



# Mayo v. Prometheus: Implications for Patents, Biotechnology, and Personalized Medicine

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## Summary

The recent enactment of the Leahy-Smith America Invents Act (AIA), P.L. 112-29, suggests congressional interest in patents on diagnostic methods. In particular, section 27 of the AIA required the U.S. Patent and Trademark Office to conduct a study on the patenting of genetic diagnostic tests. The 2012 decision of the Supreme Court in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.* also addressed these sorts of patents. The Court's decision arguably placed severe limitations on the ability of inventors to obtain diagnostic method patents.

Some observers have welcomed *Mayo v. Prometheus*, asserting that patents on diagnostic methods are harmful to healthcare and medical research. On the other hand, detractors of the opinion state that patents provide powerful incentives for innovation and public disclosure of new technologies. They believe that the Supreme Court's decision will negatively impact medical research in the areas of biotechnology and personalized medicine.

The holding in *Mayo v. Prometheus* may impact another well-publicized litigation, *Association for Molecular Pathology v. U.S. Patent & Trademark Office*. More commonly known as *Myriad*—after the name of the patent holder—this litigation may determine whether patents may appropriately issue on human genes.

Congressional policymakers may contend that current circumstances with respect to patentable subject matter are satisfactory and therefore may advocate that no further legislative action need be taken. Should Congress choose to take action, however, a number of options exist. One possibility is an amendment to the Patent Act stipulating that certain subject matter is or is not patentable. Another is to allow patents on particular inventions to issue, but to limit the remedies available to proprietors of such patents.

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Congressional recognition that the patent system plays a role in supporting U.S. innovation led to the September 16, 2011 enactment of the Leahy-Smith America Invents Act (AIA), P.L. 112-29. Among many other amendments to the Patent Act of 1952 (the “Patent Act”),<sup>1</sup> the AIA required the U.S. Patent and Trademark Office (USPTO) to “conduct a study on effective ways to provide independent, confirming genetic diagnostic test activity where gene patents and exclusive licensing for primary genetic diagnostic tests exist.” The AIA also included provisions directed towards the patentability of two distinct categories of inventions. The new law states that tax strategies “shall be deemed insufficient to differentiate a claimed invention from the prior art.”<sup>2</sup> The AIA also prohibits the issuance of a patent “directed to or encompassing” a human organism.<sup>3</sup> Under the new statutory provisions, no patent may issue to a tax strategy *per se*, or to an invention directed to or encompassing a human being, no matter how innovative that invention might be.

The 2012 decision of the U.S. Supreme Court in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*<sup>4</sup> addressed both diagnostic tests and the concept of patentable subject matter. In a unanimous opinion, the Court held that a patent claiming a method of optimizing therapies for autoimmune diseases, such as Crohn’s disease, was invalid. In so doing, the Court stressed that patents could not issue on “laws of nature” and “natural phenomena.”<sup>5</sup> Further, an invention must do “significantly more than simply describe these natural relations” to be patented.<sup>6</sup>

Some observers believe that *Mayo v. Prometheus* will significantly impact research into biotechnology and personalized medicine in the United States.<sup>7</sup> In particular, some believe that patents on diagnostic methods will be difficult to obtain or enforce in the future, dampening incentives to innovate.<sup>8</sup> On the other hand, other commentators believe that *Mayo v. Prometheus* follows established legal principles and appropriately maintains critical medical and scientific data within the public domain.<sup>9</sup> This report will review the Supreme Court’s decision and briefly consider its implications for innovation and public health.

## The Biotechnology Industry

At its simplest, biotechnology is technology based on biology; it involves the use of a broad range of techniques and procedures for modifying living organisms to suit human purposes.<sup>10</sup>

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<sup>1</sup> P.L. 82-593, 66 Stat. 792 (codified at Title 35 of the United States Code).

<sup>2</sup> AIA, § 14.

<sup>3</sup> *Id.* at § 33.

<sup>4</sup> 132 S.Ct. 1289 (March 20, 2012). Citations in this report are to the slip opinion, available at <http://www.supremecourt.gov/>.

<sup>5</sup> *Id.*, slip op. at 1.

<sup>6</sup> *Id.*, slip op. at 8.

<sup>7</sup> See Aaron S. Kesselheim & Jason Karlawish, “Biomarkers Unbound—The Supreme Court’s Ruling on Diagnostic-Test Patents,” *New England Journal of Medicine* (May 24, 2012).

<sup>8</sup> See Jeffrey L. Fox, “Industry reels as Prometheus falls and Myriad faces further reviews,” 30 *Nature Biotechnology* no. 5 (May 2012), 373.

<sup>9</sup> See American Medical Association, Statement, *AMA Welcomes Supreme Court Decision to Invalidate Prometheus Patents* (Mar. 20, 2012) (available at <http://www.ama-assn.org/ama/pub/news/news/2012-03-20-supreme-court-decision-prometheus-patents.page>).

<sup>10</sup> *What is Biotechnology?*, BIOTECHNOLOGY INDUSTRY ORGANIZATION (June 20, 2012) (available at (continued...))

Biotechnology has applications in engineering, manufacturing, food science, and, most prominently, medicine, in which it has facilitated a number of innovations.<sup>11</sup> Without biotechnology, a variety of cell and tissue culture technologies, pharmaceuticals, and combined diagnostic-therapeutic treatments could not exist.<sup>12</sup>

The biotechnology industry is relatively young and exhibits significant growth potential. Revenue for 2012 is expected to increase 3.9% to \$87 billion,<sup>13</sup> and the five-year annual growth rate for 2012 to 2017 is projected to reach 8.7%.<sup>14</sup> By comparison, the GDP of the United States is expected to expand 2.1% annually through 2017.<sup>15</sup> The biotechnology industry first attained profitability in 2009, due in part to rising revenue and increasing cost efficiencies. Profit for 2012 is expected to reach nearly \$5 billion.<sup>16</sup>

The structure of the biotechnology market is currently rather fragmented. The three largest actors, Amgen Inc., Roche Holding AG, and Monsanto Co., account for 14.0%, 11.5% and 5.8% market share respectively, while the remaining 68.7% is held by hundreds of smaller firms.<sup>17</sup> Mergers and acquisitions (M&A) within the industry steadily grew from 2007-2012, with further increases expected through 2017.<sup>18</sup> As a result, despite a projected expansion of the industry, the number of operators is expected to remain flat.<sup>19</sup>

Human health technologies represent the most significant component of the biotechnology market, accounting for 57% of revenues.<sup>20</sup> Pharmaceuticals are expected to remain the most significant component of the biotechnology market for the foreseeable future, with growth in this segment likely outpacing the rest of biotechnology.<sup>21</sup> According to the Pharmaceutical Research and Manufacturers Association (PhRMA), more than 900 biotechnology medicines are under development.<sup>22</sup>

Within the field of human health, personalized medicine represents a major avenue of growth.<sup>23</sup> Personalized medicine involves tailoring medical treatment to the individual characteristics of each patient, as well as classifying individuals based on their susceptibility to a particular disease or their response to a specific treatment.<sup>24</sup> Preventative or therapeutic interventions can then be

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<http://www.bio.org/node/517>.

<sup>11</sup> IBISWorld, IBISWorld Industry Report NN001, *Biotechnology in the US*, June 2012.

<sup>12</sup> *Id.* at 18.

<sup>13</sup> *Id.* at 5.

<sup>14</sup> *Id.*

<sup>15</sup> *Id.* at 15.

<sup>16</sup> *Id.* at 9.

<sup>17</sup> *Id.* at 30, 38.

<sup>18</sup> *Id.* at 5.

<sup>19</sup> *Id.*

<sup>20</sup> *Id.* at 17.

<sup>21</sup> *Id.*

<sup>22</sup> Pharmaceutical Research and Manufacturers Association, *PhRMA 2011 Annual Report*, 20, available at [http://www.phrma.org/sites/default/files/159/phrma\\_2011\\_annual\\_report.pdf](http://www.phrma.org/sites/default/files/159/phrma_2011_annual_report.pdf)

<sup>23</sup> IBISWorld, IBISWorld Industry Report NN001, *Biotechnology in the US*, June 2012, 17 (2012).

<sup>24</sup> *About the Personalized Medical Coalition*, PERSONALIZED MEDICAL COALITION (June 19, 2012) <http://www.personalizedmedicinecoalition.org/about>.

concentrated on those who will benefit, resulting in more efficient and effective treatment.<sup>25</sup> Among the first and most prominent examples of such interventions is Genentech's Herceptin and its companion HER2 diagnostic test.<sup>26</sup> Herceptin, a "targeted" breast cancer therapy, is prescribed only for patients whose genetic tests reveal an over-expression of the HER2 protein.<sup>27</sup> Since the Herceptin/HER2 "theranostic" intervention was introduced in 1998, it has been joined by numerous other such drug-diagnostic combinations.<sup>28</sup> The market for such diagnostic and therapeutic treatments is estimated to grow by 10% annually, reaching \$42 billion by 2015.<sup>29</sup>

Biotechnology companies often rely heavily on intellectual property rights, as patents are often the most crucial asset in a research-intensive sector that at times produces products that may be readily imitated.<sup>30</sup> Adequate patent protection improves the likelihood that biotechnology companies can appropriate their R&D results and may reduce copying by competitors.<sup>31</sup> Investors in biotechnology firms are generally well aware of the importance of patents, and the survival of such firms may depend on their convincing investors that they have a strong intellectual property protection strategy.<sup>32</sup>

Venture capital (VC) serves as the primary source of funding for small biotechnology firms.<sup>33</sup> Start-ups with patenting activity receive greater and more diverse VC funds,<sup>34</sup> with one study finding that by filing at least one patent application, a firm increases its chance of obtaining VC funding by 97%.<sup>35</sup> VC firms must carefully weigh the economic value of a company's patent portfolio in determining whether to make an investment, and the security of intellectual property is a key component in this analysis.<sup>36</sup> If changes in regulation lead to insufficient protection for biotechnology patents, VC firms may reduce investments in biotechnology and shift their focus to other, less risky industries.<sup>37</sup>

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<sup>25</sup> *Id.*

<sup>26</sup> PriceWaterhouseCoopers, *The New Science of Personalized Medicine: Translating the Promise into Practice*, 2009, 7, available at <http://pwchealth.com/cgi-local/hregister.cgi?link=reg/personalized-medicine.pdf>.

<sup>27</sup> *Id.*

<sup>28</sup> *Id.*

<sup>29</sup> *Id.* at 13.

<sup>30</sup> Esteban Burrone, *Patents at the Core: the Biotech Business*, 2006, available at [http://www.wipo.int/sme/en/documents/patents\\_biotech.htm](http://www.wipo.int/sme/en/documents/patents_biotech.htm).

<sup>31</sup> *Ibid.*

<sup>32</sup> *Ibid.*

<sup>33</sup> Gary Lauder, *Venture Capital – The Buck Stops Where?*, MEDICAL INNOVATIONS & BUSINESS JOURNAL, Summer 2010, 15, available at <http://journals.lww.com/medinnovbusiness/toc/2010/06010>.

<sup>34</sup> Jerry X. Cao, *The Informational Role of Patents in Venture Capital Financing* (June 28, 2011) available at [http://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=1678809](http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1678809)

<sup>35</sup> Carolin Häussler, *To Be Financed or Not – The Role of Patents for Venture Capital Financing* (Feb. 28, 2008) available at [http://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=1393725](http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1393725).

<sup>36</sup> Mario Cardullo, *Intellectual Property – The Basis for Venture Capital Investments*, 2004, available at [http://www.wipo.int/export/sites/www/sme/en/documents/pdf/venture\\_capital\\_investments.pdf](http://www.wipo.int/export/sites/www/sme/en/documents/pdf/venture_capital_investments.pdf)

<sup>37</sup> See *Hearing on Biologics and Biosimilars: Balancing Incentives for Innovation Before the Subcomm. on the Courts and Competition Policy of the H. Comm. on the Judiciary* (2009) (Statement of Jack Lasersohn, Board Member, National Venture Capital Association).

## Introduction to the Patent System

Innovation in the biotechnology industry is impacted by the U.S. patent system, which allows an inventor to seek the grant of a patent by preparing and submitting an application to the USPTO. USPTO officials known as examiners then determine whether the invention disclosed in the application merits the award of a patent.<sup>38</sup> USPTO procedures require examiners to determine whether the invention fulfills certain substantive standards set by the patent statute.

To be patentable, the invention must be novel, or different, from subject matter disclosed by an earlier patent, publication, or other state-of-the-art knowledge.<sup>39</sup> In addition, an invention is not patentable if “the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.”<sup>40</sup> This requirement of “nonobviousness” prevents the issuance of patents claiming subject matter that a skilled artisan would have been able to implement in view of the knowledge of the state of the art.<sup>41</sup> The invention must also be useful, a requirement that is satisfied if the invention is operable and provides a tangible benefit.<sup>42</sup>

Even if these requirements of novelty, nonobviousness, and utility are met, an invention is not patentable unless it falls within at least one category of patentable subject matter. According to section 101 of the Patent Act, an invention which is a “process, machine, manufacture, or composition of matter” may be patented.<sup>43</sup> The range of patentable subject matter under this statute has been characterized as “extremely broad.”<sup>44</sup> The courts and USPTO have nonetheless concluded that certain subject matter, including abstract ideas and laws of nature, is not patentable under section 101.<sup>45</sup> This report further discusses this legal standard below.

In addition to these substantive requirements, the USPTO examiner will consider whether the submitted application fully discloses and distinctly claims the invention.<sup>46</sup> In particular, the application must enable persons skilled in the art to make and use the invention without undue experimentation.<sup>47</sup>

If the USPTO allows the patent to issue, its owner obtains the right to exclude others from making, using, selling, offering to sell or importing into the United States the patented invention.<sup>48</sup> Those who engage in those acts without the permission of the patentee during the term of the patent can be held liable for infringement. Adjudicated infringers may be enjoined

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<sup>38</sup> 35 U.S.C. § 131.

<sup>39</sup> 35 U.S.C. § 102.

<sup>40</sup> 35 U.S.C. § 103(a).

<sup>41</sup> See *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398 (2007).

<sup>42</sup> See *In re Fischer*, 421 F.3d 1365, 1371 (Fed. Cir. 2005).

<sup>43</sup> 35 U.S.C. § 101.

<sup>44</sup> *In re Comiskey*, 554 F.3d 967 (Fed. Cir. 2009).

<sup>45</sup> See *Bilski v. Kappos*, 130 S.Ct. 3218 (2010).

<sup>46</sup> 35 U.S.C. § 112.

<sup>47</sup> See *Streck, Inc. v. Research & Diagnostic System, Inc.*, 665 F.3d 1269, 1287-92 (Fed. Cir. 2012).

<sup>48</sup> 35 U.S.C. § 271(a).

from further infringing acts.<sup>49</sup> The patent statute also provides for an award of damages “adequate to compensate for the infringement, but in no event less than a reasonable royalty for the use made of the invention by the infringer.”<sup>50</sup>

The maximum term of patent protection is ordinarily set at 20 years from the date the application is filed.<sup>51</sup> At the end of that period, others may employ that invention without regard to the expired patent.

Patent rights do not enforce themselves. Patent owners who wish to compel others to respect their rights must commence enforcement proceedings, which most commonly consist of litigation in the federal courts. Although issued patents enjoy a presumption of validity, accused infringers may assert that a patent is invalid or unenforceable on a number of grounds. The Court of Appeals for the Federal Circuit (Federal Circuit) possesses nationwide jurisdiction over most patent appeals from the district courts.<sup>52</sup> The Supreme Court enjoys discretionary authority to review cases decided by the Federal Circuit.<sup>53</sup>

## Fundamentals of Patentable Subject Matter

Section 101 of the Patent Act of 1952 allows a patent to issue upon a “process,” which the statute elsewhere defines to mean a “process, art, or method.”<sup>54</sup> Process patents claim a series of steps that may be performed to achieve a specific result. Process patents typically relate to methods of manufacture or use.<sup>55</sup> A process patent may claim a method of making a product, for example, or a method of using a chemical compound to treat a disease.

Although the statutory term “process” is broad, courts and the USPTO have nonetheless established certain limits upon the sorts of processes that may be patented. In particular, abstract ideas, mathematical algorithms, mental processes, and scientific principles have been judged not to be patentable. The Supreme Court has described these sorts of inventions as the “basic tools of scientific and technological work”<sup>56</sup> that should be “free to all men and reserved exclusively to none.”<sup>57</sup>

Prior to its issuance of *Mayo v. Prometheus*, the Supreme Court most recently considered section 101 in *Bilski v. Kappos*.<sup>58</sup> That 2010 decision addressed a claimed risk hedging method, useful in particular for commodities buyers and sellers in the energy market. The Federal Circuit had

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<sup>49</sup> 35 U.S.C. § 283. See *eBay Inc. v. MercExchange L.L.C.*, 547 U.S. 388 (2006).

<sup>50</sup> 35 U.S.C. § 284.

<sup>51</sup> 35 U.S.C. § 154(a)(2). Although the patent term is based upon the filing date, the patentee obtains no enforceable legal rights until the USPTO allows the application to issue as a granted patent. A number of Patent Act provisions may modify the basic 20-year term, including examination delays at the USPTO and delays in obtaining marketing approval for the patented invention from other federal agencies.

<sup>52</sup> 28 U.S.C. § 1295(a)(1).

<sup>53</sup> 28 U.S.C. § 1254(1).

<sup>54</sup> 35 U.S.C. § 100(b).

<sup>55</sup> See *In re Pleuddemann*, 910 F.2d 823, 826 (Fed. Cir. 1990).

<sup>56</sup> *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972).

<sup>57</sup> *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948).

<sup>58</sup> 545 F.3d 943 (Fed. Cir. 2008) (en banc), *aff'd*, 130 S.Ct. 3218 (2010).



earlier held that the claimed hedging method did not constitute patentable subject matter because it (1) was not tied to a particular machine or apparatus and (2) did not transform a particular article into a different state or thing.<sup>59</sup>

The Supreme Court subsequently agreed to hear the appeal and affirmed the Federal Circuit's patentability determination, although it did so under different reasoning. According to a majority of the Court, the "machine-or-transformation" test should not serve as the exclusive test for determining whether a claimed method was patent-eligible or not. As Justice Kennedy explained, although patents that did not meet the machine-or-transformation standard were rarely granted in earlier eras, this test "would create uncertainty as to the patentability of software, advanced diagnostic medicine techniques," and other technologies of the Information Age.<sup>60</sup> As a result, while the machine-or-transformation test provided a "useful and important clue" towards deciding the patentability of methods, it was not the "sole test."<sup>61</sup>

The Court nonetheless agreed with the Federal Circuit that the claimed hedging method was an "unpatentable abstract idea."<sup>62</sup> The Court reasoned that allowing a patent to issue on the hedging method "would pre-empt use of this approach in all fields, and would effectively grant a monopoly over an abstract idea."<sup>63</sup> The Federal Circuit was therefore affirmed.

Following *Bilski v. Kappos*, whether diagnostic methods appropriately constitute patentable subject matter remained uncertain. As noted previously, at one point the Court's decision suggests that "advanced diagnostic medicine techniques" might be patented. On the other hand, the Court confirmed that "laws of nature" could not be patented<sup>64</sup> and explained that broadly preemptive claims were likely unpatentable.<sup>65</sup> Diagnostic methods might well be classified under either of these headings. Two years after deciding *Bilski v. Kappos*, the Supreme Court would address the patentability of diagnostic methods in *Mayo v. Prometheus*.

## The *Mayo v. Prometheus* Decision

Prometheus Laboratories, Inc. is the sole licensee of two patents (U.S. Patent Nos. 6,355,623 and 6,680,302) claiming methods for determining optimal dosages of thiopurine drugs used to treat autoimmune diseases. Stated generally, the patents claim methods of: (a) administering a thiopurine drug to a patient, and (b) determining the levels of the drug or the drug's metabolites in red blood cells in the patient. The measured metabolite levels are then compared to known metabolite levels. If the measured metabolite levels in the patient are outside the known range, then the physician should increase or decrease the level of drug to be administered so as to reduce toxicity and enhance treatment efficacy. Claim 1 of the '623 patent, which reads as follows, was representative of the claims of the two patents at issue:

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<sup>59</sup> *Id.* at 954.

<sup>60</sup> 130 S.Ct. at 3227.

<sup>61</sup> *Id.*

<sup>62</sup> *Id.* at 3231.

<sup>63</sup> *Id.*

<sup>64</sup> *Id.* at 3225.

<sup>65</sup> *Id.* at 3231.

A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:

(a) administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and

(b) determining the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder,

wherein the level of 6-thioguanine less than about 230 pmol per  $8 \times 10^8$  red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and

wherein the level of 6-thioguanine greater than about 400 pmol per  $8 \times 10^8$  red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.<sup>66</sup>

Prometheus brought suit against Mayo Clinic Rochester and Mayo Collaborative Services (collectively “Mayo”) for infringement of the ‘623 and ‘302 patents. The District Court held that the two patents did not comprise patentable subject matter because they claimed a natural law—namely the correlation between thiopurine metabolite levels and the toxicity and efficacy of thiopurine drug dosages. Following an appeal, the Federal Circuit reversed. Applying the machine-or-transformation test, the Court of Appeals concluded that the patent claims called for the transformation of the human body or of blood taken from the body.<sup>67</sup>

Following its decision in *Bilski v. Kappos*, the Supreme Court directed the Federal Circuit to rehear the appeal in *Mayo v. Prometheus*.<sup>68</sup> The Court of Appeals again concluded that the claims of the ‘623 and ‘302 patents constituted patentable subject matter. According to Judge Lourie, the claims of Prometheus were “drawn not to a law of nature, but to a particular application of naturally occurring correlations, and accordingly do not preempt all uses of the recited metabolite levels and drug efficacy or toxicity.”<sup>69</sup>

Following the second Federal Circuit opinion in *Mayo v. Prometheus*, the Supreme Court again vacated the decision of the lower court.<sup>70</sup> In a unanimous decision authored by Justice Breyer, the Court concluded that the claims were directed towards natural laws and were therefore unpatentable. The Court reviewed its precedents in order to explain that phenomena of nature and abstract concepts could not be patented because the “monopolization of these basic tools through the grant of a patent might tend to impede innovation more than it would tend to promote it.”<sup>71</sup> The earlier cases recognized that all inventions at some level embody or apply laws of nature, however, and that processes that applied natural laws in a particular, useful way were eligible for patenting under § 101 of the Patent Act.

<sup>66</sup> Mayo v. Prometheus, slip op. at 5.

<sup>67</sup> 581 F.3d 1336, 1346-47 (Fed. Cir. 2009).

<sup>68</sup> 130 S.Ct. 3543 (2010).

<sup>69</sup> 628 F.3d 1347, 1355 (Fed. Cir. 2010).

<sup>70</sup> 131 S.Ct. 3027 (2011). Internal citations are to the Court’s slip opinion, which is available on the Supreme Court’s website.

<sup>71</sup> Slip op. at 2.

Applying these principles to the case at hand, the Court recognized that the claims in part recited “laws of nature,” in particular relationships between the concentration of thiopurine metabolites and the likelihood that a dosage of a thiopurine drug will prove ineffective or harmful.<sup>72</sup> However, the claims included steps in addition to the law of nature—in particular, they called for “administering” the thiopurine drug and “determining” the level of the relevant metabolites, “wherein” the drug dosage should be adjusted. According to Justice Breyer, the question before the Court was whether the claims amounted merely to the natural laws, or whether they added enough to the statement of the correlations to qualify as patent-eligible processes that applied natural laws.<sup>73</sup>

The Court reasoned that the three additional claimed steps did not suffice to render the claimed inventions patentable subject matter. Justice Breyer explained that the “administering” step referred simply to the relevant audience of the invention, namely, physicians who treat patients with certain diseases with thiopurine drugs. However, merely limiting the use of a natural law to a particular technological environment cannot render the principle patentable.<sup>74</sup>

Similarly, the “determining” step merely advised physicians to measure the level of metabolites in a patient’s blood—a step that had been done for years and was routine in the field. Justice Breyer stated that conventional or obvious pre-solution activity did not convert an unpatentable law of nature into a patent-eligible application of such law.<sup>75</sup> Finally, the “wherein” clauses simply informed physicians that they should take account of pertinent natural laws in their practices. According to Justice Breyer, an unpatentable law of nature does not become patentable merely by advising individuals to use the law.<sup>76</sup> As a result, the Court concluded that the three steps recited in the claim did not “transform unpatentable natural correlations into patentable applications of those regularities.”<sup>77</sup>

The Supreme Court’s opinion in *Mayo v. Prometheus* addressed a number of additional contentions raised during the litigation. First, the Court rejected the argument that the Prometheus patents satisfied the machine-or-transformation test. The Federal Circuit had reasoned that the patents-in-suit transformed both human blood (by analyzing it to measure metabolite levels) and the human body (by administering a thiopurine drug). Justice Breyer countered that the claims at issue required only that the metabolite levels be measured, not that human blood be transformed. And he also explained that the transformation of the human body was not pertinent to the patentability determination, for that claim limitation merely identified the group of individuals who might be interested in applying the law of nature.<sup>78</sup>

The Court also responded to the position that virtually any step beyond a statement of a law of nature should be deemed to fulfill § 101 standards. Under this view, § 101 might be satisfied fairly readily; other requirements imposed under the Patent Act, including novelty and nonobviousness, would play a more significant role in deciding whether patent should issue or

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<sup>72</sup> *Id.* at 8.

<sup>73</sup> *Id.*

<sup>74</sup> *Id.* at 9.

<sup>75</sup> *Id.* at 10.

<sup>76</sup> *Id.* at 9.

<sup>77</sup> *Id.* at 11.

<sup>78</sup> *Id.* at 19.

not. Justice Breyer rejected this proposal, stating that the policy concerns that underlie § 101 were distinct from those of the other patentability requirements.<sup>79</sup>

Third, the Court responded to concerns that rejecting the Prometheus patents would discourage diagnostic research. Justice Breyer observed that other interested parties had asserted that patents claiming the body's natural responses to illness and medical treatment should not be granted because they might limit physician access to critical scientific data. In view of these competing views, the Court was reluctant to depart from precedent denying patents on natural laws.<sup>80</sup>

## Response to *Mayo v. Prometheus*

The Supreme Court decision in *Mayo v. Prometheus* has prompted diverse reactions. Some patent lawyers with biotechnology backgrounds have reportedly issued scathing reviews of its opinion, with one describing it as “the worst patent decision in the history of the Supreme Court.”<sup>81</sup> Another is reported as stating that under “Breyer’s analysis, potentially every patent in biotechnology is not valid because most use ‘natural processes.’”<sup>82</sup> For example, suppose that a researcher discovers a new marker—such as a protein expressed by a gene that indicates a propensity to develop cancer or is an indicator of Alzheimer’s disease. Under *Mayo v. Prometheus*, this innovation might be considered a natural phenomenon that is not patentable.<sup>83</sup>

Others offered more measured criticism. Some believe that the Supreme Court did not provide sufficient guidance on the criteria needed to develop an unpatentable natural law into a patentable application of a natural law. In their view, the extent to which future diagnostic methods may be patented is unclear. This lack of clarity may discourage firms that need to support costly research and development programs in the area of diagnostics.<sup>84</sup>

Still other observers believe that the impact of *Mayo v. Prometheus* will be most keenly felt by firms focused upon diagnostics and personalized medicine. According to patent attorney Warren Woessner, predictive diagnostic methods that depend on the presence or absence of a marker, as well as diagnostic methods that measure the level of a marker, may be subject to narrow patents or may be difficult to patent at all.<sup>85</sup> Christopher Holman, a member of the faculty of the University of Missouri-Kansas City School of Law, views the Supreme Court opinion as allowing clinical labs to conduct testing “without patents in their way,” to the particular detriment of small biotech companies.<sup>86</sup>

On the other hand, some interested parties believe that *Mayo v. Prometheus* was correctly decided. Patent attorney Richard H. Stern asserted that the Supreme Court issued “a very high

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<sup>79</sup> *Id.* at 20-22.

<sup>80</sup> *Id.* at 23-24.

<sup>81</sup> See Jeffrey L. Fox, “Industry Reels as Prometheus Falls and Myriad Faces Further Reviews,” 30 *Nature Biotechnology* no. 5 (May 2012), 373.

<sup>82</sup> *Id.*

<sup>83</sup> See Patent Watch, “Drug Dosage Patent Ban Casts Doubt on Diagnostics,” 11 *Nature Reviews—Drug Discovery* (May 2012), 344.

<sup>84</sup> See Fox, *supra*.

<sup>85</sup> See Patent Watch, *supra*.

<sup>86</sup> See Fox, *supra*.

quality piece of legal craftsmanship” that resolved numerous issues with respect to § 101 and provided sufficient guidance to the intellectual property community.<sup>87</sup> In addition, the American Medical Association explained that the Supreme Court “prevented irreparable harm to patient care” by ensuring that “critical scientific data remain widely available for sound patient care and innovative medical research.”<sup>88</sup> The Chair of the AMA Board, Robert M. Wah, explained that “[m]edical innovations that provide insight into natural human biology must remain freely accessible and widely disseminated. Blocking this information from physicians and researchers inhibits future discoveries.”<sup>89</sup>

Still others observe that the patent laws of other nations disallow patents on diagnostic methods.<sup>90</sup> For example, Article 53(c) of the European Patent Convention states that “European patents shall not be granted in respect of . . . diagnostic methods practiced on the human or animal body . . . .”<sup>91</sup> As a result, the ruling in *Mayo v. Prometheus* is not necessarily out of step with global intellectual property norms.

Finally, a third group of observers believe that the impact of *Mayo v. Prometheus* upon the medical field as a whole will not be significant. Hank Greely, Director of the Center for Law and the Biosciences at Stanford University, stated that “I don’t see any reason to believe the medical world will look much different because of this decision; some players will be harmed, some will benefit.”<sup>92</sup>

## The *Myriad* Litigation

Following the Supreme Court’s opinion in *Mayo v. Prometheus*, considerable attention has been placed upon another well-publicized litigation, *Association for Molecular Pathology v. U.S. Patent & Trademark Office*.<sup>93</sup> More commonly known as *Myriad*—after the name of the patent holder—this litigation may determine whether patents may appropriately issue on isolated deoxyribonucleic acid (DNA) molecules that encode sequences identical to human genes. The USPTO has allowed inventors to obtain patents on genes for some thirty years.<sup>94</sup> But some observers believe that the reasoning of *Mayo v. Prometheus* may have an impact upon these patents because they are arguably directed towards a product of nature.<sup>95</sup>

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<sup>87</sup> Richard H. Stern, “*Mayo v. Prometheus*: No Patents on Conventional Implementations of Natural Principles and Fundamental Truths,” 34 *European Intellectual Property Review* (2012), 502.

<sup>88</sup> American Medical Association, Statement, *AMA Welcomes Supreme Court Decision to Invalidate Prometheus Patents* (Mar. 20, 2012) (available at <http://www.ama-assn.org/ama/pub/news/news/2012-03-20-supreme-court-decision-prometheus-patents.page>).

<sup>89</sup> *Id.*

<sup>90</sup> See Margaret Kubick, “An Uncertain Future: The Impact of Medical Process and Diagnostic Method Patents on Healthcare in the United States,” 9 *Northwestern Journal of Technology & Intellectual Property* (2010), 280.

<sup>91</sup> The European Patent Convention is available at <http://www.epo.org/law-practice/legal-texts/html/epc/2010/e/ar53.html>.

<sup>92</sup> See Patent Watch, *supra*.

<sup>93</sup> 653 F.3d 1329 (Fed. Cir. 2011).

<sup>94</sup> See Seth R. Ogden, “The Federal Circuit’s Decision in *Myriad*: Isolated DNA Molecules Are Patentable Subject Matter,” 61 *American University Law Review* (2011), 443.

<sup>95</sup> See William L. Warren & Stacy D. Fredrich, “Supreme Court’s *Mayo v. Prometheus* Decision Raises More Questions for Personalized Medicine,” *Genetic Engineering & Biotechnology News* (May 1, 2012).

The *Myriad* litigation commenced on May 12, 2009, when the Association for Molecular Pathology and nineteen other plaintiffs, including individual physicians, patients, and researchers, filed a lawsuit against the USPTO, Myriad Genetics, Inc. (“Myriad”), and the Directors of the University of Utah Research Foundation. The plaintiffs challenged several patents owned by Myriad that claim isolated human genes known as BRCA1 and BRCA2.<sup>96</sup> Certain alterations or mutations in these genes are associated with a predisposition to breast and ovarian cancers. Due to its intellectual property rights, Myriad is the sole commercial provider of genetic testing related to breast and ovarian cancer associated with the BRCA1 and BRCA2 genes. The plaintiffs asserted that Myriad’s gene patent claims were invalid because, in their view, human genes were naturally occurring materials that do not constitute patentable subject matter.

The U.S. District Court for the Southern District of New York sided with the plaintiffs and held that Myriad’s gene patent claims were invalid under 35 U.S.C. § 101.<sup>97</sup> Judge Sweet reasoned that Myriad’s claimed isolated DNA was not “markedly different from native DNA as it exists in nature” and therefore could not be patented.<sup>98</sup> Following an appeal, the Federal Circuit reversed this holding.<sup>99</sup> The Court of Appeals reasoned that “isolated” DNA is not merely “purified” DNA—rather, it has been “manipulated chemically so as to produce a molecule that is markedly different from that which exists in the body.”<sup>100</sup> Under this reasoning, human genes consist of patentable subject matter.

The Supreme Court subsequently agreed to hear the *Myriad* case but did not issue a ruling in the matter. Rather, on March 26, 2012, the Court vacated the judgment and remanded the matter back to the Federal Circuit with instructions to reconsider the appeal in view of *Mayo v. Prometheus*.<sup>101</sup> On August 12, 2012, the Federal Circuit again held that isolated human genes could be patented because, as explained by the Court of Appeals, “each of the claimed molecules represents a nonnaturally occurring composition of matter.”<sup>102</sup> It remains to be seen whether the Federal Circuit will rehear and reconsider its decision, or whether the Supreme Court will rule on the matter itself.

One other aspect of the *Myriad* litigation bears mention. Myriad has also raised the argument that the plaintiffs do not possess “standing” to pursue their lawsuit because they are not directly harmed by the existence of the patents. If this argument proves to be successful, a determination of whether genes may be patented or not would await future litigation.<sup>103</sup>

Should the courts reach a definitive ruling about gene patenting in *Myriad*, the implications for the biotechnology industry could potentially be significant. Dennis Crouch, a member of the law faculty of the University of Missouri, observed that under the reasoning of the District Court for

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<sup>96</sup> For example, claim 1 of U.S. Patent No. 5,747,282 recites: “An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the [following] amino acid sequence . . . .”

<sup>97</sup> 702 F.Supp.2d 181 (S.D.N.Y. 2010).

<sup>98</sup> *Id.* at 232.

<sup>99</sup> 653 F.3d 1329 (Fed. Cir. 2011).

<sup>100</sup> *Id.* at 1352.

<sup>101</sup> 132 S.Ct. 1794 (Mar. 26, 2012).

<sup>102</sup> \_\_ F.3d \_\_, 2012 WL 3518509 (Fed. Cir. Aug. 12, 2012), at \*1.

<sup>103</sup> See Megan M. LaBelle, “Standing to Sue in the *Myriad Genetics* Case,” 2 *California Law Review Circuit* (2011), 68.

the Southern District of New York, “essentially all gene patents are invalid.”<sup>104</sup> Because the USPTO has reportedly issued patents covering over 40,000 genes,<sup>105</sup> the *Myriad* ruling will potentially impact a significant amount of intellectual property.

## Congressional Issues and Options

Some observers believe that the *Mayo v. Prometheus* may prompt legislative review of the patentability of diagnostic methods, gene patents, and biotechnology more generally.<sup>106</sup> If Congress believes that the current circumstances with respect to patentable subject matter are satisfactory, then no action need be taken. Should Congress choose to take action, however, a number of options exist.

One possibility is an amendment to section 101 of the Patent Act stipulating that certain subject matter is or is not patentable. An example of this approach may be found in legislation introduced, but not enacted, in the 110<sup>th</sup> Congress, The Genetic Research and Accessibility Act, H.R. 977, would have provided:

Notwithstanding any other provision of law, no patent may be obtained for a nucleotide sequence, or its functions or correlations, or the naturally occurring products it specifies.<sup>107</sup>

The proposed amendment would not have applied to a patent issued prior to the date of enactment of the Genetic Research and Accessibility Act.<sup>108</sup>

Another option is to allow patents on particular inventions to issue, but to limit the remedies available to proprietors of such patents. The Patent Act currently stipulates that damages and injunctions are not available for patent infringement caused by "a medical practitioner's performance of a medical activity" under certain circumstances.<sup>109</sup> This provision could potentially be amended to include other categories of inventions. Such an approach was taken by the Genomic Research and Diagnostic Disability Act of 2002, which was introduced, but not enacted, in the 107th Congress.<sup>110</sup> That legislation would have created a research exemption from infringement for research on genetic sequence information and an infringement exemption for genetic diagnostic testing.

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<sup>104</sup> Dennis Crouch, *Court: Essentially All Gene Patents Are Invalid* (Mar. 30, 2010) (available at <http://www.patentlyo.com/patent/2010/03/court-essentially-all-gene-patents-are-invalid.html?cid=6a00d8341c588553ef013110028651970c>).

<sup>105</sup> Brief of Amici Curiae Rosetta Genomics, Ltd., et al. as Amici Curiae supporting Appellants (June 16, 2010), 23.

<sup>106</sup> See Fox, *supra*.

<sup>107</sup> H.R. 977, § 2(a).

<sup>108</sup> *Id.* at § 2(c).

<sup>109</sup> 35 U.S.C. § 287(c)(1).

<sup>110</sup> H.R. 3967.

## **Concluding Observations**

In *Mayo v. Prometheus*, the Supreme Court arguably limited the ability of medical innovators to patent diagnostic methods. The implications of this ruling for other laws and products of nature, including human genes, may soon be realized. Some have welcomed judicial decisions that narrow the scope of patentable subject matter, asserting that these patents are harmful to healthcare and medical research. On the other hand, some believe that patents in these fields provide powerful incentives for innovation and public disclosure of new technologies. As judicial rulings continue to influence the availability of patent protection in the healthcare and biotechnology fields, interested parties may encourage Congress to clarify the doctrine of patentable subject matter through legislative amendments.

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