

*Dov Greenbaum on*

## Will Government Efforts to Derail Patentable Subject Matter Status Quo Derail Its Efforts to Promote Personalized Medicine?

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### I. Introduction

Science and technology didn't get much play during the 2015 State of the Union<sup>1</sup>, which makes those programs that made the cut, e.g., the Precision Medicine Initiative, all the more relevant. Many of the patent issues associated with this initiative, alternatively known as personalized medicine, are also very timely, particularly with the recent release by the United States Patent and Trademark Office (USPTO) of a new revision of their subject matter guidelines.<sup>2</sup> The revision seems, on its face, to be more favorable to the personalized medicine innovation in general and the personalized medicine industry in particular than previous iterations.<sup>3</sup>

The White House, in their January 30<sup>th</sup> press conference,<sup>4</sup> clarified that this proposed two hundred and fifteen million dollar Precision Medicine Initiative,<sup>5</sup> will bring a paradigm shift to health care treatment. For example, through the use of new genomic technologies, personalized medicine promises to improve health care by providing the right drug to the right patient at the right dosage: increasing efficacy while reducing costly and dangerous adverse reactions.

Succinctly, personalized medicine therapies employ biomarker tests that can be prognostic, predictive, or diagnostic, in their nature.<sup>6</sup> More specifically, prognostic tests refer to tests configured to search biomarkers, such as genetic sequences or mRNA expression levels that would suggest that the therapy provided is changing the progression and course of the disease. Predictive tests can be those that employ data representing the presence or lack of particular biomarkers as the data informs the necessary titration and/or efficacy of the drug and/or the existence of secondary biochemical and physiological effects (pharmacodynamics) of the therapy or drugs on the individual. Diagnostic tests are used to determine and/or inform a diagnosis.

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1 <http://edition.cnn.com/2015/01/20/politics/state-of-the-union-2015-transcript-full-text/>; Note that this isn't the President's first time expressing interest in personalized medicine, *see, e.g.*, the President's comments in regard to [153 CONG. REC. 7528-29](#) (2007).

2 [http://www.uspto.gov/patents/law/exam/interim\\_guidance\\_subject\\_matter\\_eligibility.jsp](http://www.uspto.gov/patents/law/exam/interim_guidance_subject_matter_eligibility.jsp).

3 Note, other patent related issues, such as those relevant to joint and induced infringement under [35 USC §271](#) may also apply; for example, when the administration of the diagnostic and the administration of the corresponding drug are not done by the same person. *See, e.g.*, Dov Greenbaum, Cloud Computing Patent Law: Always and Never The Same 2014 Emerging Issues 7269 (2014).

4 <http://www.whitehouse.gov/blog/2015/01/30/precision-medicine-initiative-data-driven-treatments-unique-your-own-body>.

5 <http://www.whitehouse.gov/blog/2015/01/30/precision-medicine-initiative-data-driven-treatments-unique-your-own-body>.

6 Ong, Frank S., et al. "Personalized medicine and pharmacogenetic biomarkers: progress in molecular oncology testing." *Expert review of molecular diagnostics* 12.6 (2012): 593-602.

The US government is not alone in actively pursuing this line of research. Major drug companies have recently spent a lot of money to gain access to patients' genetic profiles.<sup>7 8</sup>

Axiomatically, personalized medicine often necessitates the revelation of the patient's personal genetic information to use in selecting and dosing the right medicine. Once genetic and/or other biomolecular information is collected, diagnostics tests, for example, can be run. In the lingo of the Food and Drug Administration, these are referred to as Companion Diagnostics (Cdx).<sup>9</sup> These companion diagnostics, including, chemical, biochemical, immunohistochemical, genetic, imaging or other tests, are typically paired with a particular drug and, like the drug itself also need to undergo regulatory testing and evaluation.<sup>10</sup>

For example, the drug, Herceptin (trastuzumab), a monoclonal antibody, includes a companion diagnostic test to check for the "visualization of signals achieved with directly labeled in situ hybridization probes targeting the HER2 gene and centromeric region of chromosome 17,"<sup>11</sup> i.e., to determine the existence of a particular genetic sequence within the patient. Herceptin is a cancer drug, particularly targeted to breast cancer. As the drug's mechanism targets the effects of the overexpression of a particular gene, if the breast cancer tumor does not overexpress that gene, the drug will likely have minimal therapeutic effect and potentially harm the patient. Hence the diagnostic test.

Similarly, Xalkori, (crizotinib) is a drug specifically targeted to some non-small cell lung carcinomas (NSCLC). The drug was developed following the discovery of a genetic mutation in some forms of NSCLC, where the drug is configured to act as an inhibitor of the protein expressed by the genetic mutation. The relatively fast discovery to market timeline of 4 years has been linked to the validation of the drug's companion diagnostic test, Vysis ALK Break Apart FISH Probe Kit.<sup>12</sup> An overwhelming majority of the patients that carry the mutation have shown significant reductions in their tumors when provided with the medication.<sup>13</sup>

However, outside of a small group of diseases that are closely tied to single gene mutations, much of the gathered genetic information for the development, clinical trials and eventual dispensing of these drugs will also comprise complicated statistical calculations along the way to pursuing personalized medical therapies. A concomitant revelation that a patient also has a genetic mutation however tenuously tied to say a socially stigmatized disease could have significant social and job-related impacts for the patient and their family without any actual corresponding medical apprehensions. Further, given these complicated statistics, there are concerns that many patients

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7 Matthew Harper "Surprise! With \$60 Million Genentech Deal, 23andMe Has A Business Plan" Forbes January 6, 2015 available at <http://www.forbes.com/sites/matthewherper/2015/01/06/surprise-with-60-million-genentech-deal-23andme-has-a-business-plan/>.

8 Caroline Chen, "23andMe Turns Spit Into Dollars in Deal With Pfizer" Bloomberg Business, January 12, 2015, available at <http://www.bloomberg.com/news/articles/2015-01-12/23andme-gives-pfizer-dna-data-as-startup-seeks-growth>.

9 [www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm301431.htm](http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm301431.htm).

10 <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm407328.htm>.

11 <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm301431.htm>.

12 Ong, Frank S., et al. "Personalized medicine and pharmacogenetic biomarkers: progress in molecular oncology testing." *Expert review of molecular diagnostics* 12.6 (2012): 593-602.

13 Ron Winslow and Peter Loftus, "Advances Come in War on Cancer" Wall Street Journal, June 7, 2010 available online at <http://www.wsj.com/articles/SB10001424052748704002104575291103764336126>.

will end up becoming one of the worried well or walking sick, overreacting or underreacting respectively to their newly learned genetic information.

A closely related issue is that of patient privacy and confidentiality; genetic information may need to be shared with doctors, pharmacists, families and even, intentionally or unintentionally, with third parties. As genetic data can never be fully de-identified, and the internet never forgets, the risks associated with sharing even anonymized data are huge. With an estimated one million Americans slated to be included in the President's Precision Medicine Initiative biobank, the repercussions are a non-trivial policy concern.

Additionally, the legal system does not provide consistent nor sufficient protection for the misappropriation and abuse of all this generated genetic information that comes as a result of personalized medicine. Moreover, without stronger Federal laws against the discovery and use of genetic information in obtaining health and life insurance, or in the workplace, many will be disincentivized to provide the necessary genomic information, —fearing discrimination based solely on their genetic predispositions to disease.

These social and ethical concerns notwithstanding, importantly, intellectual property law may be trending away from protecting important components of the personalized medicine process, particularly the diagnostic tests (cDX) necessary to determine and subsequently identify optimal targeted patient sub-populations in which the drug will be either effective or potentially hazardous. There is some irony here, as Obama who seems to have consistently supported this technology also had his solicitor general argue, first in an unprecedented Federal Circuit appearance, against patenting DNA in general,<sup>14</sup> and then again before the Supreme Court, in another unprecedented action, *against* the United States Patent and Trademark Office's arguably pro-diagnostics position.<sup>15</sup>

The Biotechnology Industry Organization (BIO) in an (unpublished) press release, quoted in the blog, IP Watchdog, highlights this irony: "Unfortunately, the Department of Justice's brief — to the extent it fails to fully support the patentability of such DNA-based inventions — is inconsistent with the position that agencies of the U.S. government, through both Democratic and Republican Administrations, have taken domestically and internationally for more than two decades. If adopted, the Department of Justice's position would undermine U.S. global leadership and investment in the life sciences, harm U.S. economic growth and competitiveness at home and abroad, and be counterproductive to the Administration's own initiatives to fight cancer, develop renewable sources of energy, and clean the environment by reducing dependence on fossil fuels such as petroleum."<sup>16</sup>

The Department of Justice nevertheless, sought to justify their position: "We acknowledge that this conclusion is contrary to the longstanding practice of the Patent and Trademark Office, as well as

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14 Alison Frankel, "U.S. Solicitor General to Make Unprecedented Federal Circuit Appearance in Myriad Case" The American Lawyer Feb. 24, 2011 Available at <http://www.corpcounsel.com/id=1202483155902/US-Solicitor-General-to-Make-Unprecedented-Federal-Circuit-Appearance-in-Myriad-Case#ixzz3QbPrptbo>.

15 *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. \_\_\_, 133 S. Ct. 2107, 186 L. Ed. 2d 124 (2013).

16 Gene Quinn, Department of Justice Seeks to Cripple Biotech Industry and Fundamentally Change Patent Laws IP Watchdog, Nov. 1, 2010 available online at <http://www.ipwatchdog.com/2010/11/01/departement-of-justice-seeks-to-cripple-biotech-industry-and-fundamentally-change-patent-laws/id=13062/>.

the practice of the National Institutes of Health and other government agencies that have in the past sought and obtained patents for isolated genomic DNA. The district court's judgment in this case, however, prompted the United States to reevaluate the relationship between such patents and the settled principle under Supreme Court precedent that the patent laws do not extend to products of nature. For the reasons below, the United States has concluded that isolated but otherwise unaltered genomic DNA is not patent-eligible subject matter under [35 U.S.C. § 101](#).<sup>17</sup>

The next section examines exactly what the courts have said thus far as to patent-eligible subject matter under [35 U.S.C. § 101](#).

## II. [35 USC §101](#)

Article I, Section 8, Clause 8 of the US Constitution states that Congress is empowered "To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."

As per US Code, the 'inventors' of these 'discoveries' encompass: "[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title."<sup>18</sup>

Historically, the courts have, over time, worked to flesh out the approximate definitions of this statute, along the way adding exceptions and limitations to a statute that was once defined to be as broad as encompassing "anything under the sun that is made by man."<sup>19</sup>

To this end, the courts have cabined the laws somewhat, specifically excluding laws of nature, physical phenomena, mental processes<sup>20</sup>, and abstract intellectual concepts from the scope of allowable patentable subject matter.<sup>21</sup> These judicial limitations themselves are constantly undergoing review and further elucidation.<sup>22</sup>

The diagnostics tests associated closely with personalized medicine encompass much of the Supreme Court's recent efforts in defining the judicial exclusions of patentable subject matter: DNA primers used in these tests could fall under the products of nature exception of the law,

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17 Attorneys, Appellate Staff, Civil Division U.S. Department of Justice Brief for the United States as Amicus Curiae in Support of either Party, available online at <http://graphics8.nytimes.com/packages/pdf/business/genepatents-USamicusbrief.pdf>.

18 35 U.S. Code § 101 - Inventions patentable.

19 *Diamond v. Chakrabarty*, [447 U.S. 303](#) (1980) (Citing S. Rep. No. 1979, 82d Cong., 2d Sess., 5 (1952); H. R. Rep. No. 1923, 82d Cong., 2d Sess., 6 (1952)).

20 Notably, the "mental steps" exceptions comes in and out of favor. Whereas in *Benson* it was mentioned explicitly, *Gottschalk v. Benson*, [409 US 63, 67](#) (1972) (Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work), by the time the Court got around to *Myriad* and *Alice*, mental steps had noticeably dropped out of the list of judicial exceptions: "We have long held that this provision contains an important implicit exception: Laws of nature, natural phenomena, and abstract ideas are not patentable." *Alice Corp. Pty. Ltd. v. CLS Bank Intern.*, [134 S. Ct. 2347, 2354](#) (2014).

21 *Funk Bros. Seed Co. v. Kalo Co.*, [333 US 127](#) (1948); *Gottschalk v. Benson*, [409 US 63](#) (1972); *Parker v. Flook*, [437 U. S. 584](#) (1978); *Bilski v. Kappos*, [130 S. Ct. 3218](#) (2010).

22 *Alice Corp. Pty. Ltd. v. CLS Bank Intern.*, [134 S. Ct. 2347](#) (2014).

correlations between biomarkers and drug efficiency or efficacy could fall under the physical phenomenon exception of the law, and the necessary calculations to determine drug titration, based on testing results could arguably fall under abstract intellectual concepts and mental processes.

Although often used to provide the metes and bounds of patentable subject matter, these judicial exclusions can be seen as proxies for what the Supreme Court really wants to prevent: preemption of entire ideas by the patentee. However inelegant these provided judicial exemptions seem to be, they are easier to find than the preemption of an entire idea, as patent examiners and the courts necessarily appreciate at the time of filing or even litigation whether a patent can and/or will preempt an entire idea. Effectively this implementation of preemption theory by way of specific exclusions, necessary leads to confusion in the lower courts and in the industry in general.

Arguably, some of the current confusion regarding patentable subject matter (and the Supreme Court's seeming convoluting of the law, as will be shown herein,) might stem from early exclusionary efforts relating to patentable subject matter that were decided prior to the statutory implementation of the non-obviousness doctrine in the 1952 Patent Act.<sup>23</sup> The Supreme Courts inability or lack of desire to do away with this now ill-fitting precedent has led to case law that while pre-1952 would have made sense, now confounds aspects of the post-1952 statute.<sup>24</sup>

This ill-fitting precedent continues to be relevant even in the most recent cases.

### III. Recent Supreme Court Case Law

In recently reinvigorating the formerly exceedingly low hurdle to patentability, patentable subject matter, the Supreme Court has tried (and many would argue, failed) four times in the previous 5 terms to provide a useful working definition of what and/or what is not, patentable subject matter. While their motivation to put so much judicial effort into a formerly trivial matter can be debated, they have nevertheless succeeded in muddying the waters of patent law: in some technological areas there has been a dramatic increase in [35 USC § 101](#) rejections in office actions, in some instances, simply uninspired boilerplate rejections.<sup>25 26</sup>

Three Supreme Court decisions are particularly relevant here: The biotech cases of *Mayo* and *Myriad* and the hitech software case: *Alice v CLS*.<sup>27</sup> While each of these cases failed to provide concrete direction for the patent holder and/or prosecuting attorney, what makes these decisions particularly chilling is that they were likely unpredictable at the time these patents were drafted. As Judge Newman in the Federal Circuit's *en banc Alice* ruling noted:

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23 Patent Act of 1952, Pub. L. No. 82-593.

24 Rai, Arti K. "Diagnostic Patents at the Supreme Court." *Marq. Intell. Prop. L. Rev.* 18 (2014): 1.

25 <https://ipcopy.wordpress.com/2014/07/26/uspto-starts-lobbying-rejections-from-room-101-is-this-the-post-alice-situation/>.

26 Kate Gaudry, Post-Alice Exam Stats In Software Art Units: A Bleaker Road *Law360*, (October 03, 2014, 9:39 AM ET) available online at <http://www.kilpatricktownsend.com/~media/Files/articles/2014/Post-Alice%20Exam%20Stats%20In%20Software%20Art%20Units%20A%20Bleaker%20Road.ashx>.

27 *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct. 2347(2014).

“The ascendance of section 101 as an independent source of litigation, separate from the merits of patentability, is a new uncertainty for inventors. The court, now rehearing this case en banc, hoped to ameliorate this uncertainty by providing objective standards for section 101 patent-eligibility. Instead we have propounded at least three incompatible standards, devoid of consensus, serving simply to add to the unreliability and cost of the system of patents as an incentive for innovation. With today's judicial deadlock, the only assurance is that any successful innovation is likely to be challenged in opportunistic litigation, whose result will depend on the random selection of the panel.”<sup>28</sup>

“Reliable application of legal principles underlies the economic incentive purpose of patent law, in turn implementing the benefits to the public of technology-based advances, and the benefits to the nation of industrial activity, employment, and economic growth. Today's irresolution concerning section 101 affects not only this court and the trial courts, but also the PTO examiners and agency tribunals, and all who invent and invest in new technology. The uncertainty of administrative and judicial outcome and the high cost of resolution are a disincentive to both innovators and competitors.”<sup>29</sup>

As such, the recent efforts may have a significant impact on many technological areas, including, personalized medicine.

#### **a. *Mayo v. Prometheus***

In *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*<sup>30</sup> the court unanimously ruled that Prometheus' patented method claims were invalid. The patents, described as methods to “provides a method of optimizing therapeutic efficacy and reducing toxicity associated with 6-mercaptopurine drug treatment of an immune-mediated gastrointestinal disorder such as inflammatory bowel disease”<sup>31</sup> (e.g., Crohn's Disease,) were invalid under their reading 35 US §101 and precedential earlier case law.

More specifically, the claimed methods in the 6,355,623 and 6,680,302 patents “embody findings that concentrations in a patient's blood of 6-TG or of 6-MMP metabolite beyond a certain level (400 and 7000 picomoles per 8×10<sup>8</sup> red blood cells, respectively) indicate that the dosage is likely too high for the patient, while concentrations in the blood of 6-TG metabolite lower than a certain level (about 230 picomoles per 8×10<sup>8</sup> red blood cells) indicate that the dosage is likely too low to be effective.”<sup>32</sup>

In admitting, that they are confounding patentable subject matter law with novelty law:

— “[w]e recognize that, in evaluating the significance of additional steps, the § 101 patent-eligibility inquiry and, say, the § 102 novelty inquiry might sometimes

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28 *CLS Bank Intern. v. Alice Corp. Pty. Ltd.*, [717 F. 3d 1269, 1321](#) (Fed. Cir. 2013) (en Banc).

29 *CLS Bank Intern. v. Alice Corp. Pty. Ltd.*, [717 F. 3d 1269, 1321](#) (Fed. Cir. 2013) (en Banc).

30 *Mayo Collaborative v. Prometheus Labs.*, [132 S. Ct. 1289](#), 566 U.S. 10 (2012).

31 US Patent 6,680,302.

32 *Mayo Collaborative* [132 S. Ct. at 1295](#).

overlap. But that need not always be so. And to shift the patent-eligibility inquiry entirely to these later sections risks creating significantly greater legal uncertainty, while assuming that those sections can do work that they are not equipped to do” —  
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In the end, the court ruled that method claims like exemplary claim 1 of the ‘302 patent,

“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 a level of 6-thioguanine or 6-methyl-mercaptopurine in said subject having said immune-mediated gastrointestinal disorder, [....]”

were not patentable subject matter.

The court justified this ruling in part by incorporating their policy against preemption. While it generally accepted that naturally occurring phenomena are not patentable, even if the discovery of the phenomena is considered groundbreaking, innovative, and brilliant,<sup>34</sup> the court’s policy was to limit this even further in stating that that claims are invalid when they “too broadly preempt the use of a natural law”<sup>35</sup> and prevent other parties from also using that natural law: a “... concern that patent law not inhibit further discovery by improperly tying up the future use of these building blocks of human ingenuity.”<sup>36</sup>

Still, the Court did recognize the necessary limitations on this reasoning: “too broad an interpretation of this exclusionary principle could eviscerate patent law [...] all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas [...] To that end, it has explained that an *application* of a law of nature to a known structure or process may well be deserving of patent.”<sup>37</sup>

“The Court has repeatedly emphasized this last mentioned concern, a concern that patent law not inhibit further discovery by improperly tying up the future use of laws of nature.”<sup>38</sup>

In outlining why preemption is so important that it undergirds their entire §101 jurisprudence,<sup>39</sup> the court notes “say, a typical patent on a new drug or a new way of using an existing drug, the patent claims do not confine their reach to particular applications of those laws. The presence here of the

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33 *Mayo Collaborative* [132 S. Ct. at 1304](#).

34 *Ariosa Diagnostics Inc. v. Sequenom, Inc.* 19 F. Supp. 3d 938 (N.D. Cal 2013)(citing *Myriad*, [133 S. Ct. at 2117](#)).

35 *Mayo Collaborative*, [132 S. Ct. at 1294](#).

36 *Alice Corp. Pty. Ltd. v. CLS Bank Intern.*, [134 S. Ct. 2347, 2354](#) (2014).

37 *Genetic Technologies, Ltd. V. Laboratory Corp. of America Holdings, Lab. Corp. of America, and 23andme*, [2014 U.S. Dist. LEXIS 122780, at 12](#) (D. Del. 2014) (summarizing precedent).

38 *Mayo Collaborative* [132 S. Ct. at 1301](#).

39 *Alice Corp. Pty. Ltd. v. CLS Bank Intern.*, [134 S. Ct. 2347, 2358](#) (2014).

basic underlying concern that these patents tie up too much future use of laws of nature simply reinforces our conclusion that the processes described in the patents are not patent eligible.”<sup>40</sup>

Here, the court found that the claims simply “set forth laws of nature—namely, relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm.”<sup>41</sup>

“To put the matter more succinctly, the claims inform a relevant audience about certain laws of nature; any additional steps consist of well-understood, routine, conventional activity already engaged in by the scientific community; and those steps, when viewed as a whole, add nothing significant beyond the sum of their parts taken separately.”<sup>42</sup>

While the court demanded that “to transform an unpatentable law of nature into a patent-eligible *application* of such a law, one must do more than simply state the law of nature while adding the words “apply it.””<sup>43</sup> It didn’t provide any substantive guidance into what that *je ne sais quoi* of “do more” is, just something more that “involve[ing] well-understood, routine, conventional activity previously engaged in by researchers in the field.”<sup>44</sup>

#### **b. AMP v Myriad**

In *Myriad*<sup>45</sup>, the Supreme Court, *again unanimously*, ruled in a [35 USC § 101](#) patentable subject matter case that isolated DNA material could not be patent eligible subject matter. This exact issue had been litigated twice before at the Federal Circuit, where the claims were found to be valid.<sup>46</sup> Although explicitly limiting their ruling to DNA, as distinct from a more modified cDNA, the court nevertheless struck down decades of United States Patent and Trademark Office precedent, by ruling that DNA was intrinsically a product of nature and thus excepted from §101.

According to the court, “Myriad discovered the precise location and sequence of what are now known as the BRCA1 and BRCA2 genes. Mutations in these genes can dramatically increase an individual’s risk of developing breast and ovarian cancer.”<sup>47</sup> “Knowledge of the location of the BRCA1 and BRCA2 genes allowed Myriad to [...]develop medical tests that are useful for detecting mutations in a patient’s BRCA1 and BRCA2 genes and thereby assessing whether the patient has an increased risk of cancer.”<sup>48</sup>

The case was limited to asserted composition of matter claims in US patents 5,747,282, 5,693,473 and 5,837,492, with the court noting that “had Myriad created an innovative method of manipulating genes while searching for the BRCA1 and BRCA2 genes, it could possibly have sought a

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40 *Mayo Collaborative* [132 S. Ct. at 1302](#).

41 *Mayo Collaborative* [132 S. Ct. at 1296](#).

42 *Mayo Collaborative* [132 S. Ct. at 1298](#).

43 *Mayo Collaborative* [132 S. Ct. at 1294](#).

44 *Mayo Collaborative* 132 S. Ct. at 1294.

45 *Ass’n for Molecular Pathology v. Myriad*, [133 S. Ct. 2107](#) (2013).

46 *Ass’n for Molecular Pathology v. United States PTO*, [653 F.3d 1329](#), (Fed. Cir. 2011); *Ass’n for Molecular Pathology v. United States PTO*, [689 F.3d 1303](#), (Fed. Cir., 2012).

47 [133 S. Ct at 2112](#).

48 [133 S. Ct at 2112-13](#).



method patent"<sup>49</sup> or a patent on "new *applications* of knowledge about the BRCA1 and BRCA2 genes"<sup>50</sup>

The Court, in reviewing precedential opinions — but ignoring that only one individual could be found to have (a tenuous) standing to sue the plaintiff,<sup>51</sup> and the thousands of research papers on these genes<sup>52</sup> — highlighted their preemption concern that "there would be considerable danger that the grant of patents would "tie up" the use of such tools and thereby "inhibit future innovation premised upon them."<sup>53</sup>

Thus, together, with the earlier *Mayo* decision, *Myriad* questions the subject matter eligibility of many important components of personalized medicine's diagnostics tests, including short nucleotide sequences that are used as probes in finding relevant DNA sequences, or as primers in using biochemical techniques such as Polymerase Chain Reaction (PCR) to find and amplify DNA sequences of interest. While it is unclear from the *Myriad* decision how the ruling will apply to other naturally biomolecules that might also be used in diagnostic testing, a recent Federal Circuit ruling suggests that under the Supreme Court's *Myriad* ruling, even synthetically produced primers (albeit complimentary to the natural occurring DNA) are invalid patentable subject matter.<sup>54</sup>

*Myriad* however, left many practitioners with a lot of questions: "patent lawyers are now tearing their hair out over the issue of how much modification is enough. They've created this bizarre rheostat about the amount of change that would need to take place chemically in order to justify a patent."<sup>55</sup>

For some, the *Mayo* and *Myriad* decisions allow for competing tests to be developed without the fear of infringing broad DNA and diagnostic testing patent rights, arguably promoting further (academic?) research in this area.<sup>56</sup> For others, these developments have led to concerns that companies interested in diagnostics will not be able to protect their likely substantial investment in companion diagnostic tests. (Recent, albeit limited, research could indicated that patents are less valuable in protecting innovations from infringers in this area than previously perceived.<sup>57</sup>) In some instances, uncertainty resulting from the decision could companies to keep their diagnostics tests as black box trade secrets, limiting follow-on innovation.

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49 133 S. Ct at 2119.

50 [133 S. Ct at 2120](#).

51 *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, [133 S. Ct. 2107, n3](#) (U.S. 2013).

52 *See, e.g.*, " Brief for Target Discovery, Inc. As Amicus Curiae in Support of Affirmance, March 14, 2013 available online at [file:///C:/Users/dgreenbaum/Desktop/12-398\\_affirm\\_tdi.authcheckdam.pdf](file:///C:/Users/dgreenbaum/Desktop/12-398_affirm_tdi.authcheckdam.pdf) ("[I]t is possible to observe that Myriad's patents to not prevent researchers from using BRCA genes. Since 2000, over 8,9099 articles have been published reciting BRCA1 [...] this large volume of work reflects researchers' perception that the BRCA1 gene is accessible for research.").

53 *Ass'n for Molecular Pathology v. Myriad*, [133 S. Ct. 2107, 2116](#) (2013).

54 *BRCA1- & BRCA2-Based Hereditary Cancer Test Pat. Litig. v. Amry Genetics Corp.*, No. 2014-1361, -1366, [2014 U.S. App. LEXIS 23692](#) (Fed. Cir. Dec. 17, 2014).

55 Ledford, Heidi. "BIOTECHNOLOGY Myriad ruling causes confusion." *Nature* 498.7454 (2013): 281-282.

56 Gold, Richard E., Robert Cook-Deegan, and Tania Bubela. "AMP v. Myriad: a surgical strike on blockbuster business models." *Science translational medicine* 5.192 (2013) ("The decision is not a move away from patents in general, but from ones that block huge swaths of innovative activity well beyond the contribution of the patent-holding firm.")

57 Allison, John R. and Lemley, Mark A. and Schwartz, David L., Our Divided Patent System (October 14, 2014). University of Chicago Law Review, Vol. 82, 2015, Forthcoming; Stanford Public Law Working Paper No. 2510004; Chicago-Kent College of Law Research Paper No. 2014-28. Available at SSRN: <http://ssrn.com/abstract=2510004>.

Even after the potential upheavals from *Mayo* and *Myriad*, the Supreme Court was still not finished with §101. In *Alice*<sup>58</sup>, although the case was not directly related to biotechnology, the Supreme Court case tackled another (and last?<sup>59</sup>) judicial exception to patentable subject matter: abstract ideas. (With *Mayo* focusing on laws of nature and *Myriad* on products of nature.)

### c. *Alice Corp. v. CLS Bank International*

In *Alice* the court applied its *Mayo* test to patents on computer implemented algorithms for a financial transactions escrow service.<sup>60</sup> Although the Federal Circuit's *en banc* decision was the result of a highly fractured amalgamation of 10 judges issuing 7 rulings,<sup>61</sup> the Supreme Court handily sent back *another unanimous* decision finding the claims at issue unpatentable subject matter.<sup>62</sup>

In this case, employing their *Mayo* Framework<sup>63</sup> the court ran the patents at hand through their two-part test: Are the claims in the patent directed to patent ineligible concepts – e.g., a patent ineligible abstract idea; and if so, does the claim include something “significantly more,” such that the claim isn’t overly broad and covering the entire abstract idea.

This two-step method was succinctly defined as “a search for an “inventive concept” — *i.e.*, an element or combination of elements that is “sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself.”<sup>64</sup> As described above, this *Mayo* Framework continues to conflate § 101 and [35 USC §103](#) wherein § 101 was intended to be a coarse test, allowing most of the subject matter genus to pass through, and § 103, a finer test, limiting patentability to only a subset of species within that genus. In this most current test devised by the Supreme Court, however, § 101 acts to at the outset, at the first patentability hurdle, limit the species within the genus to only those that also contain that extra significant limitation.

Like Judge Newman above, Judge Moore, in the pre-Supreme Court *Alice* Federal Circuit decision noted that the likely application of this unprecedented test will create huge uncertainty in the patent system:

“I am concerned that the current interpretation of § 101, and in particular the abstract idea exception, is causing a free fall in the patent system. The Supreme Court has taken a number of our recent decisions and, in each instance, concluded that the claims at issue were not patent-eligible. *See Bilski, Prometheus, Myriad* (under consideration). Today, several of my colleagues would take that precedent significantly further, lumping together the asserted method, media, and system

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58 *Alice Corp. v. CLS Bank International* [134 S.Ct. 2347](#) (2014).

59 *See, e.g.*, note 20.

60 US patent 5,970,479; US patent 6,912,510; US patent 7,149,720; US patent 7,725,375.

61 *CLS Bank Int'l v. Alice Corp. Pty. Ltd.*, [717 F.3d 1269](#), (Fed. Cir. 2013).

62 *Alice Corp. v. CLS Bank International*, 134 S.Ct. 2347 (2014).

63 [134 S Ct at 2355](#).

64 134 S Ct at 2355.

claims, and holding that they are all patent-ineligible under § 101. Holding that all of these claims are directed to no more than an abstract idea gives staggering breadth to what is meant to be a narrow judicial exception. And let's be clear: if all of these claims, including the system claims, are not patent-eligible, this case is the death of hundreds of thousands of patents..."<sup>65</sup>

The Supreme Court has not made the task of determining patentable subject matter any easier for the lower courts: "Distinguishing between claims that recite a patent-eligible invention and claims that add too little to a patent-ineligible abstract concept can be difficult, as the line separating the two is not always clear."<sup>66</sup>

#### IV. Recent Case Law

##### a. Ultramercial

Ultramercial,<sup>67</sup> the Federal Circuit's November 14, 2014 decision (its third stab at this case, on its second remand from the Supreme Court, after twice having found this patent valid) relating to the patentability of software, represents some of the Federal Circuit's understanding of the sum total of all Supreme Court jurisprudence in this area, and more importantly, perhaps the acquiescence to the Supreme Court's view in their arguably overzealous focus on patentable subject matter.

Ultramercial, while relating to patented methods<sup>68</sup> for distributing copyrighted media products over the Internet for advertising purposes, is not a diagnostic or personalized medicine related case per se, it does provide useful information that could be applied to all technologies where patentable subject matter is at issue.

Judge Mayer wrote in the concurrence, a basic summarizing outline of how the court will review all subsequent §101 challenges:

"First, whether claims meet the demands of [35 U.S.C. § 101](#) is a threshold question, one that must be addressed at the outset of litigation.

Second, no presumption of eligibility attends the section 101 inquiry.

Third, *Alice Corporation v. CLS Bank International*, for all intents and purposes, set out a technological arts test for patent eligibility."<sup>69</sup>

In giving a bit more guidance than the Supreme Court as to what limitations could be beneficial in the second step of the two prong analysis, the Federal Circuit opinion provided:

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65 [717 F. 3d at 1313](#).

66 *DDR Holdings, LLC v. Hotels.com, L.P.*, [773 F.3d 1245](#); (Fed. Cir. 2014).

67 *Ultramercial, Inc. v. Hulu, LLC*, [2014 U.S. App. LEXIS 21633](#) (Fed. Cir. 2014).

68 US Patent 7,346,545.

69 [2014 U.S. App. LEXIS 21633 at 717](#).

“We conclude that the limitations of the '545 claims do not transform the abstract idea that they recite into patent-eligible subject matter because the claims simply instruct the practitioner to implement the abstract idea with routine, conventional activity. None of these eleven individual steps, viewed "both individually and 'as an ordered combination,'" transform the nature of the claim into patent-eligible subject matter. The majority of those steps comprise the abstract concept of offering media content in exchange for viewing an advertisement. Adding routine additional steps such as updating an activity log, requiring a request from the consumer to view the ad, restrictions on public access, and use of the Internet does not transform an otherwise abstract idea into patent-eligible subject matter. Instead, the claimed sequence of steps comprises only "conventional steps, specified at a high level of generality," which is insufficient to supply an "inventive concept.”<sup>70</sup> And that “the use of the Internet is not sufficient to save otherwise abstract claims from ineligibility under § 101”<sup>71</sup>

Further, the Federal Circuit also allowed that the use of the *Bilski*-maligned machine or transformation test<sup>72</sup> can also be useful in assessing the second prong of the test. “A claimed process can be patent-eligible under § 101 if: "(1) it is tied to a particular [novel, i.e., not a general purpose computer] machine or apparatus, or (2) it transforms a particular article into a different state or thing.”<sup>73</sup>

## b. Ariosa Diagnostics

In *Ariosa Diagnostics*,<sup>74</sup> Sequenom was the exclusive licensee of a patent<sup>75</sup> that allowed it to provide a non-invasive prenatal test to expectant mothers using cell-free fetal DNA (cffDNA), in some examples, paternally inherited, in the mother’s blood.

The three independent method claims of the patent at issue are as follows:

1. 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.
2. A method for detecting a paternally inherited nucleic acid on a maternal blood sample, which method comprises: removing all or substantially all nucleated and a nucleated cell populations from the blood sample, amplifying a paternally inherited nucleic acid from the remaining fluid and subjecting the amplified nucleic acid to a test for the Paternally inherited fetal nucleic acid.

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70 2014 U.S. App. LEXIS 21633 at 715-16.

71 [2014 U.S. App. LEXIS 21633 at 716](#).

72 *Bilski v. Kappos*, [561 U.S. 593](#) (2010).

73 2014 U.S. App. LEXIS 21633 at 716.

74 *Ariosa Diagnostics Inc. v. Sequenom, Inc.* 19 F. Supp. 3d 938 (N.D. Cal 2013).

75 U.S. Patent No. 6,258,540.

3. A method for performing a prenatal diagnosis on a maternal blood sample, which method comprises obtaining a non-cellular fraction of the blood sample amplifying a paternally inherited nucleic acid from the non-cellular fraction and performing nucleic acid analysis on the amplified nucleic acid to detect paternally inherited fetal nucleic acid.

Ariosa claimed that these claims within the '540 patent were not eligible patentable subject matter in light of recent Supreme Court precedent in the area of patentable subject matter: arguing that all "additional limitations in the claims either apply well-understood, routine, and conventional activity to the natural phenomenon or limit the natural phenomenon to specific types of the natural phenomenon, which are also unpatentable"<sup>76</sup> Judge Ilston of the Northern District of California agreed, noting that the specification itself admitted as such and that under Supreme Court law, "It is only an innovative or inventive use of a natural phenomenon that is afforded patent protection" Drilling down further, the court noted that while the use of cffDNA may be innovative, the claimed method are routine and conventional, making the only real innovative part of the claim, the discovery of the natural phenomenon cffDNA for use in Sequenom's diagnostic."<sup>77</sup>

In citing a court case related to abstract ideas (*Flook*<sup>78</sup>), and applying it here to natural phenomenon, the court again underscored the Supreme Court's position that the listed exceptions were all simply proxies for preemption. The court paralleled the Pythagorean theorem to the existence of cffDNA: just like "the Pythagorean theorem would not have been patentable, or partially patentable, because a patent application contained a final step indicating that the formula, when solved, could be usefully applied to existing surveying techniques," paternally inherited cffDNA is not patentable simply because the claims contain steps indicating that it may be detected using existing DNA detection methods."<sup>79</sup> Similarly the court did not feel limited by the types of claims in the precedential caselaw, applying law from composition of matter claims to method claims in this case.

Finally, in noting the Supreme Court's stated overriding policy interest in preventing wholesale preemption of natural phenomena, the court further broadened this idea to include within this doctrine, even instances wherein there are alternative unpracticed or non-commercially viable options to practice the invention; "If the alternative methods are not commercially viable, then the effect of the patent in practice would be to preempt all uses of the natural phenomenon."<sup>80</sup>

### c. *Genetic Techs. Ltd. v. Agilent Techs*

In *Genetic Techs. Ltd. v. Agilent Techs., Inc.*<sup>81</sup> the plaintiff, Genetic Technologies (GTG), asserted its '179 patent against Agilent.<sup>82</sup> Judge Seeborg of the Northern District of California court, citing

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76 19 F. Supp. 3d at 949.

77 19 F. Supp. 3d at 950-1.

78 *Parker v. Flook*, [437 U.S. 584](#) (1978).

79 19 F. Supp. 3d at 951 (Note 6: "the Supreme Court has applied its § 101 jurisprudence uniformly regardless of whether the claims at issue involved a natural phenomenon, law of nature, or abstract idea") *See also*, 24 F. Supp. 3d 930, note 10.

80 19 F. Supp. 3d at 953.

81 24 F. Supp. 3d 922; (N.D. Cal. 2014).

Ultramercial,<sup>83</sup> that “[t]he affirmative defense of patent ineligibility due to unpatentable subject matter must be established by clear and convincing evidence, because every patent is presumed to be properly issued,”<sup>84</sup> ruled that the defendant did not meet its burden in showing that the claim was not meaningfully limited, as per Supreme Court precedent.

Thus, in putting a strong limitation on the use of Rule 12(b)(6) motions in patent eligible subject matter jurisprudence in general (a possible likely occurrence resulting from the Supreme Court’s overzealous attack on patentable subject matter and the USPTO’s use of boilerplate language to similarly go after §101 issues), the court noted that because the inventive concept (i.e., the second step in the Supreme Court’s two step analysis) “requires more factual development and potentially construction of the claims, Agilent’s Rule 12(b)(6) motion must be denied.”<sup>85</sup>

Like In *Ariosa Diagnostics*, the court, in subsequently assessing whether the claims preempt the broad use the law of nature, the court noted that “the relevant question for preemption purposes is whether the claims of the '179 patent preclude others from making any *practical* use of these correlations.”<sup>86</sup>

However, in this case, the court found no preemption: “All of the asserted claims require a primer pair to amplify an intron sequence. The complaint avers that at the time of the '179 patent's filing, numerous methods were available to analyze intron and exon sequences to detect genomic variations, none of which require primer pair amplification. Given the alleged availability of alternative methods of genomic analysis, clear and convincing evidence is lacking that the '179 patent impermissibly ties up the relevant field.”<sup>87</sup>

Relatedly, the court found that the amplification step of the intron sequence could plausibly provide the necessary limitations to make the claims patentable subject matter. With this plausibility the motion to dismiss could not stand.

#### **d. *Genetic Technologies, Ltd. v. Laboratory Corp. of America and 23andMe***

In another Genetic Technologies case, the Australian company asserted another patent, the ‘342 patent,<sup>88</sup> against defendants Laboratory Corporation of America and 23andMe.<sup>89</sup> The ‘342 patent provided for a genetic screen for an ACTN3 allele indicating inherited athletic performance, including: “methods for selecting or matching a sport or sporting event to an individual . . . to increase their chances of success, optimizing the training programs of individuals, and for predicting the athletic performance of individuals[,]” based on the identification of “specific gene(s) or alterations in the gene(s) that correlate with potential athletic performance.”<sup>90</sup>

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82 U.S. Patent No. 5,612,179 (“the '179 patent”).

83 *Ultramercial, Inc. v. Hulu, LLC*, [722 F.3d 1335, 1342, 1338-39](#) (Fed. Cir. 2013).

84 24 F. Supp. 3d at 927.

85 24 F. Supp. 3d 929.

86 24 F. Supp. 3d 931 (Emphasis added).

87 24 F. Supp. 3d 931.

88 U.S. Patent No. 7,615,342.

89 *Genetic Technologies, Ltd. v. Laboratory Corp. of America Holdings, Lab. Corp. of America, and 23andMe*, [2014 U.S. Dist. LEXIS 122780](#) (D. Del. 2014).

90 [2014 U.S. Dist. LEXIS 122780 at 2](#).

Claim 1, the only asserted claim reads:

1. A method to predict potential sprinting, strength, or power performance in a human comprising:
  - a) analyzing a sample obtained from the human for the presence of one or more genetic variations in a-actinin-3 (ACTN3) gene;
  - b) detecting the presence of two 577R alleles at the loci encoding amino acid number 577 of the a-actinin-3 (ACTN3) protein; and
  - c) predicting the potential sprinting, strength, or power performance of the human, wherein the presence of two copies of the 577R allele is positively associated with potential sprinting, strength, or power performance.<sup>91</sup>

The court's analysis provides a practical application of the *Alice* case, decided only months earlier. Here the court found that the claim comprises unpatentable subject matter.

In this case the court's application of *Alice* included:

- 1) Determining whether the claim is directed to a law of nature. Employing the Prometheus definition: "a relationship that is the consequence of entirely natural processes sets forth a natural law..."<sup>92</sup>

The court found that the claimed relationship between allelic variants and sport ability amounted to a natural law. In applying the second prong of the *Alice* test:

- 2) Does the claim amount to a patent eligible application of the natural law. Here the court noted that "courts examining this question tend to look first to each step of the claim, and then to the claim as a whole."<sup>93</sup>

These steps comprise: analyzing, detecting and predicting steps.

With regard to the analyzing step, the court in pointing to the description notes that: "The claim clearly does not recite a new, innovative method for such analyzation, which could be one way to effect a different outcome here."<sup>94</sup>

With regard to the detecting step: the court notes that: "It simply tells users of the process to detect the presence of two 577R alleles in the sample, again without specifying any particular method for doing so."<sup>95</sup>

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91 U.S. Patent No. 7,615,342.

92 [2014 U.S. Dist. LEXIS 122780 at 29](#).

93 [2014 U.S. Dist. LEXIS 122780 at 32](#).

94 [2014 U.S. Dist. LEXIS 122780 at 33](#) (Citations omitted).

And with regard to the predicting step, the court found that it simply “tells users of the process to predict the athletic performance of the person based on the presence of two 577R alleles in the sample, amounts to no more than an instruction apply the natural law.”<sup>96</sup>

Finally, in reviewing the claim as a whole, the court found: “Just as in *Prometheus*, this combination “amounts to nothing significantly more than an instruction to testers to apply the applicable laws.”<sup>97</sup>

### ***e. University of Utah Research Foundation et al. v. Amry Genetics Corp (Myriad II)***

In a 2014 appeal, *Myriad* asserted U.S. Patent No. 5,753,441 (“the ‘441 patent”), U.S. Patent No. 5,747,282 (“the ‘282 patent”), and U.S. Patent No. 5,837,492 (“the ‘492 patent”) against *Ambry*.<sup>98</sup> In particular, from these patents, *Myriad* appealed four composition of matter claims to synthetic DNA primers and 2 method claims involving “comparisons between the wild-type BRCA sequences with the patient’s BRCA sequences”<sup>99</sup> from an earlier denied preliminary injunction.

With regard to the primers, the court ruled that “The primers before us are not distinguishable from the isolated DNA found patent-ineligible in *Myriad* and are not similar to the cDNA found to be patent-eligible. Primers necessarily contain the identical sequence of the BRCA sequence directly opposite to the strand to which they are designed to bind. They are structurally identical to the ends of DNA strands found in nature....it makes no difference that the identified gene sequences are synthetically replicated [or single stranded – i.e., unable to occur naturally].”<sup>100</sup> This claim closely tracked an explicit example in the USPTO March 2014 guidance documents, where the USPTO also found a set of primers to be unpatentable subject matter.<sup>101</sup> What the court ignored though was the claimed set of primers is unique and not found in naturally in nature; perhaps that should have been patentable?<sup>102</sup>

The court found similarities in its ruling regarding the cloned sheep, *Dolly*: “*Dolly*, a cloned sheep—because she “is an exact genetic replica of another sheep and does not possess ‘markedly different characteristics from any farm animals found in nature.”<sup>103</sup>

The court succinctly stated the Supreme Court’s test: “First, “we determine whether the claims at issue are directed to a patent-ineligible concept. If so, we then ask, ‘what else is there in the claims before us?’... That is, we next ask whether the remaining elements, either in isolation or

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95 [2014 U.S. Dist. LEXIS 122780 at 36](#) (Citations omitted).

96 [2014 U.S. Dist. LEXIS 122780 at 37](#) (Citations omitted).

97 [2014 U.S. Dist. LEXIS 122780 at 44](#) (Citations omitted).

98 *In re BRCA1- and BRCA 2-Based Hereditary Cancer Test Patent Litigation*, [774 F.3d 755](#), 2014 U.S. App. LEXIS 23692 (Fed. Cir. 2014).

99 [2014 U.S. App. LEXIS 23692 at 5](#).

100 [2014 U.S. App. LEXIS 23692 at 8](#).

101 Guidance For Determining Subject Matter Eligibility Of Claims Reciting Or Involving Laws of Nature, Natural Phenomena, & Natural Products (Guidance) available at [http://www.uspto.gov/patents/law/exam/myriad-mayo\\_guidance.pdf](http://www.uspto.gov/patents/law/exam/myriad-mayo_guidance.pdf).

102 Chris Holman, “*Myriad II*: Another Blow to the Patenting of Biotech Innovation” *Holman’s Biotech IP Blog*, December 19, 2014. Available online at: <http://holmansbiotechblog.blogspot.co.il/2014/12/myriad-ii-another-blow-to-patenting-of.html>.

103 2014 U.S. App. LEXIS 23692 at 9.



combination with the other non-patent-ineligible elements, are sufficient to "'transform the nature of the claim' into a patent-eligible application."<sup>104</sup>

Perhaps in light of the continued beat downs by the Supreme Court in the area of patentable subject matter the court made a blanket statement: "Primers do not have such a different structure and are patent ineligible."<sup>105</sup> Ignoring perhaps the reality that primers typically come in sets, these combinations are not necessarily found to exist as such in nature. Further evidence of this acquiescing to the Supreme Court, in reviewing the method claims, the court in seemingly ruling against its own decisions in *Mayo*, and also distinguishing itself from somewhat similar method claims that both Judge Bryson of the CAFC and Justice Thomas of the Supreme Court would have found to be patentable, found the method claims to encompass unpatentable subject matter.

After determining that the claims were to ineligible abstract ideas<sup>106</sup> the court found that the balance of the method claim language only "set forth well-understood, routine and conventional activity engaged in by scientists at the time of Myriad's patent applications."<sup>107</sup> "Nothing is added by identifying the techniques to be used in making the comparison because those comparison techniques were the well-understood, routine, and conventional techniques that a scientist would have thought of when instructed to compare two gene sequences."<sup>108</sup>

While this ruling doesn't bode well for the patentee in the expected *Ariosa Diagnostics* Appeal, the court however did provide an important clue for future drafted patents: In the analysis of the first prong of the test, the court distinguished perhaps patent eligible claims as those that expressly limited the scope of what the inventors were looking to detect, i.e., "expressly identified in the specification by tables 11 and 12."<sup>109</sup>

In addition to the Federal Circuit and lower courts working through Supreme Court law in this area, the USPTO has put in substantial effort to clarify how it reads this new §101 jurisprudence.

## V. USPTO Guidelines

The United States Patent and Trademark Office issued guidance documents in March of 2014 to help practitioners better understand the current state of [35 USC § 101](#) subject matter eligibility.<sup>110</sup> The Guidance Document was particularly directed at "reciting or involving laws of nature/natural principles, natural phenomena, and/or natural products,"<sup>111</sup> and did not include guidance as to the

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104 [2014 U.S. App. LEXIS 23692 at 15-16.](#)

105 [2014 U.S. App. LEXIS 23692 at 11.](#)

106 Note that the court conflates abstract ideas with laws of nature, underlining the previous assumption that the terms are all simply proxies for the unifying idea of pre-emption.

107 [2014 U.S. App. LEXIS 23692 at 20.](#)

108 [2014 U.S. App. LEXIS 23692 at 20-21.](#)

109 [2014 U.S. App. LEXIS 23692 at 22.](#)

110 Guidance For Determining Subject Matter Eligibility Of Claims Reciting Or Involving Laws of Nature, Natural Phenomena, & Natural Products ( USPTO March 2014 Guidance) available at [http://www.uspto.gov/patents/law/exam/myriad-mayo\\_guidance.pdf](http://www.uspto.gov/patents/law/exam/myriad-mayo_guidance.pdf).

111 USPTO March 2014 Guidance.

abstract idea exception, notably still in play until the Supreme Court's *Alice* decision later that year. These guidance documents superseded the earlier ones post-*Myriad*.<sup>112</sup>

The Guidance Document was also broader than the *Myriad* guidance, and was not limited to just DNA species, but rather also “chemicals derived from natural sources (e.g., antibiotics, fats, oils, petroleum derivatives, resins, toxins, etc.); foods (e.g., fruits, grains, meats and vegetables); metals and metallic compounds that exist in nature; minerals; natural materials (e.g., rocks, sands, soils); nucleic acids; organisms (e.g., bacteria, plants and multicellular animals); proteins and peptides; and other substances found in or derived from nature.”<sup>113</sup>

Succinctly, the Guidance Document laid out that a patent claim could be patent eligible if “the claim as a whole is significantly different than the judicial exception(s).”<sup>114</sup> The document provided a number of factors to aid in this determination; “if the totality of the relevant factors weigh[s] toward eligibility, the claim qualifies as eligible subject matter.” However “[i]f the totality of the relevant factors weighs against eligibility, the claim should be rejected.”

The analysis included a three prong test:

- 1) Is The Claim Directed To One Of The Four Statutory Categories of [35 U.S.C. § 101](#)?
- 2) Does the Claim Recite or Involve A Judicial Exception?
- 3) Does The Claim As A Whole Recite Something Significantly Different Than The Judicial Exception(s)?<sup>115</sup>

Where, “Significantly Different” addresses two pathways to eligibility:

1. Product claim involving or reciting a natural product includes features or steps demonstrating a marked difference from what exists in nature; or
2. Claim involving or reciting a judicial exception must also recite meaningful limitations that add something of significance to the judicial exception.<sup>116</sup>

The Guidelines included 12 factors that needed to be weighed, 5 in favor of eligibility and 6 against, akin perhaps to the Graham factors of [35 USC §103](#) non-obviousness analysis.<sup>117</sup>

Stakeholders have had a lot of problems with these guidelines. In general, there were concerns that the guidelines were too convoluted and would promote inconsistent examiner responses. Their complexity would also leave practitioners with more questions than answers leading to overly cautious drafting. Particular concerns ranged from overly broad ineligible claims and overly narrow

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112 Supreme Court Decision in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, June 13, 2013 available at [http://www.uspto.gov/patents/law/exam/myriad\\_20130613.pdf](http://www.uspto.gov/patents/law/exam/myriad_20130613.pdf).

113 USPTO March 2014 Guidance.

114 USPTO March 2014 Guidance.

115 USPTO, Evaluating Subject Matter Eligibility Under [35 USC § 101](#): March 2014 Update PowerPoint Presentation March 19, 2014. Available online at: [http://www.uspto.gov/patents/law/exam/myriad-mayo\\_slides\\_20140319.pdf](http://www.uspto.gov/patents/law/exam/myriad-mayo_slides_20140319.pdf).

116 USPTO, Evaluating Subject Matter Eligibility Under 35 USC § 101: March 2014 Update PowerPoint Presentation March 19, 2014. Available online at: [http://www.uspto.gov/patents/law/exam/myriad-mayo\\_slides\\_20140319.pdf](http://www.uspto.gov/patents/law/exam/myriad-mayo_slides_20140319.pdf).

117 Manual of Patent Examining Procedure § 2141.

eligible claim examples, with no direction to analyze the gray areas in between; a focus on structure wherein the court's seemed to also allow for a functional analysis to find patent eligibility; as described above, the application of the guidance beyond the DNA molecules of the *Myriad* decision into Supreme Court non-precedential dicta to encompass many other naturally occurring biomolecules and their unnatural combinations – something explicitly not considered in the *Myriad* case.<sup>118</sup> In broadening their guidelines to include all biomolecules, even synthetically derived natural molecules might not be patentable.

These concerns were not just limited to the guidelines, but also with the corresponding slide deck that was provided by the USPTO in conjunction with the guidelines. This slide deck included examples not included in the guidelines themselves.<sup>119</sup> For example, the following claim was presented on page 67: “A beverage composition comprising: a) pomelo juice; and b) a preservative.” In this example, the USPTO argues that because the preservative could be natural and the combination of the preservative and the juice do not structurally change the resulting product, it doesn't matter that the preservative could also be non-natural, the claim encompasses non-patent eligible subject matter and fails: “every embodiment within the BRI [broadest reasonable interpretation] must be eligible”<sup>120</sup> It was suggested in discussions with the USPTO during a March 20, 2014 Webinar that that this would invalidate pharmaceutical claims that included a naturally occurring drug and a pharmaceutically acceptable carrier.<sup>121</sup>

In response to this widespread criticism,<sup>122</sup> the USPTO released a next (albeit not necessarily final) draft guidance document.<sup>123</sup> “[T]he guidance reflects a significant change from the examination guidance previously issued in response to *Myriad* and *Mayo*. The changes were triggered by the feedback we solicited and received from the public, as well as refinements necessitated by the *Alice Corp.* decision.”<sup>124</sup>

In the new December 2014 Guidance, the USPTO disposed of the clumsy 12 factor analysis, although still referencing the source case, allowing for the possibility that the factors could still be incorporated into the analysis; “the test for determining whether a claim is directed to a “product of nature” exception is separated from the analysis of whether the claim includes significantly more

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118 *Ass'n for Molecular Pathology v. Myriad*, [133 S. Ct. 2107, 2120](#) (2013) (“Nor do we consider the patentability of DNA in which the order of the naturally occurring nucleotides has been altered. Scientific alteration of the genetic code presents a different inquiry, and we express no opinion about the application of § 101 to such endeavors. We merely hold that genes and the information they encode are not patent eligible under § 101 simply because they have been isolated from the surrounding genetic material.”).

119 [http://www.uspto.gov/patents/law/exam/myriad-mayo\\_slides\\_20140319.pdf](http://www.uspto.gov/patents/law/exam/myriad-mayo_slides_20140319.pdf) at 67.

120 [http://www.uspto.gov/patents/law/exam/myriad-mayo\\_slides\\_20140319.pdf](http://www.uspto.gov/patents/law/exam/myriad-mayo_slides_20140319.pdf) at 73.

121 <http://www.pharmapatentsblog.com/2014/03/24/a-first-look-at-the-uspto-101-training-slides/>.

122 See, e.g., Nancy J. Linck The Linck Letter on the Myriad Guidelines, June 27, 2014 (“I applaud your efforts to harmonize past Supreme Court case law and attempt to uncover an approach that will do so and respond to the PTO’s many examiners’ questions. However, that is an impossible task, as I think you are coming to realize. It also may take you beyond the PTO’s authority by extending Myriad beyond its holding.”) (Dr. Linck was formerly Solicitor of the U.S. Patent and Trademark Office as well as service as an Administrative Patent Judge on what is today the Patent Trial and Appeal Board) available online at <http://www.laipla.net/wp-content/uploads/2014/07/LinckLetter.pdf>.

123 2014 Interim Guidance on Patent Subject Matter Eligibility A Rule by the [Patent and Trademark Office](#) on 12/16/2014 available online at: <https://www.federalregister.gov/articles/2014/12/16/2014-29414/2014-interim-guidance-on-patent-subject-matter-eligibility> (December 2014 Guidance) .

124 Peggy Focarino, “Guidance on Subject Matter Eligibility Issued” *Director’s Forum: A Blog from USPTO’s Leadership*, December 15, 2014 available online at [http://www.uspto.gov/blog/director/entry/guidance\\_on\\_subject\\_matter\\_eligibility](http://www.uspto.gov/blog/director/entry/guidance_on_subject_matter_eligibility).

than the exception;”<sup>125</sup> The subsequent accompanying USPTO PowerPoint describes this in more detail:

“Nature-based products are those products derived from natural sources that require closer scrutiny to determine whether they fall within a judicial exception [...] The term “nature-based” as used in the guidance includes both eligible and ineligible products. Eligible nature-based products are those that exhibit markedly different characteristics from any naturally occurring counterpart [...] Nature-based products that (i) are naturally occurring or (ii) are not naturally occurring but have characteristics that are not markedly different from a naturally occurring counterpart fall within an exception (law of nature or natural phenomena).”<sup>126</sup>

Moreover, other important changes in the new guidelines include, “the application of the overall analysis is based on claims *directed* to judicial exceptions (defined as claims reciting the exception, *i.e.*, set forth or described), rather than claims merely “involving” an exception;”<sup>127</sup> This “narrows the funnel” in the words of Drew Hirshfeld, Deputy Commissioner for Patent Examination Policy at the USPTO.<sup>128</sup>

Additionally, the analysis is now a two part question, which according to the USPTO is a distinct difference from the Office's prior guidance, and more like the test presented in *Mayo* and *Alice*.<sup>129</sup> In this two part question, the second half of the second part asks: “Does the Claim as a Whole Amount to Significantly More than the Judicial Exception?”<sup>130</sup> Where the USPTO provides examples of what significantly more could entail, including: “Improvements to another technology or technical field, Improvements to the functioning of the computer itself [;]Applying the judicial exception with, or by use of, a particular machine[;] Effecting a transformation or reduction of a particular article to a different state or thing [;]Adding a specific limitation other than what is well-understood, routine and conventional in the field, or adding unconventional steps that confine the claim to a particular useful application [; and,] Other meaningful limitations beyond generally linking the use of the judicial exception to a particular technological environment[.]”<sup>131</sup>

Also, the new guidelines provide for a “*markedly* different analysis focuses on characteristics that can include a product's structure, function, and/or other properties as compared to its naturally occurring counterpart in its natural state.”<sup>132</sup> According to the accompanying USPTO presentation, in the products of nature exception, markedly different characteristics includes structure, function and/or other properties, examples of which are: “ Biological or pharmacological functions or

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125 December 2014 Guidance Footnote 2.

126 Raul Tamayo, PowerPoint presentation of 2014 Interim Guidance on Patent Subject Matter Eligibility, pg. 10, January 21, 2015 available online at [http://www.uspto.gov/patents/law/exam/jan21forum\\_uspto.pdf](http://www.uspto.gov/patents/law/exam/jan21forum_uspto.pdf).

127 December 2014 Guidance Footnote 2.

128 Donald Zuhn USPTO Holds Forum on Interim Guidance -- Part I, Patent Docs, February 03, 2015 available online at <http://www.patentdocs.org/2015/02/uspto-holds-forum-on-interim-guidance-part-i.html>.

129 Donald Zuhn USPTO Holds Forum on Interim Guidance -- Part I, Patent Docs, February 03, 2015 available online at <http://www.patentdocs.org/2015/02/uspto-holds-forum-on-interim-guidance-part-i.html>.

130 December 2014 Guidelines.

131 Raul Tamayo, PowerPoint presentation of 2014 Interim Guidance on Patent Subject Matter Eligibility, pg. 15, January 21, 2015 available online at [http://www.uspto.gov/patents/law/exam/jan21forum\\_uspto.pdf](http://www.uspto.gov/patents/law/exam/jan21forum_uspto.pdf).

132 December 2014 Guidance Footnote 2 (emphasis added).

activities, e.g., a bacterium's ability to infect leguminous plants, or the protein-encoding information of a nucleic acid; Chemical and physical properties, e.g., the alkalinity of a chemical compound, or the ductility or malleability of metals; Phenotype, including functional and structural characteristics, e.g., the shape, size, color, and behavior of an organism; and Structure and form, whether chemical, genetic or physical, e.g., the physical presence of plasmids in a bacterial cell, or the crystalline form of a chemical."<sup>133</sup>

This last change acknowledges that the Funk Brothers decision allows for the analysis of structure, function and utility, not just structure.<sup>134</sup>

In the revised guideline supplemental example set for nature based products,<sup>135</sup> the USPTO revisited the Pomelo Juice example: "A beverage composition comprising pomelo juice and an effective amount of an added preservative."<sup>136</sup> In this case, the USPTO, in applying the changes of the new guidelines, found the claim to be patent eligible.

"Because the claim is a nature-based product, i.e., a combination of a naturally occurring substance (pomelo juice) with an added preservative, the nature-based combination is analyzed to determine whether it has markedly different characteristics from any naturally occurring counterpart(s) in their natural state. In this case, there is no naturally occurring counterpart to the claimed combination, so the combination is compared to the individual components as they occur in nature. The specification indicates that the preservative can be natural or non-natural in origin, but that regardless of its origin, when an effective amount of preservative is mixed with the pomelo juice, the preservative affects the juice so that it spoils much more slowly (spoil in a few weeks) than the naturally occurring juice by itself (spoil in a few days). This property (slower spoiling) of the claimed combination is markedly different from properties of the juice by itself in nature. Accordingly, the claimed combination has markedly different characteristics, and is not a "product of nature" exception. Thus, the claim is not directed to an exception (Step 2A: NO), and qualifies as eligible subject matter."<sup>137</sup>

Importantly for personalized medicine related patents: Section I.B.3.provides for a streamline eligibility that "can be used for a claim that may or may not recite a judicial exception but, when viewed as a whole, clearly does not seek to tie up any judicial exception such that others cannot practice it. Such claims do not need to proceed through the full analysis herein as their eligibility will be self-evident."<sup>138</sup> As such, diagnostics that are configured to not preempt the natural phenomenon, e.g., by having a specific and particular method limitation, and that include a clear and purposeful inventive step, may be able to avoid the bulk of the analysis.<sup>139</sup>

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133 Raul Tamayo, PowerPoint presentation of 2014 Interim Guidance on Patent Subject Matter Eligibility, pg. 12, January 21, 2015 available online at [http://www.uspto.gov/patents/law/exam/jan21forum\\_uspto.pdf](http://www.uspto.gov/patents/law/exam/jan21forum_uspto.pdf).

134 *Funk Bros. Seed Co. v. Kalo Co.*, [333 US 127, 131](#) (1948); see also, *Ass'n for Molecular Pathology v. Myriad*, [133 S. Ct. 2107, 2117](#) (2013) (The Court held that the composition was not patent eligible because the patent holder did not alter the bacteria in any way.) (emphasis added).

135 [http://www.uspto.gov/patents/law/exam/mdc\\_examples\\_nature-based\\_products.pdf](http://www.uspto.gov/patents/law/exam/mdc_examples_nature-based_products.pdf).

136 [http://www.uspto.gov/patents/law/exam/mdc\\_examples\\_nature-based\\_products.pdf](http://www.uspto.gov/patents/law/exam/mdc_examples_nature-based_products.pdf) at 2.

137 [http://www.uspto.gov/patents/law/exam/mdc\\_examples\\_nature-based\\_products.pdf](http://www.uspto.gov/patents/law/exam/mdc_examples_nature-based_products.pdf) at 2.

138 December 2014 Guidance, Section I.B.3.

139 Millen, White, Zelano and Branigan PC : Updated Mayo/Myriad/Alice Patent Eligibility Interim Guidance" January 19, 2015, available online at <http://www.mwzb.com/news-Mayo-Myriad-Alice-patent-eligibility-01192015.html>.

Notably, however, there were no specific diagnostic claim examples provided in the guidelines, perhaps indicating that the law here is far from settled.

## VI. Conclusions

If this Administration is interested in supporting personalized medicine, it has a funny way of showing it, particularly as the their overt efforts in overturning the status quo of some areas of patent law seem to go against the conventional wisdom that patents promote innovation, particularly in the area of biotechnology. Whether or not this conventional wisdom proves true,<sup>140</sup> companies and their investors in the biotechnology industry believe it to be true, and as such, efforts to weaken patents in this area will likely have an effect on investment and innovation.

In light of the seeming animosity by the Supreme Court, and now the Federal Circuit to the status quo of personalized medicine related claims, practitioners can still rely on the USPTO which seems to still be at least responsive to the concerns of the industry, as indicated by the revised guidelines. However, until a final set of guidelines is released there remains some concern that the future guidelines may not be as sympathetic, particularly in light of recent CAFC case law.

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140 Allison, John R. and Lemley, Mark A. and Schwartz, David L., Our Divided Patent System (October 14, 2014). University of Chicago Law Review, Vol. 82, 2015, Forthcoming; Stanford Public Law Working Paper No. 2510004; Chicago-Kent College of Law Research Paper No. 2014-28. Available at SSRN: <http://ssrn.com/abstract=2510004>.