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## Confusion Abounds Regarding Patent Eligibility Within the Biotechnology Community

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## CONFUSION ABOUNDS REGARDING PATENT ELIGIBILITY WITHIN THE BIOTECHNOLOGY COMMUNITY

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### I. Introduction

On October 6, 2014, oral arguments were made before the United States Court of Appeals for the Federal Circuit concerning patents claiming BRCA 1<sup>1</sup> and BRCA 2 Polymerase Chain Reaction<sup>2</sup> (“PCR”) primers. These arguments were made subsequent to the Supreme Court’s decision in *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*<sup>3</sup>

Involved in the case were patents held by Myriad which “cover[ed] compositions of matter and methods relating to the BRCA1 and BRCA2 genes.”<sup>4</sup> Myriad sued Ambry, claiming that Ambry had infringed their patents and seeking a preliminary injunction. The District Court denied the injunction due to claim invalidity, holding that the claims were directed to ineligible subject matter and not patentable under 35 U.S.C §101. Myriad appealed the District Court’s decision to the Court of Appeals for the Federal Circuit. The question presented was whether Myriad’s claims were directed to §101 judicial exceptions, and therefore patent ineligible subject matter.

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<sup>1</sup> *BRCA*, in ENCYCLOPEDIA OF GENOMICS AND PROTEOMICS IN MOLECULAR MEDICINE 173-74 (Detlev Ganten & Klaus Ruckpaul eds., 2006) (defined as “Breast Cancer Susceptibility Gene”).

<sup>2</sup> *Polymerase Chain Reaction*, in ENCYCLOPEDIA OF GENOMICS AND PROTEOMICS IN MOLECULAR MEDICINE, *supra* note 1, at 1443 (defined as “[a] method for rapidly amplifying a small amount of DNA using a heat-stable polymerase and two oligonucleotide primers”).

<sup>3</sup> *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013).

<sup>4</sup> *In re BRCA1-, BRCA2-Based Hereditary Cancer Test Patent Litigation*, 3 F. Supp. 3d 1213, 1227 (D. Utah 2014).

At oral argument Petitioner, Myriad, presented a novel argument in which they attempted to redefine the term conventional<sup>5</sup> in the context of the *Alice* two part test.<sup>6</sup> Respondent, Ambry Genetics, contended that Myriad’s claim for the BRCA1 and BRCA2 primers should be invalidated, because the claim sought to patent an abstract idea, without the “claim amount[ing] to significantly more than the abstract idea itself.”<sup>7</sup> According to Ambry, Myriad simply applied a “conventional, routine, and well-understood”<sup>8</sup> technique to the underlying patent ineligible abstract idea – the BRCA gene – and as such the primer patents should be invalidated under the *Alice* test. Challenging Ambry’s assertion that primer creation using the BRCA gene sequence should result in patent ineligible subject matter, the judges queried<sup>9</sup> what Myriad could have done in order to satisfy the “significantly more than the abstract idea” element of the *Alice* test. Contemplating solutions to the significantly more criteria, the judges advanced the idea of adding a tag<sup>10</sup> to the BRCA primer, and questioning whether this addition would satisfy the *Alice* test.

In response, Myriad advanced an argument attempting to shoehorn the addition of a primer into the “significantly more”<sup>11</sup> part of the *Alice* test, on the theory that the combination of a primer and the BRCA sequence qualify as an improvement to the BRCA gene.

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<sup>5</sup> Foster Dobry, What Do You Mean Conventional?! (Nov. 11, 2014) (unpublished E-brief) (on file with author) (analyzing Myriad’s contention to redefine conventional in light of the *Alice* test for patent eligibility of abstract ideas.).

<sup>6</sup> Memorandum from Deputy Commissioner for Patent Examination Policy Andrew H. Hirschfield to Patent Examining Corps (June 25, 2014) [hereinafter Hirschfield Memo], available at [http://www.uspto.gov/patents/announce/alice\\_pec\\_25jun2014.pdf](http://www.uspto.gov/patents/announce/alice_pec_25jun2014.pdf).

<sup>7</sup> *Id.* at 3.

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

<sup>9</sup> Oral Argument at 33:42, *Univ. of Utah Research v. Ambry Genetics Corp.*, No. 2014-1361 (Fed. Cir. Oct. 6, 2014), available at <http://www.caafc.uscourts.gov/oral-argument-recordings/all/university-of-utah.html>

<sup>10</sup> *Tag*, in GEORGE P. RÉDEI, *ENCYCLOPEDIA OF GENETICS, GENOMICS, PROTEOMICS, AND INFORMATICS* 1927 (3d ed. 2008) (defined as “[i]dentifying a gene by the insertion of a transposon, an insertion element, a transformation vector, or by annealing with a DNA probe”).

<sup>11</sup> Hirschfield Memo, *supra* note 5.

## **II. Myriad Contends That Primer Creation Resulted in a Man Made Product**

On appeal, Myriad contended that the creation of PCR primers from the BRCA sequence resulted in an unconventional man-made product with utility beyond that of isolated DNA, and therefore the primer claims were directed toward patent eligible subject matter. Myriad analogized the creation of the primer to the plasmid transformation performed in *Chakrabarty*.<sup>12</sup>

*Chakrabarty* employed a conventional technique – transformation<sup>13</sup> – to introduce plasmids into a bacterium. It was previously known that certain species of bacteria were able to degrade portions of crude oil, however Chakrabarty’s bacterium had the capability to degrade multiple elements of crude oil.<sup>14</sup> Myriad utilized the ruling in *Chakrabarty* to suggest that despite the fact that Myriad used a conventional technique to create the primers did not automatically result in the BRCA sequence being a product of nature. In short, merely utilizing a conventional technique in creating the primers, according to Myriad, did not preclude patent eligibility.

### **A. Ambry Argues That Myriad Should Be Denied Patent Protection Because the Primers Fail the Two-Part *Alice* Test**

In countering Myriad’s comparison to the transformation process employed in *Chakrabarty*, Ambry analogized Myriad’s primer creation process to the computer implemented abstract idea in *Alice Corp. Pty. v. CLS Bank International*.<sup>15</sup> The Court in *Alice* outlined a two

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<sup>12</sup> *Diamond v. Chakrabarty*, 447 U.S. 303 (1980).

<sup>13</sup> *Transformation, in RÉDEI, supra* note 9, at 2005 (defined as “[i]nformation transfer by naked DNA fragments or plasmid, obviating traditional sexual or asexual processes in prokaryotes and in eukaryotes”).

<sup>14</sup> Douglas Robinson & Nina Medlock, *Diamond v. Chakrabarty: A Retrospective on 25 Years of Biotech Patents*, 17 INTELL. PROP. & TECH. L.J. 12 (2005).

<sup>15</sup> *Alice Corp. Pty. v. CLS Bank Int’l.*, 134 S. Ct. 2347 (2014).

part test for determining the patentability of inventions under 35 U.S.C. § 101,<sup>16</sup> and the test was later formalized in a memorandum by the Deputy Commissioner of Patent Examination.<sup>17</sup>

### **1. Deputy Commissioner’s Memorandum Detailing the Patentability of Abstract Ideas**

In his memorandum, the Deputy Commissioner of the United States Patent and Trademark Office (“USPTO”) outlined the two part *Alice* test, and further clarified what the USPTO considers an abstract idea and what possibly qualifies as something “significantly more than the abstract idea itself.”<sup>18</sup> Part one of the test is to determine whether the “claim is directed to an abstract idea,”<sup>19</sup> and therefore patent ineligible. The USPTO listed four categories of abstract ideas, including: “fundamental economic practices,” “certain methods of organizing human activities,” “an idea of itself,” and “mathematical relationships/formulas.”<sup>20</sup> However, under part two of the *Alice* test, an abstract idea may be patent eligible if the claim added something significantly more than the abstract idea.

Under part two of the *Alice* test what qualifies as significantly more, includes, but is not limited to: “improvements to another technology or technical field,” “improvements to the functioning of the computer itself,” or a “meaningful limitation beyond generally linking the use of an abstract idea to a particular technological environment.”<sup>21</sup> Additionally, the USPTO included items that specifically did not qualify as significantly more. These included simply

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<sup>16</sup> 35 U.S.C. § 101 (2014) (defining “Inventions Patentable”) (“Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.”).

<sup>17</sup> Hirschfield Memo, *supra* note 5, at 3.

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

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

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

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

adding the words “apply it” to a claim, and requiring no more than a generic computer to implement a “well-understood, routine, and conventional” practice known in “the industry.”<sup>22</sup>

## **2. *Alice Corp. Pty. v. CLS Bank International***

*Alice* concerned the implementation of a “computerized scheme for mitigating ‘settlement risk’ via the use of a computer system.”<sup>23</sup> All the claims of *Alice*’s patents required the use of a generic computer. The Court, in applying the test it had outlined in *Mayo*,<sup>24</sup> found that the mitigation of “settlement risk” was an abstract idea, and because the idea of settlement risk was simply employed using a generic computer system, the claims failed to “amount[] to significantly more than the abstract idea itself.”<sup>25</sup> Because *Alice* had attempted to patent an abstract idea without utilizing an inventive step, the court invalidated *Alice*’s patents.

At oral argument, *Ambry* specifically mentioned part two of the *Alice* test concerning the use of a “generic computer to perform . . . a well-understood, routine, and conventional activity . . . known to the industry.”<sup>26</sup> *Ambry* stated *Myriad*’s addition of the primer to the isolated BRCA sequence was, in essence, using a generic computer – the primer – to transform the abstract idea – the BRCA sequence – into patentable subject matter, and as such the BRCA primer failed part two of the test.

Analogizing the use of a primer to requiring a generic computer, as in *Alice*, presents a potential issue with the second part of the test, because there are potentially two valid ways to view the creation of the primers under the *Alice* test. The first is the view taken by *Ambry* that

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<sup>22</sup> *Id.*

<sup>23</sup> *Alice Corp. Pty. v. CLS Bank Int'l.*, 134 S. Ct. 2352 (2014).

<sup>24</sup> *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1297 (2012).

<sup>25</sup> Hirschfield Memo, *supra* note 5, at 3 (describing part two of the *Alice* test).

<sup>26</sup> Oral Argument at 24:25, *Univ. of Utah Research v. Ambry Genetics Corp.*, No. 2014-1361 (Fed. Cir. Oct. 6, 2014), available at <http://www.ca9.uscourts.gov/oral-argument-recordings/all/university-of-utah.html>

employing a primer is simply akin to using a generic computer to implement an abstract idea. As noted by the district court,<sup>27</sup> primer use in PCR sequencing is ubiquitous, and protocol for the creation and use of primers in PCR are numerous.

A second way to view the creation of the primers, however, is that the primer is an “improvement[] to the functioning of the computer itself.”<sup>28</sup> In essence, Myriad improved the function of the BRCA sequence, because they applied it in a way that has never before been employed. As the court noted, no individual had ever combined the BRCA sequence with PCR primer, and therefore this step could be seen as an improvement.<sup>29</sup> Furthering the improvement point of view, on rebuttal Myriad reiterated that adding the primer to the BRCA sequence absolutely improved the function of the patent ineligible BRCA sequence because the sequence was given new utility in that it identified the target mutation.<sup>30</sup>

In short, the primer or probe application to the BRCA sequence could be viewed as both (1) improving the function of the abstract idea, and (2) applying a well-understood, routine, and conventional method to an abstract idea. The first interpretation may qualify as significantly more under the *Alice* test, the second likely not. This two view interpretation supports the Myriad’s assertion that “the biotech community is at sea;”<sup>31</sup> alluding to the fact that the Biotech community is unsure how to interpret recent decisions, and thus are without bearing with which to guide their voyage. The Federal Circuit will hopefully shed light onto what qualifies as “something more than the abstract idea itself,” providing the biotech community with some precedential ruling which they may follow.

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<sup>27</sup> *In re BRCA1-, BRCA2-Based Hereditary Cancer Test Patent Litigation*, 3 F. Supp. 3d 1213, 1227 (D. Utah 2014).

<sup>28</sup> Hirschfield Memo, *supra* note 5, at 3.

<sup>29</sup> Oral Argument at 32:28.

<sup>30</sup> *Id.* at 39:00.

<sup>31</sup> *Id.* at 16:07-16:08.

## **B. What Steps Could Myriad Have Taken to Qualify as Implementing Something More Than the Abstract Idea Itself?**

In response to Ambry’s argument, the court questioned whether much, if anything, related to the BRCA sequence could be patent eligible. The court posed two questions to Ambry in an attempt to elucidate what patentable subject matter might result from the BRCA primers: (1) simply give an example of an application of the BRCA that would be patent eligible<sup>32</sup>; and (2) whether attaching a tag to the primer would confer patentable subject matter.<sup>33</sup>

### **1. Ambry Provides an Example of an Application of the BRCA Gene That Likely Would Be Patent Eligible**

Ambry contended that an *in vitro*<sup>34</sup> assay<sup>35</sup> application of the isolated BRCA sequence could be patent eligible subject matter. Applying the BRCA primer to an *in vitro* assay, according to Ambry, would be analogous to *Chakrabarty*<sup>36</sup>, “where other genetic material was put inside a bacterium to create a new . . . life form not found in nature.”<sup>37</sup> Additionally, Ambry’s argument distinguishes<sup>38</sup> Myriad’s primer claims from those claimed in *Diamond v. Diehr*.<sup>39</sup>

Presenting an assay as an application that would result in patentable subject matter is a weak analogy. It is difficult, if not impossible, to draw a meaningful distinction between an *in*

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<sup>32</sup> *Id.* at 34:08.

<sup>33</sup> *Id.* at 31:09.

<sup>34</sup> *In Vitro*, in RÉDEI, *supra* note 9, at 982 (defined as a “reaction or culture [that] is carried out in a “glass” vessel rather than in an intact cell or in natural culture condition”).

<sup>35</sup> *Assay*, in RÉDEI, *supra* note 9, at 152 (defined as “a test for mutagenic effectiveness or efficiency or the velocity of a chemical reaction catalyzed by enzymes or the test of function of any biological process”).

<sup>36</sup> *Diamond v. Chakrabarty*, 447 U.S. 303 (1980).

<sup>37</sup> Oral Argument at 36:34.

<sup>38</sup> *Id.* at 29:06.

<sup>39</sup> *Diamond v. Diehr*, 450 U.S. 175 (1981).

*vitro* assay and PCR. Both of these processes involve *in vitro* analysis for the detection of a particular analyte<sup>40</sup> in the case of an assay, or gene sequence in the case of PCR. The only difference that could be drawn is that an assay typically measures for the presence of one sequence, while PCR can be used to amplify and identify single or multiple genetic sequences. On balance, Ambry's contention that an assay utilizing the BRCA gene may be patent eligible versus a PCR application utilizing the BRCA gene being patent ineligible is weak, given the similarities of the two processes.

Ambry also distinguished the holding in *Diamond* from the current appeal before the court. In *Diamond*, the Court found that the implementation of a well-known mathematical equation to the vulcanization process of rubber was an inventive step, as the concept would later be known. The claimed method takes a patent ineligible law of nature – the Arrhenius Equation<sup>41</sup> – and applies it using a rubber molding apparatus, which constantly measured the temperature of uncured rubber inside, adjusting the cure time with each measurement to ensure proper curing. Applying the equation to the curing process was held to be an inventive step, and as such, this particular application was patent eligible. *Diamond* did not seek to “pre-empt the use of the Arrhenius Equation,” rather, *Diamond* simply used the “equation in conjunction with all of the other steps” to produce properly cured rubber.<sup>42</sup>

Distinguishing *Diamond* from *Myriad*, Ambry contended that the PCR application of the law of nature – the BRCA sequence – to primers for PCR was not inventive, but instead conventional, and therefore implementation of the BRCA sequence via PCR primers was not

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<sup>40</sup> *Analyte*, in ENCYCLOPEDIA OF MICROFLUIDICS AND NANOFUIDICS 47 (Dongqing Li et al. eds., 2008) (defined “analyte” as “the substance or chemical constituent that is undergoing analysis”).

<sup>41</sup> *Arrhenius Equation*, in ENCYCLOPEDIA OF POLYMERS 66-67 (Jan W. Gooch ed., 2007) (defined as “[a] classical equation describing how rates of chemical reactions increase with rising absolute temperature”).

<sup>42</sup> *Diamond*, 450 U.S. at 187.

patent eligible. Moreover, granting Myriad patent protection for the BRCA sequence would likely preempt the use of the BRCA sequence. In short, the BRCA primer employs conventional techniques to a law of nature that, if granted patent protection, would preempt use of the sequence. Therefore, the BRCA primer for use in PCR should not be patent eligible. On the other side of the coin, using the BRCA sequence in an *assay* for the detection of one analyte would *not* preempt the use of the BRCA sequence and, therefore, according to the *Alice* court should be patent eligible.

## **2. Ambry Contends That the Tag Hypothetical Would Not Result in Patent Eligible Subject Matter Because the Primer Will Hybridize with or Without the Tag**

In analyzing the tag hypothetical posed by the court, Ambry argued that merely adding a tag to the PCR primer did not confer patentability on the primer.<sup>43</sup> Ambry stated that this was due to the fact that the tag is placed on the primer in order to report the hybridization of the primer to the target sequence. Mirroring the district court's Watson-Crick hybridization finding<sup>44</sup>, Ambry argued that hybridization would occur with or without the tag. Therefore, the tag does not confer any additional utility upon the patent ineligible BRCA sequence. Furthermore, allowing Myriad to patent a tagged BRCA primer would preempt the use of the BRCA sequence in PCR applications. Preemption of all PCR uses of a law of nature is contrary to the public policy outlined in *Mayo*<sup>45</sup>; thus a tagged primer should not qualify as patent eligible.

### **III. The District Court Denies Myriad's Preliminary Injunction, Finds BRCA Primer Likely Unpatentable Subject Matter Because It Is Conventional, Routine,**

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<sup>43</sup> Oral Argument at 31:16.

<sup>44</sup> *In re BRCA1-, BRCA2-Based Hereditary Cancer Test Patent Litigation*, 3 F. Supp. 3d 1213, 1266 (D. Utah 2014).

<sup>45</sup> *Mayo Collaborative Servs. v. Prometheus Labs. Inc.*, 132 S. Ct. 1289, 1294 (2012).

### **and Well-understood**

Following a hearing for a preliminary injunction that would have barred Ambry's sale of less expensive BRCA tests, Myriad's request for a preliminary injunction was denied. Myriad argued that the "probes, primers, and [assays]"<sup>46</sup> were an inventive step "because they utilize the BRCA1 and BRCA2 sequences."<sup>47</sup> Moreover, the method claims could not qualify as "conventional, routine, or well-understood" because the claims are limited to a specific application (PCR) and as such were not "routine at the time the patents were filed because it was impossible as a practical matter to create or perform [PCR] without the knowledge of the BRCA1 and BRCA2 sequences."<sup>48</sup>

The district court quickly disposed of Myriad's argument, holding that converting the BRCA 1 and BRCA 2 sequences to primers, probes, or assays involved steps that were conventionally used in nearly every lab across the country when attempting to create PCR primers.<sup>49</sup> The protocol for the creation of the primers, the reagents used in the creation of the primers, and the laboratory devices needed were commonplace, and do not transform unpatentable subject matter into patentable subject matter.<sup>50</sup> Furthermore, simply limiting the application of the BRCA genes to the specific field of PCR did not allow for circumvention of the "prohibition against patenting abstract ideas."<sup>51</sup>

The district court's analysis centers on the fact that in creating the primers based on the BRCA sequences, Myriad did not perform any step that qualified the claim as something

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<sup>46</sup> *In re BRCA1-, BRCA2-Based Hereditary Cancer Test Patent Litigation*, 3 F. Supp.3d at 1269.

<sup>47</sup> *Id.*

<sup>48</sup> *Id.* at 1270 (citing Plaintiffs' Reply Brief at 58).

<sup>49</sup> *Id.*

<sup>50</sup> *Id.*

<sup>51</sup> *Bilski v. Kappos*, 561 U.S. 593, 611 (2010) (quoting *Diamond v. Diehr*, 450 U.S. 175, 191 (1981)).

“significantly more” than the BRCA sequence itself. The protocol followed to create the BRCA primers was conventional, and as such those steps did not transform the patent ineligible BRCA sequence into a patent eligible claim.<sup>52</sup> The court stated that Myriad was essentially attempting to “preempt use of laws of nature” by claiming the BRCA primer, and “foreclosing the . . . means to study and test for BRCA1 and BRCA2” was contrary to public policy.<sup>53</sup>

Further analysis by the district court focused on the alleged utility added by Myriad, regarding the BRCA primers. The court found, unpersuasive, the argument that primers “have a utility beyond naturally occurring DNA” due to the fact that the primers will “function like natural DNA during replication” because of another natural law – Watson-Crick base pairing.<sup>54</sup>

#### **A. On Appeal, Myriad Contends Primers Are Patentable Because Steps Taken by Myriad Were Not Conventional**

During oral argument,<sup>55</sup> Myriad contended that primers created from the isolated BRCA sequence were patentable, because the primers were unconventional man-made products that had new utility in PCR reactions. Furthermore, Myriad argued that the court erred because its holding would require that every inventor who discovers a new law of nature would need to implement a new, non-conventional process in order to patent the law of nature.<sup>56</sup> Additionally, Myriad disputed the Watson-Crick base pair finding of the district court, arguing that the primer sequences alone did not hybridize to the BRCA gene in nature.<sup>57</sup> Myriad attempted to

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<sup>52</sup> *In re BRCA1-, BRCA2-Based Hereditary Cancer Test Patent Litigation*, 3 F. Supp. 3d 1213, 1270-71 (D. Utah 2014).

<sup>53</sup> *Id.*

<sup>54</sup> *Id.* at 1266.

<sup>55</sup> Oral Argument at 5:52, *Univ. of Utah Research v. Ambry Genetics Corp.*, No. 2014-1361 (Fed. Cir. Oct. 6, 2014), *available at* <http://www.cafc.uscourts.gov/oral-argument-recordings/all/university-of-utah.html>

<sup>56</sup> *Id.*

<sup>57</sup> *Id.* at 12:05.

distinguish steps taken in their preparation of PCR primers from steps taken in *Mayo* and *Funk Bros.*, where patent protection was denied.<sup>58</sup>

### **1. *Mayo Collaborative Services v. Prometheus Laboratories, Inc.***

*Mayo*, “concern[ed] patent claims covering processes that help doctors who use thiopurine drugs to treat patients with [Crohn’s disease and ulcerative colitis] determine whether a given dosage level is too low or too high.”<sup>59</sup> In its most basic form, the *Mayo* patents dealt with a law of nature regarding metabolism of thiopurine and directed physicians simply to apply the law. The claims did not claim any process that was significantly more than the law of nature exception. As a result, patent protection was invalidated on the claim concerning the level of “certain thiopurine metabolites”<sup>60</sup> because the claim simply stated to “apply it.”<sup>61</sup> The court held that the “claimed processes” did not qualify for patent protection because they “involve well-understood, routine, conventional activity”<sup>62</sup> commonly engaged in by practitioners in the field. The court denied patent protection, holding, for policy reasons, that “upholding the patents would risk disproportionately tying up the use of the underlying natural laws, inhibiting their use in the making of further discoveries.”<sup>63</sup>

### **2. *Funk Bros. Seed Co. v. Kalo Inoculant Co.***

In *Funk Bros.*, respondent discovered a new inoculant mixture of bacteria from the genus *Rhizobium* which lacked the inhibitive effect present in previous mixtures, and obtained patent protection on said *Rhizobia* mixture.<sup>64</sup> Kalo Inoculant sued for patent infringement, alleging

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<sup>58</sup> *Id.* at 12:11.

<sup>59</sup> *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1294 (2012).

<sup>60</sup> *Id.*

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

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

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

<sup>64</sup> *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948).

Funk Bros. violated their patent.<sup>65</sup> Funk Bros. counter claimed, seeking a declaratory judgment that Kalo's patent was invalid, because it sought to claim patent ineligible subject matter in the form of a law of nature.<sup>66</sup>

Prior to the date of the patent application, it was common knowledge that species of leguminous plants were greatly benefited by the presence of certain Rhizobia – bacteria which fix nitrogen into a form useable by plants. Typically, only one species of Rhizobia was used to inoculate one species of plants, as Rhizobia species meant for one plant may mutually inhibit Rhizobia species meant for other plant species.<sup>67</sup> The inventor in this case discovered that certain Rhizobia could be combined in an inoculant that would work with many different species of plants, while not exhibiting mutual inhibition. The Supreme Court held that the discovery of the non-inhibition was a fact of nature, and therefore was not eligible for patent protection, because it was the “handiwork of nature and hence . . . not patentable.”<sup>68</sup>

Attempting to distinguish their discovery from those of *Mayo* and *Funk Bros.*, Myriad analogized their primers to the bacteria and plasmid combination in *Chakrabarty*. In *Chakrabarty*, a patent was granted on a bacterium created via the conventional process of transformation.<sup>69</sup> Four plasmids<sup>70</sup> conferring a metabolic pathway for the degradation of hydrocarbons were transformed into the bacterium, resulting in patentable subject matter. The

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

<sup>66</sup> *Id.*

<sup>67</sup> *Id.*

<sup>68</sup> *Id.* at 131.

<sup>69</sup> *Transformation*, in RÉDEI, *supra* note 9, at 2005 (defined as “[i]nformation transfer by naked DNA fragments or plasmid, obviating traditional sexual or asexual processes in prokaryotes and in eukaryotes”).

<sup>70</sup> *Plasmid*, in RÉDEI, *supra* note 9, at 1506-07 (defined as a “dispensable genetic element, which can propagate independently and can be maintained within the (bacterial) cell, and may be present in yeast and mitochondria of a number of organisms. The plasmids may be circular or linear double-stranded DNA.”).

Court held that the claimed bacterium was, in fact, patentable subject matter because, although the unaltered bacterium is a product of nature, the combination of plasmid and bacteria is a product of man.<sup>71</sup> The claimed bacterium had to be created in the lab, and was not found in nature, weighing in favor of finding the engineered bacterium patent eligible.

In short, Myriad asserted that because the primer for BRCA based PCR reactions was created in a lab, with conventional techniques, the primers were analogous to *Chakrabarty*, and therefore resulted in patent eligible subject matter. The difficulty in distinguishing *Chakrabarty* and the present case has been noted in at least one jurisdiction outside the United States. In the opinion of the Federal Circuit of Australia, the court, in dicta, stated that it was difficult to reconcile the opinion of the Court in *Chakrabarty* with its holding in AMP.<sup>72</sup>

At a high level of abstraction, the comparison made by Myriad to *Chakrabarty* is sound. Both parties invented a product that is not found in nature, having new utility conferred to it by man, the result of which had never before been observed. However, delving into the substance of what is actually being attempted by Myriad reveals some troubling policy concerns. Allowing a hypothetical biotech company to obtain patent protection for a DNA sequence will essentially prevent any other entity from developing tests or other applications of the patented sequence. This would stymie innovation in the field of genetic research, as only the patent holder could utilize the sequence. This preemptive effect is what the Court sought to prevent in *Mayo*<sup>73</sup>, and therefore, the district court, for policy reasons, is sound in denying the motion for temporary injunction.

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<sup>71</sup> *Diamond v. Chakrabarty*, 447 U.S. 303 (1980).

<sup>72</sup> *D'Arcy v. Myriad Genetics, Inc.*, [2014] FCAFC 115 (Austl.).

<sup>73</sup> *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1294 (2012).

## B. Myriad's Watson-Crick Base Pairing Counter-argument

At oral argument, Myriad countered the Watson-Crick analysis made by the district court in denying the preliminary injunction. Myriad, in essence, argued that primers when put together in a petri dish, would not hybridize according to Watson-Crick hybridization principles<sup>74</sup>, and therefore, this was not a case of man adding “natural utility unchanged from nature.”<sup>75</sup>

Myriad, in using this analogy, was attempting to distinguish primer creation from the bacteria inhibition found in *Funk Bros.* In *Funk Bros.*<sup>76</sup>, multiple types of bacteria were placed in a solution that provided all the benefits of Rhizobia nitrogen fixation, without the bacteria inhibiting the effectiveness of each other. Man, in *Funk Bros.*, was required to do no more than combine the bacteria in a petri dish, and the law of nature was exhibited via non-inhibition<sup>77</sup>. In contrast, when the primers were placed in a petri dish, the Watson-Crick base pairing would not occur, and this fact made the primer creation inherently different from non-inhibition in *Funk Bros.* It therefore follows, according to Myriad, because man did not add anything to the bacteria in *Funk Bros.*, and patent protection was rightly denied, it follows that when man *has* added new utility, as is the present case, patent protection should be granted.<sup>78</sup>

The response by Myriad misses the point made by the district court. The court pointed out that just because primers functioned as primers in PCR did not make them “markedly different from that of naturally occurring DNA.”<sup>79</sup> Myriad, in short, attempted to make an inapt

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<sup>74</sup> Oral Argument at 12:05, *Univ. of Utah Research v. Ambry Genetics Corp.*, No. 2014-1361 (Fed. Cir. Oct. 6, 2014), available at <http://www.cafc.uscourts.gov/oral-argument-recordings/all/university-of-utah.html>

<sup>75</sup> *Id.* at 11:59.

<sup>76</sup> *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948).

<sup>77</sup> Oral Argument at 12:22

<sup>78</sup> *Id.* at 12:11.

<sup>79</sup> *In re BRCA1-, BRCA2-Based Hereditary Cancer Test Patent Litigation*, 3 F. Supp. 3d 1213, 1266 (D. Utah 2014).

comparison to *Funk Bros.* The comparison fails because in *Funk Bros.*, all the ingredients needed for non-inhibition were added, including the Rhizobia inoculant, “bacterial nutrients,”<sup>80</sup> and “moist powder”<sup>81</sup> medium. Without these key components, the bacteria would not exhibit the law of nature. The same reasoning goes for PCR primers. They are primers for a PCR reaction, not simply DNA fragments in isolation. For the Watson-Crick hybridization to occur all the components of PCR must be present, including isolated DNA, “heat-stable polymerase”<sup>82</sup>, and the primers. Therefore, Myriad’s statement that the primers alone would not produce any Watson-Crick hybridization is absolutely true. However, taking all the necessary components into account renders this analogy inapposite.

#### **IV. The USPTO Provides Interim Guidance on Nature-based Products**

The USPTO occasionally releases what they refer to as “Interim Guidance.” The purpose of the interim guidance is to “set[] out the Office’s interpretation of” confusing or unclear areas of patent law.<sup>83</sup> The guidance does not have the force of law, and as such is not persuasive authority to the courts.<sup>84</sup> The USPTO released such a guidance in December of 2014 dealing with §101<sup>85</sup> patent eligible subject matter. The focal point of the interim guidance is the flow chart<sup>86</sup> detailing how to determine what qualifies as patent eligible subject matter. Part 1 and 2

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<sup>80</sup> U.S. Pat. No. 2,200,532 col. 2 1.5-12 (filed Aug. 24, 1938).

<sup>81</sup> *Id.* at col. 1 1.60-66, col. 2 1.1-4.

<sup>82</sup> *Heat-stable Polymerase*, in *ENCYCLOPEDIA OF ASTROBIOLOGY* 1648 (Muriel Gargaud et al. eds., 2011) (defined as “polymerase extracted from the thermophilic bacteria *Thermus aquaticus*. It is the DNA polymerase of choice for PCR as it can withstand the high temperatures of the process.”).

<sup>83</sup> 2014 Interim Guidance on Patent Subject Matter Eligibility, 79 Fed. Reg. 74619 (Dec. 16, 2014).

<sup>84</sup> *Id.*

<sup>85</sup> 35 U.S.C. § 101 (2012).

<sup>86</sup> 79 Fed. Reg. at 74621.

of the *Alice/Mayo* test<sup>87</sup> are present and comprise steps 2A and 2B.<sup>88</sup> The first step in establishing patent eligibility is to determine whether the claim is “to a process, machine, manufacture or composition of matter.”<sup>89</sup> If the claim is directed to any of the listed potentially §101 eligible categories, the examiner then moves to the *Alice/Mayo* part of the test. Under this part, if the claim is directed to any judicially recognized exceptions,<sup>90</sup> the claim must recite something significantly more than the exception itself to qualify for patent protection.

#### **A. Nature Based Products Supplement to 2014 Interim Eligibility Guidance**

Likely the most useful element – at least to the biotech community – of the recently released interim guidance is the accompanying supplement, which lists examples of potentially patent eligible nature-based subject matter. Key to resolving the nucleic acid patent eligibility issue recently raised in litigation<sup>91</sup> is an example Nature-based claim, which claims a nucleic acid sequence and tag.<sup>92</sup> In short, the issue raised by the panel at oral argument concerned whether patent eligibility was conferred upon a nucleic acid via use of a tag.<sup>93</sup> Such a tag could employ fluorescence or radioactivity in reporting primer hybridization to the target sequence. The court’s presumption was that the addition of a tag by man would result in the BRCA sequence eligible under §101.

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<sup>87</sup> Hirschfield Memo, *supra* note 5.

<sup>88</sup> *Id.*

<sup>89</sup> 79 Fed. Reg. at 74621.

<sup>90</sup> *Id.* at 74622 (defined as those claims that are “directed to a . . . law of nature, a natural phenomenon, or an abstract idea).

<sup>91</sup> *In re BRCA1-, BRCA2-Based Hereditary Cancer Test Patent Litigation*, 3 F. Supp. 3d 1213 (D. Utah 2014).

<sup>92</sup> U.S. Patent & Trademark Office, Nature-Based Product Examples 9-10 (Dec. 16, 2014) [hereinafter Nature-Based Product Examples].

<sup>93</sup> Oral Argument at 31:09, *Univ. of Utah Research v. Ambry Genetics Corp.*, No. 2014-1361 (Fed. Cir. Oct. 6, 2014), *available at* <http://www.ca9.uscourts.gov/oral-argument-recordings/all/university-of-utah.html>

Ambry was challenged by the court<sup>94</sup> regarding the addition of a tag creating patent eligible subject matter. Ambry responded<sup>95</sup> that the tag added contributed nothing to the BRCA sequence. In essence, the tag did not alter binding of the DNA, hybridization would occur with or without such a tag. The nucleic acid hypothetical claim provided by the USPTO,<sup>96</sup> however, rejects this reasoning and points to the conclusion that adding a tag to an isolated nucleic acid sequence would transform the product into patent eligible subject matter. This is due to the fact that the combination of the nucleic acid and the tag are not found in nature.<sup>97</sup> The reason cited for granting patent eligibility to the tag/nucleic acid sequence is that the combination of the tag and primer contains both functional and structural characteristics which amount to alterations “of a marked difference”<sup>98</sup> from those in nature, and thus patent protection may be warranted. The example given for a structural difference<sup>99</sup> is the new molecule now comprises two separate molecules as compared to the natural DNA, and the example given as to the functional difference<sup>100</sup> is that the new molecule is now fluorescent. In short, adding a tag to the nucleic acid satisfies the § 101 patent eligibility inquiry due to the marked differences between natural nucleic acids and tagged nucleic acids. In short, the tagged nucleic acids amount to significantly more than naturally occurring nucleic acids.

The ramifications of the interim guidance and the examples provided are that if an application for the BRCA 1 and 2 sequences at issue in *Ambry* were submitted today, the sequences, if tagged, would likely result in the USPTO finding them patent eligible. However,

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<sup>94</sup> *Id.*

<sup>95</sup> *Id.* at 31:09.

<sup>96</sup> Nature-Based Product Examples, *supra* note 91, at 9-10.

<sup>97</sup> *Id.* at 11.

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

<sup>99</sup> *Id.*

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

as stated before, the interim guidance is not binding on the courts, and as such they may still rule in contradiction to a USPTO finding of patent eligibility.<sup>101</sup> In short, according to the USPTO, the addition of a tag or probe results in a new molecule that is markedly different from a naturally occurring sequence, and this marked difference results in patent eligibility for the new molecule.

However, concerns are raised when considering the result of allowing a nucleic acid sequence, such as the BRCA gene, and tag combination to be patent eligible. *Mayo* specifically mentioned the issue courts have with allowing applicants to “tying up” scientific truths.<sup>102</sup> Allowing discoverers of particular genes, which alone are not patent eligible, to simply add a tag to the gene and confer patent protection over the entire gene would essentially prevent use of the gene by any other person. In theory, sophisticated parties could claim the sequence with any number of tags, known or theoretical, and prevent other parties from using a particular sequence and any tag combination in any other process. Combining a tag and nucleic acid sequence may result in essentially locking up a law of nature, and that goes against public policy.<sup>103</sup>

Regardless of how large the potential is for locking up laws of nature, after issuance of the interim guidance at least determining patent eligibility of nucleic acids is now much clearer. Any inventor attempting to determine whether a particular nucleic acid sequence may be patent eligible simply need look to the flowchart and examples, and tailor their claims to the example patent eligible nucleic acid claims listed. The interim guidance should alleviate some of the issues raised as a consequence of recent Supreme Court decisions, and hopefully the biotech

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<sup>101</sup> The CAFC did just this in *University of Utah v. Ambry*, in finding that Myriad’s patents were directed toward patent ineligible subject matter. The guidance provided an example that appeared to show that the USPTO would have approved the claim under § 101.

<sup>102</sup> *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1294 (2012).

<sup>103</sup> *Id.*

community now has a means for efficiently navigating concerns regarding nucleic acid patent eligibility.

## V. Conclusion

The biotech community remains in the dark as to what will qualify as patent eligible subject matter. Courts are not bound to follow guidance issued by the USPTO, and in the recently published decision *University of Utah v. Ambry Genetics* the court did exactly that -- declining to follow the interim guidance and finding Myriad's claims invalid.<sup>104</sup> Attempting to resolve the issue will take additional precedent, and in the meantime inventors will need to juggle satisfying both the USPTO's guidance, in order to get a patent issued, and the Court of Appeals for the Federal Circuit – in order for an issued patent to survive being invalidated. The likely result lead to inventors being unable to claim certain elements for fear of said elements being invalidated.

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<sup>104</sup> *BRCA1- & BRCA2-Based Hereditary Cancer Test Patent Litig. v. Ambry Genetics Corp.*, 774 F.3d 755 (Fed. Cir. 2014).