

# PATENTING DIAGNOSTICS: A NONCOMPLEMENTARY POLICY\*

## I. INTRODUCTION

“[O]ne of the promises of precision medicine is not just identifying [diseases] . . . ; it is also empowering individuals to monitor and take a more active role in their own health.”<sup>1</sup> Precision medicine is based upon individualized care that uses a patient’s genetic makeup to diagnose and treat the patient.<sup>2</sup> In 2015 President Obama announced the Precision Medicine Initiative, which aims to accelerate biomedical discoveries that aid in individualizing the diagnosis and treatment of diseases.<sup>3</sup>

Although in its infancy, precision medicine is already changing lives.<sup>4</sup> For example, Angelina Jolie famously authored a *New York Times* opinion article discussing her decision to have a double mastectomy after a genetic test revealed she had an eighty-seven percent risk of developing breast cancer.<sup>5</sup> Jolie’s risk of developing breast cancer is now less than five percent.<sup>6</sup> Precision medicine also is a valuable tool in treating diseases.<sup>7</sup> For example, former NBA player Kareem Abdul-Jabbar was diagnosed with leukemia caused by a genetic mutation.<sup>8</sup> Although

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\* Alison Slaughter, Ph.D., J.D. Candidate, Temple University Beasley School of Law, 2021. The author holds a Ph.D. in Pharmaceutics and Pharmaceutical Chemistry. Thank you to Professor Mary Levy for advising me. Thank you to Brittany Steane, Emily Berg, and Jeremy Gradwohl for their thoughtful insights and input. Thank you to the *Temple Law Review* staff for their hard work in editing this piece. Finally, thank you to Michael for his endless support and encouragement.

1. President Barack Obama, Remarks by the President in Precision Medicine Panel Discussion (Feb. 25, 2016), <http://obamawhitehouse.archives.gov/the-press-office/2016/02/25/remarks-president-precision-medicine-panel-discussion> [<https://perma.cc/56JJ-5SBR>] [hereinafter President Obama, Precision Medicine Panel Remarks].

2. FDA, PAVING THE WAY FOR PERSONALIZED MEDICINE: FDA’S ROLE IN A NEW ERA OF MEDICAL PRODUCT DEVELOPMENT 6 (2013), <http://www.fdanews.com/ext/resources/files/10/10-28-13-Personalized-Medicine.pdf> [<https://perma.cc/G8G5-VH4T>].

3. See *The Precision Medicine Initiative*, WHITE HOUSE: PRESIDENT BARACK OBAMA, <http://obamawhitehouse.archives.gov/precision-medicine> [<https://perma.cc/FLE6-77N4>] (last visited Oct. 17, 2019). The mission statement of the Precision Medicine Initiative is as follows: “To enable a new era of medicine through research, technology, and policies that empower patients, researchers, and providers to work together toward development of individualized care.” *Id.*

4. *Id.*

5. Angelina Jolie, Opinion, *My Medical Choice*, N.Y. TIMES (May 14, 2013), <http://www.nytimes.com/2013/05/14/opinion/my-medical-choice.html> [<https://perma.cc/5Q4Z-F8T3>]. Jolie chose to have a genetic test performed after her mother died of breast cancer. *Id.*

6. *Id.* (“I can tell my children that they don’t need to fear they will lose me to breast cancer.”).

7. *The Precision Medicine Initiative*, *supra* note 3.

8. See Press Release, NBA, Abdul-Jabbar Partners with Novartis Oncology (Nov. 10, 2009), <http://web.archive.org/web/20091114164127/http://www.nba.com/2009/news/11/10/kareem.release/> [<https://perma.cc/9WZA-YJ6D>].

once fatal, doctors treated Abdul-Jabbar with a drug that targeted the mutation.<sup>9</sup> He credits his survival to precision medicine.<sup>10</sup>

In discussing the Precision Medicine Initiative, President Obama noted that the initiative “won’t work unless we have the private sector coming up with innovation” and that “[w]e want to encourage that kind of innovation.”<sup>11</sup> One way to further the goals of the Precision Medicine Initiative is to incentivize innovation through the patent system.<sup>12</sup> However, courts have struggled with determining how to confine the scope of patent claims so that innovation is not hindered.<sup>13</sup> In the context of diagnostics, the tools used in precision medicine, courts have erred on the side of caution—severely limiting the inventions that can be patented—out of fear that overbroad patent claims could have a chilling effect on innovation in that area.<sup>14</sup> At the same time, courts have also intensified the requirements for patent infringement claims.<sup>15</sup> This has been especially prevalent in the case of method patents that involve multiple entities performing each step of the method.<sup>16</sup> However, without the ability to patent their products, many private sector companies refrain from moving forward with product development.<sup>17</sup>

This Comment discusses the ways that patent law jurisprudence falls short in promoting innovation in precision medicine. Section II provides an overview of the diagnostic field and the patent eligibility of diagnostics as well as suggestions for drafting patent-eligible claims for diagnostics. Section III discusses the doctrine of divided infringement, when more than one entity performs steps in a patented method. Section III then argues the limitations placed on patent eligibility for diagnostic method claims render many of these patents unenforceable against infringement. Thus, this Comment suggests that the courts have created a problem where, in order to obtain a patent for a diagnostic, an inventor must include limitations that then make the claims unenforceable. This Comment further argues—in direct conflict with the Precision

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9. *See id.*

10. *The Precision Medicine Initiative*, *supra* note 3.

11. President Obama, Precision Medicine Panel Remarks, *supra* note 1.

12. *See* Marshall Phelps, *Do Patents Really Promote Innovation? A Response to The Economist*, FORBES (Sept. 16, 2015, 2:42 PM), <http://www.forbes.com/sites/marshallphelps/2015/09/16/do-patents-really-promote-innovation-a-response-to-the-economist/#3c79fdb51921> [<https://perma.cc/T6R7-NBVW>] (“[P]atents are *strongly correlated* with increased innovation, knowledge sharing, and economic growth.”).

13. *See infra* Part II.B for a discussion on the limitations courts have placed on patent-eligible subject matter.

14. *See* Timothy R. Holbrook, *Method Patent Exceptionalism*, 102 IOWA L. REV. 1001, 1008 (2017) (arguing that courts have ignored the “technological context” and “carved out processes for exceptional treatment regardless of any potential policy concerns”).

15. *See* Rachel E. Sachs, *Innovation Law and Policy: Preserving the Future of Personalized Medicine*, 49 U.C. DAVIS L. REV. 1881, 1913 (2016) (noting that recent patent infringement case law has made it “more difficult for courts to assign liability”).

16. *See id.* at 1913, 1918 (“[When] treatment steps are by definition performed by physicians, rather than diagnostic laboratories, this is tantamount to requiring applicants to write divided method claims.”).

17. *See* Erik P. Harmon, Note, *Promoting the Progress of Personalized Medicine: Redefining Infringement Liability for Divided Performance of Patented Methods*, 42 HOFSTRA L. REV. 967, 968–69 (2014) (arguing that the “decision to invest in the discovery of useful genetic markers will turn . . . on [the] ability to enforce . . . patent rights against competitors”).

Medicine Initiative—this problem is specific to diagnostics that diagnose either the risk for developing a disease or untreatable diseases.

## II. PATENTING MOLECULAR DIAGNOSTICS

Diagnostic tests provide a patient with personalized information about her specific biological processes so that she can make informed healthcare decisions.<sup>18</sup> The Human Genome Project, which provided the first sequence of an entire human genome, prompted the goal of precision medicine.<sup>19</sup> Accordingly, precision medicine seeks to use information about a patient’s genome as a major factor in preventing, diagnosing, and selecting treatments for a disease.<sup>20</sup> As DNA sequencing technology has advanced, and therefore the price of whole-genome sequencing has reduced,<sup>21</sup> both research and clinical practice have focused heavily on a precision medicine approach.<sup>22</sup>

Part II.A provides an overview of the types of molecular diagnostics and how each type is used in preventing, diagnosing, and selecting treatments for a disease. Part II.B then discusses the patent eligibility of molecular diagnostics. Finally, Part II.C provides an analysis of how to draft claims for molecular diagnostics that are patent eligible.

### A. *Molecular Diagnostics*

Molecular diagnostics are tools used to detect variants in a person’s genetic code.<sup>23</sup> Thus, molecular diagnostics identify biomarkers—genes that are indicators of disease, how a patient will respond to medication, or how a patient’s body is working.<sup>24</sup> Knowledge that a patient has a variant allows physicians to treat the patient more effectively.<sup>25</sup> For example, after knowing a patient has a genetic variant, a physician

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18. See FDA, *supra* note 2, at 29.

19. See NAT’L RESEARCH COUNCIL OF THE NAT’L ACADS., TOWARD PRECISION MEDICINE 77 (2011). The terms “personalized medicine” and “precision medicine” are often used interchangeably to mean “tailoring of medical treatment to the individual characteristics of each patient . . . [by] classify[ing] individuals into subpopulations that differ in their susceptibility to a particular disease, in the biology and/or prognosis of those diseases they may develop, or in their response to a specific treatment.” See *id.* at 124. The term “precision medicine” will be used throughout this Comment.

20. See, e.g., Matthew Meyerson, *Human Genetic Variation and Disease*, 362 LANCET 259, 259 (2003) (discussing the role of single-nucleotide polymorphisms in disease susceptibility and pharmacogenomics).

21. Elizabeth G. Phimister et al., *Realizing Genomic Medicine*, 366 NEW ENG. J. MED. 757, 757 (2012) (estimating the cost of whole-exome and whole-genome sequences to be \$1,000).

22. Jeremy A. Greene & Joseph Loscalzo, *Putting the Patient Back Together—Social Medicine, Network Medicine, and the Limits of Reductionism*, 377 NEW ENG. J. MED. 2493, 2493 (2017) (“In the 21st century, the framework of biomedical research and clinical practice has begun to shift away from universal models of disease . . . toward an approach that celebrates ‘personalized medicine’ and focuses . . . on the whole person as a unit of analysis.”).

23. See George P. Patrinos & Wilhelm J. Ansorge, *Molecular Diagnostics: Past, Present, and Future*, in MOLECULAR DIAGNOSTICS 1, 1 (George P. Patrinos & Wilhelm J. Ansorge eds., 2d ed. 2010).

24. See FDA, *supra* note 2, at 10, 58 (explaining the relationship between molecular diagnostics and biomarkers).

25. See Patrinos & Ansorge, *supra* note 23, at 5. For example, when Angelia Jolie had a mutation in her BRCA1 gene, a biomarker for breast cancer, she therefore had an increased risk for breast cancer. See Jolie, *supra* note 5.

could predict the likelihood that the patient will develop a disease, identify a disease that is causing symptoms, or select a type or dose of a medication that will improve the patient's condition.<sup>26</sup> This Part discusses the different types of molecular diagnostics and provides examples of how molecular diagnostics are currently used in precision medicine. Part II.A.1 describes companion diagnostics. Part II.A.2 describes complementary diagnostics. Part II.A.3 discusses the differences between physician-administered and direct-to-consumer molecular diagnostics.

### 1. Companion Diagnostics

The U.S. Food and Drug Administration (FDA) defines a companion diagnostic as a medical device that “provides information that is essential for the safe and effective use of a corresponding drug or biological product.”<sup>27</sup> Some companion diagnostics identify patients who would respond to a specific treatment, while others identify patients for whom a specific treatment is not recommended.<sup>28</sup> In 1998 the FDA approved the first companion diagnostic, HercepTest.<sup>29</sup> HercepTest measures the level of HER-2, a biomarker for breast cancer.<sup>30</sup> HercepTest is the companion to Herceptin, which treats breast cancer by targeting HER-2, and therefore is only recommended for patients in which HER-2 is overexpressed.<sup>31</sup>

Currently, there are thirty-seven FDA-approved companion diagnostics, and almost all of them are companions to cancer therapeutics.<sup>32</sup> For example, the FDA recently approved Foundation Medicine's companion diagnostic, which identifies mutations in 324 genes to identify patients who would benefit from one or more of eighteen specific cancer therapeutics.<sup>33</sup> However, companies are also beginning to incorporate companion diagnostics into other types of therapeutics, including those for

26. See Patrinos & Ansorge, *supra* note 23, at 8.

27. *Companion Diagnostics*, FDA, <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm407297.htm> [https://perma.cc/A66L-EWAC] (last updated Dec. 7, 2018).

28. See *id.*

29. Letter from Susan Alpert, Dir., Ctr. for Devices and Radiological Health, to Gretchen M. Murray, Assistant Manager, Regulatory Affairs, DAKO Corp. (Sept. 25, 1998), [http://www.accessdata.fda.gov/cdrh\\_docs/pdf/P980018.pdf](http://www.accessdata.fda.gov/cdrh_docs/pdf/P980018.pdf) [https://perma.cc/2TGH-92DG]; see also Agata Zieba et al., *Molecular Tools for Companion Diagnostics*, 29 NEW BIOTECHNOLOGY 634, 634 (2012).

30. See Zieba et al., *supra* note 29, at 634–35.

31. See *HercepTest Identifies Breast Cancer Tumors That Overexpress HER2*, CANCER NETWORK (Oct. 1, 1998), <http://www.cancernetwork.com/breast-cancer/herceptest-identifies-breast-cancer-tumors-overexpress-her2> [https://perma.cc/U8XR-PY88].

32. See *List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools)*, FDA, <http://www.fda.gov/medicaldevices/productsandmedicalprocedures/invitrodiagnostics/ucm301431.htm> [https://perma.cc/8F3L-3L6L] (last updated Oct. 29, 2019). Note that not all diagnostics require FDA approval. See Rebecca Eisenberg & Harold Varmus, *Insurance for Broad Genomic Tests in Oncology*, 358 SCIENCE 1133, 1133 (2017) (noting that the FDA “has declined to [regulate genetic tests] when the same laboratory that develops the tests performs the testing service rather than selling tests to others”).

33. *FoundationOne CDx – P170019*, FDA, <http://www.fda.gov/medical-devices/recently-approved-devices/foundationone-cdx-p170019> [https://perma.cc/JH8L-JQS8] (last updated Dec. 22, 2017); see also FOUND. MED., INC., FOUNDATION ONE CDX 1–4 (2017), [http://www.accessdata.fda.gov/cdrh\\_docs/pdf17/P170019C.pdf](http://www.accessdata.fda.gov/cdrh_docs/pdf17/P170019C.pdf) [https://perma.cc/FK5F-L8VK].

cardiovascular, neurological, and infectious diseases.<sup>34</sup> The market for companion diagnostics is expected to be more than \$7 billion within the next five years, underscoring its importance in personalized healthcare.<sup>35</sup>

## 2. Complementary Diagnostics

Complementary diagnostics include various types of tests that “can improve disease management, early diagnosis, patient risk stratification and drug monitoring related to associated therapeutics.”<sup>36</sup> However, unlike companion diagnostics, complementary diagnostics are not necessarily used in conjunction with specific treatments.<sup>37</sup> Rather, complementary diagnostics can diagnose diseases that do not currently have treatments or assess patients’ risks of developing diseases in the future.<sup>38</sup>

Two of the most significant uses of complementary diagnostics are risk assessment and early diagnosis.<sup>39</sup> For example, women who have certain mutations in BRCA1/2 genes “have up to an 85 percent lifetime chance of developing breast cancer, compared to a 13 percent chance among the general female population.”<sup>40</sup> This information can prompt preventative measures, such as mastectomies, chemoprevention, and earlier and more frequent mammograms.<sup>41</sup>

Similarly, complementary diagnostics can facilitate an early diagnosis<sup>42</sup> or provide a prognosis.<sup>43</sup> In many cases, having a diagnosis can change the course of treatments used and influence lifestyle choices.<sup>44</sup> For example, in one study, the identification of a mutation in the CDK13 gene, which is linked to a congenital heart

34. *Companion Diagnostics Beyond Oncology*, BIOPHARMADIVE (Sept. 28, 2018), <http://www.biopharmadive.com/news/companion-diagnostics-beyond-oncology/533209/> [<https://perma.cc/J8TS-3ZY4>].

35. *See Companion Diagnostics Market Size Is Projected To Be Around US\$ 7 Billion by 2024*, MARKETWATCH (Aug. 20, 2018, 11:15 AM), <http://www.marketwatch.com/press-release/companion-diagnostics-market-size-is-projected-to-be-around-us-7-billion-by-2024-2018-08-20> [<https://perma.cc/VUT8-CMGS>].

36. Christopher-Paul Milne et al., *Complementary Versus Companion Diagnostics: Apples and Oranges?*, 9 BIOMARKERS MED. 25, 26 (2015).

37. *Id.*

38. *See id.* (defining complementary diagnostics as “tests that can improve disease management, early diagnosis, patient risk stratification and drug monitoring related to associated therapeutics, but do not require a regulatory link to a specific therapeutic”).

39. *See* PERSONALIZED MED. COAL., *THE PERSONALIZED MEDICINE REPORT 9* (2017).

40. *Id.*

41. *Id.*

42. *Diagnostic Biomarkers*, PERSONALIZED MED. COALITION, [http://www.personalizedmedicinecoalition.org/Education/Diagnostic\\_Biomarkers](http://www.personalizedmedicinecoalition.org/Education/Diagnostic_Biomarkers) [<https://perma.cc/K7KV-MQFZ>] (last visited Oct. 18, 2019). A diagnostic biomarker is used to “confirm that a patient has a particular health disorder.” *Id.*

43. *Prognostic Biomarkers*, PERSONALIZED MED. COALITION, [http://www.personalizedmedicinecoalition.org/Education/Prognostic\\_Biomarkers](http://www.personalizedmedicinecoalition.org/Education/Prognostic_Biomarkers) [<https://perma.cc/4F92-KPWK>] (last visited Oct. 18, 2019). A prognostic biomarker is used to “indicate how a disease may develop in an individual.” *Id.*

44. *See* Kimberly Splinter et al., *Effect of Genetic Diagnosis on Patients with Previously Undiagnosed Disease*, 379 NEW ENG. J. MED. 2131, 2135–36 (2018).

defect, led to repurposing a known treatment to treat the disease.<sup>45</sup> In other cases, identification of a mutation has led to improved genetic counseling.<sup>46</sup> Complementary diagnostics like these can shorten the “medical odyssey” that frequently occurs in diagnosing diseases.<sup>47</sup> This can lead to improved clinical outcomes.<sup>48</sup>

### 3. Physician-Administered and Direct-to-Consumer Tests

Traditionally, health professionals, including licensed physicians and genetic counselors, have performed genetic testing.<sup>49</sup> Prenatal testing, a common example, tests for a wide variety of diseases and disorders, including trisomy 21 and cystic fibrosis.<sup>50</sup> In the mid-to-late 1990s, Myriad Genetics (Myriad) began offering physicians its testing services for mutations in BRCA1/2 genes.<sup>51</sup> Myriad currently provides several versions of its BRCA diagnostic test for clinicians.<sup>52</sup> After sending a sample for Myriad to test, the physician receives a report that describes the results.<sup>53</sup> Additionally, some reports describe possible prophylactic measures for the physician to consider and discuss with the patient.<sup>54</sup>

In contrast to diagnostic tests ordered by physicians, direct-to-consumer tests are “marketed directly to consumers without the involvement of a health care provider.”<sup>55</sup> These tests are rising in popularity, as more than twelve million people have purchased direct-to-consumer genetic testing services.<sup>56</sup> In 2018 the FDA authorized 23andMe,

45. *See id.* app. at 16.

46. *See id.* app. at 15–28. Genetic counseling teaches patients who have tested positive for a mutation in a biomarker about the significance of the mutation so they can make informed decisions about their healthcare. PERSONALIZED MED. COAL., *supra* note 39, at 42.

47. Splinter et al., *supra* note 44, at 2138.

48. *See id.* at 2135–36.

49. *See Genetic Testing*, AM. MED. ASS’N, <http://www.ama-assn.org/delivering-care/precision-medicine/genetic-testing> [https://perma.cc/82RA-4VTN] (last visited Nov. 11, 2019).

50. Ricki Lewis, *A Brief History of Genetic Testing*, SCI. PROGRESS (May 5, 2008), <http://web.archive.org/web/20190604205028/https://scienceprogress.org/2008/05/a-brief-history-of-genetic-testing/> [https://perma.cc/9RX2-FDS3].

51. E. Richard Gold & Julia Carbone, *Myriad Genetics: In the Eye of the Policy Storm*, 12 GENETICS MED. S39, S42 (Apr. Supp. 2010).

52. *See All Products*, MYRIAD GENETICS, INC., <http://myriad.com/products-services/all-products/overview/> [https://perma.cc/2BD8-YAKM] (last visited Oct. 19, 2019).

53. *See MYRIAD GENETICS, INC., COMPREHENSIVE BRACANALYSIS®: BRCA1 AND BRCA2 ANALYSIS RESULT 1* (2011), [http://d1izdzz43r5o67.cloudfront.net/sample-results/CompBRAC\\_POS.pdf](http://d1izdzz43r5o67.cloudfront.net/sample-results/CompBRAC_POS.pdf) [https://perma.cc/HYK5-L3R2] (sample report).

54. *See MYRIAD GENETICS, INC., GENETIC RESULT – INTEGRATED BRACANALYSIS®: BRCA1 AND BRCA2 ANALYSIS* (2016), <http://s3.amazonaws.com/myriad-library/sample-results/Integrated+BRAC+POS.pdf> [https://perma.cc/2H5W-6ANG] (providing a sample report with management tools for cancer risks specific to a patient’s genetic test results).

55. *Direct-to-Consumer Tests*, FDA, <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm624726.htm> [https://perma.cc/8JBT-BBAD] (last updated Nov. 1, 2018).

56. Ellen Matloff, *Healthcare Providers Can’t Afford To Ignore Direct-to-Consumer Genetic Testing*, FORBES (Apr. 25, 2018, 11:05 AM), <http://www.forbes.com/sites/ellenmatloff/2018/04/25/health-care-providers-cant-afford-to-ignore-direct-to-consumer-genetic-testing> [https://perma.cc/4TFQ-9RKB]. The direct-to-consumer genetic testing boom is due, in part, to the decrease in cost of genome sequencing and to the availability of using genetic testing as a method of genealogy. Scott Bowen & Muin J. Khoury, *Consumer*

one of the leading direct-to-consumer testing companies, to market its tests to consumers to detect their genetic health risks<sup>57</sup> and to identify how their bodies metabolize therapeutics.<sup>58</sup> After sending in a saliva sample, 23andMe sends customers a report describing the results of the genetic variants for which the test screens.<sup>59</sup> If a person has one of these variants, the report describes the disease, discusses how the variant influences the likelihood that she will develop the disease, and instructs her to discuss the results with a healthcare professional.<sup>60</sup>

### B. Molecular Diagnostic Patent Eligibility

Section 101 of Title 35 of the United States Code provides that an inventor may obtain a patent for any novel “process, machine, manufacture, or composition of matter.”<sup>61</sup> Although Congress intended patent-eligible subject matter to “include anything under the sun that is made by man,”<sup>62</sup> an inventor may not obtain a patent for unlimited subject matter. For example, it is well established that mathematical formulae, abstract ideas, and physical phenomena are not patent eligible.<sup>63</sup> This Part discusses the patent eligibility of molecular diagnostic methods and diagnostic testing compositions.

#### 1. Patenting Molecular Diagnostic Methods

Although laws of nature, such as mathematical formulae and natural products, are not patent eligible,<sup>64</sup> a method that uses or involves a law of nature may be patent

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*Genetic Testing Is Booming: But What Are the Benefits and Harms to Individuals and Populations?*, CTRS. FOR DISEASE CONTROL & PREVENTION: GENOMICS & PRECISION HEALTH (June 12, 2018), <http://blogs.cdc.gov/genomics/2018/06/12/consumer-genetic-testing/> [<https://perma.cc/Q4J8-SJV9>].

57. Press Release, U.S. Food & Drug Admin., FDA Authorizes, with Special Controls, Direct-to-Consumer Test That Reports Three Mutations in the BRCA Breast Cancer Genes (Mar. 6, 2018), <http://www.fda.gov/news-events/press-announcements/fda-authorizes-special-controls-direct-consumer-test-reports-three-mutations-brca-breast-cancer> [<https://perma.cc/63BL-54Y8>]; see also Erika Check Hayden, *The Rise, Fall and Rise Again of 23andMe*, 550 NATURE 174, 175 (2017) (“23andme has always been the most visible face of direct-to-consumer genetic testing, and it is more formidable now than ever before.”). 23andMe offers genetic testing to determine risk for developing diseases such as late-onset Alzheimer’s disease, Parkinson’s disease, and breast cancer. *Direct-to-Consumer Tests*, *supra* note 55.

58. See *Direct-to-Consumer Tests*, *supra* note 55.

59. See, e.g., *Parkinson’s Disease*, 23ANDME (Apr. 17, 2017), [http://medical.23andme.com/wp-content/uploads/2017/09/Parkinson\\_one\\_G2019S.pdf](http://medical.23andme.com/wp-content/uploads/2017/09/Parkinson_one_G2019S.pdf) [<https://perma.cc/DU5T-KANJ>] (sample report).

60. See *id.*

61. 35 U.S.C. § 101 (2018).

62. *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980) (quoting S. REP. NO. 82-1979, at 5 (1952)).

63. *Id.* (providing “a new mineral discovered in the earth or a new plant found in the wild” as patent-ineligible subject matter).

64. The often-cited examples of laws of nature include Einstein’s finding of  $E=mc^2$  or Newton’s discovery of the law of gravity. *E.g., id.*

eligible.<sup>65</sup> Rather, if the method as a whole “perform[s] a function which the patent laws were designed to protect,” it is patent-eligible subject matter.<sup>66</sup>

The U.S. Court of Appeals for the Federal Circuit first considered whether diagnostic methods are patent eligible in 1989.<sup>67</sup> The *In re Grams*<sup>68</sup> court considered the patent eligibility of a method that comprises the steps of performing laboratory tests to identify measurements of specific parameters and both the use and analysis of the data to determine the existence of an abnormal condition.<sup>69</sup> The court held that the sole tangible step of performing a laboratory test on a patient to obtain data was insufficient to transform the use of an algorithm into patent-eligible subject matter.<sup>70</sup> Accordingly, the method patent was invalid because it claimed patent-ineligible subject matter.<sup>71</sup>

Courts have used the “machine-or-transformation test” to determine whether a method is patent eligible.<sup>72</sup> The Supreme Court has used the machine-or-transformation test many times to distinguish an abstract idea or natural law from a patent-eligible method that merely involves the abstract idea or natural law.<sup>73</sup> This test requires the patent-eligible method either be “tied to a particular machine” or “transform[] a particular article into a different state or thing.”<sup>74</sup> The Federal Circuit determined that a claimed method must satisfy the machine-or-transformation test to be patent eligible.<sup>75</sup> However, the Supreme Court later clarified in *Bilski v. Kappos*<sup>76</sup> that the machine-or-transformation test is merely one factor to consider when determining

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65. See *Diamond v. Diehr*, 450 U.S. 175, 187–88 (1981) (“[An] equation is not patentable in isolation, but when a process . . . is devised which incorporates it in a more efficient solution of the equation, that process is at the very least not barred at the threshold [of] § 101.”).

66. *Id.* at 192. Courts have repeatedly stated that a patent should be awarded only for “a product of human ingenuity.” *Chakrabarty*, 447 U.S. at 309.

67. See *In re Grams*, 888 F.2d 835, 837 (Fed. Cir. 1989).

68. 888 F.2d 835 (Fed. Cir. 1989).

69. See *In re Grams*, 888 F.2d at 836–37 (describing the challenged patent claim).

70. See *id.* at 839 (“[The] necessary antecedent steps of establishing values for the variables in [an] equation cannot convert the unpatentable method to patentable subject matter.” (quoting *In re Christensen*, 478 F.2d 1392, 1394 (C.C.P.A. 1973))).

71. *Id.* at 840–41.

72. *E.g.*, *Bilski v. Kappos*, 561 U.S. 593, 604 (2010) (“This Court’s precedents establish that the machine-or-transformation test is a useful and important clue, an investigative tool, for determining whether some claimed inventions are processes under § 101.”); *Cochrane v. Deener*, 94 U.S. 780, 788 (1876) (explaining that a method is “an act or series of acts, performed upon the subject-matter to be transformed and reduced to a different state or thing”).

73. See, *e.g.*, *Diamond v. Diehr*, 450 U.S. 175, 191–92 (1981) (clarifying that merely limiting the use to “a particular technological environment” does not impart patent eligibility on an otherwise patent-ineligible process); *Parker v. Flook*, 437 U.S. 584, 594 (1978) (holding that a method for monitoring catalytic conversion conditions in the petrochemical and oil-refining industries is patent ineligible because the “algorithm is assumed to be within the prior art” and therefore “the application, considered as a whole, contains no patentable invention”); *Gottschalk v. Benson*, 409 U.S. 63, 71–72 (1972) (holding that use of an algorithm to convert decimals numbers into binary code is not a patent-eligible method).

74. *In re Bilski*, 545 F.3d 943, 954 (Fed. Cir. 2008) (en banc), *aff’d sub nom. Bilski v. Kappos*, 561 U.S. 593 (2010).

75. *Id.* at 955–56 (noting that the machine-or-transformation test is the sole “test for determining patent eligibility of a process under § 101”).

76. 561 U.S. 593 (2010).



whether a method is patent eligible.<sup>77</sup> Although the machine-or-transformation test was helpful in determining patent eligibility of in the industrial age, it may be insufficient for determining patent eligibility of inventions in the information age (including inventions related to diagnostic testing) because it would require that the method be tied to a specific machine.<sup>78</sup> Although the Court held that patent eligibility of claims involving abstract ideas or natural laws should be assessed with the goal of balancing inventor interests with limiting monopolies over natural laws, it provided little guidance regarding the additional factors to be considered.<sup>79</sup>

Two years later, the Court further refined the inquiry for patent eligibility, specifically in the context of diagnostic methods, in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*<sup>80</sup> Prometheus was the exclusive licensee of a patent claiming a method for optimizing therapeutic efficacy of a treatment.<sup>81</sup> The method included the following steps: (1) administering a drug to a subject having a gastrointestinal disorder, and (2) determining the level of a specific metabolite.<sup>82</sup> The patent claim required that the level of the metabolite indicate a need to change the amount of the drug administered to the subject.<sup>83</sup>

The Court set forth a two-step test to determine whether claims are patent eligible.<sup>84</sup> The first step is to determine whether the claims involve a law of nature.<sup>85</sup> If the claims involve a law of nature, the next step is to determine “whether the claims do significantly more than simply describe these natural relations.”<sup>86</sup> Therefore, claims involving a law of nature are only patent eligible if they (1) include “enough” additional steps or components that apply the law of nature, and (2) consequently “amount[] to significantly more than a patent upon the natural law itself.”<sup>87</sup>

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77. See *Bilski*, 561 U.S. at 604 (“The machine-or-transformation test is not the sole test for deciding whether an invention is a patent-eligible ‘process.’”).

78. See *id.* at 605 (plurality opinion) (“[T]he machine-or-transformation test would create uncertainty as to the patentability of software, advanced diagnostic medicine techniques, and inventions based on linear programming, data compression, and the manipulation of digital signals.”).

79. See *id.* at 605–06 (declining to opine on the patent eligibility of “technologies from the Information Age” but rather providing guidelines for balancing “protecting inventors and not granting monopolies over procedures that others would discover by independent, creative application of general principles”).

80. 566 U.S. 66 (2012).

81. *Mayo*, 566 U.S. at 74–75. Prometheus was the licensee of U.S. Patent Numbers 6,355,623 and 6,680,302. *Id.* Claim one of the 6,355,623 patent was used as the representative claim. *Id.*

82. U.S. Patent No. 6,355,623 col. 4 ll. 7–12 (filed Apr. 8, 1999).

83. *Id.*

84. See *Mayo*, 566 U.S. at 77–80; see also *Alice Corp. v. CLS Bank Int’l*, 573 U.S. 208, 217–21 (2014) (explaining the *Mayo* two-step test); U.S. PATENT & TRADEMARK OFFICE, MANUAL OF PATENT EXAMINING PROCEDURE § 2106 (9th ed. rev. 8., Jan. 2018) (providing guidelines using the *Mayo* two-step test for determining subject matter eligibility).

85. See *Mayo*, 566 U.S. at 77. This step can be extended to other judicial exceptions, such as abstract ideas or physical phenomena. See, e.g., *Alice*, 573 U.S. at 217–21 (applying the *Mayo* two-step test to claims involving an abstract idea).

86. *Mayo*, 566 U.S. at 77.

87. *Id.* at 73, 77 (noting that the critical inquiry is whether the claims include “enough to their statements of the correlations to allow the processes they describe to qualify as patent-eligible processes that apply natural laws”).

The *Mayo* Court determined that the claimed method involved a law of nature—the relationship between metabolites and the dosage of thiopurine that will cause harm.<sup>88</sup> Next, the Court determined whether the claims added additional elements that sufficiently transformed the claims into a patent-eligible method that applied the natural law.<sup>89</sup> To answer this question, the Court first analyzed each limitation of the claimed method separately.<sup>90</sup> The first step of the claimed method<sup>91</sup> merely identified the established audience of physicians who treat autoimmune disorders using a specific class of drugs.<sup>92</sup> The second step of the claimed method<sup>93</sup> involved only the determination of the blood metabolite concentration through any appropriate means.<sup>94</sup> Finally, the “wherein” clauses, which limit the scope of the claim,<sup>95</sup> only described the natural law of the relationship between the metabolite level and appropriate dosage of the drug.<sup>96</sup> The Court determined these steps were routine in the field, established “[pre]-solution activity,” and therefore were insufficient to make an application of a natural law patent eligible.<sup>97</sup>

Even if each step of the method is not patent eligible when read in isolation, the claim as a whole may nonetheless be patent eligible if the combination or order of the steps adds something more to the method that is not embodied by any single step.<sup>98</sup> Here, however, these steps “amount[ed] to nothing significantly more than an instruction to doctors to apply the applicable laws when treating their patients.”<sup>99</sup> The Court explained that adding general, conventional steps to the law of nature did not make the claims patent eligible because the claimed methods “tie up the doctor’s subsequent treatment decision whether that treatment does, or does not, change in light of the inference he has drawn using the correlations.”<sup>100</sup> The Court reasoned this result

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88. *Id.* at 77–80.

89. *Id.*

90. *Id.* at 78–79.

91. Step (a) of claim 1 recited “administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder.” U.S. Patent No. 6,355,623 col. 20 ll. 13–15 (filed Apr. 8, 1999).

92. *See Mayo*, 566 U.S. at 78 (“[D]octors used thiopurine drugs to treat patients suffering from autoimmune disorders long before anyone asserted these claims.”).

93. Step (b) of claim 1 comprised “determining the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder.” ‘623 Patent col. 20 ll. 16–17.

94. *Mayo*, 566 U.S. at 78–79 (noting that the physician may determine the metabolite levels “through whatever process the doctor or the laboratory wishes to use” and that the “methods for determining metabolite levels were well known in the art”).

95. The “wherein” clauses of claim 1 described that when the level of the 6-thioguanine is “less than about 230 pmol per  $8 \times 10^8$  red blood cells[ ], it] indicates a need to increase the amount of said drug,” while when the level of the 6-thioguanine is “greater than about 400 pmol per  $8 \times 10^8$  red blood cells[ ], it] indicates a need to decrease the amount of said drug subsequently administered to said subject.” ‘623 Patent col. 20 ll. 18–24.

96. *See Mayo*, 566 U.S. at 78 (“[T]hese clauses tell the relevant audience about the laws while trusting them to use those laws appropriately where they are relevant to their decisionmaking.”).

97. *Id.* at 79–80 (alteration in original) (quoting *Parker v. Flook*, 437 U.S. 584, 590 (1978)).

98. *See id.* at 79 (noting that a combination of steps may be patent eligible even if each of the steps themselves were “well known and in common use before the combination was made” (quoting *Diamond v. Diehr*, 450 U.S. 175, 188 (1981))).

99. *Id.*

100. *Id.* at 86–87.

is contrary to the underlying policy of patents because it “threaten[s] to inhibit the development” of specific treatment regimens, and therefore the claimed methods are not patent-eligible subject matter.<sup>101</sup>

In the wake of *Mayo*, the Federal Circuit has considered the types of steps that add “something more” to a diagnostic method claim.<sup>102</sup> For example, the court considered the patent eligibility of a claimed method of determining the risk of fetal Down’s syndrome, which included (1) measuring the level of a biomarker, and (2) determining the risk of Down’s syndrome by comparing the level of the biomarker to the level of a control.<sup>103</sup> The Federal Circuit held that the method was not patent eligible because the relationship between the risk of fetal Down’s syndrome and the biomarker level is “an eternal truth that ‘exists in principle apart from any human action.’”<sup>104</sup> The court stressed that the claimed method, as a whole, did not require the “doctor [to] act on the calculated risk.”<sup>105</sup>

Similarly, the Federal Circuit held a method for detecting paternally inherited DNA patent ineligible.<sup>106</sup> The method included two steps: (1) “amplifying [the] paternally inherited nucleic acid from [maternal] serum,” and (2) “detecting the presence of [the] paternally inherited nucleic acid.”<sup>107</sup> The court reasoned that the method was patent ineligible because it was based on a natural phenomenon, fetal DNA in the serum of pregnant women, and the routine nature of the steps of amplifying and detecting DNA did not add enough to make the claim patent eligible.<sup>108</sup>

In contrast, *Vanda Pharmaceuticals Inc. v. West-Ward Pharmaceuticals International Ltd.*<sup>109</sup> held a method of diagnosing and treating a patient with schizophrenia patent eligible.<sup>110</sup> The Vanda patent claimed a method for treating a schizophrenic patient with a specific drug using the following steps: (1) determining whether the patient is a poor metabolizer via a diagnostic test, (2) administering a low dose of the drug if the patient is a poor metabolizer, and (3) administering a higher dose of the drug if the patient is not a poor metabolizer.<sup>111</sup> However, the court held that the Vanda claims were patent eligible because they were not “directed to patent-ineligible subject matter.”<sup>112</sup> First, the court distinguished this case from *Mayo* because the

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101. *Id.*

102. *See, e.g., Vanda Pharm. Inc. v. West-Ward Pharm. Int’l Ltd.*, 887 F.3d 1117 (Fed. Cir. 2018), *petition for cert. filed sub. nom., Hikma Pharm. USA Inc. v. Vanda Pharm. USA Inc.*, 2018 WL 6819525 (U.S. Dec. 20, 2018) (No. 18-817); *Cleveland Clinic Found. v. True Health Diagnostics LLC*, 859 F.3d 1352 (Fed. Cir. 2017); *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015); *PerkinElmer, Inc. v. Intema Ltd.*, 496 F. App’x 65 (Fed. Cir. 2012).

103. *Intema*, 496 F. App’x at 69–70.

104. *Id.* at 70–71 (quoting *Mayo*, 566 U.S. at 77).

105. *Id.* at 71.

106. *Ariosa*, 788 F.3d at 1378.

107. *Id.* at 1373–74.

108. *Id.* at 1376–77.

109. 887 F.3d 1117 (Fed. Cir. 2018), *petition for cert. filed sub. nom., Hikma Pharm. USA Inc. v. Vanda Pharm. USA Inc.*, 2018 WL 6819525 (U.S. Dec. 20, 2018) (No. 18-817).

110. *Vanda*, 887 F.3d at 1135–36.

111. U.S. Patent No. 8,586,610 col. 17 ll. 5–20 (filed Sept. 30, 2005).

112. *Vanda*, 887 F.3d at 1134.

Vanda patent was directed to a method of treating a disease.<sup>113</sup> In contrast, the Mayo patent claims were “directed to a diagnostic method based on the ‘relationships between concentrations of certain metabolites . . . and the likelihood that a dosage . . . will prove ineffective or cause harm.’”<sup>114</sup> Thus, it was important that the claims were “directed to a method of using iloperidone to treat schizophrenia.”<sup>115</sup>

The court further distinguished *Mayo* by explaining that the Vanda patent claims did not “tie up the doctor’s subsequent treatment decision.”<sup>116</sup> The Mayo patent claims merely recited that a certain result “‘indicate[d]’ a need to increase or decrease a [specific dosage]” while the Vanda patent claims recited the step of *using* the results of the diagnostic test to carry out a dosage regimen.<sup>117</sup> Thus, the presence of this additional step transformed the method into a method of using the drug in a safer or more effective manner rather than merely one that required a physician to generically apply a law of nature.<sup>118</sup>

## 2. Patenting Compositions for Use in Diagnostic Testing

While patents claiming diagnostic methods protect the *method* of diagnosing and/or treating a disease or disorder, diagnostic composition claims intend to protect the *sequence* of the molecule that the diagnostic method is based upon or a reagent for use in the diagnostic method.<sup>119</sup> However, when the molecule is a product of nature or is derived from a product of nature, these claims may also be patent-ineligible subject matter.<sup>120</sup> Genes, which are often the biomarker analyzed in diagnostic methods,<sup>121</sup> do not exist in isolation, but rather exist as part of the DNA of chromosomes.<sup>122</sup> Therefore, the question becomes whether isolation of a product that exists in nature is patent-eligible subject matter.

Myriad discovered that mutations in BRCA1/2 genes resulted in a significantly increased susceptibility to cancer and owned several patents claiming specific

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113. *See id.*

114. *Id.* (quoting *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66, 77 (2012)).

115. *See id.* at 1134–35 (“This case, however, is not *Mayo*. . . [T]he claims in *Mayo* were not directed to a novel method of treating a disease.”).

116. *Id.* at 1135 (quoting *Mayo*, 566 U.S. at 86).

117. *Id.* (quoting *Mayo*, 566 U.S. at 75).

118. *See id.* The claimed method of treating schizophrenia requires steps of determining a patient’s CYP2D6 genotype via a genotype assay and administering iloperidone at specific dosages depending on the result of the assay. *Id.* at 1134. The requirement of administering a specific dose of iloperidone transforms the natural phenomenon of the relationship between the CYP2D6 genotype and iloperidone into patent-eligible subject matter because the claims are now “‘a new way of using an existing drug’ that is safer for patients because it reduces the risk of” side effects. *Id.* at 1135 (quoting *Mayo*, 566 U.S. at 87).

119. For example, a method may be claimed by including a step of determining the sequence of a gene in a biological sample, while a corresponding composition claim would be directed toward the specific sequence of the gene. *See, e.g.*, U.S. Patent Application No. 11/126,385 (filed May 10, 2005) (claiming a diagnostic polypeptide marker and a method of diagnosing renal disease by measuring the polypeptide in urine).

120. *See* Dan L. Burk, *The Curious Incident of the Supreme Court in Myriad Genetics*, 90 NOTRE DAME L. REV. 505, 513–17 (2014) (discussing the differences between laws of nature and products of nature).

121. *See supra* Part II.A for a discussion of diagnostic methods.

122. Helen Pearson, *What Is a Gene?*, 441 NATURE 398, 399 (2006).

BRCA1/2 sequences.<sup>123</sup> Myriad offered three levels of BRCA testing: (1) identifying whether a person had a specific mutation, (2) identifying whether a person had any of the three most common types of that specific mutations, and (3) sequencing the entire BRCA1/2 genes.<sup>124</sup> Myriad aggressively enforced its patents; it sent cease and desist letters to institutions that also provided BRCA testing and notified others that planned to provide BRCA testing to its patients.<sup>125</sup> As a result of Myriad's ardent patent enforcement, the American Civil Liberties Union represented twenty plaintiffs seeking a declaratory judgment that Myriad's patents were invalid because they were directed toward patent-ineligible subject matter.<sup>126</sup>

In reviewing the patent eligibility of isolated DNA, the Supreme Court reaffirmed the *Mayo* holding that laws of nature cannot be patented.<sup>127</sup> In *Association for Molecular Pathology v. Myriad Genetics, Inc.*,<sup>128</sup> the Court did not use the two-step *Mayo* test to determine eligibility, but rather confined its analysis to whether the sequence was "naturally occurring."<sup>129</sup> Myriad's patents claimed both genomic DNA (gDNA)<sup>130</sup> and complementary DNA (cDNA),<sup>131</sup> which encode the BRCA protein.<sup>132</sup> With respect to the gDNA sequence, the Court found that "Myriad did not create anything" and that "separating [a] gene from its surrounding genetic material is not an act of invention."<sup>133</sup> Even though the isolation of the gDNA sequence "severs chemical bonds and thereby creates a nonnaturally occurring molecule," the difference in chemical structure is unimportant to the claim, which is concerned with the information stored within the DNA sequence.<sup>134</sup> In contrast, the Court found that "cDNA does not present the same obstacles" because it is artificially created and is distinct from the DNA sequence found in nature.<sup>135</sup> Accordingly, the *Myriad* Court held that while

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123. *E.g.*, U.S. Patent No. 5,837,492 (filed Apr. 29, 1996); U.S. Patent No. 5,747,282 (filed June 7, 1995); U.S. Patent No. 5,693,473 (filed June 7, 1995).

124. Jorge L. Contreras, *Narratives of Gene Patenting*, 43 FLA. ST. U. L. REV. 1133, 1146 (2016).

125. *Id.* at 1145–46 (noting that at least nine facilities discontinued BRCA testing as a result of Myriad's patents).

126. Sandra S. Park, *Gene Patents and the Public Interest: Litigating Association for Molecular Pathology v. Myriad Genetics and Lessons Moving Forward*, 15 N.C. J.L. & TECH. 519, 527, 529 (2014) ("We represented twenty plaintiffs: four national associations of pathologists and geneticists; six individual geneticists; two genetic counselors; two breast cancer and women's health groups; and six patients.").

127. *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 589 (2013).

128. 569 U.S. 576 (2013).

129. *Myriad*, 569 U.S. at 580; *see also* Burk, *supra* note 120, at 506 (noting that the relationship between *Mayo* and *Myriad* "remains unarticulated").

130. Genomic DNA is DNA that is isolated from cells or is identical to DNA in cells. *See Complementary DNA*, A DICTIONARY OF BIOLOGY (Elizabeth Martin & Robert Hine eds., 7th ed. 2015) (ebook); *Genome*, A DICTIONARY OF BIOLOGY (Elizabeth Martin & Robert Hine eds., 7th ed. 2015) (ebook).

131. Complementary DNA is a "form of DNA prepared in the laboratory[,] . . . [which] unlike genomic DNA, . . . contains no noncoding sequences." *Complementary DNA*, *supra* note 130.

132. *Myriad*, 569 U.S. at 584 (noting that Myriad claimed an isolated DNA coding for the wild-type BRCA1 protein, which encompasses the gDNA sequence and an isolated cDNA sequence encoding the wild-type BRCA1 protein that does not include introns).

133. *Id.* at 591.

134. *Id.* at 593.

135. *Id.* at 594–95. The Court distinguished cDNA as not occurring in nature because cDNA does not include introns. *See id.*

gDNA is patent ineligible because it is a “product of nature,” cDNA is distinct from a natural product and is therefore patent eligible.<sup>136</sup>

Following the Supreme Court’s lead, the Federal Circuit similarly found that primers—small, single-stranded DNA molecules that are used to sequence a gene or a region of a gene—were patent ineligible because they “claim the same nucleotide sequence as naturally occurring DNA.”<sup>137</sup> The Federal Circuit explained that primers do not have “a unique structure, different from anything found in nature” because primers are segments of the naturally occurring nucleic acid sequence and use DNA’s inherent ability to bind to a complementary strand of DNA.<sup>138</sup> Accordingly, the primers were not patent-eligible subject matter.<sup>139</sup>

### C. *Satisfying Section 101: Claim Limitations*

Little clarity has been provided as to the types of claim limitations that are sufficient to satisfy the “something more” inquiry under the *Mayo/Myriad* framework.<sup>140</sup> Since the Court decided *Myriad* in 2013, in cases involving Section 101 challenges, those in which the adverse party asserts the claims are invalid for not being patent-eligible subject matter under Section 101, the Federal Circuit has only upheld claims as being directed toward patent-eligible subject matter in eighteen out of 143 selected cases.<sup>141</sup> However, some guidance can be pulled from *Vanda*<sup>142</sup> and the United States Patent and Trademark Office’s (USPTO) administrative guidelines.<sup>143</sup> The USPTO provides eligibility guidance, which gives examples of claims and eligibility analyses in a variety of technical areas.<sup>144</sup> While not binding,<sup>145</sup> these guidelines give

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136. *Id.* at 580.

137. *In re BRCA1- and BRCA2-Based Hereditary Cancer Test Patent Litig.*, 774 F.3d 755, 758–59 (Fed. Cir. 2014). The Federal Circuit analyzed a single representative claim from Myriad’s U.S. Patent No. 5,747,282:

A pair of single-stranded DNA primers for determination of a nucleotide sequence of a BRCA1 gene by a polymerase chain reaction, the sequence of said primers being derived from human chromosome 17q, wherein the use of said primers in a polymerase chain reaction results in the synthesis of DNA having all or part of the sequence of the BRCA1 gene.

*Id.* at 759 (quoting U.S. Patent No. 5,747,282 col. 155 ll. 23–29 (filed June 7, 1995)).

138. *See id.* at 761.

139. *Id.*

140. *See, e.g.*, Joyce C. Li, Note, *Preemption, Diagnostics, and the Machine-or-Transformation Test: Federal Circuit Refinement of Biotech Method Eligibility*, 32 BERKELEY TECH. L.J. 379, 389 (2017) (“[Patent eligibility] remains a gray area despite the Court’s attempts to clarify the doctrine . . .”).

141. *See Subject Matter Eligibility Court Decisions*, U.S. PAT. & TRADEMARK OFF., [http://www.uspto.gov/sites/default/files/documents/ieg-sme\\_crt\\_dec.xlsx](http://www.uspto.gov/sites/default/files/documents/ieg-sme_crt_dec.xlsx) [https://perma.cc/8UF6-LAAX] (last updated Oct. 3, 2019).

142. *See Vanda Pharm. Inc. v. West-Ward Pharm. Int’l Ltd.*, 887 F.3d 1117, 1133–36 (Fed. Cir. 2018) (explaining and applying the Supreme Court’s two-step framework to determine patent subject matter eligibility under Section 101), *petition for cert. filed sub. nom.*, *Hikma Pharm. USA Inc. v. Vanda Pharm. Inc.*, 2018 WL 6819525 (U.S. Dec. 20, 2018) (No. 18-817).

143. *See* 2019 Revised Patent Subject Matter Eligibility Guidance, 84 Fed. Reg. 50 (Jan. 7, 2019).

144. *Subject Matter Eligibility*, U.S. PAT. & TRADEMARK OFF., <http://www.uspto.gov/patent/laws-and-regulations/examination-policy/subject-matter-eligibility> [https://perma.cc/8CQE-DCMT] (last updated Oct. 17, 2019).

tangible examples of patent-eligible subject matter under the *Mayo/Myriad* analysis.<sup>146</sup> From the life sciences examples, two strategies emerge: (1) specific methods of detection, discussed in Part II.C.1; and (2) methods of treatment, discussed in Part II.C.2.<sup>147</sup>

### 1. Specific Methods of Detection

One strategy for protecting diagnostic methods is to claim a method of detecting the biomarker.<sup>148</sup> The USPTO gives two examples of method of detection claims, which it deems to be directed toward patent-eligible subject matter.<sup>149</sup> First, the eligibility guidelines provide an example based on Myriad's BRCA1/2 discovery.<sup>150</sup> A method for identifying a BRCA1 mutation by comparing the sequence of the BRCA1 gene isolated from a sample to the wild type is not patent eligible because it "merely requires a comparison of two pieces of information."<sup>151</sup> In contrast, a claim is patent eligible when it includes a detection or amplification step that was not used as a "routine or conventional" technique for detecting or amplifying DNA.<sup>152</sup>

When unconventional steps are included in a method claim, the patent owner cannot exclude others from using other routine steps to analyze the biomarker.<sup>153</sup> For example, consider the USPTO's example of using a nonconventional method to amplify DNA in the sequencing of BRCA1.<sup>154</sup> A competitor could simply use traditional polymerase chain reaction (PCR) to determine the BRCA1 sequence,

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145. *Cleveland Clinic Found. v. True Health Diagnostics LLC*, 760 F. App'x 1013, 1020 (Fed. Cir. 2019) ("While we greatly respect the [US]PTO's expertise on all matters relating to patentability, including patent eligibility, we are not bound by its guidance."); see also Courtenay C. Brinckerhoff & Jennifer L. Best-Martin, *Federal Circuit Finds Detection Claims Invalid Under 101*, FOLEY & LARDNER LLP: PHARMAPATENTS (Oct. 11, 2018), <http://www.pharmapatentsblog.com/2018/10/11/federal-circuit-invalidates-detection-claims-under-101/> [<https://perma.cc/9NZG-UKB2>] (noting that the Federal Circuit recently published a decision that appears to contradict claim 1 of example 29).

146. See U.S. PATENT & TRADEMARK OFFICE, SUBJECT MATTER ELIGIBILITY EXAMPLES: LIFE SCIENCES 9–16, 23–28 (2016), <http://www.uspto.gov/sites/default/files/documents/ieg-may-2016-ex.pdf> [<https://perma.cc/C36W-E2T6>].

147. Example 29 "illustrates the application of the significantly more analysis to diagnostic and treatment claims using a hypothetical disease," *id.* at 9, and example 31 demonstrates the analysis for methods of "[s]creening [f]or [g]ene [a]lterations," *id.* at 23.

148. See *id.* at 9–11, 26–28.

149. See *id.*

150. See *id.* at 23–28. See also *supra* Part II.B.2 for a discussion of Myriad's BRCA1 discovery and patent litigation.

151. U.S. PATENT & TRADEMARK OFFICE, *supra* note 146, at 25 (citing *Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office*, 689 F.3d 1303 (Fed. Cir. 2012), *aff'd in part, rev'd in part on other grounds sub nom.* *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576 (2013)). The Federal Circuit evaluated the exemplary claim during the BRCA1/2 patent litigation and struck it down as being directed toward patent-eligible subject matter. *Id.* at 23–25.

152. *Id.* at 26–28.

153. See *id.* (distinguishing method claims that are patent eligible from those that are merely routine or conventional); Michael R. Woodward, Note, *Amending Alice: Eliminating the Undue Burden of "Significantly More,"* 81 ALB. L. REV. 329, 354–56 (2018) (arguing that the *Mayo* and *Alice* standard blurs the patent-eligibility requirement of patent-eligible subject matter with the patent-eligibility requirements of novelty and nonobviousness).

154. See U.S. PATENT & TRADEMARK OFFICE, *supra* note 146, at 27–28.

thereby circumventing the diagnostic method patent.<sup>155</sup> In fact, should an inventor discover a novel and nonobvious method of analyzing a biomarker, it may be more advantageous to claim a method that is silent as to the analysis of any one specific biomarker.<sup>156</sup>

The USPTO also notes that there are some methods of detection that do not involve a judicial exception.<sup>157</sup> For example, a claim directed to a method of detecting a protein in a patient does “not recite or describe” a natural law when it (1) obtains a plasma sample; and (2) contacts the protein with a reagent, such as an antibody, to detect binding between the reagent and the protein.<sup>158</sup> The USPTO interprets *Mayo* to mean that the specific steps of administering and determining “are not themselves natural laws,” and therefore a claim reciting these steps is not directed toward a natural law.<sup>159</sup>

Claims that do not involve a judicial exception, while subject to some of the same concerns as including unconventional steps in a claim for identifying a mutation,<sup>160</sup> can be tailored to identify specific mutations in a specific gene and therefore can be valuable diagnostic method claims.<sup>161</sup> However, courts have been hesitant to embrace these types of claims.<sup>162</sup> In *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*,<sup>163</sup> the Federal Circuit struck down claims for detecting fetal DNA, which circulates in the mother’s blood.<sup>164</sup> Fetal DNA can be used to determine characteristics of the fetus noninvasively.<sup>165</sup> However, the court held that the method was nothing more than merely a “general instruction to doctors to apply routine, conventional techniques when seeking to detect [fetal DNA].”<sup>166</sup> Similarly, the Federal Circuit held a claim as patent ineligible that was directed to a method for identifying an elevated metabolite concentration that included the steps of (1) contacting the sample with an antibody,

155. *See id.*

156. A claim to a new method of analyzing nucleic acids or proteins could be applied broadly to all biomarkers.

157. *See* U.S. PATENT & TRADEMARK OFFICE, *supra* note 146, at 11.

158. *Id.*

159. *Id.* (quoting *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66, 78 (2012)).

160. *See supra* notes 153–156 and accompanying text for a discussion of the criticisms of requiring unconventional steps in patent claims.

161. *See* U.S. PATENT & TRADEMARK OFFICE, *supra* note 146, at 10–11. Example 29 describes that a claim comprising the steps of (1) obtaining a sample and (2) detecting whether a specific biomarker is present is “not directed to an exception . . . and is [patent] eligible.” *Id.*

162. *See, e.g.*, *Cleveland Clinic Found. v. True Health Diagnostics, LLC*, 760 F. App’x 1013, 1017–18 (Fed. Cir. 2019) (holding Cleveland Clinic’s claims were “directed to the natural law that blood MPO levels correlate with atherosclerotic CVD,” even though the claims recited “a method of detecting elevated MPO”); *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1373–74, 1377 (Fed. Cir. 2015).

163. 788 F.3d 1371 (Fed. Cir. 2015).

164. *Ariosa*, 788 F.3d at 1377.

165. *See id.* at 1373 (noting that the patented invention “created an alternative for prenatal diagnosis of fetal DNA that avoids the risks of widely-used techniques that took samples from the fetus or placenta”).

166. *Id.* at 1373–74, 1377 (striking down a claim which required “[a] method for detecting a paternally inherited nucleic acid of fetal origin performed on a maternal serum or plasma sample from a pregnant female, which method comprises amplifying a paternally inherited nucleic acid from the serum or plasma sample and detecting the presence of a paternally inherited nucleic acid of fetal origin in the sample” (quoting U.S. Patent No. 6,258,540 col. 23 ll. 61–67)).



(2) detecting the level of the metabolite, and (3) comparing the levels to a standard.<sup>167</sup> The court noted that a “rephrasing of the claims does not make them less directed to a natural law.”<sup>168</sup> Thus, the distinction that the claimed method was directed to a technique for detecting the metabolite was “overly superficial” and merely rephrased a natural law.<sup>169</sup>

Further, in *Roche Molecular Systems, Inc. v. CEPHEID*,<sup>170</sup> the Federal Circuit invalidated method claims that required the physician to use discrete reagents for detecting a biomarker.<sup>171</sup> Roche’s patent claimed a method for detecting a bacterium using specific reagents that bind to the bacterium’s DNA.<sup>172</sup> The court held the patent invalid because it “exploit[ed] the . . . law of nature” that the reagent bound to the target biomarker.<sup>173</sup>

The reactions to *Ariosa* and *CEPHEID* were critical.<sup>174</sup> In a concurring opinion in *CEPHEID*, Judge O’Malley expressed concern that the underlying holdings in *Myriad* and *In re BRCA1- and BRCA2-Based Hereditary Cancer Test Patent Litigation*<sup>175</sup> were broad and should be revisited.<sup>176</sup> While the legal and scientific communities may advocate for refining the Section 101 doctrine, the Supreme Court seems uninterested in hearing another subject matter eligibility case any time soon, as it frequently denies certiorari for questions involving patent subject matter eligibility.<sup>177</sup>

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167. *Cleveland Clinic*, 760 F. App’x at 1016–18.

168. *Id.* at 1019.

169. *Id.* at 1018–19.

170. 905 F.3d 1363 (Fed. Cir. 2018).

171. *CEPHEID*, 905 F.3d at 1372–74.

172. *Id.* at 1365–66.

173. *Id.* at 1372–74 (invalidating a method of detecting *Mycobacterium tuberculosis* comprising the steps performing PCR using one of eleven enumerated primers and detecting “the presence or absence of a PCR amplification product”).

174. See, e.g., Brinckerhoff & Best-Martin, *supra* note 145 (noting that it is troubling the court’s “analysis comments on the naturally occurring state of the biological sample and reminds us of their finding that the primers used in the methods are ‘indistinguishable’ from naturally occurring segments of DNA”); Thomas Goldstein, *Ariosa v. Sequenom: Dire Consequences for Biomedicine Require Rehearing En Banc by CAFC*, IPWATCHDOG (Sept. 13, 2015), <http://www.ipwatchdog.com/2015/09/13/ariosa-v-sequenom-dire-consequences-for-biomedicine-require-rehearing-en-banc-by-cafc/id=61415/> [https://perma.cc/9AEP-BKEP] (“The ironic result will be that a ‘preemption’ doctrine designed to ensure that fundamental discoveries remain a public good will instead prevent them from being made or taught to the world.”); Kevin E. Noonan, *Roche Molecular Systems, Inc. v. Cepheid* (*Fed. Cir. 2018*), PATENT DOCS (Oct. 10, 2018), <http://www.patentdocs.org/2018/10/roche-molecular-systems-inc-v-cepheid-fed-cir-2018.html> [https://perma.cc/6B33-ANVK] (arguing that courts have held that claims using nucleic acids are patent ineligible “despite lip service to a mythic ‘something more’ that would distinguish a patent-eligible method”).

175. 774 F.3d 755 (Fed. Cir. 2014).

176. *CEPHEID*, 905 F.3d at 1381 (O’Malley, J., concurring).

177. See Gene Quinn & Steve Brachmann, *Supreme Court Denies Cert in Two-Way Media v. Comcast, Refuses Another 101 Case*, IPWATCHDOG (Oct. 18, 2018), <http://www.ipwatchdog.com/2018/10/18/supreme-court-denies-cert-two-way-media-v-comcast/id=102398/> [https://perma.cc/63JD-CCGE].

## 2. Methods of Treatment

A second strategy in protecting diagnostic methods is to claim a method of treating a subject that tests positive for a specific biomarker.<sup>178</sup> Method of treatment claims have a longstanding history of patent eligibility.<sup>179</sup> Accordingly, because methods of treating diseases have been squarely adopted as patent-eligible subject matter, courts may be more receptive to patents claiming diagnostic methods so long as they are accompanied by a treatment.<sup>180</sup> This is consistent with *Mayo*'s requirement that the claims must "do more than simply state the law of nature while adding the words 'apply it.'"<sup>181</sup> The Federal Circuit in *PerkinElmer, Inc. v. Intema Ltd.*<sup>182</sup> further noted that a method of treatment claim that does not "require[] that a doctor act on the calculated risk" that the diagnostic method establishes is not patent eligible.<sup>183</sup>

The USPTO provides two examples of patent-eligible methods of "diagnosing and treating" a disease or disorder where the subject is diagnosed after detection of a specific biomarker in a biological sample and is then administered a treatment for the disease or disorder.<sup>184</sup> In one example, the claim comprises diagnosing the subject with a disease or disorder and then administering vitamin D to the subject.<sup>185</sup> The step of administering vitamin D transforms the method into patent-eligible subject matter because, in the hypothetical disease, administering vitamin D is not conventionally used to treat the disease.<sup>186</sup> Thus, one option is to add an "administering" step that is somehow unconventional or inventive in view of the current treatments for the disease.<sup>187</sup>

This type of claim limitation works well for companion diagnostics that analyze biomarkers to identify patients who will respond positively or negatively to a given drug.<sup>188</sup> Thus, companion diagnostics provide administering steps and are therefore patent eligible because they treat only the specific patient population for which the

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178. See U.S. PATENT & TRADEMARK OFFICE, *supra* note 146, at 10–11, 14–15.

179. See Todd Martin, *Patentability of Methods of Medical Treatment: A Comparative Study*, 82 J. PAT. & TRADEMARK OFF. SOC'Y 381, 400 (2000) ("[T]he patent laws of the U.S. regarding patentability of methods of medical treatment are very liberal.").

180. See *Vanda Pharm. Inc. v. West-Ward Pharm. Int'l Ltd.*, 887 F.3d 1117, 1136 (Fed. Cir. 2018) (holding patent-eligible claims were "directed to a specific method of treatment for specific patients using a specific compound at specific doses to achieve a specific outcome"), *petition for cert. filed sub. nom.*, *Hikma Pharm. USA Inc. v. Vanda Pharm. Inc.*, 2018 WL 6819525 (U.S. Dec. 20, 2018) (No. 18-817); *Rapid Litig. Mgmt. Ltd. v. CellzDirect, Inc.*, 827 F.3d 1042, 1048–49 (Fed. Cir. 2016) (noting that patents for methods of "treating cancer with chemotherapy . . . or treating headaches with aspirin" claim "processes to achieve a desired outcome").

181. *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66, 72 (2012).

182. 496 F. App'x 65 (Fed. Cir. 2012).

183. *Intema*, 496 F. App'x at 71.

184. See U.S. PATENT & TRADEMARK OFFICE, *supra* note 146, at 10–11, 14–15 (explaining that the additional step of "administering an effective amount of anti-tumor necrosis factor (TNF) antibodies to the diagnosed patient" or "administering an effective amount of topical vitamin D to the diagnosed patient" transforms the law of nature into patent-eligible subject matter).

185. *Id.* at 14.

186. *Id.*

187. See *id.*

188. See *supra* Part II.A.1 for a discussion of companion diagnostics.

therapeutics are effective.<sup>189</sup> For example, Foundation Medicine's companion diagnostic identifies mutations in a gene associated with lung cancer to predict patients who would respond to non-small cell lung cancer treatments afatinib, gefitinib, and erlotinib.<sup>190</sup> A method claim that incorporates a step for detecting the genetic mutation and a step of administering one of these treatments when the mutation is detected adds an additional step that transforms the claim into patent-eligible subject matter.<sup>191</sup>

In the second example, the claim comprises diagnosing the subject with a disease or disorder and then administering a specific antibody to the subject.<sup>192</sup> While administering the antibody was previously known to treat the disease, the claim as a whole "integrate[s] the [natural law] into the diagnostic and treatment process, and amount[s] to more than merely diagnosing . . . and instructing a doctor to generically 'treat it.'"<sup>193</sup> Thus, another option to ensure patent eligibility is to include an administering step in the method claim, even if the step is not unconventional or inventive in view of the current treatments.<sup>194</sup> The administering step meaningfully limits using the law of nature so that there is a correlation between a specific biomarker and the presence or likelihood of developing a disease.<sup>195</sup>

Unlike companion diagnostics, complementary diagnostics are not necessarily used in combination with specific treatments.<sup>196</sup> For example, some complementary diagnostics can detect diseases before traditional clinical exams would be able to or can detect diseases that clinical exams are unable to detect.<sup>197</sup> For these types of complementary diagnostics, claims directed toward complementary diagnostic methods could be written to include treatment steps that encompass many treatments of the diseases.<sup>198</sup>

Complementary diagnostics also include tests that assess the risk that the patient will develop a disease or disorder.<sup>199</sup> For example, Myriad offers a diagnostic test to identify mutations in BRCA1/2 genes.<sup>200</sup> Women who have certain mutations in

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189. See *supra* notes 28–33 and accompanying text for examples of companion diagnostics that identify appropriate patients for treatment.

190. FOUND. MED., INC., *supra* note 33, at 1.

191. *Cf.*, e.g., U.S. PATENT & TRADEMARK OFFICE, *supra* note 146, at 14–15 (concluding that steps of administering an unconventional treatment or a specific treatment transforms the claim into patent-eligible subject matter). It is important to note that these claims, even if directed toward patent-eligible subject matter, still need to meet the requirements of novelty and nonobviousness to be patent eligible. See 35 U.S.C. §§ 102–03 (2018).

192. U.S. PATENT & TRADEMARK OFFICE, *supra* note 146, at 15.

193. *Id.*

194. *See id.*

195. *See id.*

196. Milne et al., *supra* note 36, at 26.

197. *See* Splinter et al., *supra* note 44, at 2131 (describing the results of genetic testing on patients who "have an undiagnosed condition despite thorough evaluation by a health care provider").

198. *See* U.S. PATENT & TRADEMARK OFFICE, *supra* note 146, at 15 (providing an example of a diagnostic method for diagnosing a disease that was difficult to diagnose with traditional clinical examination).

199. *See* Milne et al., *supra* note 36, at 26.

200. *See supra* notes 51–54 and accompanying text for a brief discussion of Myriad's diagnostic tests. Myriad attempted to protect this test by claiming nucleic acids encoding BRCA1/2 genes and isolated BRCA1/2 proteins, as well as the nucleic acid primers used to sequence the genes. U.S. Patent No. 5,837,492

BRCA1/2 genes, and therefore have an increased risk of developing breast cancer, can undertake preventative measures to reduce the likelihood of developing breast cancer.<sup>201</sup> Exemplary preventative measures include mastectomies, chemoprevention, and earlier and more frequent mammograms.<sup>202</sup> To capture diagnostic methods for determining the patient's risk of developing a disease or disorder, the claim must include some active steps on the part of the physician that she performs specifically *because* the patient has the increased risk of developing the disease or disorder.<sup>203</sup> Indeed, the USPTO has allowed claims that include a step of "administering . . . active surveillance."<sup>204</sup> These patents define active surveillance as "observation and regular monitoring without invasive treatment."<sup>205</sup> However, these terms could be modified to encompass all types of preventative treatment.<sup>206</sup>

### III. ENFORCING DIAGNOSTIC METHOD PATENTS

Section 271 of Title 35 of the United States Code sets forth the causes of action a patent owner has available against both direct and indirect infringers.<sup>207</sup> Part III.A discusses the infringement of diagnostic method claims when more than one person is involved in carrying out the patented method. Part III.B then argues claim limitations required for patent eligibility render many patents protecting complementary diagnostics unenforceable against infringement. Thus, the problem of the divided infringement loophole is specific to diagnostics that diagnose the risk for developing a disease or diagnose untreatable diseases.

#### A. *Infringement of Diagnostic Method Patents*

The causes of action a patent owner has available against anyone who "makes, uses, offers to sell, or sells" a patented invention are set forth in Section 271.<sup>208</sup> Section 271(a) codified the common law definition of direct infringement<sup>209</sup> and states that anyone who "makes, uses, offers to sell, or sells any patented invention . . . infringes

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(filed Apr. 29, 1996); U.S. Patent No. 5,747,282 (filed June 7, 1995); U.S. Patent No. 5,693,473 (filed June 7, 1995). However, these claims were invalidated because they were a product of nature and therefore patent ineligible. *See supra* notes 123–139.

201. PERSONALIZED MED. COAL., *supra* note 39, at 9.

202. *Id.*

203. *See Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66, 86–87 (2012) (noting that the claims "tie up the doctor's subsequent treatment decision whether that treatment does, or does not, change in light of the inference he has drawn using the correlations").

204. *E.g.*, U.S. Patent No. 9,605,319 col. 110 l. 30 (filed Aug. 30, 2011); *id.* at col. 109 l. 45–col. 110 l. 32 (claiming a method of treating prostate cancer comprising of determining the expression of a panel of genes and administering "active surveillance" to the patient when the expression of the genes is "lower than a threshold index value"); *see also* U.S. Patent No. 9,976,188 col. 91 ll. 52–61 (filed May 5, 2017) (claiming a method of treating prostate cancer comprising of determining the expression of the TPX2 gene and administering "active surveillance" to the patient when TPX2 is "lower than a threshold index value").

205. '319 Patent col. 42 ll. 53–56.

206. *See* PERSONALIZED MED. COAL., *supra* note 39, at 9.

207. 35 U.S.C. § 271(a) (2018).

208. *Id.* § 271(a)–(c).

209. Note, *Section 271(b) of the Patent Act of 1952: Confusion Codified*, 66 YALE L.J. 132, 136 (1956).

the patent.”<sup>210</sup> Similarly, Section 271(b) codified the common law doctrine of induced infringement<sup>211</sup> and states that anyone who “actively induces infringement of a patent shall be liable as an infringer.”<sup>212</sup> However, it is a well-established rule that infringement must be predicated on an act of direct infringement.<sup>213</sup>

Infringement of a method patent generally requires that the alleged infringer perform each step of the method.<sup>214</sup> However, when two or more parties perform different steps of a patented method, even if each step of the patented method is performed, there is no direct infringement.<sup>215</sup> In terms of diagnostic method patents, often different entities perform the steps of identifying a variant in the patient’s genome and the subsequent treatment.<sup>216</sup> Part III.A.1 discusses the doctrine of direct infringement. Part III.A.2 discusses the doctrine of induced infringement.

### 1. Direct Infringement

To be liable for infringement of a patented method, the alleged infringer must perform each step of the claimed method.<sup>217</sup> This requirement creates a “divided infringement loophole” when two or more parties independently perform only a part of the method, but when combined the parties perform each step of the patented method.<sup>218</sup> This Part discusses when direct infringement occurs in instances of divided infringement.

#### a. *Pre-Akamai*

Courts have long grappled with the challenging balance of limiting the breadth of infringement while protecting the patentee’s property interest.<sup>219</sup> While “[i]t would be unfair . . . for the mastermind . . . to escape liability,” the Federal Circuit resisted imposing liability when the parties merely cooperate at an arm’s length in *BMC Resources, Inc. v. Paymentech, L.P.*<sup>220</sup> For example, BMC Resources owned a patent for a method for processing debit transactions using touchtone telephones that required

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210. 35 U.S.C. § 271(a).

211. Note, *supra* note 209, at 137, 139 (noting that “paragraph[] (b) . . . [was] intended as a codification of prior case law”).

212. 35 U.S.C. § 271(b).

213. *Aro Mfg. Co. v. Convertible Top Replacement Co.*, 365 U.S. 336, 341 (1961).

214. Holbrook, *supra* note 14, at 1014.

215. Leland L. Black, Comment, *Patenting and Protecting Personalized Medicine Innovation Post-Mayo, Myriad, and Limelight*, 95 N.C. L. REV. 493, 510–11 (2017); see also Lynda J. Oswald, *The “Strict Liability” of Direct Patent Infringement*, 19 VAND. J. ENT. & TECH. L. 993, 1015 (2017) (“The Patent Act does not address the complicated issue of assigning direct infringement liability where various steps of a method or process patent are performed by different parties, particularly parties who are co-equals or who have no contractual or other type of relationship with each other.”).

216. See Sachs, *supra* note 15, at 1918 (pointing out that laboratories usually perform the “determining” step while physicians perform the “treatment” step).

217. See Black, *supra* note 215, at 510–11.

218. *Id.*

219. See Holbrook, *supra* note 14, at 1010–12 (comparing the possibility of overbreadth in composition patents and method patents).

220. 498 F.3d 1373, 1381 (Fed. Cir. 2007), *overruled by* *Akamai Techs., Inc. v. Limelight Networks, Inc. (Akamai II)*, 692 F.3d 1301 (Fed. Cir. 2012) (en banc) (per curiam), *rev’d*, 572 U.S. 915 (2014).

the “combined action of several participants, including the payee’s agent . . . , a remote payment network . . . , and the card-issuing financial institution[.]”<sup>221</sup> Paymentech used a method that included each step of BMC’s patented method, but the Federal Circuit determined Paymentech would only be liable for infringement if it “directed or controlled the behavior of the financial institutions that performed those claimed method steps that Paymentech did not perform.”<sup>222</sup> Although the court noted that this rule may seem to create a “loophole,” a party “cannot avoid infringement [liability] . . . by contracting out steps of a patented process to another entity.”<sup>223</sup> The court suggested that patentees solve the problem of divided infringement by drafting claims “to focus on one entity.”<sup>224</sup>

In *Muniauction, Inc. v. Thomson Corp.*,<sup>225</sup> the Federal Circuit invoked the requirement that the defendant must direct or control the entire process even when the defendant and its users jointly performed the method.<sup>226</sup> The court underscored the fact that the relationship between the parties in no way determines whether the defendant has sufficiently controlled or directed the other parties—the users in Thomson’s case—“such that [the defendant] can be said to have performed every step of the asserted claims.”<sup>227</sup> Thus, because Thomson did not itself perform each step of the method and did not request another party to perform the additional steps as its representative, it did not infringe Muniauction’s patented method.<sup>228</sup>

*b. The Akamai Standard*

In a series of decisions, the Federal Circuit and the Supreme Court reevaluated the standard for determining direct infringement of method claims when no single party performs each step of the method.<sup>229</sup> Akamai and Limelight are companies that specialize in delivery of content that is maintained on their servers.<sup>230</sup> Akamai brought an action against Limelight for infringing its patent.<sup>231</sup>

Akamai’s patent claimed methods for retrieving information in a computer network using a novel method of hosting and distributing content.<sup>232</sup> The method required (1) replicating content, (2) tagging objects, and (3) serving the object in response to a request.<sup>233</sup> Limelight completed each step of the claimed method except

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221. *Id.* at 1375.

222. *Id.* at 1378.

223. *Id.* at 1381.

224. *Id.*

225. 532 F.3d 1318 (Fed. Cir. 2008).

226. *Muniauction*, 532 F.3d at 1329.

227. *Id.*

228. *Id.* at 1330.

229. *See* *Limelight Networks, Inc., v. Akamai Techs., Inc. (Akamai III)*, 572 U.S. 915 (2014); *Akamai Techs., Inc. v. Limelight Networks, Inc. (Akamai V)*, 797 F.3d 1020 (Fed. Cir. 2015) (en banc) (per curiam); *Akamai II*, 692 F.3d 1301 (Fed. Cir. 2012) (en banc) (per curiam), *rev’d*, 572 U.S. 915 (2014).

230. *See Akamai II*, 692 F.3d at 1306.

231. *See id.* Akamai is the exclusive licensee of U.S. Patent No. 6,108,703. *Id.*

232. U.S. Patent No. 6,108,703 col. 1 ll. 8–13 (filed May 19, 1999).

233. *Id.* at col. 19 ll. 6–25 (claim 19).

for the “tagging” step, which it instructed its customers to complete.<sup>234</sup> Although, under the standard set forth by *Muniauction*, Limelight did not directly infringe Akamai’s patent under Section 271(a), rather the Federal Circuit held that Limelight induced infringement under Section 271(b).<sup>235</sup> Therefore, a defendant who performed some steps of a method patent and encouraged others to perform the rest could be liable for inducement of infringement even if no one was liable for direct infringement.<sup>236</sup>

Limelight appealed the Federal Circuit’s decision in *Akamai Techs., Inc. v. Limelight Networks, Inc. (Akamai II)*,<sup>237</sup> and the Supreme Court granted certiorari to answer the question of whether a defendant may “be liable for inducing infringement of a patent under 35 U.S.C. § 271(b) when no one has directly infringed the patent under § 271(a) or any other statutory provision.”<sup>238</sup> Interpreting the infringement statute, the Court looked to Section 271(f)(1), which provides a specific provision for induced infringement of patents where the combination is made outside of the United States.<sup>239</sup> The Court held that the language of Section 271(f)(1) demonstrates that “when Congress wishes to impose liability for inducing activity that does not itself constitute direct infringement, it knows precisely how to do so.”<sup>240</sup> Accordingly, the Court held that liability for induced infringement “must be predicated on direct infringement.”<sup>241</sup> However, the Court left the door open for a finding of infringement based on a direct infringement theory under Section 271(a) because it explicitly declined to address whether the Federal Circuit’s *Muniauction* holding was correct.<sup>242</sup>

On remand, the Federal Circuit reconsidered whether Limelight infringed Akamai’s patent under Section 271(a).<sup>243</sup> Direct infringement under Section 271(a) occurs only when “all steps of a claimed method are performed by or attributable to a single entity.”<sup>244</sup> The court determined that if multiple actors perform the steps of the claimed method, infringement exists only if the each of the actions can be “attributed to a single entity,” which occurs when the “entity directs or controls [the] others’ performance,” or “the actors form a joint enterprise.”<sup>245</sup> To be liable under a joint enterprise theory, there must be (1) an “agreement” among the actors, (2) “a common

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234. *See Akamai II*, 692 F.3d at 1306 (explaining that Limelight instructed its customers to modify the content rather than completing that step itself).

235. *Id.* at 1306–07 (“Because the reasoning of our decision today is not predicated on the doctrine of direct infringement, we have no occasion at this time to revisit any of those principles regarding the law of divided infringement as it applies to liability for direct infringement under 35 U.S.C. § 271(a).”).

236. *Id.* at 1317–18.

237. 692 F.3d 1301 (Fed. Cir. 2012) (en banc) (per curiam), *rev’d*, 572 U.S. 915 (2014).

238. *Akamai III*, 572 U.S. 915, 917 (2014).

239. *Id.* at 922–23.

240. *Id.*

241. *Id.* at 920–21, 923.

242. *See id.* at 926 (declining to address whether the “*Muniauction* rule for direct infringement” was valid because “the question on which [the Court] granted certiorari did not involve § 271(a)” and because the “petitioner did not address that important issue in its opening brief”).

243. *Akamai V*, 797 F.3d 1020, 1022 (Fed. Cir. 2015) (en banc) (per curiam) (providing itself with the “opportunity to revisit the § 271(a) question” (quoting *Akamai III*, 572 U.S. at 926)).

244. *Id.* The court used well-established vicarious liability principles to determine when an entity is responsible for an infringement action of another. *Id.* at 1023.

245. *Id.* at 1022–23.

purpose,” (3) “a community of pecuniary interest in that purpose,” and (4) an “equal right of control.”<sup>246</sup> Alternatively, an entity “directs or controls” another’s infringing action if the entity “conditions participation in an activity or receipt of a benefit upon performance of a step or steps of a patented method and establishes the manner or timing of that performance.”<sup>247</sup> Here, Limelight conditioned its customers’ use of the product by requiring customers to complete the tagging step, and it established the manner as well as the timing of the performance.<sup>248</sup> Therefore, the court reinstated the jury verdict, and found Limelight liable for direct infringement of Akamai’s patented method.<sup>249</sup> Accordingly, although there must always be a direct infringer in an induced infringement action,<sup>250</sup> direct infringement can be shown if (1) multiple actors who are involved in performing the steps of the method form a joint enterprise, or (2) an entity conditions participation on performance of one or more steps of a patented method and determines the manner or timing of the performance.<sup>251</sup>

## 2. Induced Infringement

In *Eli Lilly & Co. v. Teva Parenteral Medicines, Inc.*,<sup>252</sup> the Federal Circuit applied the divided infringement test to methods of treatment using the guidelines set forth in the Supreme Court’s holding in *Akamai* and the Federal Circuit’s holding on remand.<sup>253</sup> Patentee Eli Lilly brought an action against Teva for allegedly infringing its patent that claimed a method for “administering pemetrexed disodium.”<sup>254</sup> Eli Lilly’s claimed method requires “administering an effective amount of folic acid and an effective amount of a methylmalonic acid lowering agent followed by administering an effective amount of pemetrexed disodium.”<sup>255</sup> Eli Lilly asserted a combination of physician and patient action infringed its claimed method: a patient self-administered folic acid and a physician administered vitamin B12 and pemetrexed disodium.<sup>256</sup> Eli Lilly satisfied the first prong of the *Akamai* test because physicians conditioned receipt of the pemetrexed disodium on patients’ performances of the step of administering folic acid.<sup>257</sup> Eli Lilly also satisfied the second prong because physicians decided when and

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246. *Id.* at 1023 (quoting RESTATEMENT (SECOND) OF TORTS § 491 cmt. c (AM. LAW INST. 1965)).

247. *Id.*

248. *Id.* at 1024–25 (“Lime-light’s customers do not merely take Limelight’s guidance and act independently on their own. Rather, Limelight establishes the manner and timing of its customers’ performance so that customers can only avail themselves of the service upon their performance of the method steps.”).

249. *Id.* at 1025.

250. *Akamai III*, 572 U.S. 915, 920–21 (2014).

251. *Akamai V*, 797 F.3d at 1023.

252. 845 F.3d 1357 (Fed. Cir. 2017).

253. *Eli Lilly*, 845 F.3d at 1364–68.

254. *Id.* at 1362.

255. U.S. Patent No. 7,772,209 col. 10 ll. 55–60 (filed July 11, 2007).

256. *Eli Lilly*, 845 F.3d at 1362.

257. *Id.* at 1365–67. The first prong of the *Akamai* test requires conditioning “participation in an activity or receipt of a benefit” on completion of one or more steps of the patented method. *Id.* (quoting *Akamai V*, 797 F.3d 1020, 1023 (Fed. Cir. 2015) (en banc) (per curiam)). Here, the relevant benefit was not a reduction in toxicity when the patient self-administered folic acid because that was “not a benefit that physicians [could] condition” as it was a natural consequence of folic acid pretreatment. *Id.* at 1365. Rather,



how much folic acid the patients take.<sup>258</sup> Accordingly, the physicians' actions directly infringed Eli Lilly's patent under Section 271(a).<sup>259</sup>

Even though the physicians' actions directly infringed the patent, the court still needed to determine whether Teva induced the physicians' infringement under Section 271(b).<sup>260</sup> To be liable for induced infringement under Section 271(b), the infringer must have "specific intent and [take] action to induce infringement."<sup>261</sup> In the context of methods of treatment where a physician directly infringes a patent, the pharmaceutical company induces infringement where its prescribing information describes "an infringing use" of the product in a manner to allow an inference of "an affirmative intent to infringe the patent."<sup>262</sup> Although it is immaterial that physicians may ignore prescribing information instructions, ambiguous instructions that require physicians to use outside material to "understand the alleged implicit encouragement" are insufficient to show that the pharmaceutical company intended to infringe the patent.<sup>263</sup> Here, there was significant emphasis on the requirement of taking folic acid prior to administering the pemetrexed disodium.<sup>264</sup> Therefore, the court reasoned Teva induced infringement of the Eli Lilly patent under Section 271(b) and was barred from selling its generic version of ALIMTA until the Eli Lilly patent expires.<sup>265</sup>

#### B. Applying *Akamai* to Infringement of Diagnostic Method Claims

Infringement must be based on an act of direct infringement.<sup>266</sup> However, in diagnostic methods, different entities often perform the steps of identifying a variant in the patient's genome and the subsequent treatment steps.<sup>267</sup> Thus, in order to infringe a diagnostic method claim, the performance of each step of the claim must be "attributed to a single entity."<sup>268</sup>

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the relevant benefit was the treatment itself and the decreased toxicity merely was the "reason why physicians would condition the receipt of pemetrexed treatment" on the patient's completion of the step of administering folic acid. *Id.*

258. *Id.* at 1367. The second prong of the *Akamai* test requires establishing "the manner or timing of that performance." *Akamai V*, 797 F.3d at 1023. Here, the prescribing information provided specific instructions for physicians to instruct patients to self-administer folic acid and warned physicians of "consequences of non-compliance." *Eli Lilly*, 845 F.3d at 1367. Further, it was immaterial whether patients sought additional information about folic acid from sources other than the treating physician. *Id.*

259. *Eli Lilly*, 845 F.3d at 1368.

260. *Id.* (noting that the "mere existence of direct infringement by physicians, while necessary," is insufficient for induced infringement (quoting *Takeda Pharm. U.S.A., Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 631 (Fed. Cir. 2015))).

261. *Id.* (quoting *Takeda*, 785 F.3d at 631).

262. *Id.* (quoting *Takeda*, 785 F.3d at 631).

263. *Id.* at 1369 (quoting *Takeda*, 785 F.3d at 634).

264. *See id.* at 1369.

265. *Id.* at 1361.

266. *See Aro Mfg. Co. v. Convertible Top Replacement Co.*, 365 U.S. 336, 341 (1961).

267. *See Sachs*, *supra* note 15, at 1918 (pointing out that laboratories usually perform the "determining" step while physicians perform the "treatment" step).

268. *Akamai V*, 797 F.3d 1020, 1023 (Fed. Cir. 2015) (en banc) (per curiam).

Some have suggested that careful claim drafting can be used to avoid a divided infringement loophole.<sup>269</sup> These suggestions center around a common theme: draft claims that turn on a single entity.<sup>270</sup> For example, in *BMC Resources, Inc. v. Paymentech, L.P.*,<sup>271</sup> the court suggested that the patentee could have “featured references to a single party’s supplying or receiving each element of the claimed process” rather than requiring “four different parties perform different acts within one claim.”<sup>272</sup> Similarly, for diagnostic method claims, some suggest that the steps should focus on the physician’s actions.<sup>273</sup> However, these strategies only work in limited situations.<sup>274</sup> This Part analyzes whether, in the absence of a joint enterprise,<sup>275</sup> claims that satisfy Section 101, and are therefore patent eligible, can be attributed to a single entity using the *Akamai* standards.<sup>276</sup>

### 1. Companion Diagnostics

Patent-eligible claims directed toward methods of treatment for companion diagnostics are relatively straightforward.<sup>277</sup> As discussed in Part II.C.2, a method claim is likely patent eligible when it contains a step for detecting the expression of a gene or the presence of a mutation in the gene as well as a step of administering a specific therapeutic that is effective when the patient has the genetic mutation.<sup>278</sup> In this method, a laboratory or diagnostic company usually performs the “detecting” step, while the physician performs the “administering” step.<sup>279</sup> Thus, in order to be liable for

269. See, e.g., *BMC Res., Inc. v. Paymentech, L.P.*, 498 F.3d 1373, 1381 (Fed. Cir. 2007), *overruled by Akamai II*, 692 F.3d 1301 (Fed. Cir. 2012) (en banc) (per curiam), *rev’d*, 572 U.S. 915 (2014); Black, *supra* note 215, at 518–22; Katie Silikowski, Comment, *A Methodical Look at Divided Infringement*, 15 J. MARSHALL REV. INTELL. PROP. L. 780, 794–96 (2016).

270. See, e.g., *BMC*, 498 F.3d at 1381; Black, *supra* note 215, at 521–22; Silikowski, *supra* note 269, at 794–96.

271. 498 F.3d 1373 (Fed. Cir. 2007).

272. *BMC*, 498 F.3d at 1381. See *supra* notes 220–224 and accompanying text for a review of BMC’s patented method.

273. Silikowski, *supra* note 269, at 794–96 (providing an example of physician-focused steps using the *Eli Lilly* claims, considering “[i]nstructing the patient to administer pemetrexed disodium” rather than “administration of pemetrexed disodium”).

274. Compare *infra* Part III.B.1, with *infra* Part III.B.2 for a review of the differences in enforcing companion diagnostic patent claims and complementary diagnostic patent claims.

275. Actors who complete separate steps of a patented method but as a joint enterprise are liable “as if each is a single actor.” *Akamai V*, 797 F.3d 1020, 1023 (Fed. Cir. 2015) (en banc) (per curiam). To be a joint enterprise, *Akamai* requires that there be proof of four elements: “(1) an agreement, express or implied, among the members of the group; (2) a common purpose to be carried out by the group; (3) a community of pecuniary interest in that purpose, among the members; and (4) an equal right to a voice in the direction of the enterprise.” *Id.*

276. Absent a joint enterprise, the actions can be attributed to a single entity when it “conditions participation in an activity or receipt of a benefit upon performance of a step or steps of a patented method and establishes the manner or timing of that performance.” *Id.*

277. See *supra* notes 188–191 and accompanying text discussing how method claims for companion diagnostics contain an administering step that transforms the claim into patent-eligible subject matter.

278. See *supra* notes 188–191 and accompanying text for an analysis for how a method claim can be transformed into patent-eligible subject matter.

279. See Sachs, *supra* note 15, at 1918 (explaining that the inclusion of more innovative steps in method claims has led to more than one individual being involved in their performance).

infringement, either the diagnostic company must condition performance of the detecting step on the physician administering a specific therapeutic or the physician must condition performance of the administering step on the diagnostic company performing the detecting step.<sup>280</sup>

It is unlikely that a diagnostic company would condition detecting the expression of a gene or the presence of a mutation in the gene on the physician administering a specific therapeutic.<sup>281</sup> For example, in Foundation Medicine's companion diagnostic,<sup>282</sup> the package insert specifically states that it does not require the physician to administer any specific treatment.<sup>283</sup> In contrast, a physician is likely to condition administering a specific treatment on the diagnostic company detecting a mutation.<sup>284</sup> For instance, in some cases administering a specific therapeutic may be ineffective if the patient has a specific genotype.<sup>285</sup>

Further, the physicians also establish the manner and timing of performance because, like the physicians in *Eli Lilly* who required patients to take folic acid before administering pemetrexed,<sup>286</sup> the physicians in these situations require the detection of the expression or mutation before administering the treatment.<sup>287</sup> Accordingly, only in this situation would a physician directly infringe the patented method.

Importantly, the Patent Act shields physicians from liability when their medical activity "constitutes an infringement."<sup>288</sup> However, this provision does not shield companies that induce physicians to infringe a patented method from liability under

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280. See *Eli Lilly & Co. v. Teva Parenteral Meds.*, 845 F.3d 1357, 1365 (Fed. Cir. 2017) (determining that the physicians conditioned pemetrexed treatment on the patients self-administering the folic acid pre-treatment); *Akamai V.*, 797 F.3d 1020, 1023 (Fed. Cir. 2015) (en banc) (per curiam) ("In those instances [of conditioned participation], the third party's actions are attributed to the alleged infringer such that the alleged infringer becomes the single actor chargeable with direct infringement.").

281. See, e.g., *FOUND. MED., INC.*, *supra* note 33, at 1 (providing instructions for use of its companion diagnostic).

282. See *supra* notes 33, 190 and accompanying text for a review of Foundation Medicine's companion diagnostic.

283. *FOUND. MED., INC.*, *supra* note 33, at 2 ("Decisions on patient care and treatment must be based on the independent medical judgment of the treating physician, taking into consideration all applicable information concerning the patient's condition, such as patient and family history, physical examinations, information from other diagnostic tests, and patient preferences, in accordance with the standard of care in a given community.").

284. See, e.g., *Highlights of Prescribing Information, GILOTRIF® (Afatinib)*, BOEHRINGER INGELHEIM, [http://www.boehringer-ingelheim.us/sites/us/files/documents/gilotrif\\_0.pdf](http://www.boehringer-ingelheim.us/sites/us/files/documents/gilotrif_0.pdf) [<https://perma.cc/TQ43-Z4JP>] (last visited Nov. 20, 2019) (stating that afatinib should be used in patients with nonresistant EGFR mutations).

285. See, e.g., *id.* (stating that afatinib should not be used in patients with resistant EGFR mutations). See also *supra* notes 30–31 and accompanying text for an example of a therapeutic that is only indicated for patients who test positive for a specific biomarker.

286. See *Eli Lilly & Co. v. Teva Parenteral Meds.*, 845 F.3d 1357, 1367–68 (Fed. Cir. 2017).

287. See *Table of Pharmacogenomic Biomarkers in Drug Labeling*, FDA, <http://www.fda.gov/drugs/science-and-research-drugs/table-pharmacogenomic-biomarkers-drug-labeling> [<https://perma.cc/Q5HP-947Q>] (last updated Sept. 3, 2019) (providing a list of therapeutic products for which the labeling includes "specific actions to be taken based on . . . biomarker information").

288. 35 U.S.C. § 287(c)(1) (2018); see also Holbrook, *supra* note 14, at 1021–23 (discussing the legislative history and applicability of the medical activity provision).

Section 271(b).<sup>289</sup> To be liable for induced infringement under Section 271(b), the infringer must have shown “specific intent and action to induce infringement,” which can be inferred, for example, from prescribing information.<sup>290</sup> In cases where a therapeutic is ineffective if the patient has a specific genotype, the pharmaceutical insert describes when the physician should use the medication.<sup>291</sup> Thus, in these situations, the pharmaceutical company could be held liable for infringing a diagnostic method patent.

## 2. Complementary Diagnostics

Patent-eligible claims directed toward methods of treatment for complementary diagnostics are murkier than companion diagnostics.<sup>292</sup> As discussed in Part II.C.2, a method claim that contains a step for detecting the expression of a gene or the presence of a mutation in the gene as well as a step of administering a genus of treatments or administering “active surveillance” may be patent eligible.<sup>293</sup> Similar to companion diagnostics, usually a laboratory or diagnostic company performs the detecting step, while the physician performs the administering step.<sup>294</sup> Thus, the diagnostic company must condition performing the detecting step on the physician administering one or more treatments within the genus or active surveillance. Alternatively, the physician must condition performing the administering step on the diagnostic company performing the detecting step.<sup>295</sup>

It is unlikely that a diagnostic company would condition detecting the expression of a gene or the presence of a mutation in the gene on the physician administering a specific therapeutic.<sup>296</sup> For example, in Myriad’s BRCA diagnostic test, which provides physicians an analysis of the risk the patient will develop breast or ovarian cancer, Myriad detects the mutations in the BRCA1/2 genes and sends the physician a report describing the results as well as possible prophylactic measures for the physician to consider and discuss with the patient.<sup>297</sup> However, the report specifically states that it

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289. Holbrook, *supra* note 14, at 1022 (“[A] company that provides a device and instructions for using the device to perform a patented method could be liable for induced infringement even though the doctor would be immune.”).

290. *Eli Lilly*, 845 F.3d at 1368 (quoting *Takeda Pharm. U.S.A., Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 631 (Fed. Cir. 2015)).

291. See, e.g., *Highlights of Prescribing Information, GILOTRIF® (Afatinib)*, *supra* note 284 (stating that afatinib should be used in patients with nonresistant EGFR mutations).

292. See *supra* notes 196–206 and accompanying text for an example of limitations in method claims for complementary diagnostics that transform the claim into patent-eligible subject matter.

293. See *supra* notes 203–206 and accompanying text discussing the patent eligibility of claims involving active surveillance. It is important to note that although the suggested claim limitations are consistent with the USPTO guidelines and issued patents, claims with comparable limitations have not been challenged at the Federal Circuit.

294. See Sachs, *supra* note 15, at 1918.

295. See *Eli Lilly*, 845 F.3d at 1365; *Akamai V*, 797 F.3d 1020, 1023–24 (Fed. Cir. 2015) (en banc) (per curiam).

296. See, e.g., FOUND. MED., INC., *supra* note 33, at 1, 4 (providing instructions for use of Foundation Medicine’s companion diagnostic).

297. MYRIAD GENETICS, INC., *supra* note 54.

does not require the physician to administer any specific treatment.<sup>298</sup> Further, unlike companion diagnostics, a physician is unlikely to condition administering a treatment on the diagnostic company detecting a mutation because other clinical evaluations, such as family history, may be sufficient to determine a treatment.<sup>299</sup> Accordingly, because the physician does not condition the treatment step on the detecting step, she would not directly infringe the patented method.

Even if a physician conditions the treatment step on the detecting step,<sup>300</sup> she is shielded from liability when her medical activity “constitutes an infringement.”<sup>301</sup> However, unlike companion diagnostics, there is often no entity that induces the physician to infringe. For example, if the physician conditions the treatment step of prophylactic surgery on the results of a diagnostic test, there would be no entity that has prescribed such a procedure.<sup>302</sup> Thus, in these situations, owners of a diagnostic method patent would have no cause of action against infringement.

#### IV. CONCLUSION

Precision medicine is the future of medicine. It has the ability to provide predictive diagnosis, early diagnosis, and treatment targeted to the underlying causes of diseases, creating a system that is more cost-effective and provides improved patient care.<sup>303</sup> President Obama articulated, the Precision Medicine Initiative “won’t work unless we have the private sector coming up with innovation.”<sup>304</sup> However, the courts have frequently either struck down diagnostic method patents<sup>305</sup> or created an enforcement loophole by requiring that a single entity perform each step of a patented method.<sup>306</sup>

In shaping the patent-eligible subject matter and patent infringement doctrines, courts have discriminated between the diagnostic methods that can treat a disease and those that merely diagnose an untreatable disease or assess the patient’s risk of

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298. *Id.*

299. *See, e.g.,* Stacy Simon, *Should You Get Genetic Testing for Cancer Risk?*, AM. CANCER SOC’Y (Sept. 18, 2019) <http://www.cancer.org/latest-news/should-you-get-genetic-testing-for-cancer-risk.html> [<https://perma.cc/A92U-FGJS>].

300. For example, in aggressive preventative measures such as prophylactic surgery, a physician may condition treatment based on the results of a diagnostic test. *See NCI Dictionary of Cancer Terms*, NAT’L CANCER INST., <http://www.cancer.gov/publications/dictionaries/cancer-terms/def/prophylactic-surgery> [<https://perma.cc/95F7-3SZY>] (last visited Oct. 21, 2019) (defining prophylactic surgery).

301. 35 U.S.C. § 287(c)(1) (2018); *see also* Holbrook, *supra* note 14, at 1021–23 (discussing the legislative history and applicability of the medical activity provision).

302. *See, e.g.,* Robert Klitzman & Wendy Chung, *The Process of Deciding About Prophylactic Surgery for Breast and Ovarian Cancer: Patient Questions, Uncertainties, and Communication*, 152A AM. J. MED. GENETICS PART A 52, 52 (2009) (discussing the physician’s flexibility in determining whether to proceed with prophylactic surgery).

303. During a panel discussion, President Obama argued that precision medicine “promises to reduce costs, provide much better care, [and] make our entire health care system much more effective.” President Obama, Precision Medicine Panel Remarks, *supra* note 1.

304. *Id.*

305. *See supra* Part II.B for a discussion of the difficulties in patenting diagnostics.

306. *See supra* Part III.B for a discussion of the divided infringement loophole in molecular diagnostics.

developing a disease in the future. In doing so, courts have strayed from the public policy backdrop of patents and the Precision Medicine Initiative. In order to incentivize precision medicine, specifically preventative or prophylactic precision medicine,<sup>307</sup> the Court or Congress must close this divided infringement loophole.

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307. See *supra* Part III.B.2 for a discussion of diagnostics which diagnose an untreatable disease or assess the patient's risk of developing a disease.