicly available, thereby creating a more efficient market for patents.²⁸⁶ By making this type of information easily accessible, even without license terms, costs in clinical laboratories could be reduced,²⁸⁷ and interested parties would have a better idea of where new opportunities for licenses and new innovation exist.

CONCLUSION

Developments such as the SACGHS gene-patent recommendations and the *Myriad* case have made the patentability of genes a highly visible issue. Because of the controversial nature of gene patents and the strong opinions that they engender, these developments largely amount to overreactions that would do more harm than good. Broadly precluding patent protection for isolated DNA, as was suggested in *Myriad I*, would threaten to unravel sectors of the biotechnology industry. The SACGHS recommendation of broad exemptions for genetic testing for the purposes of both research and patient care would be no better, as these purposes are often the primary commercial uses envisioned by patent holders. Without the guarantee of exclusivity in these markets, patent holders will be unlikely to invest in the development and commercialization of genetic diagnostic tests, especially with the possibility of increased FDA regulation on the horizon.

Instead, it is advisable to consider alternative solutions that more directly and precisely address the primary concerns surrounding gene patents: impeded research and impeded patient access to high-quality genetic diagnostic tests. Gathering appropriate information will

285. This type of idea has been suggested by others. See Jeffrey L. Furman, Fiona Murray & Scott Stern, *More for the Research Dollar*, 468 NATURE 757, 758 (2010) (“A standardized, accessible database of such transactions . . . would reduce future transaction costs for innovators trying to build on ideas with many different patented elements.”).

286. See Mark A. Lemley & Nathan Myhrvold, *How To Make a Patent Market*, 36 HOFSTRA L. REV. 257, 258 (2007) (“[Requiring publication of patent assignment and license terms] will help rationalize patent transactions, turning them from secret, one-off negotiations into a real, working market for patents. And by making it clear to courts and the world at large what the normal price is for patent rights, it will make it that much harder for a few unscrupulous patent owners to hold up legitimate innovators . . .”).

287. See *supra* note 108 and accompanying text.

facilitate a determination of whether limited exemptions for confirmatory diagnostic testing and whole-genome sequencing might be particularly beneficial. Furthermore, increased transparency would facilitate increased innovation, which may in turn improve both the standard of care and patient access by driving costs down. These solutions strike an appropriate balance between ensuring maximum patient access to high-quality, gene-based technologies and maintaining the protection and incentives needed to create and develop those technologies in the first place.