Title: Patenting Natural Compounds – Effect of *Association for Molecular Pathology v. Myriad Genetics, Inc.* Supreme Court Ruling on Gene Patents

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The U.S. Supreme Court's June 13, 2013 ruling in *Association for Molecular Pathology v. Myriad Genetics, Inc.*[1] ("*Myriad"*) — that naturally occurring DNA sequences are not patentable — may have serious, and perhaps unintended, consequences on issued patents, pending patent applications and future biotechnology inventions. In *Myriad*, the unanimous Court ruled that DNA sequences found in nature, such as isolated genomic DNA, are not patentable subject matter under Section 101 of the Patent Act, as codified in 35 U.S.C. §101 ("Section 101").

Until *Myriad*, the United States Patent and Trademark Office (USPTO) Utility Examination Guidelines allowed that "[a]n isolated and purified DNA molecule that has the same sequence as a naturally occurring gene is eligible for a patent … ."[2] Under this policy, by the end of 2010 the USPTO had granted over fifteen thousand patents containing claims to isolated nucleic acids with naturally occurring sequences, with an estimated excess of eight thousand such patents still in effect as of May 2013.[3] These patents cover nucleic acids relevant to many fields, including medicine, agriculture, energy and food and beverage manufacturing. After *Myriad*, claims to nucleic acids with naturally occurring sequences are now at risk of invalidation. Of equal concern is that, immediately following *Myriad*, Deputy Commissioner for Patent Examination Policy Andrew Hirshfeld directed the Patent Examining Corps to "reject product claims drawn solely to naturally occurring nucleic acids or fragments thereof, whether isolated or not, as being ineligible subject matter under 35 U.S.C. § 101,"[4] thereby putting potentially hundreds of pending patent application claims in jeopardy of rejection.

Concerns have also been raised as to the scope of the *Myriad* holding. According to Jim Greenwood, President and CEO of the Biotechnology Industry Organization (BIO), the *Myriad* decision could "create business uncertainty for a broader range of biotechnology inventions."[5]

For example, *Myriad* leaves unanswered the questions of whether isolated non-nucleic acid natural compounds are patentable and, if so, under what conditions?

Whether *Myriad* is narrowly applied only to nucleic acids or broadly interpreted to apply to all naturally occurring biomolecules is an unresolved question with significant implications for biotechnology innovation.[6] The *Myriad* Court held that "[a] naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated."[7] Although *Myriad* did not address naturally occurring compounds other than DNA, its emphasis on the non-patentability of isolated naturally occurring compounds raises concerns that it could be applied to invalidate claims to isolated naturally occurring small compounds, proteins, polypeptide sequences, antibodies, lipids, steroids and other naturally occurring biomolecules. Indeed, the words "natural" or "naturally" appear 34 times in the opinion and words with the root "isolate" appear 34 times.

Between 1981 and 2010, 19% of new chemical entities (NCEs) approved by the FDA were isolated and purified natural products or biotechnologically produced peptides or proteins, some of which may be identical to natural compounds.[8] Thus, application of *Myriad* to isolated naturally occurring compounds other than DNA could potentially affect the patentability of therapeutic agents that are widely used in medicine, in addition to compounds used in other fields. On the other hand, *Myriad* does not exclude the possibility that an isolated natural compound may be patentable if it is shown to be "new and useful" and not merely a natural phenomenon. Under Section 101 of the Patent Act, "[w]hoever invents or discovers any new and useful … composition of matter, or any new and useful improvement thereof, may obtain a patent therefor … ."[9] Nonetheless, as the *Myriad* Court reiterated, laws of nature, natural phenomena, and abstract ideas are long-held exceptions to patentable subject matter – exceptions

that are "not without limits" and, in determining whether subject matter is patentable, a balance must be struck between incentivizing invention versus removing the basic tools of scientific invention, such as natural phenomena, from the public domain.[10]

Applying these principles, the *Myriad* Court found that Myriad's discovery of the location and sequence of the BRCA1and BRCA2 genes "fell squarely within the law of nature exception."[11] Moreover, the Court found that "separating [a] gene from its surrounding genetic material is not an act of invention."[12] As the Court explained, Myriad's claims were "focus[ed] on the genetic information encoded in the … genes"[13] and did not "rely in any way on the chemical changes that result from the isolation of a particular section of DNA."[14] Thus, applying this reasoning, the Court held that Myriad's claims to "genes and the information they encode are not patent eligible under §101 simply because they have been isolated from the surrounding genetic material."[15]

Assuming that *Myriad* is applicable to isolated naturally occurring compounds other than DNA, *Myriad* can still be interpreted to mean that such compounds are patent eligible if the inventors reveal some characteristic distinguishing them from their natural counterparts, thereby demonstrating a "new and useful … composition of matter."[16] Indeed, the *Myriad* Court acknowledged that the process of isolation of a segment of genomic DNA creates a nucleic acid compound chemically distinct from the naturally occurring gene. However, the Court found that this structural difference was not adequate to confer any "new and useful" property on the isolated nucleic acid sequence. That is, both the isolated and natural DNA sequence bear the same informational properties and Myriad failed to demonstrate any additional properties beyond that which were "useful."

The patentability of isolated natural compounds having "new and useful" characteristics is consistent with prior jurisprudence. In a Federal court decision from 1911, *Parke-Davis & Co. v. H.K. Mulford Co*.[17], Judge Learned Hand explained that purified adrenaline "became for every practical purpose a new thing commercially and therapeutically," because the purified adrenaline had properties distinct from the compound *in situ*. Later courts similarly found patentable purified naturally occurring compounds.[18] These compounds were determined to be patentable even though the claimed products were isolated from nature because the isolated and purified compounds possessed some property that provided a therapeutic advantage compared to the natural compounds. That is, isolation alone did not render the claimed product patentable; the fact that it had some "new and useful" property compared to the naturally occurring compound made it patentable.

Whether *Myriad* will be applied broadly to isolated naturally occurring compounds other than DNA, and what constitutes a sufficient "new and useful" property to render an isolated naturally occurring compound patentable, will remain unclear until courts apply *Myriad* in future litigations. Until then, the uncertainty currently surrounding what constitutes a patentable invention, in the wake of *Myriad*, may have the unintended consequence of dampening innovation and stifling discovery of new medicines.

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[1] *Association for Molecular Pathology v. Myriad Genetics, Inc.,* 133 S.Ct. 2107, 2109 (2013).
[2] Utility Examination Guidelines (USPTO), 66 Fed. Reg. 4, 1092-1099 (Jan. 5, 2001).
[3] Gregory D. Gaff, Zhen Lei, Carol Nottenburg, Sooyoung Oh, Philip G. Pardey & Devon Phillips, *Not quite a myriad of gene patents*, 31Nature Biotechnology, May 2013, at 404-10.
[4] Memorandum from Andrew H. Hirshfeld, Deputy Comissioner for Patent Examination Policy, *Guidance For Determining Subject Matter Eligibility Of Claims Reciting Or Involving Laws Of Nature, Natural Phenomena, & Natural Products* (March 2014)(available at http://www.uspto.gov/patents/law/exam/myriad-mayo_guidance.pdf).

[5] Statement from Jim Greenwood, President and CEO of the Biotechnology Industry Organization (BIO)(June 13, 2013) (Roy Zwahlen, *Myriad Supreme Court Decision: BIO' Statement*, Patently Biotech, June 2013(August 21, 2013), http://www.biotech-now.org/public-policy/patently-biotech/2013/06/myriad-supreme-court-decision-bios-statement#.
[6] Although, since this article was written, the USPTO issued a *Guidance For Determining Subject Matter Eligibility Of Claims Reciting Or Involving Laws Of Nature, Natural Phenomena, & Natural Products* (March 2014) ("March 2014 USPTO Guidance") which broadly applies *Myriad* to all natural products, this USPTO interpretation of the *Myriad* holding is not binding on the courts, leaving the question unresolved. Memorandum from Andrew H. Hirshfeld, Deputy Comissioner for Patent Examination Policy, *Guidance For Determining Subject Matter Eligibility Of Claims Reciting Or Involving Laws Of Nature, Natural Phenomena, & Natural Products* (March 2014)(available at http://www.uspto.gov/patents/law/exam/myriad-mayo_guidance.pdf).
[7] *Myriad*, 133 S.Ct. at 2111.
[8] Gordon M. Cragg & David J. Newman, *Natural Products as Sources of New Drugs over the 30 Years from 1981 to 2010*, 2012 J. Nat. Prod.75(3), at 311-35.
[9] 35 U.S.C. § 101
[10] *Myriad*, 133 S.Ct. at *2116
[11] *Id.* at *2117
[12] *Id.*
[13] *Id.* at *2110
[14] *Id.* at *2118
[15] *Id.* at *2120
[16] The March 2014 USPTO Guidance instructs the Patent Examining Corps to balance several factors to determine whether claims involving laws of nature, natural phenomena or natural products are patentable. According to the March 2014 USPTO Guidance, a claim reciting or involving a natural product, which "includes, but is not limited to: 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," is patent ineligible unless a factor-based analysis show that the claim is "*significantly different*" from the natural product. However, marked or significant differences resulting from routine activity or human manipulation of natural processes may still weigh in favor of patentability. Thus, a natural product that acquires a property that confers a therapeutic advantage via the process of isolation may be patent eligible if the product claim recites significant differences. March 2014 USPTO Guidance at 2.
[17] *Parke-Davis & Co. v. H.K. Mulford Co*., 189 F. 95, 103 (S.D.N.Y. 1911),
[18] *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991); *Merck & Co. v. Olin Mathieson Chemical Corp.*, 253 F.2d 156 (4th Cir. 1958*); In re Bergstrom*, 427 F. 2d 1394 (C.C.P.A. 1970).