American University Law Review

Volume 63 | Issue 1 Article 5

2013

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Keywords
United States. Supreme Court, United States. Court of Appeals (Federal Circuit), Association for Molecular Pathology v. Myriad Genetics Inc. (Supreme Court case), Patent suits -- United States, Human genes -- Lawsuits & claims, Mayo Collaborative Services v. Prometheus Laboratories (Supreme Court case), Judgments -- United States -- States, Actions & defenses (Law) -- United States

COMMENTS

TAKE OFF YOUR GENES AND LET THE DOCTOR HAVE A LOOK: WHY THE *MAYO* AND *MYRIAD* DECISIONS HAVE INVALIDATED METHOD CLAIMS FOR GENETIC DIAGNOSTIC TESTING

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Ass'n for Molecular Pathology v. U.S. Patent & Trade Office *sent shockwaves through the legal community, when the U.S. District Court for the Southern District of New York rejected a series of patents held by Myriad Genetics, Inc. The court invalidated all of Myriad's compositional patents for human genes and its method patents for diagnosing genetic predispositions to breast cancer. While commentators have discussed the ethical implications of allowing patent rights to human genes in great detail, the Court's ruling on Myriad's method claims went by comparatively unnoticed.*

The ability to test a patient's genetic profile for predisposition to cancer and other diseases is an incredible achievement in the field of personalized medicine. Whether these tests deserve patent protection is a hotly debated issue that involves weighing the interests of both incentivizing research and making these tests available to the general public. This Comment analyzes the legal framework established by the Supreme Court and U.S. Court of Appeals for the

* Note & Comment Editor, *American University Law Review*, Volume 63; JD Candidate, May 2014, *American University Washington College of Law;* B.S. Biology, 2011, *The College of William and Mary.* First and foremost, I would like to thank Professor Jonas Anderson for his constant guidance, support, and encouragement through the Comment process. Additionally, I would like to thank the entire *American University Law Review* staff, who put a significant amount of time and energy into this piece. Any mistakes are my own. Finally, I would like to thank my family for their unconditional love and unwavering support throughout my entire law school experience. Mom and Dad, thank you in particular for supplying me with my own genetic material.

Federal Circuit to decide patent eligibility for genetic diagnostic tests. It concludes that, while the world was spellbound by the ethical quandary of compositional claims on human genes, the recent Supreme Court and Federal Circuit decisions have surreptitiously eliminated genetic diagnostic tests as patentable subject matter under § 101 of the United States Patent Act.

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"We are on the leading edge of a true revolution in medicine, one that promises to transform the traditional 'one size fits all' approach into a much more powerful strategy that considers each individual as unique and as having special characteristics that should guide an approach to staying healthy."[1]

INTRODUCTION

On March 3, 1986, the U.S. Department of Energy announced the Human Genome Project: an unparalleled endeavor to decode the entire human genome and one day develop "new diagnostic, preventative and therapeutic tools."[2] Nearly thirty years later, humanity has finally begun to harvest the fruits of this mammoth endeavor.[3] New technology, made possible by genetic research, allows doctors to use a patient's unique genetic profile to prevent,

1. Tiana Leia Russell, *Unlocking the Genome: The Legal Case Against Genetic Diagnostic Patents*, 16 MARQ. INTELL. PROP. L. REV. 81, 81 (2012) (quoting FRANCIS S. COLLINS, THE LANGUAGE OF LIFE: DNA AND THE REVOLUTION IN PERSONALIZED MEDICINE, at xxiii-xxiv (2010)).

2. OFFICE OF HEALTH & ENVTL RESEARCH, U.S. DEP'T OF ENERGY, SEQUENCING THE HUMAN GENOME: SUMMARY REPORT OF THE SANTA FE WORKSHOP 1 (1986) [hereinafter SUMMARY REPORT], *available at* http://web.ornl.gov/sci/techresources/Human_Genome/publicat/1986santafereport.pdf; *see also* Robert Kanigel, *The Genome Project*, N.Y. TIMES (Dec. 13, 1987), http://www.nytimes.com/1987/12/13/magazine/the-genome-project.html?pagewanted=all&src=pm (describing the Human Genome Project as "the biggest, costliest, most provocative biomedical research project in history, and the United States must embark on it immediately").

3. *See* Russell, *supra* note 1, at 82 ("Although personalized medicine remains in its early stages, its potential to improve patients' lives cannot be overstated."); *see also* Birgit Verbeure, *Patent Pooling for Gene-Based Diagnostic Testing*, *in* GENE PATENTS AND COLLABORATIVE LICENSING MODELS 3, 15 (Geertrui Van Overwalle ed., 2009) (explaining that currently, over a "thousand genetic diseases can be diagnosed through available tests").

diagnose, and treat disease.[4] As research efforts continue, this practice—known as "personalized medicine"[5]—continues to promise cheaper, more effective healthcare and incredible diagnostic capability.[6]

Despite the benefits personalized medicine has already produced, the field remains in its infancy.[7] Unfortunately, courts have struggled with encouraging the growth of this industry while simultaneously ensuring equitable access to its benefits.[8] This tension between encouraging innovation and maintaining accessibility—which mirrors the central conflict of patent law itself[9]—has resulted in a heated debate as to whether human genes and genetic diagnostic tests ought to receive patent protection.[10] Supporters of patent protection for genes and genetic tests argue that, without protection, researchers will no longer be incentivized to invest in personalized medical research.[11] Opponents respond that patent monopolies impede access and have a chilling effect on cooperative research efforts.[12]

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4. Russell, *supra* note 1, at 82 (explaining that with advances in genetic diagnostic methods, doctors are able to use an individual's unique genetic code to personalize treatments).

5. *Genetics Home Reference*, NATIONAL INST. OF HEALTH, http://ghr.nlm.nih.gov/glossary=personalizedmedicine (last updated June 24, 2013) (defining "personalized medicine" as "us[ing] an individual's genetic profile to guide decisions made in regard to the prevention, diagnosis, and treatment of disease").

6. Russell, *supra* note 1, at 82 ("'[M]ost of the promise offered by the sequencing of the human genome still lies ahead.'" (quoting COLLINS, *supra* note 1, at 3)).

7. *Id.*

8. *Id.* at 83 (describing whether genes and genetic tests deserve patent protection as a "hotly debated issue"); *see also* Stephen H. Schilling, *DNA as Patentable Subject Matter and a Narrow Framework for Addressing the Perceived Problems Caused by Gene Patents*, 61 DUKE L.J. 731, 732 (2011) (highlighting the arguments of those who object to gene patenting, such as the ethical implications of restricting access to genetic tests or the negative impact of gene patents on foundational research).

9. *See* Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1305 (2012) (concluding that patent protection is a "two-edged sword" that provides both incentives but also obstacles to creation and invention).

10. *See* Russell, *supra* note 1, at 82 ("As our understanding of the linkages between genetic mutations and diseases has grown, so has a heated debate over whether patents on genes are deserving of patent protection.").

11. *See, e.g.*, Schilling, *supra* note 8, at 772 (arguing that precluding patent protection for isolated DNA sequences would "unravel sectors of the biotechnology industry," due to decreased investment in response to the lack of a guarantee of market exclusivity).

12. *See e.g.*, Russell, *supra* note 1, at 83 (listing the policy arguments against gene patents including the "chilling effect" on research); Sean MacKenzie, Note, *Recognizing the Building Blocks of Life as Products of Nature:* Association for Molecular Pathology*'s Rightful Exclusion of Genetic Information from Patentable Subject Matter*, 32 WHITTIER L. REV. 367, 393 (2011) (arguing that property rights on products of nature, such as genes, preempt research that could advance the cause of personalized medicine and thus frustrate the very purpose of the patent system).

In 2011, this conflict came to a head in *Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office*[13] (*Myriad I*). Myriad Genetics, Inc. (Myriad), a genetic researcher, held patents on two genes associated with a high incidence of breast and ovarian cancer as well as patents for genetic diagnostic tests, which identified a predisposition to these cancers in a patient.[14] On an initial remand from the Supreme Court, the U.S. Court of Appeals for the Federal Circuit held that (1) isolated genetic sequences remained eligible for patent protection,[15] and (2) Myriad's diagnostic method patents were not eligible for patent protection.[16] The Supreme Court vacated and remanded the case for further consideration[17] in light of its holding in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*[18] (*Mayo*), which held that simple, naturally occurring correlations were unpatentable.[19]

On remand again in 2012, the Federal Circuit's decision in *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*[20] (*Myriad II*) remained nearly identical to its decision in *Myriad I*. The Federal Circuit upheld Myriad's compositional patent claims on isolated genes,[21] and rejected Myriad's genetic diagnostic patents.[22] This time, however, the court's reasoning was buttressed by the Supreme Court's logic in *Mayo*.[23] The court's holding in *Myriad II* on compositional patents

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13. 653 F.3d 1329 (Fed. Cir. 2011), *vacated*, 132 S. Ct. 1794 (2012) (mem.), *remanded to* 689 F.3d 1303 (Fed. Cir. 2012), *aff'd in part, rev'd in part on other grounds*, 133 S. Ct. 2107 (2013).

14. *See id.* at 1334–35 (describing the specific DNA sequences and diagnostic methods claimed).

15. *See id.* at 1354 (noting that such compositional patents had been granted by the U.S. Patent and Trade Office (USPTO) for the last thirty years and that changes to such a longstanding practice should come from Congress).

16. *See id.* at 1357 (concluding that Myriad's claims failed to satisfy the machine-or-transformation test because they did not include any transformative steps).

17. Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 132 S. Ct. 1794 (2012) (mem.).

18. 132 S. Ct. 1289 (2012).

19. *See id.* at 1302 (explaining that Prometheus's method is tied up in the statistical relationship between metabolite levels and levels of appropriate medication and suggesting a patent for Prometheus's method would preempt the total use of this correlation); *see also infra* notes 121–132 and accompanying text (providing an overview of the *Mayo* analysis).

20. 689 F.3d 1303 (Fed. Cir. 2012), *aff'd in part, rev'd in part on other grounds*, 133 S. Ct. 2107 (2013).

21. *Id.* at 1333. *But see id.* at 1343 (Bryson, J., concurring in part and dissenting in part) ("If I were deciding this case on a blank canvas, I might conclude that an isolated DNA sequence that includes most or all of a gene is not patentable subject matter.").

22. *See id.* at 1335 (majority opinion) ("Myriad's claimed methods of comparing or analyzing nucleotide sequences are only directed to the abstract mental process of comparing two nucleotide sequences.").

23. *Id.* (explaining that the method claims in *Myriad II* were actually weaker than those in *Mayo* because they lacked any kind of "Mayo-like step of determining,"

garnered considerable media attention and sparked much controversy.[24] However, while the world questioned the wisdom of patenting genes themselves, the Federal Circuit's holding on Myriad's genetic diagnostic tests may have surreptitiously sounded the death knell for genetic diagnostic patents altogether.

This Comment argues that, when viewed in conjunction with the Supreme Court's holding in *Mayo*, *Myriad II* categorically invalidated genetic diagnostic method patents because any diagnostic test is an exploitation of a simple correlation between the presence of a disease allele and the likelihood for developing that disease. Part I of this Comment provides an overview of the current patent legal landscape as well as the method patents at issue. Part II contends that the Supreme Court's decision in *Mayo* combined with the Federal Circuit's holding in *Myriad II*—along with other medical patent cases—creates a three-part test for diagnostic and therapeutic method claims. Part II also looks at patents that were granted by the U.S. Patent and Trademark Office (USPTO) before and after the *Myriad II* decision, and applies this three-part test to investigate those patents' validity. This Comment concludes that due to these recent decisions, patent law can no longer adequately protect genetic diagnostic methods.

I. SECTION 101 AND THE THRESHOLD TEST FOR PATENTABILITY

The U.S. Constitution empowers Congress to "promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings

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which required researchers to measure a physical change); *see also infra* notes 132–133 and accompanying text.

24. *See, e.g.*, Katherine Booth, *Isolated DNA Patents: Incentivizing Medical Research or Selling Human Identity?:* Association for Molecular Pathology v. U.S. Patent and Trademark Office, 40 J.L. MED. & ETHICS 413, 416 (2012) ("There are strong moral and philosophical arguments against isolated DNA patents."); Schilling, *supra* note 8, at 772 (referring to such objections to compositional DNA claims as "overreactions that would do more harm than good"). These controversial compositional claims seem to have eclipsed the Court's ruling on genetic diagnostic tests. *See, e.g.*, Daniel Fisher, *D.C. Court Upholds Myriad Breast-Cancer Patents, Snubbing Supreme Court*, FORBES (Aug. 16 2012), http://www.forbes.com/sites/danielfisher/2012/08/16/d-c-court-upholds-myriad-breast-cancer-patents-snubbing-supreme-court/2 (discussing the *Myriad* decision but focusing on the compositional claims); Jonathan Stempel, *Myriad Wins Gene Patent Ruling from US Appeals Court*, REUTERS (Aug. 16, 2012, 4:23 PM), http://www.reuters.com/article/2012/08/16/us-myriad-patent-idUSBRE87F12K20120816 (dedicating only one sentence to *Myriad*'s method claims). Recently, the Supreme Court has ruled on the admissibility of compositional gene patents, thus ending this portion of the debate—at least temporarily. *See* Ass'n for Molecular Pathology v. Myriad Genetics, Inc. (*Myriad III*), 133 S. Ct. 2107, 2118–19 (2013) (holding that, although isolated gene fragments are unpatentable, manmade cDNA may receive patent protection).

and Discoveries."[25] This enables Congress to grant inventors the absolute right to exclude others from making, using, or selling their inventions.[26] These exclusionary rights are conferred through patents, which are granted by the USPTO.[27] Although Congress has broad authority to grant patents to inventors, the Constitution forbids granting any patent that hinders innovation or fails to promote the scientific welfare of the United States.[28] Thus, the provisions of the United States Patent Act—specifically 35 U.S.C. §§ 101, 102, 103, and 112—place limits on patentability and attempt to ensure that only patents that encourage innovation are granted.[29]

Section 101 of the Patent Act, referred to as the "threshold test" for patentability, explicitly limits patent protection to any "process, machine, manufacture, or composition of matter."[30] The Supreme Court has read § 101 to implicitly exclude any "laws of nature, natural phenomena and abstract ideas" from patent protection.[31] These principles were not created through human ingenuity but are naturally occurring and therefore, "free to all men and reserved exclusively to none."[32] Allowing inventors the right to monopolize such laws of nature would result in enormous market power, which would tend to stifle innovation rather than encourage it.[33]

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25. U.S. CONST. art. I, § 8, cl. 8.
26. 35 U.S.C. § 271(a) (2006).
27. *Id.* § 2(a)(1).
28. U.S. CONST. art. I, § 8, cl. 8.; *Allen v. Ideal Prod., Inc.*, 300 F. Supp. 349, 351 (W.D. Pa. 1969) ("The very power of Congress to grant a patent is limited and delineated by the purpose proclaimed in the constitutional grant itself. . . . 'To promote the Progress of Science and the useful Arts' . . . ." (quoting Automatic Radio Mfg, Co. v. Hazletine Research, 339 U.S. 827, 836–37 (1950))).
29. *See* 35 U.S.C. §§ 101–03, 112 (requiring that patents are only given to inventions that are useful, novel, nonobvious, and described in detail). *See generally* Mayo Collaborative Servs. v. Prometheus Labs., Inc. 132 S. Ct. 1289, 1303–04 (2012) (describing the different statutory hurdles that prevent frivolous patents).
30. 35 U.S.C. § 101.
31. Diamond v. Diehr, 450 U.S. 175, 185 (1981); *see also Mayo*, 132 S. Ct. at 1293 (explaining that one could not patent a newly discovered mineral or a mathematical formula such as $E = mc^2$).
32. *Diehr*, 450 U.S. at 185 (quoting Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980)).
33. MacKenzie, *supra* note 12, at 374–75 (describing why courts deny patent protection to "fundamental truths" or "principles of nature"). A good example of the Court's reasoning for these exceptions can be found in *O'Reilly v. Moorse*, 56 U.S. (15 How.) 62 (1853). In 1837 Samuel F.B. Morse sought a patent for the telegraph and stated in his claim that he "[did] not propose to limit [himself] to the specific machinery or parts of machinery described in the forgoing specification and claims; the essence of [his] invention being . . . electro-magnetism." *Id.* at 112. The Supreme Court held that an inventor could not patent electro-magnetism, a law of nature. *Id.* at 120. Such broad patent protection would inhibit future inventors from making more efficient, or creative uses of electro-magnetism. *Id.* at 120–21.

A. The Difficulty of Method Claims: Benson*,* Flook*, and* Diehr

Applying the exceptions of § 101 can be very difficult when assessing the patentability of process claims, also known as "method claims."[34] The three cases discussed in this section establish the Court's framework for determining the patentability of method claims. Taken together, *Benson*, *Flook*, and *Diehr* confirm the Court's reluctance to allow patents on claims that preempt natural law and foreshadow the difficulty in determining patentability for evaluating novelty in a method claim.

In 1972, in *Gottschalk v. Benson*,[35] the Supreme Court attempted to draw a line between "a[n] idea itself," and a "useful structure created with the aid of knowledge of scientific truth" for a method claim.[36] In that case, an inventor attempted to patent an algorithm that converted binary-coded decimal numerals into pure binary code.[37] The Court held that this method claim was too abstract to be considered a patentable invention.[38] The Court's reasoning rested on the fact that the inventor applied mathematical principles that could not be used except in connection with a computer.[39] Thus, the inventor's patent on the computer algorithm would preempt the mathematical formula and, in practical effect, would be a patent on the mathematical principle itself.[40]

Six years later, in *Parker v. Flook*,[41] the Supreme Court rejected another computer algorithm, which, it claimed, preempted an entire mathematical concept.[42] In *Flook*, the inventor sought to obtain a patent on an alarm system claiming a method comprising of (1) determining the value of a variable, (2) using that variable to calculate a new alarm limit, and (3) determining the new alarm

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34. Russell, *supra* note 1, at 86 ("[T]he fundamental principles exception can be a difficult standard to apply particularly when assessing the patentability of process claims.").

35. 409 U.S. 63 (1972).

36. *Id.* at 67 (alteration in original).

37. *See id.* at 66–67 (describing exactly how the method, called the BCD system, worked, which simply "varie[d] the ordinary arithmetic steps a human would use").

38. *See id.* at 68 ("Here the 'process' claim is so abstract and sweeping as to cover both known and unknown uses of the BCD to pure binary conversion.").

39. See *id.* at 71–72 (summarizing the court's reasoning that a mathematical formula is not patentable).

40. *Id.*; *see also* Russell, *supra* note 1, at 89–90 (explaining that this rationale—namely, that an invention which entirely preempts a natural law is unpatentable—is a fundamental principle of determining the patentability of a method claim).

41. 437 U.S. 584 (1978).

42. *See id.* at 594–95 (stressing the fact that a claim which merely restates a mathematical formula cannot be patented, even if the formula is used for a specific purpose, such as in this case (citing *In re* Richman, 563 F.2d 1026, 1030 (1977))).

limit.[43] There, the inventor attempted to escape the logic of *Benson* by claiming that the "post-solution" activity of adjusting the alarm limit after the calculation prevented the method from preempting the entire mathematic principle within the patent.[44] The Supreme Court disagreed, explaining that "[t]he notion that post-solution activity, no matter how conventional or obvious in itself, can transform an unpatentable principle into a patentable process exalts form over substance."[45] Thus, the Court eliminated the possibility of circumventing the rule against patenting an abstract idea by merely attaching the abstract idea to a specific technological environment, which would entirely pre-empt its use.[46]

In 1981, in *Diamond v. Diehr*[47] the Supreme Court upheld a method patent on a computer algorithm for the first time.[48] In this case the inventors sought patent protection for a method of molding rubber into cured precision products using a mathematical formula and a computer to complete many steps of the process.[49] The Court found that the patent in this case did not preempt an entire mathematical formula, but instead claimed an industrial process for the creation of a consumer product.[50] The Court held that a process claim reciting a fundamental principle of nature could be allowed patent protection; however, "an inquiry must be made into whether the claim is seeking patent protection for that formula in the abstract."[51]

Thus, after *Diehr* the key inquiry was whether the process sought to patent a formula in the abstract or whether the process went beyond a recitation of some abstract principle. Together, these three cases suggest that, to be patentable, a method claim cannot completely preempt the natural law upon which it is based.[52]

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43. *See id.* at 586. The invention in *Flook* was a method of setting an alarm limit for a catalytic conversion process. *Id.* at 585. During a catalytic conversion process temperature, pressure, and flow rates fluctuate. *Id.* These rates must be carefully monitored to ensure that they remain within normal parameters. *Id.* An alarm limit is a predetermined unsafe threshold. *Id.* Whenever a temperature, pressure, or flow rate exceeds an alarm limit an alarm is triggered, which signals the presence of an abnormal condition. *Id.*

44. *Id.* at 590.

45. *Id.*

46. *See* Russell, *supra* note 1, at 90 (noting that, under the Court's reasoning in *Flook*, if a claim does not disclose another inventive concept, apart from a fundamental principle, natural law, or correlation, it is unpatentable under § 101).

47. 450 U.S. 175 (1981).

48. *Id.* at 193.

49. *Id.* at 178–79.

50. *Id.* at 191.

51. *Id.*

52. Russell, *supra* note 1, at 89–90 (explaining the importance of preemption in the Supreme Court's reasoning in its patent decisions).

B. The Machine-or-Transformation Test: A Bright-Line Clue

Eventually, the Federal Circuit examined the Supreme Court's reasoning in *Diehr*, *Flook*, and *Benson*, and tried to extrapolate a bright-line rule. This "definitive test" would greatly simplify the determination of whether a method was appropriate subject matter under § 101. The Federal Circuit sat en banc in *In re Bilski*[53] to decide whether a method for hedging risk qualified as patentable subject matter under § 101.[54] The court set forth the "machine-or-transformation" test as the "correct test" for validity under § 101.[55] Under this test an inventor can demonstrate that his process claim satisfies § 101 by "showing that his claim is tied to a particular machine, or by showing that his claim transforms an article."[56]

The inventors conceded that their method of hedging risk was not tied to a machine or machinated process; however, they claimed their method "transform[ed] the relationships" between various players in the industry.[57] The Federal Circuit disagreed, stating that manipulations of legal obligations, relationships, and business risks are abstractions and not physical substances.[58] As such, the method was held unpatentable.[59]

The Supreme Court granted certiorari and upheld the judgment[60] but rejected the notion that the "machine-or-transformation" test was determinative for patentability.[61] The Supreme Court did, however,

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53. 545 F.3d 943 (Fed. Cir. 2008) (en banc), *aff'd sub nom. on other grounds*, Bilski v. Kappos, 130 S. Ct. 3218 (2010), *remanded to* 659 F.3d 1057 (Fed. Cir. 2011). The Federal Circuit described the § 101 inquiry as "hardly straightforward" and discussed the "limited usefulness" of Supreme Court precedent, *id.* at 954, until the establishment of the machine-or-transformation test by the Supreme Court. *See infra* notes 60–64 and accompanying text (discussing the subsequent Supreme Court decision).

54. *In re Bilski*, 545 F.3d at 949–50.

55. *See id.* at 955 (describing the Supreme Court's definitive "machine-or-transformation" test that determines whether a process claim is designed to cover only a specific application of a fundamental principle rather than the abstract principle itself); *see also id.* at 961 (listing rejected tests such as the physical steps test and physical limitations test in favor of the machine-or-transformation test for a § 101 inquiry).

56. *Id.* at 961. *See generally* Angela D. Follet, Note, *The Problem with* Bilski*: Medical Diagnostic Patent Claims Reveal Weaknesses in a Narrow Subject Matter Test*, 7 U. ST. THOMAS L.J. 229, 240–41 (2009) (providing an overview of the rationale behind the machine-or-transformation test: a claim must be limited to particular applications of a fundamental principle).

57. *In re Bilski*, 545 F.3d at 64.

58. *Id.* at 963.

59. *Id.* at 966.

60. *See* Bilski v. Kappos, 130 S. Ct. 3218, 3231 (2010) (holding the petitioner's process claim as invalid under § 101 because their claims attempted to patent the use of an abstract idea to a particular field).

61. *Id.* at 3226.

reason that the test was an "important and useful clue" and investigative tool for determining patentability.[62] The Court reiterated that the correct standard for patentability was inquiring as to whether a method amounted to laws of nature or abstract ideas.[63] Nevertheless, the Supreme Court failed to offer any additional guidance other than referring to its previous logic in *Diehr, Flook* and *Benson*.[64]

C. Method Patents in a Biomedical Context: Non-Genetic Diagnostic Method Patents

Diagnostic method patents have been at the center of a considerable amount of controversy and have raised significant equity and ethical concerns.[65] The Supreme Court and the Federal Circuit have had two major opportunities to tackle these challenging ethical issues: *Laboratory Corp. of America Holdings v. Metabolite Laboratories, Inc.*[66] and *Classen Immunotherapies, Inc. v. Biogen IDEC*.[67] These cases, discussed below, set forth a basic framework for understanding how courts examine diagnostic method patents.

1. Metabolite Laboratories

In *Metabolite Laboratories, Inc. v. Laboratory Corp. of America Holdings*,[68] the Federal Circuit upheld a patent that claimed a method for detecting B vitamin deficiency in a patient.[69] Metabolite Laboratories' method was composed of (1) assaying a body fluid for an elevated level of a certain protein, homocystine, and (2) correlating an elevated level of homocystine in body fluid with a B vitamin deficiency.[70] Laboratory Corporation of America challenged this patent on multiple grounds; however, it did not challenge the correlation as unpatentable subject matter under § 101 until it

62. *Id.*
63. *Id.* at 3238–39.
64. *Id.* at 3235, 3238–39; *see also* Asher Hodes, Note, *Diagnosing Patentable Subject Matter*, 26 BERKELEY TECH. L.J. 225, 228–29 (2011) (explaining that many commentators have observed this lack of Supreme Court guidance).
65. *See generally* Hodes, *supra* note 64, at 229–30 (detailing examples of controversial court decisions, and disputes dealing with diagnostic medical patents).
66. 548 U.S. 124 (2006) (per curiam) (dismissing the writ of certiorari as improvidently granted).
67. 659 F.3d 1057 (Fed. Cir. 2011), *cert. denied sub nom.* GlaxoSmithKline v. Classen Immunotherapies, Inc., 133 S. Ct. 973 (2013).
68. 370 F.3d 1354 (Fed. Cir. 2004), *cert. dismissed per curiam*, 548 U.S. 124 (2006).
69. *Id.* at 1358.
70. *Id.* at 1358–59.

petitioned for certiorari to the Supreme Court.[71] Although the Court granted certiorari, it subsequently dismissed the writ as improvidently granted.[72] Justice Breyer dissented to the dismissal, joined by Justices Stevens and Souter.[73]

Justice Breyer attacked Metabolite's patent, stating that there was little doubt that the correlation between the protein and the related biological result was a natural phenomenon.[74] He explained that claim thirteen's process simply instructed the user to "(1) obtain test results and (2) think about them."[75] Justice Breyer argued that this transformative step was irrelevant because it was not at the core of the patent and, thus, could not have altered the patent's overall subject matter.[76] However, despite the aggressive tone of his dissent, the Federal Circuit has declined to follow Justice Breyer's reasoning.[77]

2. Classen

In *Classen Immunotherapies, Inc. v. Biogen IDEC*,[78] the U.S. District Court for the District of Maryland held that a method of discovering an optimal immunization schedule was only a simple correlation and, thus, unpatentable subject matter under § 101.[79] The claimed

71. *See* Brief for the United States as Amicus Curiae at 16, *Lab Corp.*, 548 U.S. 124 (No. 04-607), 2005 WL 3533248 (noting that no § 101 challenge was asserted nor did any of the lower courts address the issue).

72. *Lab. Corp.*, 548 U.S. at 125; *see also* Hodes, *supra* note 64, at 230 (suggesting that certiorari was revoked due to the failure to raise the patentable subject matter issue prior to its petition).

73. *Lab. Corp.*, 548 U.S. at 125 (Breyer, J., dissenting).

74. *See id.* at 135 (adding "[t]hat is what the petitioner argues. It is what the Solicitor General has told us. Indeed, it is close to what the respondents concede." (citation omitted)); *see also id.* at 137–38 ("[The claims] embody only the correlation between homocystine and vitamin deficiency that the researchers uncovered.").

75. *Id.* at 136.

76. *See id.* at 135, 137–38 (expounding that the steps involved in the process did not embody much beyond a natural phenomenon); *see also* Hodes, *supra* note 64, at 230–31 (referencing Justice Breyer's assertion that the "measuring step" needed to measure the amino acids was immaterial for purposes of qualifying the method for patentability under § 101).

77. *See, e.g.*, Prometheus Labs., Inc. v. Mayo Collaborative Servs., 628 F.3d 1347, 1356 n.2 (Fed. Cir. 2010) (explicitly declining to examine Justice Breyer's reasoning in *Lab. Corp.* because a dissent is not controlling law and *Lab. Corp.* involved claims for a business method), *rev'd*, 132 S. Ct. 1289 (2012); *see also* Hodes, *supra* note 64, at 241 (predicting that a broad application of Justice Breyer's standard would invalidate all correlative diagnostic patents, including those in *Prometheus* and *Myriad* because it would be impossible to draft a valid patent if courts presumed that claims preclude all applications of the natural processes involved in an invention's operation).

78. No. WDQ-04-2607, 2006 WL 6161856 (D. Md. Aug. 16, 2006), *aff'd*, 304 F. App'x 866 (Fed. Cir. 2008), *vacated*, 130 S. Ct. 3541 (2010), *remanded to* 659 F.3d 1057 (Fed. Cir. 2011), *cert. denied sub nom.* GlaxoSmithKline v. Classen Immunotherapies, Inc., 133 S. Ct. 973 (2013).

79. *See id.* at *5 ("[The] patents describe little more than an inquiry of the extent of the proposed correlation between vaccines and chronic disorders. . . . [T]he Court finds they are an attempt to patent an unpatentable natural phenomenon.").

process involved: (1) identifying two groups of mammals of the same species, with Group A having been immunized according to immunization schedule one, and Group B having been immunized according to immunization schedule two; and (2) comparing the effectiveness of the first and second immunization schedules.[80] In 2008, the Federal Circuit affirmed the district court's decision and cited *In re Bilski* for support.[81] Then, after rejecting the "machine-or-transformation" test in *Bilski*,[82] the Supreme Court granted certiorari in *Classen* and—on the same day—remanded it to the Federal Circuit.[83]

On remand, the Federal Circuit reversed its earlier decision and held that Classen's method of optimizing an immunization schedule was patentable subject matter under § 101.[84] The court relied upon the key "immunization step" in moving this method from an abstract idea into a valid method patent.[85] The court suggested that this immunization step was transformative for the purposes of the "machine-or-transformation" test.[86] Collectively, *Classen*, *Metabolite*, *Myriad*, and *Mayo* set the framework for determining the future patentability of medical diagnostic tests based on a patient's genetic material.[87]

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80. Classen Immunotherapies, Inc. v. Biogen IDEC, 659 F.3d 1057, 1060 (Fed. Cir. 2011), *cert. denied sub nom. GlaxoSmithKline*, 133 S. Ct. 973.

81. *See* Classen Immunotherapies, Inc. v. Biogen IDEC, 304 F. App'x 866, 867 (Fed. Cir. 2008) (explaining that the claims failed the "machine-or-transformation" test (citing *In re* Bilski, 545 F.3d 943, 954 (Fed. Cir. 2008) (en banc)).

82. 130 S. Ct. 3218, 3226 (2010) (declining to recognize the "machine-or-transformation" test as determinative for purposes of determining what constitutes a "process").

83. Classen Immunotherapies, Inc. v. Biogen IDEC, 130 S. Ct. 3541, 3541 (2010), *remanded to* 659 F.3d 1057 (Fed. Cir. 2011).

84. *Classen*, 659 F.3d at 1068.

85. *See id.* (arriving at its conclusion by looking at the invention as a whole, including the scope asserted by the patentee); *see also* PerkinElmer, Inc. v. Intema Ltd., 496 F. App'x 65, 71 n.2 (Fed. Cir. 2012) (denying the patentability of the claims at issue because, unlike in *Classen*, there was no "further act" moving the recited concepts to a specific application), *cert. denied*, No. 12-1372, 2013 WL 2155734 (Oct. 7, 2013).

86. *See Classen*, 659 F.3d at 1068 (describing the actual immunization of an animal as a "transformative" step).

87. *See* John D. Lopinksi, *Clash of the Titans: How the* Prometheus, Myriad, *and* Classen *Cases Are Shifting the Sands*, *in* THE IMPACT OF RECENT PATENT LAW CASES AND DEVELOPMENTS 149, 150–51 2011) (arguing that the future of biotech patent law is found within *Myriad*, *Mayo*, and *Classen* because these cases provide a rationale for including a particular description in biotech patent applications in order to increase the likelihood that a claim will be patentable under § 101). *See generally* Hodes, *supra* note 64, at 230–34, 236–37 (detailing the various courts' reasoning in these four cases as the roadmap to understanding genetic diagnostic correlation methods as patentable subject matter).

D. The Stage Is Set for Method Patents: Understanding the Legal Framework

As described above, case precedent leading up to the court's determination in *Myriad* occurred in three phases: (1) a concern for preemption (*Benson*, *Flook*, and *Diehr*);[88] (2) the machine-or-transformation test (*Bilski)*;[89] and (3) the Court's attempt to define the scope and boundaries of diagnostic methods (*Classen* and *Metabolite*).[90]

In *Benson*, *Flook*, and *Diehr*, the Court's decisions established that a method patent cannot entirely preempt all uses of a law of nature; and that meaningless "post-solution activity" would be irrelevant to the issue of patentability.[91] In *Bilski*, the Supreme Court rejected the "machine-or-transformation" test as a definitive rule for patentability under § 101 and instead insisted that the test was merely a useful clue.[92] Finally, in *Classen* and *Metabolite*, the Supreme Court and Federal Circuit found the "machine-or-transformation" test useful in determining the patentability for diagnostic procedures.[93] Taken together, these cases suggest that a transformation is only valid if it occurs at the core of the patent and involves a novel step.[94]

With these cases, the Supreme Court and Federal Circuit provided a legal foundation capable of addressing the problems posed by diagnostic and genetic patents. The next Supreme Court cases, *Mayo* and *Myriad*, expanded and solidified this framework.

E. Before Genetic Patents: A Brief Biology Primer

Before delving into an argument about the patentability of genetic diagnostic tests, a brief introduction to molecular biology and genetics is helpful. DNA is a chemical molecule composed of several

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88. *Supra* note 52 and accompanying text.
89. *Supra* notes 60–63 and accompanying text.
90. *See supra* notes 78–86 and accompanying text (providing the facts of *Classen* of an example of how the "machine-or-transformation" test influences the court's analysis).
91. *See supra* notes 41–45 and accompanying text.
92. *See supra* notes 60–64 and accompanying text (outlining the holding in *Bilski* and emphasizing the rejection of the "machine-or-transformation" test as determinative).
93. *See supra* text accompanying note 86 (describing the influence of the "machine-or-transformation" test in *Classen*); *see also* PerkinElmer, Inc. v. Intema Ltd., 496 F. App'x 65, 71 n.2 (Fed. Cir. 2012) (explaining that the immunization was a "further step," that moved the "abstract scientific principle to specific application"), *cert. denied*, No. 12-1372, 2013 WL 2155734 (Oct. 7, 2013).
94. *See supra* notes 66–86 (describing *Classen* and *Lab. Corp.*); *see also PerkinElmer*, 496 F. App'x at 71 n.2 (explaining that the immunization was a "further act," one that moved the "abstract scientific principle to specific application").

subparts known as nucleotides.[95] Genetic DNA is composed of four different kinds of nucleotides: A, G, C, and T, which are chemically bonded together in varying combinations.[96] For example, a DNA fragment may be: G-A-C-G-A-C, G-G-T-G-G-C, or some other combination of nucleotides.[97] Full DNA chains involve thousands of nucleotides strung together.[98] A person's cellular machinery can read this sequence of nucleotides and recognize them as a subset of smaller discrete units, known as genes.[99]

A gene, the basic unit of heredity, is a subpart of the genome; it is a person's sum total of DNA.[100] A gene is a particular stretch of nucleotides that usually encodes for one particular protein.[101] Genes are responsible for the inheritance of discrete traits such as sex, race, and disease predisposition.[102]

For the most part, DNA is the same from person to person.[103] Everyone shares almost the exact overall nucleotide sequence and, therefore, the same genes.[104] The normal version of a gene is known as the "wild-type" gene.[105] Occasionally, a person's cellular machinery makes a mistake and gives a person a new nucleotide sequence in a particular gene.[106] This event results in a mutated version of the same gene.[107] These mutations are heritable and some are correlated with an increased risk of particular diseases.[108]

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95. MacKenzie, *supra* note 12, at 371.
96. *Id.*
97. *See id.* (explaining that sequencing determines the arrangement of nucleotides).
98. Russell, *supra* note 1, at 94.
99. *See* Schilling, *supra* note 8, at 734 (describing nucleotides as "spell[ing] out biological messages" for the cell).
100. George Dandalides, *The Patentability of Isolated DNA Sequences Deoxyribonucleic Acid (DNA)*, 14 TUL. J. TECH. & INTELL. PROP. 283, 283 (2011).
101. *See* Schilling, *supra* note 8, at 734 n.14 (explaining that proteins are molecules responsible for performing the majority of a cell's functions, including directing most of a cell's chemical processes, generating movements, sensing signals, and maintaining structures).
102. *See* Russell, *supra* note 1, at 94 (providing that genes contain exons, necessary for the creation of proteins, and introns, which contain regulatory sequences that affect a body's rate of production of the protein encoded by a gene).
103. *See* Dandalides, *supra* note 100, at 284 (noting that although only less than one percent of nucleotides within the genes vary slightly between individuals, these variances cause the unique differences among individuals, ranging from skin and eye color to variations presenting significant consequences to a person's health).
104. *Id.*
105. *See* Russell, *supra* note 1, at 95 (explaining that "wild-type" genes do not have any variations, but that when variations do occur, they occur at different magnitudes, resulting in varying levels of health risks).
106. *Id.*
107. *See id.* (relaying that small scale mutations manifest as slight sequence differences between the same genes in different individuals and large mutations can include the addition or elimination of substantial chromosomal regions).
108. *See id.* (explaining that in some cases a certain mutation may make a disease

DNA sequencing is a procedure that allows researchers to determine the specific order of nucleotides within a DNA strand.[109] When a "wild-type" gene is sequenced, the researcher knows the ordinary combination of nucleotides for the "normal" version of the gene.[110] If doctors know the "wild-type" version of a gene, they can—with relative ease—take a DNA sample from a patient and compare the patient's particular gene against the "wild-type" version of that gene.[111] If the two match, the patient has the normal "wild-type" gene.[112] If they differ, the patient has a mutated version of the gene.[113] If this particular mutation corresponds with a predisposition to a disease condition, then the doctor can inform the patient, and the two can begin to take preventative measures.[114]

F. Considering Mayo *and* Myriad*: The Emerging Rule of Genetic Patents*

1. The three step-inquiry and Mayo*: Naturally occurring correlations with meaningless post or pre-solution activity are unpatentable under § 101*

In *Mayo*, the Supreme Court considered two method patents held by Prometheus Labs, which claimed methods for determining the optimal level of medicine—6-Tgioguanine ("6-TG")—to give to a patient with Crohn's Disease.[115] If the concentration of 6-TG in the bloodstream was too high, one could suffer from significant complications and side effects.[116] If the concentration of 6-TG was

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condition all but certain). For example cystic fibrosis (CF), a disease affecting the lungs, pancreas, and sweat glands, is actually caused by a genetic mutation, which is passed down from parent to child. Kristine Barlow-Stewart, *Fact Sheet # 33, Cystic Fibrosis*, CENTER FOR GENETICS EDUC. 1 (Nov. 2012), http://www.genetics.edu.au/Publications-and-Resources/Genetics-Fact-Sheets/FS33KBS.pdf. *See generally Conditions: Cystic Fibrosis*, GENETICS HOME REFERENCE, http://ghr.nlm.nih.gov/condition/cystic-fibrosis (last updated August, 2012) (explaining, in detail, how genetic mutations may cause or contribute to disease conditions, and how these mutations are inherited).

109. Russell, *supra* note 1, at 95.

110. *Id.*

111. *Id.* at 95–96 (describing that this type of comparison can occur when researchers attempt to locate genes tied to various conditions using linkage analysis).

112. *Id.* at 95.

113. *Id.*

114. *Id.* (emphasizing the usefulness and difficulty in locating a particular genetic mutation tied to a specific disease condition).

115. *See* Mayo Collaborative Servs. v. Prometheus Labs., Inc. 132 S. Ct. 1289, 1295 (2012) (detailing the patent's findings that distinct concentrations of 6-TG or 6-MMP metabolite in a patient's blood could indicate that the dosage was either too high or too low to be effective).

116. *See* U.S. Patent No. 6,355,623 col.1 l.66 (filed Apr. 8, 1999) ("Complications associated with [6-TG] drug treatment include allergic reactions, neoplasia, opportunistic infections, hepatitis, bone marrow suppression, and pancreatitis."), *invalidated by Mayo*, 132 S. Ct. 1289.

too low, the treatment would be ineffective.[117] Prometheus had found the therapeutic sweet spot and claimed a process for finding the appropriate dose of 6-TG to give to a patient by: (1) giving 6-TG to a patient with Crohn's; (2) taking a blood sample from that patient and determining the concentration of 6-TG in their bloodstream, and (3) making a determination regarding a threshold concentration level of 6-TG in the patient's blood.[118] If the level of 6-TG was above a threshold concentration (400 picomoles per $8x10^8$ red blood cells), the patient would receive less 6-TG; if the level of 6-TG was below a certain threshold concentration (230 picomoles per $8x10^8$ red blood cells), the patient would receive more 6-TG.[119] This method relied upon the natural relationship between the concentration of 6-TG in the bloodstream and the likelihood of harmful side effects or ineffectiveness.[120] Before examining the patents, the Court cited *Benson*, *Flook*, and *Diehr*, and explained that a process that "preempt[s] the use of a natural law" could not be patented.[121] The question before the court then became whether the patent claims added *enough* to the correlation statements to make the described claims "patent-eligible" processes that applied natural laws.[122]

a. Mayo*'s method patents: U.S. Patent No. 6,680,302 and U.S. Patent No. 6,355,623*

The two patents at issue in *Mayo* were the '302 Patent and the '623 Patent.[123] Before beginning its analysis the Court warned that any attempt to monopolize a law of nature would not be rewarded with a patent.[124] Then, the Court initiated its inquiry by separating out the distinct steps of the methods at issue.[125]

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117. *Mayo*, 132 S. Ct. at 1295.

118. *See id.* (labeling the steps as the "administering" step, the "determin[ation]" step, and the "wherein" step).

119. *Id.* (quoting the '623 Patent). The same method could be accomplished by measuring the level of 6-metyl-mercaptopurine (6-MMP) in the patient's blood stream after administering 6-TG. *Id.*

120. *Id.*

121. *Id.* at 1294; *see also id.* (asserting that the Court's precedents forewarn against determining patent eligibility too broadly or without careful examination as to whether the patent contains an "inventive concept" as opposed to an insignificant post-solution activity).

122. *Id.* at 1298.

123. *Id.* at 1295 (suggesting that the two patents were nearly identical; although, the '302 Patent provided a more precise therapeutic range when measuring 6-MMP).

124. *See id.* at 1297 (analogizing to the Greek scholar Archimedes, and asserting that "Archimedes [could not] have secured a patent for his famous principle of flotation by claiming a process consisting of simply telling boat builders to refer to that principle in order to determine whether an object will float"); *see also* Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948) (construing "law of nature"

The Court looked at the "administering" step, which instructed a doctor to dose a patient with 6-TG.[126] The court noted that doctors have been treating Crohn's disease with 6-TG for many years, so this step was merely an attempt "to limit the use of [a] formula to a particular technological environment."[127] As such, it did not add anything to the law of nature, which in this case, was the naturally occurring correlation between levels of 6-TG in the blood and harmful side effects for patients.[128]

Second, the court looked at the "wherein" step. For this patent, the step simply described the relevant concentration thresholds for 6-TG.[129] The Court stated that this step merely informed a doctor about a natural correlation and suggested that the doctor take this correlation into consideration.[130] The Court likened this step to a situation where Einstein might simply explain his basic law to linear accelerator operators and trust them to use it.[131]

Third, the Court looked at the final "determining" step, which involved taking a blood sample and measuring the levels of 6-TG.[132] The process of taking a blood sample and measuring metabolite levels was considered commonplace by the scientific community, and the court analogized this step to the "conventional or obvious [pre/post] solution activity" in *Bilski* which was incapable of turning a law of nature into a patentable process.[133]

After examining the steps of the patent separately and determining that nothing new was being added to the law of nature—other than conventional and widely used pre-solution activity—the Court

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to include any phenomenon of nature, such as the heat of the sun, electricity, or the qualities of metals or bacterium).

125. *See Mayo*, 132 S. Ct. at 1297–98 (separating the claims into three steps—an "administering" step, a "determining" step, and a "wherein" step—to demonstrate how these additional steps were insufficient to transform the nature of the claims because they simply inform a targeted audience about the relevance of natural laws).

126. *Id.* at 1297.

127. *Id.* at 1291 (internal quotation marks omitted). The Court, however, insisted that the "administering step," although albeit a transformation, was irrelevant because it simply helped pick out individuals who would be interested in applying the law of nature. *Id.* at 1297; *see also* Douglas L. Rodgers, *After* Prometheus*, are Human Genes Patentable Subject Matter?*, 11 Duke L. & Tech. Rev. 434, 454, 456–60 (2013) (arguing that, more than anything else, the steps of a method must include an innovative step).

128. *See Mayo*, 132 S. Ct. at 1294 (proffering that an *application* of a law of nature to a new and useful end may be patentable, but that such protection cannot be afforded to a claim that merely recited a law of nature while adding the words "apply it").

129. *Id.* at 1297.

130. *Id.*

131. *Id.*

132. *Id.* at 1297–98.

133. *Id.*

considered the steps as a whole.[134] Yet, even when considering the three steps as a part of an ordered combination, the Court found that nothing new was added to the law of nature.[135] Thus, these patents simply amounted to a set of instructions telling doctors to measure the level of the relevant metabolite, use the relevant laws of nature to calculate toxicity, and reassess use of the drug given the relevant law of nature.[136]

In *Mayo*, the Court determined the method's patentability by first separating out the steps of the method to consider whether any of the steps added anything to the law of nature that was not "well-understood, routine, conventional activity."[137] Next, the Court considered the method as a whole to see if, as a system, the process added anything to the law of nature.[138] Prometheus asserted that its process passed the "machine-or-transformation" test by (1) transforming the human body when administering 6-TG, and (2) by transforming the patient's blood when analyzing the metabolites.[139] Without much explanation, the Supreme Court immediately dismissed the first transformation as "irrelevant."[140] Regarding the second transformation, the Court gave only two brief justifications: (1) the step could theoretically be satisfied without transforming the blood "should science develop a totally different system for determining metabolite levels," and (2) the machine-or-transformation test was merely an important clue that did not trump the Court's initial inquiry into whether the patented process was simply a law of nature.[141]

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134. *Id.* at 1298.
135. *Id.*
136. *See id.* at 1299–1300 (emphasizing that these steps simply instructed doctors to apply the law of nature in a particular way when treating their patients). It is crucial to note that the Court was referring only to the steps *surrounding* the law of nature as "well-understood, routine, conventional activity." *Id.* at 1298. In contrast, the law of nature itself had never before been discovered and was incredibly useful. *See id.* at 1295 (noting that researchers' discovery was a correlation between "metabolite levels and likely harm or ineffectiveness" of 6-TG). Nevertheless, without producing a novel, unconventional, or non-routine activity, Prometheus was unable to obtain its patent. *Id.* at 1298.
137. *Id.* at 1298.
138. *Id.*
139. *Id.* at 1302.
140. *Id.* at 1302–03 (disagreeing with Prometheus's position that the claimed processes were patentable by asserting that the step could be accomplished without transforming the blood).
141. *Id.* at 1303.

b. Explanations for transformations: Help from Flook, Diehr, *and* Metabolite

There are two potential explanations as to why transformations like the ones alleged in *Mayo* are insufficient for patentability. First, the transformation was routine and thus added nothing significant to the method. Second, the transformation was not central to the method claim. The Court in *Mayo* did not explicitly discuss either of these reasons but, as outlined below, they are deduced from the Court's reasoning.

i. The transformation was routine

The first reason for rejecting the Prometheus patent was that there was nothing new about analyzing a patient's blood after administering a well-known and commonly used drug.[142] These steps could not add enough novelty to raise the method above a simple law of nature.[143] Although these transformations occurred, they amounted to meaningless pre/post-solution activity.[144]

The difference between transformative steps and meaningless pre/post-solution activity can be found by comparing *Flook* and *Diehr*. In *Flook*, the presence of an alarm was not enough to raise an algorithm based on a law of nature to patentability.[145] The Court simply considered the alarm to be a conventional and obvious post-solution activity.[146] On the other hand, in *Diehr* an algorithm was held patentable.[147] There, the process was used to produce cured synthetic rubber.[148] The *Diehr* method resulted in a nonobvious and useful product; thus, it was deemed to be an "industrial process."[149] The key to differentiating these cases is recognizing that the *Diehr* method resulted in a useful and nonobvious product,[150] whereas the *Flook* method merely included a conventional and previously-available

142. *See supra* note 127 and accompanying text (noting that doctors have been treating Crohn's disease with 6-TG for many years).
143. *See Mayo*, 132 S. Ct. at 1297–98 (explaining that the drugs used for the method had been used "long before anyone asserted [the] claims," that the "methods for determining metabolite levels were well known in the art," and that therefore, the additional steps were routine).
144. *See id.* at 1298 (explaining that the "determining" step is meaningless, well-understood post-solution activity).
145. *See* Parker v. Flook, 437 U.S. 584, 593–95 (1978) (explaining that the claims could not be protected by a patent, not simply because the only novel feature of the method was a mathematical formula, but because once the mathematical formula was *applied*, the claims as a whole contained no patentable invention).
146. *Id.* at 591.
147. Diamond v. Diehr, 450 U.S. 175, 192–93 (1981).
148. *Id.* at 187.
149. *Id.* at 192.
150. *Id.* at 191–92.

alarm.[151] Applying this logic to *Mayo* potentially leads to the conclusion that transformations are only significant for the purposes of method claims if they themselves are unconventional and nonobvious or result in a nonobvious product.[152]

Additional support for this theory is found in Justice Breyer's dissent from the denial of certiorari in *Metabolite*. There, Justice Breyer explained that using an *unpatented* and well-understood procedure for "transforming" blood samples during one step of a patented method, although leading to a "useful, concrete, and tangible result" should be considered irrelevant in determining whether a patent is valid.[153] This view, taken together with the Supreme Court's reasoning in *Flook* and *Benson*, indicates that a transformation must involve or produce a novel or nonobvious material to be relevant for the § 101 patentability analysis.

Recently, the Federal Circuit had an opportunity to expand on this rationale in *PerkinElmer, Inc. v. Intema Ltd.*[154] There, the Federal Circuit examined a patented method of determining a fetus's chances of having Down Syndrome.[155] The patent was comprised of two steps: (1) *measuring* the levels of certain biological markers in the blood, and (2) *determining* whether those levels indicated a heightened risk of Down Syndrome.[156] The Federal Circuit explained

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151. *Flook*, 437 U.S. at 594–95; *see also* Gottschalk v. Benson, 409 U.S. 63, 70 (1972) (explaining that processes "involving mechanical operations and producing a *new and useful result*" are generally patentable (emphasis added) (quoting Expanded Metal Co. v. Bradford, 214 U.S. 366, 385–86 (1909))).

152. *See* Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1292 (2012) (contrasting *Diehr* and *Flook*, both of which addressed processes using mathematical formulas; and, explaining that in *Diehr* the additional steps of the process integrated the equation into the process as a whole, transforming the process into an inventive application of the formula, while in *Flook* the additional steps of the process were not limited to a particular application).

153. *See* Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc., 548 U.S. 124, 136 (2006) (Breyer, J., dissenting) (emphasizing that it was illogical to interpret whether it mattered that the test results themselves were obtained through an unpatented procedure because many procedures could involve "the use of empirical information obtained through an unpatented means that might have involved transforming matter").

154. 496 F. App'x 65, 71 (Fed. Cir. 2012) (construing the validity of a patent disclosing specific screening methods meant to estimate the risk of fetal Down Syndrome after the U.S. District Court for the District of Massachusetts held the asserted claims unpatentable because they were anticipated and obvious, and therefore granted summary judgment), *cert. denied*, No. 12-1372, 2013 WL 2155734 (Oct. 7, 2013).

155. *See id.* at 67 (acknowledging this test as beneficial compared to other tests that carry a significant risk of miscarriage).

156. *See id.* at 66–67 (discussing the patent at issue and explaining that the key difference between representative claims one and twenty was that in claim twenty patients were screened into either "screen positive" or "screen negative" groups, with only "screen negative" patients undergoing testing in the second trimester)).

that the measuring step was an insufficient transformation to make the claim patent-eligible because the available measurement procedures were already known and, therefore, nothing more than "conventional or obvious pre-solution activity."[157]

ii. The transformation was not central to the method claims

Another explanation for the unpatentability of the transformations in *Mayo* could be that the transformation was not central to the method being claimed. Although the Supreme Court never explicitly mentioned this reason in *Mayo*, Justice Breyer did explain that measuring metabolite levels could theoretically be satisfied without transforming the blood if science developed a new method for making this determination that did not involve transforming the blood.[158] In other words, this step was not a crucial part of the overall method.

Although the Supreme Court did not explicitly consider this step in *Mayo*, courts generally have held that a transformation needs to be central to the claims of the method to raise the method above the § 101 bar.[159] For example, in *Bilski*, the Federal Circuit explained that a transformation "must be central to the purpose of the claimed process."[160] Although the Federal Circuit failed to elaborate on this point, Justice Breyer's dissent in *Metabolite* is again informative. There, Justice Breyer argued that a step, that simply instructed a person to measure products in a patient's bloodstream, could not be a valid transformation.[161] Justice Breyer explained, "[w]hy should it matter if the test results themselves were obtained through . . . the transformation of blood? Claim 13 is indifferent to that fact, for it

157. *Id.* at 71 (internal quotation marks omitted).

158. Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1303 (2012).

159. *See, e.g.*, *In re* Bilski, 545 F.3d 943, 962 (Fed. Cir. 2008) (concluding that the "machine-or-transformation test" is the sole test to determine patentability and providing that if the claimed process transforms a particular article into a different state or thing, it is patent-eligible), *aff'd sub nom. on other grounds*, Bilski v. Kappos, 130 S. Ct. 3218 (2010); SmartGene v. Advanced Biological Labs., SA 852 F. Supp. 2d 42, 62 (D.D.C. 2012) (explaining that one of the guidelines to determine if a claimed process is patent eligible under the machine or transformation test is whether the transformation is central to the process instead of mere manipulation of abstract nonphysical objects or substances); Bancorp Servs., LLC v. Sun Life Assurance Co. of Can., 771 F. Supp. 2d 1054, 1066 (E.D. Mo. 2011) (concluding that a claim was not patentable because the claims did "not transform the raw data into anything other than more data and are not representations of any physically existing objects").

160. *Bilski*, 545 F.3d at 962.

161. *See* Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc., 548 U.S. 124, 125, 136–38 (2006) (Breyer, J., dissenting) (per curiam) (arguing that respondents' described process was *not* a process for transforming blood or any other matter).

tells the user to use any test at all."[162] Thus, if a transformation is unnecessary for the central purpose of the patent, it should not be considered when determining patentability. Additionally, careful drafting that writes a natural law, correlation, or phenomenon into the patent's process does not elevate the process to patentability.[163] Thus, the transformation in *Metabolite* was trivial to the patent; it did not matter how the user measured the blood or whether that measurement involved a transformation.[164] Similarly, in *Mayo*, how the user obtained 6-TG measurements from the patient, and whether that step involved a transformation, was irrelevant to the purpose of the patent.[165]

2. Myriad*: Genetic diagnostic tests are simple correlations at their core*

a. Genetic diagnostics and biology

As discussed above, DNA sequencing is a procedure that allows researchers to determine the specific order of nucleotides within a DNA strand.[166] This technique allows researchers to determine whether an individual has the normal ("wild type") version of a gene or a mutated version of a gene.[167] If the individual has a mutated gene, and this particular mutation corresponds with a predisposition to a disease condition, then the doctor can inform the patient and the two can begin to take preventative measures.[168]

Myriad held compositional patents on the "wild-type" and mutant versions of two genes: BRCA1 and BRCA2.[169] Mutant BRCA genes correspond to a very high incidence of breast and ovarian cancers;[170] thus, they are incredibly helpful in identifying a patient's

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162. *Id.* at 136.
163. *Id.* at 137.
164. *See id.* at 136 (suggesting that the administering step is unimportant in determining patentability).
165. *See* Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1303 (2012) (concluding that the "administering" step is "irrelevant"); see *also* Bilski v. Kappos, 130 S. Ct. 3218, 3227 (2010) (explaining that recent case law has deemed the machine-or-transformation test not exhaustive; rather, it is merely a "clue to the patentability" of a claimed process).
166. *Myriad II*, 689 F.3d 1303, 1311 (Fed. Cir. 2012), *aff'd in part, rev'd in part on other grounds*, 133 S. Ct. 2107 (2013).
167. *Id.* at 1341 (Moore, J., concurring in part).
168. *See, e.g.*, *id.* at 1314 (majority opinion) (describing the usefulness of results in determining an appropriate course of cancer treatment).
169. *See Myriad III*, 133 S. Ct. at 2113. It is important to note that compositional patents differ from method patents, where the claims are for a process rather than a gene or molecule itself. *See Myriad II,* 689 F.3d at 1310 (describing Myriad's method claims as diagnostic methods focused on identifying specific mutations associated with breast or ovarian cancer).
170. *Myriad III*, 133 S. Ct. at 2113.

predisposition to cancer.[171] Additionally, Myriad held that diagnostic method patents, which attempted to claim the process of comparing the "wild-type" BRCA genes to a patient's specific BRCA genes to determine whether a patient was predisposed to these cancers.[172] This comparative process allows a doctor to take a DNA sample from a patient, determine whether the patient has the BRCA mutant gene, and thus identify patients with a higher likelihood of developing breast and ovarian cancer.[173] If a patient discovers that she carries a mutated BRCA1 and BRCA2 gene, she could then take steps to manage and treat her risk of cancer.[174] The Federal Circuit initially rejected these method patents.[175] The Supreme Court then vacated the Federal Circuit's decision and remanded the case following its decision in *Mayo*.[176]

b. Comparing and analyzing methods: Myriad *on remand*

On remand, the Federal Circuit was instructed to consider *Myriad* in light of the Supreme Court's decision in *Mayo*.[177] The Association for Molecular Pathology brought an action against Myriad alleging that fifteen claims from seven patents were ineligible subject matter under § 101.[178] Six of the challenged claims were method claims.[179] The Court separated these method claims into two

171. *See, e.g.*, *Consumers Have Few Negative Reactions to the Results of Genetic Testing for Cancer Mutations, Study Shows*, SCI. DAILY (Feb. 12, 2013), http://www.sciencedaily.com/releases/2013/02/130212075428.htm (explaining that a small percentage of breast cancers occur in women who have a genetic predisposition for the disease, which is usually due to mutations in either the BRCA1 or BRCA2 gene).

172. *See Myriad II*, 689 F.3d at 1310, 1314 (describing how large sets of DNA samples from families with inherited breast and ovarian cancers allowed Myriad to correlate the occurrence of cancer in individual family members with the inheritance of specific marker DNA sequences, which in turn facilitated Myriad's diagnostic testing services).

173. *Id.* at 1314.

174. *See* Russell, *supra* note 1, at 100 (noting a patient's "range of options for managing their risk of cancer, including increased surveillance, prophylactic surgery, chemoprevention, and risk avoidance").

175. *Myriad I*, 653 F.3d 1329, 1334 (Fed. Cir. 2011), *vacated sub nom.* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 132 S. Ct. 1794 (2012) (mem.), *remanded to* 689 F.3d 1303.

176. *Myriad Genetics*, 132 S. Ct. 1794 (order granting cert., vacating judgment, and remanding case).

177. *See Myriad II*, 689 F.3d at 1308 (detailing the remand instructions given by the Supreme Court).

178. *Id.* at 1309.

179. *Id.* at 1333. Specifically, plaintiffs challenged method claims of: U.S. Patent No. 5,753,411 (filed Nov. 27, 1996), U.S. Patent No. 5,710,001 (filed Jun. 7, 1995), and U.S. Patent No. 5,709,999 (filed Jun. 7, 1995). Plaintiffs also challenged method claims one, two, and twenty of U.S. Patent No. 6,033,857 (filed Mar. 20, 1998).

subgenres: (1) comparing and analyzing methods, and (2) therapeutic screening methods.[180]

Most of Myriad's method claims involved analyzing and comparing a patient's BRCA gene sequence with the "wild-type" sequence to identify mutations corresponding with a predisposition to breast and ovarian cancers.[181] The comparing and analyzing method claims were each composed of a single step.[182] That step included either "analyzing" a sequence of a BRCA gene from a patient to check for certain mutations or "comparing" a patient's BRCA gene with the "wild-type" and mutant versions of the BRCA gene.[183]

The Federal Circuit first explained that a simple comparison or analysis is an unpatentable mental step.[184] Unfortunately for Myriad, the only real substance to either of its method claims was a simple comparison.[185] The Federal Circuit noted this point stating, "the step of comparing two DNA sequences is the entire process that is claimed."[186] Thus these method claims were held unpatentable.[187]

Myriad, much like Prometheus, attempted to circumvent the Court's logic by claiming that its process necessarily incorporated two transformative steps: (1) extracting DNA from a human sample, and (2) sequencing the BRCA DNA molecule.[188] The Federal Circuit immediately rejected this characterization because these two additional steps were not referenced within Myriad's actual method claims.[189] The court continued that, without these extra steps, Myriad's claims were weaker than the claims in *Mayo* because they lacked any potentially transformative steps, such as administering a drug or obtaining a metabolite sample from a patient.[190] As such, the

180. *Id.* at 1334–35.
181. *Id.* at 1309.
182. *Id.*
183. *Id.*
184. *See id.* at 1334 (relying on Gottschalk v. Benson, 409 U.S. 63, 67 (1972), to explain that a comparison falls outside the scope of § 101 because it is an unpatentable mental process, one of "the basic tools of scientific and technological work").
185. *See id.* (explaining that the act of comparing a BRCA sequence from a tumor and non-tumor sample is "nothing more than the abstract mental steps" required to compare two different things, thus is an unpatentable mental process).
186. *Id.* at 1335.
187. *See id.* at 1334 (rejecting, additionally, the argument that the comparison step was an application of an abstract idea as part of a process, which is patentable).
188. *Id.* at 1335; *see also supra* Part I.E-F (explaining how the patent holder in *Mayo* attempted to use the "machine-or-transformation" test to avoid the Supreme Court's holding that its claim was a recitation of a law of nature).
189. *See Myriad II*, 689 F.3d at 1335 (rejecting the argument because the claims themselves contained no further steps other than performing the comparison and because "comparing" or "analyzing" does not mean "extracting" or "sequencing").
190. *See id.* (comparing the comparison and analysis steps in Myriad's patent

Court invalidated Myriad's sequencing and analysis claims as abstract mental processes.[191]

c. The therapeutic methods

Myriad's therapeutic method claimed a process of screening potential cancer therapeutics and comprised of four steps: (1) growing cells transformed with a mutated BRCA gene, (2) placing half of these cells in the presence of a compound suspected of being a cancer therapeutic, (3) keeping the other half of these cells from such compounds, and (4) comparing the growth rate of both groups of cells.[192] The Federal Circuit began analyzing this claim by looking at the first step of the claimed process.[193] Immediately, the Court noted that the first step added something significant to the law of nature.[194] The act of transforming cells by introducing a mutant BRCA gene was a step that resulted in an unnatural manmade cell with enhanced functionality.[195] The court deemed this therapeutic method claim patentable subject matter because the first step took the claim beyond simply adding the words "apply it" and, thus, transformed a law of nature into a patent-eligible application of the law.[196]

The Federal Circuit's opinion teaches two important lessons to inventors for drafting valid method patents. First, simply "growing" cells, although a physically transformative step, is probably not sufficient to render a method claim patentable.[197] The key fact in *Myriad* was not that the company grew cells, but that the cells were a

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to the "administering" and "determining" steps rejected by the Supreme Court in *Mayo*).

191. *See id.* (explaining that the process could be completed by "mere introspection alone").

192. *See id.* at 1336.

193. *Id.*

194. *Id.* (comparing the transformed cells to the manmade cells from *Chakrabarty* and concluding that this kind of transformation satisfies § 101 patentability requirements for method claims).

195. *See id.* (emphasizing that the transforming of cells requires more than simply "comparing" cells and concluding that the manmade nature of the cells makes them patent-eligible).

196. *See id.* (noting that there was patent-eligibility for a novel and nonobvious manmade cell even if the cell yielded from a well-known and established process or method). The Federal Circuit limited its holding because the method pertained only to the specific host cells that were transformed with specific genes, suggesting that these manmade cells were the key to patentability for this method claim. *Id.* at 1337.

197. *See id.* at 1336 (reasoning that "the abstract mental step of looking at two numbers and 'comparing' two host cells' growth rates" would be insufficient for purposes of § 101).

product of human ingenuity, not nature.[198] Therefore, purely physical changes, *even if central and necessary for the success of the method*, may not alone be sufficient for patentability.[199] Second, if a method involves or results in a nonobvious, novel product, that method is likely patentable subject matter under § 101.[200] Thus, a diagnostic method may become patentable if it can tie itself to a novel or nonobvious product, such as a diagnostic drug or genetic test kit.[201]

d. Myriad*'s return to the Supreme Court*

After the Federal Circuit's second ruling, the Supreme Court once again granted Myriad's petition for certiorari.[202] In its recent decision, the Supreme Court only addressed the patentability of Myriad's composition claims for isolated BRCA genes and manmade cDNA.[203] The court expressly noted that it did not consider the patentability of any method claims.[204] Thus, to the extent this Comment discusses the patentability of methods of genetic diagnostic testing, the Supreme Court's recent decision is simply inapplicable.[205]

198. *See id.* ("The transformed, man-made nature of the underlying subject matter in claim 20 makes the claim patent-eligible. The fact that the claim also includes the steps of determining the cells' growth rates and comparing growth rates does not change the fact that the claim is based on a man-made, non-naturally occurring transformed cell—patent-eligible subject matter.").

199. *See id.* (requiring that the claim be a product of man, not of nature).

200. *See id.* ("By definition, however, performing operations, even known types of steps, on, or to create, novel, *i.e.*, transformed subject matter is the stuff of which most process or method invention consists . . . . In situations where the objects or results of such steps are novel and nonobvious, they should be patent-eligible.").

201. *See, e.g.*, Optigen, LLC, v. Int'l Genetics, Inc., 777 F. Supp. 2d 390, 403–04 (N.D.N.Y. 2011) (showing a case brought for patent infringement in which there was no question as to the validity of a compositional claim on a physical genetic diagnostic test kit).

202. Ass'n for Molecular Pathology v. Myriad Genetics Inc., 133 S. Ct. 694 (2012) (granting certiorari but limiting the scope of review to only whether human genes themselves were patentable).

203. *See Myriad III*, 133 S. Ct. 2107, 2112, 2119 (2013) (emphasizing that the Supreme Court's decision does not implicate method patents). *See generally* Caile Morris, Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, No. 12-398, slip op. (U.S. June 13, 2013)*, AM. U. BUS. L. REV. BLOG (Aug. 26, 2013), http://www.aublr.org/2013/08/assn-for-molecular-pathology-v-myriad-genetics-inc-no-12-398-slip-op-u-s-june-13-2013-available-at-httpwww-supremecourt-govopinions12pdf12-398_1b7d-pdf (providing a brief overview of the Supreme Court's most recent decision).

204. *Myriad III*, 133 S. Ct. at 2119.

205. *Id.*

II. TOGETHER, *MAYO* AND *MYRIAD* CATEGORICALLY ELIMINATED PATENTS FOR METHODS OF DIAGNOSING GENETIC PREDISPOSITIONS TO ILLNESS.

The Supreme Court's holding in *Mayo* and the Federal Circuit's holding in *Myriad II* have likely eliminated genetic diagnostic methods as patentable subject matter under § 101. This is not to say that there is no practical way for genetic diagnostic tests to be protected by patent law. Quite the contrary, companies, such as Myriad, may still be able to maintain monopolies on diagnostic tests. So long as a company holds a compositional patent on a method of *implementing* the diagnostic test, the overall test may still receive patent protection.[206] Additionally, the Supreme Court has suggested that a novel method of identifying a mutated gene within a patient might also be patentable.[207] This possibility, however, is outside the scope of this Comment. Regardless of whether compositional claims might offer respite for inventors, specific method claims themselves likely cannot be granted patent protection.

A. Synthesizing a Rule from Mayo *and* Myriad *To Provide a Framework for Understanding Method Patents for Diagnostic Procedures*

1. The three-step inquiry

Mayo and *Myriad*, when viewed in the context of prior Supreme Court precedent, provide a framework for understanding method patents for diagnostic procedures. Specifically, a test for patentability may be extrapolated from the Supreme Court's and Federal Circuit Court of Appeal's logic. When determining whether a particular diagnostic method is patentable subject matter under § 101 the Court will (1) identify the end purpose of the patented method, and whether the end purpose entirely preempts a natural law;[208] (2) look at each step of the patented method one-by-one to determine whether the step is an abstract mental process or whether it adds any "non-conventional" step to the process;[209] and (3) determine whether

206. *See infra* notes 313–318 and accompanying text.
207. *Myriad III*, 133 S. Ct. at 2119–20.
208. *See, e.g.*, Parker v. Flook, 437 U.S. 584, 585 (1978) (defining, first, the purpose of the patent at issue—to update an alarm limit).
209. *See, e.g.*, Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1297–98 (2012) (considering individually each step of the method—an "administering" step, a "wherein" step, and a "determining" step—after defining the method's overall purpose).

the combination of the steps as a whole transform the process into something more than the sum of its parts.[210]

The first step in any method patentability inquiry is to identify the end purpose of the patent. This principle can be traced back to the Supreme Court's reasoning in *Benson*, *Flook*, and *Diehr*. For example, in *Benson* the Court's first step was to identify the purpose of the patent—in that case, the ability to convert signals from binary-coded decimal form into pure binary form.[211] Unfortunately for Benson, the necessary mathematical algorithm would be completely preempted because the algorithm involved had no substantial practical application without using a computer; accordingly, the patented mathematical formula would, in effect, be a patent on the algorithm itself.[212] Likewise in *Flook*, the Court first identified the purpose of the method—updating an alarm limit.[213] The Court found that, although this purpose seemed narrower than simply claiming the mathematical formula, it had no relevant limiting factors in any of its steps other than conventional and well-known post solution activity.[214]

The decision in *Mayo* highlighted the importance of the first step of this analysis. In *Mayo*, the Court identified the purpose of Prometheus's patent as identifying the optimal level of 6-TG to give a patient.[215] The Court explained that achieving this end was only made possible by Prometheus's discovery of the correlation between 6-TG concentration in the blood and ill-effects in a patient.[216] This correlation was the "law of nature" Prometheus attempted to patent; an identification crucial to the Court's reasoning.[217]

The second step of the analysis—analyzing a method claim step-by-step—was essential in *Mayo* to determine if any of the steps described

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210. *See, e.g.*, *id.* at 1298 ("[T]o consider the three steps as an ordered combination adds nothing to the laws of nature that is not already present when the steps are considered separately." (citing Diamond v. Diehr, 450 U.S. 175, 188 (1981))).

211. *See* Gottschalk v. Benson, 409 U.S. 63, 64–67 (1972) (beginning the Court's analysis by describing how the patent as a whole functioned to convert binary-coded decimals into pure binary numerals).

212. *See id.* at 68, 71–72 (explaining that although the method could be carried out without a computer, any practical use depended on a computer).

213. *Flook*, 437 U.S. at 586.

214. *See id.* at 595 (observing that a claimed method is nonstatutory when the claim is directed to a method of calculating, even if the algorithm is designed for a specific purpose (quoting *In re* Richman, 563 F.2d 1026, 1030 (Fed. Cir. 1977))).

215. *Mayo*, 132 S. Ct. at 1296–97.

216. *See id.* at 1297 (explaining that "the [cor]relation itself exists in principle apart from any human action").

217. *See id.* (identifying the correlation as the "natural law" that Prometheus attempted to exploit and advancing to the second prong of the inquiry as to whether any step in the process added something more to transform that natural law).

more than just natural law to make the claims patent-eligible.[218] This step of the analysis proved determinative in *Myriad*, when the Federal Circuit examined Myriad's therapeutic method claim.[219] The first step of that method involved a manmade organism, which immediately elevated the claim above a simple recitation of natural law.[220] Accordingly, a transformation in any step allows for patent-eligibility for a method claim when that transformation is both (1) central to the claim and (2) results or involves a non-routine, nonobvious product or procedure.[221]

The third step in the analysis, introduced by the Supreme Court in *Mayo*, acts as a failsafe device.[222] If the individual steps of a method patent merely "inform a relevant audience about certain laws of nature," and only include "well-understood, routine, conventional activity already engaged in by the scientific community," the only way a claimed method can be patentable is if, when viewed as a whole, it is more than "the sum of [its] parts."[223] Although such a situation is theoretically possible, the Court in *Mayo* provided no examples.[224]

2. Reexamining Myriad's comparing and analyzing claims

In *Myriad*, the Federal Circuit was unable to fully apply the Supreme Court's step-by-step *Mayo* analysis to Myriad's "comparing" and "analysis" patents because these patents had only one step per method. Each single-step involved a simple abstract mental process, making any step-by-step analysis impossible. Therefore, the Federal Circuit's logic left open the hypothetical question: what if Myriad had claimed a process involving (1) *extracting* DNA from a human sample, (2) *sequencing* that sample, and then (3) *comparing* that sample to the known "wild-type" and mutant versions of the same gene?[225]

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218. *See id.* (addressing individually each of the three steps—the "determining" step, "administering" step, and the "wherein" step—to determine whether the claim allowed the processes to qualify for a patent).

219. *Myriad II*, 689 F.3d 1303, 1336 (Fed. Cir. 2012) (explaining that the very first step of the method was premised on the use of transformed, manmade host cells), *aff'd in part, rev'd in part on other grounds*, 133 S. Ct. 2107 (2013).

220. *See id.* (arguing that performing operations—even operations that involve known types of steps—to create novel subject matter transforms the nature of the claim to patent-eligible subject matter).

221. *See supra* notes 115–141 and accompanying text (detailing the standard by which the *Mayo* court considered Prometheus's method patents).

222. See *Mayo*, 132 S. Ct. at 1298 (describing this third step as simply instructing doctors to engage in conventional activity that scientists in the field have already been engaging in).

223. *Id.*

224. *Id.*

225. This kind of claim has already been submitted to the USPTO. *See, e.g.*, Biomarker for Successful Aging Without Cognitive Decline, U.S. Patent No. 8,216,787 (filed Apr. 14, 2010).

Applying the three-part test identified above, the first step is to identify the purpose of the method and the law of nature or abstract process that the method claim is attempting to use.[226] According to the abstracts and specifications of their patents, Myriad's invention related to diagnosing a predisposition to breast cancer.[227] Much like Prometheus's method claims in *Mayo*, which patented a method in an attempt to protect the correlation it discovered between certain levels of 6-TG and drug efficiency, Myriad attempted to protect the correlation between the presence of the mutant BRCA gene in a patient and a heightened likelihood of breast and ovarian cancer.[228] Thus, like in *Mayo*, the law of nature being exploited here is essentially a correlation, which the court has already deemed an unpatentable abstract principle.[229]

After identifying the purpose of the method and the law of nature being utilized, the next step is to determine whether any of the individual steps of the proposed method add to this law of nature.[230] In *Mayo*, the Supreme Court clarified that a "well-understood, routine, [or] conventional" step adds "nothing" significant to the method and is thus insufficient to move the claim from an unpatentable natural correlation to an application of those occurrences, which could comprise a patentable claim.[231]

The first step of the hypothetical Myriad patent is *extracting* DNA. In the specification of its patent, Myriad identified several potential methods for isolating and extracting DNA.[232] These methods were

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226. *See supra* notes 208–210 and accompanying text (outlining the three-part test for diagnostic method patents).

227. *See* U.S. Patent No. 5,709,999 col.1 l.20–22 (filed Jun. 7, 1995) ("Specifically, the present invention relates to methods and materials used to isolate and detect a human breast and ovarian cancer predisposing gene . . . . More specifically, the invention relates to germline mutations in the BRCA1 gene and their use in the diagnosis of predisposition to breast and ovarian cancer."), *invalidated by Myriad II*, 689 F.3d 1303 (Fed. Cir. 2012), *aff'd in part, rev'd in part on other grounds*, 133 S. Ct. 2107 (2013).

228. *See Myriad II*, 689 F.3d at 1315–16 (explaining that the reason the suit against Myriad was brought in the first place was to stop other practitioners from providing BRCA diagnostic tests); '999 Patent at col.4 l.22–23 ("Identification of a breast cancer susceptibility locus would permit the early detection of susceptible individuals . . . .").

229. *See generally* '999 Patent (describing the method as involving screening suspected BRCA1 mutant alleles, and that the presence of a mutant allele means a greater susceptibility to breast cancer).

230. *Supra* text accompanying note 218.

231. *See* Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1298 (2012) (requiring significant post-solution activity for a claim to be elevated to be patentable).

232. '999 Patent at col.13 l.4–8 ("This can be determined by testing DNA from any tissue of the person's body. Most simply, blood can be drawn and DNA extracted from the cells of the blood. In addition, prenatal diagnosis can be

attributed to publicly available journals and are generally well-known techniques.[233] The Supreme Court's reasoning in *Flook* and *Diehr* indicate that a transformation, which involves obvious and conventional procedures or products, is insufficient on its own to satisfy the § 101 bar.[234] Extracting DNA is a conventional step used in a range of different genetic tests, and therefore, is likely insufficient to satisfy the § 101 bar.[235] Additionally, this step cannot be considered a "transformation" because as the Court discussed in *Mayo*, it could theoretically become irrelevant in the near future should an entirely new system be developed for identifying a person's DNA code.[236] For both of these reasons, the Court would likely not have viewed the hypothetical extraction step as a "transformation."

The second step in the hypothetical process is *sequencing* DNA. Utilized since the beginning of the Human Genome Project, DNA sequencing is just as banal a step as extracting.[237] Given its current ubiquity in modern scientific inquiry in environments ranging from criminal enforcement to paternity tests featured on daytime talk shows, sequencing can almost certainly be considered a conventional step.[238]

The last step of the inquiry is to determine whether the steps as a whole add anything to elevate the law of nature to patentable subject matter.[239] In Myriad's diagnostic claims, there was no transformation of significant magnitude that was found in its therapeutic claim.[240]

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accomplished by testing fetal cells, placental cells or amniotic cells for mutations of the BRCA1 gene.").

233. *Id.*; *see also Myriad III*, 133 S. Ct. 2107, 2119 (2013) ("[T]he processes used by Myriad to isolate DNA . . . were well understood, widely used, and fairly uniform . . . ." (internal quotation marks omitted)).

234. *See supra* text accompanying notes 116–136 (examining whether the patented claims sufficiently add enough to their statements of the correlations as to allow the processes that they describe to be patent-eligible).

235. *See* Russell, supra note 1, at 103 (referring to steps such as sequencing and analyzing as "nothing more than a data-gathering step").

236. *Mayo*, 132 S. Ct. at 1303.

237. *See* SUMMARY REPORT, *supra* note 2, at 1 (explaining that the analysis begins "with the task of ordering overlapping recombinant DNA fragments obtained from purified human chromosomes"); *see also* '999 Patent (explaining several different known methods to identify and screen for specific DNA sequences); Kanigel, *supra* note 2 (explaining that the ability to sequence DNA began the genomic revolution).

238. *See* Kanigel, *supra* note 2, (noting that once a physical genome map is completed, companies can sell information on DNA bases to be used in such instances)*; see also* Russell, *supra* note 1, at 103 (explaining that "data-gathering" steps are insignificant).

239. *See supra* text accompanying notes 182–184 (describing the holding that comparing and analyzing a patient's gene sequence with the "wild-type" sequence is unpatentable).

240. *Compare Myriad II*, 689 F.3d 1303, 1335 (Fed. Cir. 2012) (asserting that Myriad attempts to read into its claims the additional steps of "extracting" and "sequencing," but the use of these terms does not), *aff'd in part, rev'd in part on other grounds*, 133 S. Ct. 2107 (2013), *with id.* (incorporating the creation of novel manmade cells within

Additionally, similar to the patent in *Mayo*, the hypothetical Myriad patent can be summed up as (1) measuring, by any method, the current levels of the relevant metabolite, and (2) applying particular laws of nature to understand that the presence of a mutation correlates to a heightened susceptibility to breast and ovarian cancers.[241] It is highly unlikely that a court would find that this method, taken as a whole, added anything to the basic "law of nature." Even with terms such as sequencing and analyzing, the steps add nothing, either by themselves or taken together, and therefore cannot overcome the § 101 statutory bar. Thus these patents would likely be invalidated if challenged.

3. Reexamining Myriad's therapeutic claims

In light of the Supreme Court's decision to uphold Myriad's therapeutic patent claims, it may seem unreasonable to suggest that together *Mayo* and *Myriad* categorically eliminate diagnostic method patents; however, once the *Mayo/Myriad* test is applied to Myriad's therapeutic patents the distinction becomes clear.

Applying the three-part *Mayo/Myriad* test, the first step is to identify the purpose of the method and the law of nature or abstract process that the method claim is attempting to use.[242] According to the patent specification, the purpose of the therapeutic claim was to provide "methods of screening drugs for cancer therapy *to identify suitable drugs for restoring BRCA1 gene product function*."[243] Nevertheless, this claim has a different purpose than Myriad's other claims; the purpose of the therapeutic claim is to identify a suitable drug, not a predisposition to cancer in a patient.[244] This is unlike a diagnostic patent, which would be used to detect the presence of or predisposition to cancer in a patient.[245] To identify these drugs, Myriad's therapeutic method claims instruct the user to "(1) grow[] host cells *transformed* with an altered *BRCA1* gene in the presence or absence of a potential cancer therapeutic, (2) determin[e] the growth rate of the host cells with or without the potential therapeutic, and (3) compar[e] the growth rate of the host cells."[246] Myriad

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the method, or imply any "processing" of a human sample).

241. *Mayo*, 132 S. Ct. at 1299.

242. *See supra* text accompanying notes 208–210 (identifying the three steps of the test).

243. U.S. Patent No. 5,747,282 (filed June 7, 1995) (emphasis added).

244. *See id.* (relating the invention to the screening of drugs for cancer therapy).

245. *See id.* (describing different therapies associated with cancers caused by a mutation in the BRCA1 gene, such as gene therapy, protein replacement therapy and protein mimetics).

246. *Myriad II*, 689 F.3d 1303, 1336 (Fed. Cir. 2012), *aff'd in part, rev'd in part on other grounds*, 133 S. Ct. 2107 (2013).

further claimed that the law of nature being used in its method was the correlation between growth rates and the effectiveness of a potential cancer therapeutic.[247]

After identifying the purpose of the method and the law of nature being utilized, the next step is to determine whether any of the steps of the proposed method add a non-conventional element to this law of nature.[248] In its decision, the Federal Circuit immediately saw that the first step of the patent—growing transformed manmade cells—added a significant non-conventional step to the method.[249] The court explained that unlike in Myriad's genetic diagnostic claims, the results of such therapeutic steps are novel and nonobvious, and thus, were patent-eligible.[250] Myriad's therapeutic claim did not just exploit and preempt a law of nature, which would lead to ineligibility, because it involved incorporating a novel manmade organism to use during experimentation.[251] Because the claim did not cover all methods of determining the therapeutic effect of a compound, and instead was just tied to a specific type of therapeutic, the claim survived § 101.[252]

B. Applying the Mayo*/*Myriad *Test to Claims in Method Patents*

Testing for a genetic predisposition is essentially testing for the presence of a particular gene that correlates strongly with a predisposition to cancer. Accordingly, *any* genetic test is an attempt to exploit this correlation, much like the patent in *Mayo*. In *Mayo*, the Supreme Court held that to be patentable, methods attempting to exploit a correlation must include a non-frivolous, non-conventional step.[253] Myriad met this standard in its therapeutic claim by requiring the use of a novel, transformed host cell.[254]

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247. *See id.* at 1335–36 (suggesting that a correlation between slower growth rate in the presence of a potential therapeutic and the compound being a cancer therapeutic does not preempt a scientific principle).

248. *See supra* text accompanying notes 184–187 (referencing the holding that a simple comparison or analysis does not add anything new, and therefore is an unpatentable step).

249. *See Myriad II*, 689 F.3d at 1336 (emphasizing that Myriad's therapeutic claim employs transformative steps that "are a product of man, not of nature").

250. *Id.*

251. *See id.* (including "the steps of determining the cells' growth rates and comparing growth rates [in the larger claim] does not change the fact that the claim is based on a man-made, non-naturally occurring transformed cell—patent-eligible subject matter").

252. *Id.* at 1336–37.

253. *Id.* at 1336.

254. *See id.* at 1336–37 (hinging patentability on specific host cells transforming with specific genes and growing "in the presence or absence of a specific type of therapeutic").

Nevertheless, a patentee making a claim for genetic diagnostic tests would likely be unable to add such a novel approach to the patent's steps because once a disease allele has been identified it is relatively easy to identify its presence in a patient.[255] Additionally, there are many readily available tools a researcher can employ to determine whether a disease allele is present.[256] Applying the rationale from *Mayo* and *Myriad* to currently held patents for genetic diagnostic tests illustrates the difficulty associated with trying to instill novelty into a correlative genetic diagnostic test.

1. Patents granted before Myriad

Many patents granted by the USPTO before the decision in *Myriad* tend to follow the same "analyze" and "compare" formula that was invalidated in *Myriad*. United States Patent No. 7,479,380[257] and U.S. Patent No. 8,211,638[258] provide examples for applying the *Mayo/Myriad* test to existing patents.[259] Both the '380 Patent and the '638 Patent disclosed a method for determining predispositions for disease and both methods were composed of two steps: (1) detecting a mutation in the patient, and (2) determining whether the patient had a disease predisposition based on the presence or absence of the mutation.[260] These kinds of method claims are likely invalidated by the current three-step test for method patentability.

Walking through the three-step test, courts must first identify the purpose of the method claim.[261] The purpose of the claim is used to identify a predisposition to a disease, or a genetic disease condition itself.[262] To accomplish this task, the inventor relies on a correlation

255. *See* Verbeure, *supra* note 3, at 15 (explaining that the development of gene-based diagnostic testing does not require a large investment); *see also* Russell, *supra* note 1, at 103 (explaining that the process of identifying known mutations is a simple data gathering step).

256. *See* Verbeure, *supra* note 3, at 15 (among the various tests that are currently available, over a thousand genetic diseases can be diagnosed); *see also Myriad III*, 133 S. Ct. 2107, 2119 (2013) (explaining that there are processes which may be used to isolate DNA which are "well understood, widely used, and fairly uniform").

257. Method for Assessing Behavioral Predisposition, U.S. Patent No. 7,479,380 (filed July 11, 2003).

258. Genetic Polymorphisms Associated with Liver Fibrosis, Method of Detection and Uses Thereof, U.S. Patent. No. 8,211,638 (filed Apr. 29, 2010).

259. As seen in the *Mayo* and *Myriad* tests, both of these patents rely on the existence of certain environmental specificities to find a connection between possessing a gene and being a risk for a disorder. *See generally* '380 Patent (providing the patent is for determining behavioral predisposition); '638 Patent (stating the patent as a method for associating a specific polymorphism with liver fibrosis).

260. *See* '380 Patent; '638 Patent.

261. *Supra* text accompanying notes 211–217.

262. *See* '380 Patent at [57] ("The present invention relates to diagnostic methods for assessing predisposition of a subject to a mental disorder phenotype . . . ."); '638 Patent at [57] ("The present invention is in the field of fibrosis diagnosis and therapy

between the existence of a genetic mutation, and the disease phenotype.[263] As seen in *Mayo*, when a method's purpose depends upon a natural correlation, the steps are then considered separately and must add something significant to the law of nature.[264]

The two steps in the '638 Patent and '380 Patent mirror the failed method claims from *Myriad*. Much like in *Myriad*, the "determining" and "comparing" steps only inform a person using these methods of a naturally occurring correlation and suggest consideration of this correlation when determining an increased likelihood of disease.[265] Additionally, because the "determining" step necessitates other steps, such as obtaining a sample from the patient or profiling a subject's allele via a nucleic acid microarray, this step is not enough for patentability for two reasons. First, because these steps were not claimed steps in the first place;[266] and, second, because even if these steps were claimed within the overall method claim, they would likely amount to banal pre-solution activity.[267] The procedures for obtaining genetic samples from patients or sequencing those samples are conventional, well-known steps.[268] Indeed, those steps are so ordinary that the claimed methods assume that a person with ordinary skill in the art already knows the requirements for "determining" a mutation.[269]

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and in particular liver fibrosis diagnosis and therapy . . . .").

263. *See* '380 Patent (relating a mental disorder phenotype and an at-risk allele of a brain function gene); '638 Patent (relating particular nucleic acid molecules and methods of using the nucleic acid and protein).

264. *See supra* text accompanying notes 184–87 (explaining that mental steps that simply involve making comparisons add nothing to natural law).

265. *See Myriad II*, 689 F.3d 1303, 1335 (Fed. Cir. 2012) (noting that Myriad's method patents contained only "comparing" and "analyzing" steps which were not transformative), *aff'd in part, rev'd in part on other grounds*, 133 S. Ct. 2107 (2013).

266. *See id.* (explaining that the extracting and sequencing steps were not mentioned in the claim, and thus would not be considered for validity).

267. *See supra* text accompanying notes 142–44 (explaining that administering tests will not be considered transformative).

268. *Id.*; *see* Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 702 F. Supp. 2d 181, 200 (S.D.N.Y. 2010), (noting that the techniques used for sequencing are well-known and used daily by scientists in the field of genetics), *aff'd in part, rev'd in part, Myriad I*, 653 F.3d 1329, 1334 (Fed. Cir. 2011), *vacated sub nom.* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 132 S. Ct. 1794 (2012) (mem.), *remanded to* 689 F.3d 1303, *aff'd in part, rev'd in part on other grounds*, 133 S. Ct. 2107; *see also Myriad II*, 689 F.3d at 1335 ("extracting" and "sequencing"—i.e., obtaining a sample and testing it—is insufficient for patentability).

269. *See* U.S. Patent No. 7,479,380 col.2 l.55–58 (filed July 11, 2003) (the method steps include "determining whether the subject carries a two- or three-repeat allele of a variable . . . and concluding that the subject is predisposed to the phenotype if the subject carries the two- or three-repeat allele"); U.S. Patent No. 8,211,638 (filed Apr. 29, 2010) (detailing a method comprising of testing a human's nucleic acid and correlating the presence or absence of an allele at certain positions on the nucleotide); *see also* '380 Patent col.7 l.9 (explaining in the specification that a "wide range of profiling tests exist" which a physician should already be aware of).

Other patents granted before the decision in *Myriad* included "pre-solution" steps such as obtaining a sample from a patient[270] or running PCR amplifications.[271] These steps refer to unpatented, routine procedures that amount to nothing more than common data-gathering steps.[272] Transformations that do not involve or produce nonobvious or novel material are insufficient to elevate a method claim above the § 101 bar.[273] Therefore, patents that were approved before *Mayo* and *Myriad* should now be considered unpatentable because they do not add anything novel to the process.

2. Patents granted after Myriad

Since the Federal Circuit decided *Myriad II* in August 2012, several patent applications for genetic diagnostic tests have cleared the USPTO.[274] The method claims that have passed through the USPTO can be divided into three general groups: (1) those that have added terms and unnecessary extra steps to their core method claim, (2) those that are phrased in such a way so as to incorporate physical biological structures in their claims, and (3) those that capture the method claim inside a compositional claim. This section discusses these claims and argues that if challenged, a court would likely invalidate them in light of the *Mayo/Myriad* test.

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270. *See, e.g.*, U.S. Patent No. 7,521,190 col.175 l.39–40 (filed Mar. 2, 2007) ("A method for detecting in an individual the presence or absence of a mutant PKD gene comprising: (a) obtaining a nucleic acid sample . . . and (b) detecting the presence or absence of one or more mutations . . . .").

271. *See, e.g.*, U.S. Patent No. 7,638,308 col.13 l.56 (filed Jul. 6, 2005) (describing the method for disease diagnosis as "running PCR amplification . . . and DNA typing the resulting PCR amplification products"); U.S. Patent No. 8,221,979 col.139 l.2–5 (filed Nov. 16, 2011) ("A method for diagnosing Noonan syndrome . . . comprising amplifying all or part of a . . . (SOS1) nucleic acid molecule . . . and detecting a mutation in the SOS1 nucleic acid molecule . . . ."). PCR stands for Polymerase Chain Reaction, and is a method of replicating DNA. Karmin T. MacKnight, *The Polymerase Chain Reaction (PCR): The Second Generation of DNA Method Analysis Takes Hold*, 9 SANTA CLARA COMPUTER & HIGH TECH L.J. 287 304–08 (1993). Generally speaking PCR is a "DNA photocopy machine," which makes thousands of DNA copies from one sample. *Id.* This process allows researchers to identify the presence of specific genes in a given DNA sample. *See generally id.* (explaining exactly how PCR is used).

272. *See* Russell, *supra* note 1, at 102 (suggesting that data collecting steps are generally meaningless post-solution activities).

273. *See supra* text accompanying notes 184–87 (discussing the Federal Circuit's rejection of method claims involving only mental steps, asserting "the step of comparing two DNA sequences is the entire process that is claimed").

274. *See, e.g.*, Method of Profiling Gene Expression in a Subject Having Alzheimer's Disease, U.S. Patent No. 8,257,922 (filed Apr. 9, 2010); Methods For Predicting & Treating Tumors Resistant to Drug, Immunotherapy & Radiation, U.S. Patent No. 8,257,928 (filed Sep. 7, 2011).

a. Escaping Mayo *and* Myriad*: throwing science at the wall*

Generally speaking, claims for genetic diagnostic patents have three basic steps: (1) obtaining a DNA sample from a patient, thereby establishing a providing, collecting, or obtaining step, (2) sequencing that DNA sample, and (3) comparing the patient's DNA sequence to other known wild-type and mutant strands to determine if the patient has a mutation.[275]

To escape the result of *Mayo* and *Myriad*, some patents have attempted to add several steps and terms to their diagnostic method claims. A prime example is U.S. Patent No. 8,236,500.[276] This patent claims

> A method, comprising: a) *providing*; i) an individual suspected of having a predisposition to schizophrenia; ii) a nucleic acid derived from said individual, wherein said nucleic acid comprises an alpha7 nicotinic acid receptor regulatory allele; b) *detecting* at least one polymorphism within said alpha7 regulatory allele, wherein said polymorphism comprises –1831 C/A of SEQ ID NO: 181; and c) *correlating* the presence of said at least one polymorphism with a predisposition to schizophrenia.[277]

This method can be unpacked into the three basic steps for genetic testing: (1) taking a particular DNA sample from a patient, (2) determining whether the gene is the "wild-type" or mutant version, and (3) analyzing whether the person likely has a predisposition to schizophrenia if the gene is mutated.[278] However, when applying the *Mayo/Myriad* test, it becomes clear that adding extra terms or steps cannot raise a correlative test above the § 101 bar.

In determining whether or not the '500 Patent is a valid method claim under § 101 pursuant to the *Mayo/Myriad* test, the purpose of the claim and the law of nature at use must first be identified.[279]

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275. *See, e.g.*, U.S. Patent No. 8,236,500 (filed May 29, 2009) (listing the providing, detecting, and correlating steps). Patenting genetic diagnostic methods has become more difficult in light of recent Supreme Court decisions. *See* Russell, *supra* note 1, at 92 (explaining the difficulty inherent in diagnostic patents because they need to show a claim for a fundamental principle rather than a series of steps).

276. Promoter Variants of the Alpha-7 Nicotinic Acetylcholine Receptor, U.S. Patent No. 8,236,500 (filed May 29, 2009).

277. *Id.* at col.189 l.1–14 (emphasis added).

278. *Id.* Viewed this way, a pattern for genetic diagnostic tests begins to emerge that may be unavoidable. *Compare id.* (exemplifying the three-step process of (1) providing, (2) detecting, and (3) correlating), *with* Mayo Collaborative Servs. v. Prometheus Labs., Inc. 132 S. Ct. 1289, 1303 (2012) (explaining the three steps of the *Mayo* patent), *supra* text accompanying notes 239–41 (listing the steps of the hypothetical *Myriad* patents), *and supra* text accompanying notes 259–60 (detailing the steps in the patents granted before *Myriad*, which passed the § 101 bar because they added something new or novel to the method).

279. *See supra* text accompanying notes 242–44 (pointing out that the purpose of

Here, the stated purpose is to diagnose a predisposition to schizophrenia, and the law of nature at issue is a correlation between a mutant gene and the disease condition.[280] The next step is to analyze the method steps one-by-one to determine if they add anything significant to the law of nature.[281]

The patent claim's first step involves obtaining a sample from a patient. This step is very similar to the first proposed step in the hypothetical Myriad patent.[282] Simply obtaining a sample has generally been held insufficient for method patentability.[283] The second step of the '500 Patent is to detect at least one polymorphism.[284] In effect, this step is identical to the *Myriad* step of "analyzing" a particular gene for a mutation.[285] Moreover, in *PerkinElmer*, the Federal Circuit made clear that a "measuring" step by itself is insufficient to raise a claim to patentability.[286] Here, there is no specific, novel, or unique method of "detecting" required; the patent simply instructs the user to somehow detect the presence of a mutation.[287] Thus, this step can be discarded as an "abstract mental process" that could be completed through "mere inspection alone."[288] The final step in the '500 patent is correlating the presence of a mutant gene with a predisposition to schizophrenia,[289] which is clearly the recitation of the "law of nature."[290]

Myriad's claim had a different purpose than its other claims, and thus the method did not pass the § 101 bar).

280. '500 Patent; *see, e.g.*, *Myriad II*, 689 F.3d 1303, 1314 (Fed. Cir. 2012) (describing the correlation between mutations in certain genes and breast cancer), *aff'd in part, rev'd in part on other grounds,* 133 S. Ct. 2107 (2013).

281. *See supra* text accompanying notes 249–52 (clarifying that the addition of something significant to the laws of nature includes steps that are novel and nonobvious, such as incorporating a man-made organism into experimentation).

282. *See supra* text accompanying notes 232–33 (stating that the first step of the hypothetical Myriad patent is extracting).

283. *See, e.g.*, *Mayo*, 132 S. Ct. at 1303 (explaining that taking blood from a patient was not a transformation and could not raise the method to the required level of patentability); *see also* Russell, *supra* note 1, at 102 (suggesting that data gathering steps, such as collecting samples, "can also fairly be characterized as insignificant extra-solution activity.").

284. *See generally* '500 Patent (allowing the user to detect, by any method, the presence of the polymorphism and explaining several different methods of detection).

285. *See Myriad II*, 689 F.3d at 1334 (holding that analyzing two gene sequences falls outside the scope of § 101 because the patents claim only abstract mental processes).

286. *See* PerkinElmer, Inc. v. Intema, Ltd., 496 F. App'x 65, 71 (Fed. Cir. 2012) (holding that measuring steps are insufficient to make claims patent-eligible because the step simply directs users to measure screening markers, but the users can still use any method they wish), *cert. denied*, No. 12-1372, 2013 WL 2155734 (Oct. 7, 2013).

287. *See* '500 Patent (demonstrating several ways to detect a polymorphism).

288. *See Myriad II*, 689 F.3d at 1335 (differentiating Myriad's claim from any "*Mayo*-like" transformative step because Myriad's claim involves abstract mental processes).

289. '500 Patent at col.3–4 l.43–3.

290. *See* Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1297

This patent's steps add nothing unconventional or novel to the overall process, and the steps certainly do not come close to the "administering" and "determining" steps that the court concluded to be transformative in Myriad's therapeutic claims.[291] Thus, the method is nothing more than an attempt to monopolize the correlation between a particular genetic mutation and a predisposition to a disease condition. If challenged, the '500 Patent should be invalidated under the *Mayo/Myriad* test.

b. Escaping Mayo *and* Myriad*: incorporating physical structures*

In the Federal Circuit's decision in *Myriad*, the company attempted to argue that the "sequencing" method claim referred to the manipulation of the physical DNA molecule itself, not simply to the information held within the molecule's structure.[292] The Federal Circuit disagreed and held that the patent only claimed the abstract process of comparing two sequences; not the physical manipulation of biological structures.[293] Some diagnostic patents granted by the USPTO since the Federal Circuit decided *Myriad* incorporate the physical manipulations of biological structures in their method claims.[294]

A good example of this incorporation phenomenon can be found in U.S. Patent No. 8,263,337[295] that discloses another method for determining a genetic disposition to schizophrenia. Unlike in the *Myriad* patent, the '337 Patent explicitly describes the targeted sequence and even the targeted polymorphism as the difference between the inclusion of an "A" allele or a "G" allele at nucleotide polymorphism rs135667, which correlates with a predisposition to schizophrenia, and not just the targeted gene.[296] Using the

(2012) (identifying the correlation in Prometheus's claim as a natural law and thus the claim was unpatentable because it simply "inform[s] a relevant audience about certain laws of nature" and merely adds "additional steps consist[ing] of well-understood, routine, conventional activity" is invalid under § 101).

291. *See Myriad II*, 689 F.3d at 1335 (explaining that the therapeutic claim passed the § 101 bar because it involved the creation of novel manmade cells, which were central to the purpose of the process involved).

292. *See id.* (adding that the claims Myriad defended were indistinguishable from the claims that the Supreme Court invalidated under § 101 in *Mayo*).

293. *See id.* ("[T]he claims only recite mental steps, not the structure of physical DNA molecules.").

294. *See, e.g.*, U.S. Patent No. 8,323,906 col.4 l.47–55 (filed Dec. 17, 2008) (describing use of a specific nucleotide sequence to determine host expression).

295. Genetic Markers of Schizophrenia, U.S. Patent No. 8,263,337 (filed Oct. 27, 2011).

296. *Id.* at col.44 l.23–35.

Mayo/Myriad three-step test provides guidance as to whether this specificity raises the method above the § 101 bar.[297]

The first step is simple; the purpose of the patent is to correlate a genetic anomaly with a predisposition of schizophrenia.[298] Next, each step of the method must be considered individually.[299] The first step of the '337 Patent involves determining whether a particular gene (the CERK haplotype) is present within the patient.[300] Much like the determining steps in *Mayo* or *PerkinElmer*, this step does not explain *how* to determine whether this anomaly exists, but leaves that up to the user.[301] In both *Mayo* and *PerkinElmer* this kind of discretionary determining step was insufficient to meet the § 101 bar.[302]

The second step of the '337 Patent is a "wherein" clause, which states the exact polymorphisms that correspond to a predisposition to schizophrenia.[303] The patent relies on the correlation between the presence of a polymorphism and a predisposition to schizophrenia.[304] Although this patent identifies the specific nucleotide to be examined, it still remains an abstract idea—a comparison that could be accomplished by mere introspection alone.[305] Providing greater specificity cannot transform the nature of the method.[306] Here, the

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297. *See supra* text accompanying notes 231–35 (explaining that because extracting DNA is such a commonly used step in a wide array of genetic tests, it is insufficient to satisfy the § 101 bar).

298. '337 Patent col.44 l. 23–35.

299. *See supra* text accompanying notes 237–38 (illustrating that this step applied to the first step of the hypothetical patent in *Myriad* of extracting DNA).

300. '337 Patent col.44 l.34–39. Whether the particular gene is present determines if the subject has an increased risk of developing schizophrenia. *Id.* col.44–45 l.63–3.

301. *See* Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1297 (2012) (describing Mayo's "determining step" as alerting the doctor to determine the level of the relevant metabolites in the blood, using whatever process he or she wishes); PerkinElmer, Inc. v. Intema Ltd., 496 F. App'x 65, 71 (Fed. Cir. 2012) (requiring the "ineligible mental step" of "comparing" measurements with data on affected pregnancies in order to determine the risk of fetal Down's syndrome), *cert. denied*, No. 12-1372, 2013 WL 2155734 (Oct. 7, 2013).

302. *See Mayo*, 132 S. Ct. at 1298 (explaining that using an unpatented natural correlation technique was insufficient for patent eligibility under § 101); *PerkinElmer*, 496 F. App'x at 71 (comparing the claim to the one in *Mayo*, which amounted to a mere "suggestion" that a doctor take a mental step and included no requirement that a doctor act on the calculated risk, thus making both claims ineligible for patents under § 101).

303. '337 Patent col.44 l.36–40.

304. *Id.* at col.2 l.15.

305. *See Myriad II*, 689 F.3d 1303, 1335 (Fed. Cir. 2012) (explaining that narrowing the claim to a specific genetic region was insufficient because the key still remained the comparison, an abstract mental process), *aff'd in part, rev'd in part on other grounds*, 133 S. Ct. 2107 (2013).

306. Prometheus could not escape the § 101 bar even though it identified the specific biological structure required for its correlation, 6-TG, so it seems unlikely that genetic diagnostics would be able to escape § 101 this way. *See Mayo*, 132 S. Ct. at 1294 (reiterating the Court's instructions that to transform an unpatentable law of

two different structures are still simply being compared, which is an abstract mental process.[307] It does not matter how specifically these structures are described; the key lies in the comparison, not their structures.[308]

The final step is to consider the method as a whole, and as a whole, '337 offers nothing beyond the correlation between a particular genetic mutation and a predisposition to disease.[309] Additionally, there is no non-frivolous or non-traditional transformation anywhere in this patent.[310] While the inventor may argue that transformations must occur during the "determination" step, the Supreme Court's decision in *Mayo* and the Federal Circuit's decision in *PerkinElmer* demonstrate that a measuring or determination step must include some novel, nonobvious procedure to rise above the § 101 bar.[311]

Incorporating biological structures into the method claim of a genetic diagnostic test should not raise a patent to pass the § 101 statutory bar. The key inquiry in these method claims does not concern the structure of the genes or the specific locus of a relevant sequence, but rather the fact that the very presence of a mutation statistically correlates with a disease condition.[312] Thus, although these kinds of patents identify specific biological structures, because the process remains identical to other genetic diagnostic tests they cannot pass the *Mayo/Myriad* three-part test.

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nature into something patent-eligible, restating the law of nature and adding the words "apply it" is not enough).

307. *See id.* at 1293 (explaining that the term "analyzing," when used to describe the mental process of comparing two different things, is nothing more than an "abstract intellectual concept[]" that is not patentable).

308. *See id.* at 1294 (emphasizing that the method claimed must demonstrate additional elements (or a combination of elements) to ensure that the patent involves more than ubiquitous activity performed by experts in the field or just a patent upon the natural law itself).

309. *See supra* text accompanying notes 184–87 (noting that comparison or analysis is not patentable).

310. *See supra* text accompanying notes 142–57 (explaining that to be relevant a transformation within a method claim must involve a novel product or step, and must be central to the actual purpose of the method).

311. *See Mayo*, 132 S. Ct. at 1303–04 (correcting the government's claim that anything beyond stating a new law of nature is patentable by showing precedent requires something nonobvious or novel); PerkinElmer, Inc. v. Intema, Ltd., 496 F. App'x 65, 71 (Fed. Cir. 2012) (explaining that obvious changes in measuring steps are insufficient to make a law of nature patent-eligible), *cert. denied*, No. 12-1372, 2013 WL 2155734 (Oct. 7, 2013).

312. Genetic Markers of Schizophrenia, U.S. Patent No. 8,263,337 col.44 l.23–35 (filed Oct. 27, 2011) (explaining that an individual will have an "increased risk of schizophrenia," if they have a certain mutation in his CERK haplotype).

c. Escaping Mayo *and* Myriad*: reliance on compositional claims*

Despite the challenges, there is a way for a method of genetic diagnostic testing to gain patent protection. A certain genetic illness may be successfully patented if the method claim is captured by a compositional claim.[313] An inventor may easily obtain a patent on a diagnostic test kit or on an eligible diagnostic drug.[314] For example, an inventor may manufacture a test kit for international distribution.[315] This test kit would be sold to physicians and allow them a simple way to test for genetic predisposition to a disease, such as cystic fibrosis.[316] Alternatively, this test kit could also be sold directly to consumers for testing at home. Either way, the test kit itself might be eligible for a patent on its compositional claim.[317] These compositional patents may provide protection for the genetic diagnostic method as a whole; however, it is *not* a patent on the genetic diagnostic method itself. These compositional patents may simply serve to preempt others from using the diagnostic test kit, and therefore the methods employed by the test kit.[318]

CONCLUSION

While the patent world was fixated on *Myriad* because of its controversial holdings on patents for isolated DNA fragments, the case's holding on diagnostic method claims was largely ignored. When combined with the Supreme Court's previous ruling in *Mayo*, *Myriad*'s holding may very well require interpretation of 35 U.S.C.

313. *See* Nicholas J. Landau, *The Practical Lessons of* Myriad, LAW360 (Sept. 4, 2012, 11:56 AM), www.law360.com/articles/374258/print?section=appellate (advising that after the *Myriad* decision, inventors may wish to rely more heavily on compositional claims instead of method claims to maintain patent protection on diagnostic tests); *supra* text accompanying notes 177–73 (explaining that Myriad's claimed compositional patents on BRCA1 and BRCA2 were quite helpful in identifying a patient's predisposition to breast and ovarian cancers).

314. *See* Christopher M. Holman, *Learning from Litigation: What Can Lawsuits Teach Us About the Role of Human Gene Patents in Research and Innovation?*, 18 KAN. J.L. & PUB. POL'Y 215, 248 (2009) (predicting an increase of genetic diagnostic testing litigation due to the rising popularity and prevalence of personalized medicine). *But see* Schilling, *supra* note 8, at 760 (explaining that there are two kinds of tests for diagnosing genetic predispositions, ones which occur in a laboratory without a kit—and therefore, ostensibly outside the realm of patent protection—and ones that customers can take at home with a kit).

315. Schilling, *supra* note 8, at 760.

316. *Id.* at 760; Lauren B. Solberg, *Over the Counter but Under the Radar: Direct to Consumer Genetic Tests and FDA Regulation of Medical Devices* 11 VAN J. ENT. & TECH. L. 711, 717–18 (2009).

317. Schilling, *supra* note 8, at 760.

318. *See, e.g.*, Optigen, LLC, v. Int'l Genetics, Inc., 777 F. Supp. 2d 390, 404–05 (N.D.N.Y. 2011) (illustrating an instance in a patent infringement case where it was undisputed that the defendant was aware of the plaintiff's patents).

§ 101 in such a way as to foretell the end of patent protection for genetic diagnostic tests.

Section 101 of the United States Patent Act prohibits any patent that attempts to claim a law of nature, natural phenomena, or abstract idea.[319] Applying these exceptions can be very difficult when assessing the patentability of method claims and especially difficult when considering diagnostic method claims.[320] The Supreme Court and the Federal Circuit have laid the foundation for understanding method patents in three phases. First, in *Benson*, *Flook*, and *Diehr*, the courts explained that to be patentable subject matter, a method claim could not wholly preempt a natural law, and meaningless post-solution activity could not raise a method to patentability. Then, in *Bilski*, the Supreme Court rejected the "machine-or-transformation" test as a determinative factor in patentability. Finally, in *Metabolite* and *Classen*, the courts determined that transformations were still useful clues to deterring patentability for methods if they were central to the claims and involved a novel or nonobvious product.[321] These cases set the framework for *Mayo* and *Myriad*, which created a foundation for understanding the patentability of genetic diagnostic tests.

Together *Mayo* and *Myriad* established a three-part test for determining diagnostic method patentability: (1) identify the end purpose of the patented method and whether that end purpose entirely preempts a natural law; (2) look at each step of the method to determine whether a step is an abstract mental process or adds any "non-conventional" element to the process; and (3) determine whether the combination of the individual steps as a whole transforms the process into something more than the sum of its parts. Furthermore, the transformation might raise a method claim to the level of patentability if the transformation is central to the process and involves a novel or nonobvious process.

Applying this test to patents, granted before and after *Myriad* was decided, demonstrates that genetic diagnostic patents categorically fail the three-part test. Neither incorporating physical biological structures nor incorporating a longer list of enumerated steps can raise a genetic test to the level of patentability because a genetic test is, at its core, simply a correlation.

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319. 35 U.S.C. § 101 (2006); *see also* Diamond v. Diehr, 450 U.S. 175, 185 (1981) (explaining the three statutory exclusions to the United States Patent Act).
320. Russell, *supra* note 1, at 86.
321. *Supra* text accompanying notes 209–24.

New correlations between genes and disease conditions are being made rapidly as science progresses further into the era of personalized medicine. For better or worse, the *Mayo/Myriad* decisions, which likely strip genetic diagnostic tests of their patentability, ensure that such tests are not monopolized, remain available to all, and are held exclusively by none.