Patenting DNA Sequences after the US *Myriad* Decision: New Frontiers or Just More of the Same?

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Abstract

The recent United States Supreme Court decision in *Association for Molecular Pathology v Myriad Genetics Inc* determined that a naturally occurring DNA sequence is not patentable. This is a significant finding by a superior United States court after more than 20 years of contentious debate about the merits of patenting DNA. This article reviews the decision and considers its likely effects on existing and future claims over DNA sequences. The article concludes that even though the decision might be heralded as a significant limitation on DNA patenting, in fact, probably very little has changed and DNA remains eminently patentable. The decision is really a triumph of form over substance.

Introduction

Ever since the United States Supreme Court decision in *Diamond v Chakrabarty* stating “anything under the sun that is made by man”,¹ and establishing that living human-made biological organisms were patentable subject matter under the United States Patent Act, the reach of patents over biological materials has been complicated and contested.² This is partly a consequence of the broad language of the patent

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¹ Noting, of course, that this is a misleading quotation from the legislative history of the Patent Act the full quote being: “A person may have ‘invented’ a machine or a manufacture, which may include anything under the sun made by man, but it is not necessarily patentable under § 101 unless the conditions of the title are fulfilled”: S Rep. No 1979, 82d Cong., 2d Sess., 5 (1952); H.R.Rep. No.1923, 82d Cong., 2d Sess. 6 (1952).

² *Diamond v Chakrabarty*, 447 U.S. 303, 309 (1980); 35 U.S.C. §101. For an overview of the significance of this case see Douglas Robinson and Nina Medlock, “Diamond v Chakrabarty: A Retrospective on 25 Years of Biotech Patents” (2005) 17 *Intellectual Property & Technology Law Journal* 12.

thresholds. The United States *Constitution* provides a very general power to make laws about patents:

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.³

This has been expressed in the *United States Code* (35 U.S.C. § 101) with the threshold standard for patenting as:

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.

Over time the language of this threshold standard has been given “wide scope”⁴ albeit with limits including that a “manufacture” or “composition of matter” described as the “laws of nature, physical phenomena, and abstract ideas”⁵ and “[p]henomenon of nature, though just discovered, mental processes, and abstract intellectual concepts”⁶ are not patentable.⁷ The significance of the Supreme Court’s *Diamond v Chakrabarty* decision was to expressly allow a claim to a genetically engineered bacterium itself where the question before the Court was whether the claimed bacterium constituted a “manufacture” or “composition of matter” within the meaning of the United States Patent Act:⁸

the patentee has produced a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility. His discovery is not nature’s

³ *Constitution*, Article I, § 8, cl 8.

⁴ *Bilski v. Kappos*, 130 S.Ct. 3218, 3225 (2010); *JEM Ag Supply Inc v. Pioneer Hi-Bred International Inc*, 534 U.S. 124, 131 (2001); *Diamond v. Chakrabarty*, *op. cit.* note 2 at 308.

⁵ *Diamond v. Chakrabarty*, *ibid.* at 309. See also *Mayo Collaborative Services v. Prometheus Laboratories Inc*, 132 S.Ct. 1289, 1293 (2012); *Bilski v. Kappos*, *ibid.* at 3226; *Diamond v. Diehr*, 450 U.S. 175, 185 (1981).

⁶ *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972).

⁷ See *Association for Molecular Pathology v. United States Patent and Trademark Office*, 702 F.Supp.2d 181, 218-219 (2010).

⁸ *Op. cit.* note 2 at 307.

handiwork but his own; accordingly it is patentable subject matter under §101 [United States Patent Act].⁹

While this was a narrow question before the Supreme Court the effect of the court's conclusion was to liberalise the conceptions about what kinds of biological materials were patent eligible, including claiming DNA sequences isolated from biological organisms.¹⁰ Isolated DNA sequences were then framed as mere chemicals irrespective of their biological origin, association or function.¹¹ The following decades witnesses a cascade of DNA sequence patents,¹² albeit there remained concerns about the eligibility of patents claiming DNA sequences that were identical to those found in "nature".¹³ The unresolved, and perhaps unresolvable, issue is where to draw the line between objects and materials that satisfy the threshold standards of a "manufacture" or "composition of matter"?¹⁴

⁹ *Op. cit.* note 2 at 310.

¹⁰ The analysis in this article distinguishes between "naturally occurring segments of DNA" and "complementary DNA (cDNA), which contains the same protein-coding information found in a segment of natural DNA but omits portions within the DNA segment that do not code for proteins": see *Association for Molecular Pathology v. Myriad Genetics Inc.*, 133 S.Ct. 2107, 2111-2112 (2013). See also *Association for Molecular Pathology v. United States Patent and Trademark Office*, 689 F.3d 1303, 1310-1314 (2012); *Association for Molecular Pathology v. United States Patent and Trademark Office*, 653 F.3d 1329, 1335-1339 and 1361-1363 (2011); *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 7 at 192-212.

¹¹ See, for example, *Amgen Inc v. Chugia Pharmaceutical Co.*, 927 F.2d 1200, 1206 (1991) providing: "A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it".

¹² See, for example, Gregory Graff, Devon Phillips, Zhen Lei, Sooyoung Oh, Carol Nottenburg and Philip Pardey, "Not Quite a Myriad of Gene Patents" (2013) 31 *Nature Biotechnology* 404, 405. See also *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 10 at 1343-1344.

¹³ There is a huge literature questioning the merits and legality of DNA sequence patenting: see, for example, Dianne Nicol, "On the Legality of Gene Patents" (2005) 29 *Melbourne University Law Review* 809.

¹⁴ *Funk Brothers Seed Co v. Kalo Inoculant Co.*, 333 U.S. 127, 134-135 (1948) providing: "[S]uch terms as 'the work of nature' and the 'laws of nature' ... are vague and malleable terms infected with too much ambiguity and equivocation. Everything that happens may be deemed 'the work of nature',

DNA provided a unique challenge to the “manufacture” or “composition of matter” analysis because DNA is both a chemical *and also* an information-carrying medium where the information is preserved in the isolated chemical and essential to the utility of the chemical as a molecular tool. The recent United States Supreme Court decision in *Association for Molecular Pathology v Myriad Genetics Inc* is a significant development and a pronouncement from of superior court about this controversy.¹⁵ Justice Thomas delivered the opinion of the Court (Roberts CJ, and Kennedy, Ginsburg, Breyer, Alito, Sotomayor and Kagan JJ)¹⁶ with Justice Scalia joining the judgement except for his careful qualification that he was unable to affirm the details about the molecular biology about genes and heredity.¹⁷ The question before the Supreme Court had been reduced to the validity of composition claims from three of Myriad’s patents – US Patent 5,747,282 (the ‘282 patent; claims 1, 2, 5, 6, and 7), US Patent 5,693,473 (the ‘473 patent; claim 1), and US Patent 5,837,492 (the ‘492 patent; claims 1, 6, and 7) (see Table 1) – and “whether a naturally occurring segment of [DNA] is patent eligible under 35 U.S.C. §101 by virtue of its isolation from the rest of the human genome”.¹⁸ The Supreme Court’s ultimate decision was clearly stated and held:

that a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated, but that cDNA is patent eligible because it is not naturally occurring.¹⁹

and any patentable composite exemplifies in its properties ‘the laws of nature’. Arguments drawn from such terms for ascertaining patentability could fairly be employed to challenge almost every patent”.

¹⁵ There is a long history to these patents: see, for examples, Richard Gold and Julia Carbone, “Myriad Genetics: In the Eye of the Policy Storm” (2010) 12 *Genetics in Medicine* S39; Matthew Rimmer, “Myriad Genetics: Patent Law and Genetic Testing” (2003) 25 *European Intellectual Property Review* 20.

¹⁶ *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2110.

¹⁷ *Ibid.* at 2120.

¹⁸ *Ibid.* at 2111. In accepting the appeal the Supreme Court order provided: “The petition for a writ of certiorari is granted limited to Question 1 [‘Are human genes patentable?’] presented by the petition”: *Association for Molecular Pathology v. Myriad Genetics Inc*, 133 S.Ct. 694 (2012).

¹⁹ *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2111.

The decision appears to draw a clear distinction between the patent eligibility of a “naturally occurring DNA segment” and “not naturally occurring [cDNA]”. The following analysis reviews the lower court decisions²⁰ and then provides a detailed analysis of the Supreme Court jurisprudence on this matter in the context of the decision in *Association for Molecular Pathology v Myriad Genetics Inc.* After this the analysis considers the likely effect of the decision. The question addressed by this article is whether the United States Supreme Court’s decision establishes any important limitations on DNA sequence patenting? The article concludes that the Supreme Court’s decision is very narrowly focussed and that its impact is likely to be minor.

United States District Court decision

The litigation commenced when the plaintiffs Association for Molecular Pathology and others sought a summary judgement in the United States District Court for the Southern District of New York that fifteen claims in seven patents were invalid.²¹ District Judge Sweet reduced the question before the court to whether “isolated human genes and the comparison of their sequences [are] patentable” and decided that each of the DNA sequence claims, the methods for “comparing” and “analysing”

²⁰ Notably the decisions in this matter were in order the United States District Court for the Southern District of New York about lack of subject matter jurisdiction and standing (*Association for Molecular Pathology v. United States Patent and Trademark Office*, 669 F.Supp.2d 365 (2009)), the United States District Court for the Southern District of New York about the invalidity of patent claims (*Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 7), the United States Court of Appeals, Federal Circuit about an appeal United States District Court for the Southern District of New York about lack of subject matter jurisdiction and standing and the invalidity of patent claims (*Association for Molecular Pathology v. United States Patent and Trademark Office*, 653 F.3d 1329 (2011)), the United States Supreme Court vacating the decision and remanding the matter (*Association for Molecular Pathology v. Myriad Genetics Inc*, 132 S.Ct. 1794 (2012)), the United States Court of Appeals, Federal Circuit re-examination about an appeal United States District Court for the Southern District of New York about lack of subject matter jurisdiction and standing and the invalidity of patent claims (*Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 10) and then an appeal to the Supreme Court (*Association for Molecular Pathology v. Myriad Genetics Inc*, 133 S.Ct. 694 (2012)).

²¹ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 7 at 184.

DNA sequences to assess predispositions to breast and ovarian cancer, and ‘comparing’ cell growth rates in the presence of cancer therapeutics were invalid.²² This involved assessing the patentability of the composition claims and then the method claims, albeit this article only addresses the composition claims and not the “comparing” and “analysing” claims.²³

The starting point was the United States Patent Office existing practice of granting patents to claims over DNA sequences of “isolated DNA”:²⁴

This practice is premised on the view that DNA should be treated no differently from any other chemical compound, and that its purification from the body, using well-known techniques, renders it patentable by transforming it into something distinctly different in character [from naturally occurring DNA].²⁵

The plaintiffs asserted that the composition claims to both naturally occurring DNA and cDNA were “products of nature” and so patent ineligible.²⁶ District Judge Sweet agreed, first finding that there was no requirement to defer to the United States Patent Office practice,²⁷ and secondly rejecting the assertion that granted patent claims were constitutionally protected and protected by the United States’ commitment to international treaties.²⁸ District Judge Sweet then addressed the detail of the

²² *Ibid.* at 185.

²³ Notably District Judge Sweet concluded that the method claims “analysing” and “comparing” sequences under the then Federal Circuit “machine or transformation” standard from *In re Bilski*, 545 F.3d 943, 952 and 961-962 (2008) (subsequently the “machine or transformation” standard was determined to be “not the sole test for deciding whether an invention is a patent-eligible ‘process’”, but rather “a useful and important clue, an investigative tool, for determining whether some claimed inventions are processes under § 101”: *Bilski v. Kappos*, *op. cit.* note 4 at 3227) were not patentable: “even if the method claims-in-suit were construed to include the physical transformations associated with isolating and sequencing DNA, they would still fail the “machine or transformation” test under § 101 for subject matter patentability”: *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 7 at 236-237.

²⁴ *Ibid.* at 185.

²⁵ *Ibid.* at 185.

²⁶ *Ibid.* at 220.

²⁷ *Ibid.* at 220-221.

²⁸ *Ibid.* at 221-222.

composition claims analysing the Supreme Court authority for two related propositions:²⁹

(a) That products of nature are not patentable:

Supreme Court precedent has established that products of nature do not constitute patentable subject matter absent a change that results in the creation of a fundamentally new product.³⁰

(b) That purifying natural compounds are not patentable:

the clear line of Supreme Court precedent and accompanying lower court authorities, stretching from *American Wood-Paper* through to *Chakrabarty*, establishes that purification of a product of nature, without more, cannot transform it into patentable subject matter. Rather, the purified product must possess “markedly different characteristics” in order to satisfy the requirements of § 101.³¹

District Judge Sweet then determine whether the isolated DNA identified in the patent claims possessed “markedly different characteristics” from the DNA found in its natural state within human cells.³² For District Judge Sweet it was significant that DNA had “unique qualities as a physical embodiment of information”³³ so that it was

²⁹ The authority considered was *Diamond v. Chakrabarty*, *op. cit.* note 2 at 310 (“the patentee has produced a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility. His discovery is not nature’s handiwork, but his own”); *Funk Brothers Seed Co v. Kalo Inoculant Co*, *op. cit.* note 14 at 130 (“did not create a state of inhibition or of non-inhibition in the bacteria. Their qualities are the work of nature. Those qualities are of course not patentable”); *American Fruit Growers Inc v. Brogdex Co*, 283 US 1, 13 (1931) (“There must be transformation; a new and different article must emerge having a distinctive name, character, or use”); *Cochrane v. Badische Anilin & Soda Fabrik*, 111 U.S. 293 (1884) (“Calling it artificial alizarine did not make it a new composition of matter, and patentable as such”); *American Wood-Paper Co v. Fibre Disintegrating Co*, 90 U.S. 566, 593 (1874) (“A process to obtain [an extract] from a subject from which it has never been taken may be the creature of invention, but the thing itself when obtained cannot be called a new manufacture”).

³⁰ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 7 at 222.

³¹ *Ibid.* at 227.

³² *Ibid.* at 227-228.

³³ *Ibid.* at 229.

more than just a mere chemical or analogous to a mere chemical, and that the structural and functional differences between the native DNA and various isolates were *not* “markedly different”.³⁴ While noting that “[t]here will almost inevitably be some identifiable differences between a claimed invention and a product of nature” this was not the relevant standard.³⁵ Instead:

the appropriate § 101 inquiry is whether, considering the claimed invention as a whole, it is sufficiently distinct in its fundamental characteristics from natural phenomena to possess the required “distinctive name, character, [and] use”.³⁶

Significantly, District Judge Sweet considered that cDNA was also *not* “markedly different”, both in its sequence and its function, and so it too was not patentable.³⁷ The result of District Judge Sweet’s analysis was that neither the naturally occurring DNA nor the cDNA composition claims were valid because they “constitute[d] un-patentable subject matter under 35 U.S.C. § 101”.³⁸

United States Court of Appeals, Federal Circuit decisions

Following the conclusion of an appeal to the United States Court of Appeals, Federal Circuit³⁹ there was a successful petition to the Supreme Court that vacated and remanded the matter back to the Federal Circuit.⁴⁰ The Federal Circuit again considered the matter with Circuit Judges Lourie, Bryson and Moore each delivering

³⁴ *Ibid.* at 228-229.

³⁵ *Ibid.* at 229.

³⁶ *Ibid.* at 229 citing *Diamond v. Chakrabarty*, *op. cit.* note 2 at 309-310 citing *Hartranft v. Wiegmann*, 121 U.S. 609 (1887).

³⁷ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *ibid.* at 230-231.

³⁸ *Ibid.* at 232 and 238.

³⁹ See *Association for Molecular Pathology v. United States Patent and Trademark Office*, 653 F.3d 1329 (2011).

⁴⁰ *Association for Molecular Pathology v. Myriad Genetics Inc.*, 132 S.Ct. 1794 (2012). The cases was remanded for further consideration in light of its decision in *Mayo Collaborative Services v. Prometheus Laboratories Inc.*, *op. cit.* note 5: see *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 10 at 1308.

separate opinions variously concurring and dissenting.⁴¹ The outcome of the decision was to reverse the lower court to findings and conclude that isolated sequences of naturally occurring DNA are patent ineligible (Circuit Judge Bryson dissenting)⁴² and that cDNA was patent eligible.⁴³ Each decision provides a different perspective.

Circuit Judge Lourie characterised the United States District Court decision as:

that isolated DNA molecules fall within the judicially created “products of nature” exception to § 101 because such isolated DNAs are not “markedly different” from native DNAs ... The court relied on the fact that, unlike other biological molecules, DNAs are the “physical embodiment of information”, and that this information is not only preserved in the claimed isolated DNA molecules, but also essential to their utility as molecular tools.⁴⁴

Circuit Judge Lourie rejected the District Court analysis returning to the characterisation of DNA as a chemical that has been artificially created by means of its isolation:

The isolated DNA molecules before us are not found in nature. They are obtained in the laboratory and are man-made, the product of human ingenuity. While they are prepared from products of nature, so is every other composition of matter. All new chemical or biological molecules, whether made by synthesis or decomposition, are made from natural materials. For example, virtually every medicine utilized by today’s medical practitioners, and every manufactured plastic product, is either synthesized from natural materials (most often petroleum fractions) or derived from natural plant materials. But, as such, they are different from natural materials, even if they are ultimately derived from them. The same is true of isolated DNA molecules.⁴⁵

Circuit Judge Lourie then characterises each of the parties’ claims:

- (a) *Myriad (that DNA is patent eligible)* – Myriad argued that “isolated” DNA does not exist in nature and “that isolated DNAs, unlike native DNAs, can be

⁴¹ *Ibid.* at 1333-1358 (Circuit Judge Lourie), 1358-1373 (Circuit Judge Moore) and 1358-1381 (Circuit Judge Bryson).

⁴² *Ibid.* at 1309 (Circuit Judge Lourie), 1337 (Circuit Judge Moore) and 1348 (Circuit Judge Bryson).

⁴³ *Ibid.* at 1309 (Circuit Judge Lourie), 1337 (Circuit Judge Moore) and 1356 (Circuit Judge Bryson).

⁴⁴ *Ibid.* at 1317.

⁴⁵ *Ibid.* at 1325.

used as primers and probes for diagnosing cancer”.⁴⁶ Myriad further argued that the product of nature exception was also unworkable as every composition of matter was to some degree “composed of natural materials”.⁴⁷

- (b) *Plaintiffs (that DNA is patent ineligible)* – The Plaintiffs argued that “isolated” DNA was a natural phenomena and product of nature and excluded from patentability, and “because isolated DNAs retain part of the same nucleotide sequence as native DNAs, they do not have any ‘markedly different’ characteristics”.⁴⁸ The Plaintiffs further argued that the “isolated DNA claims pre-empt products and laws of nature, excluding anyone from working with the BRCA genes and the genetic information they convey”.⁴⁹
- (c) *Government amicus curiae (the naturally DNA is patent ineligible and cDNA is patent eligible)* – The Government argued that naturally occurring DNA was the “product[] of nature, since their nucleotide sequences exist because of evolution, not man” and so excluded from patentability.⁵⁰ Meanwhile cDNA was “DNA molecules engineered by man” was patentable “because, with rare exceptions, they do not occur in nature, either in isolation or as contiguous sequences within a chromosome”.⁵¹

The determinative distinction for Circuit Judge Lourie between patent ineligible DNA and patent eligible DNA under the product of nature exception was about the change in the composition on isolation:

One distinction, therefore, between products of nature and human-made invention for purposes of § 101 turns on a change in the claimed composition’s identity compared with what exists in nature. Specifically, the Supreme Court has drawn a line between compositions that, even if arrayed in useful combinations or harnessed to exploit newly discovered properties, have similar

⁴⁶ *Ibid.* at 1325.

⁴⁷ *Ibid.* at 1325.

⁴⁸ *Ibid.* at 1326.

⁴⁹ *Ibid.* at 1326.

⁵⁰ *Ibid.* at 1326.

⁵¹ *Ibid.* at 1326.

characteristics as in nature, and compositions that human intervention has given “markedly different”, or “distinctive”, characteristics ... Applying this test to the isolated DNAs in this case, the challenged claims are drawn to patent-eligible subject matter because the claims cover molecules that are markedly different – have a distinctive chemical structure and identity – from those found in nature.⁵²

Circuit Judge Lourie concluded that “isolated DNA is not just purified DNA” and that the isolated DNA had “been manipulated chemically so as to produce a molecule that is markedly different from that which exists in the body”.⁵³ As a consequence isolated DNA was patent eligible. Further cDNA was “even more the result of human intervention into nature and are hence patent-eligible subject matter”.⁵⁴ He then recited the importance of a covalent bond in distinguishing between molecules⁵⁵ presumably because the covalent bonds are broken and remade during isolation with the isolated molecules having potentially different covalent bonds to the native DNA in the human cells – this is a “conversion to a different molecular entity”.⁵⁶ And then he rejects the argument that “because the claimed isolated DNAs retain the same nucleotide sequence as native DNAs, they do not have any ‘markedly different’ characteristics”.⁵⁷

it is the distinctive nature of DNA molecules as isolated compositions of matter that determines their patent eligibility rather than their physiological use or benefit. Uses of chemical substances may be relevant to the non-obviousness of these substances or to method claims embodying those uses, but the patent eligibility of an isolated DNA is not negated because it has similar informational properties to a different, more complex natural material. The claimed isolated DNA molecules are distinct from their natural existence as portions of larger entities, and their informational content is irrelevant to that fact ... genes are in fact materials having a chemical nature and, as such, are best described in patents by their structures rather than by their functions.⁵⁸

⁵² *Ibid.* at 1327-1328.

⁵³ *Ibid.* at 1328.

⁵⁴ *Ibid.* at 1329.

⁵⁵ *Ibid.* at 1329-1330.

⁵⁶ *Ibid.* at 1332.

⁵⁷ *Ibid.* at 1330.

⁵⁸ *Ibid.* at 1330.

Circuit Judge Moore joined Circuit Judge Lourie in accepting that both isolated DNA and cDNA claims were valid.⁵⁹ Her analysis reduced her inquiry into the patentability of cDNAs, short DNA sequences (ranging from the 15-mers up to the full length sequence isolates) and then full-length DNA sequences. She reasoned that cDNA was patent eligible because it does not “exist in nature” as the introns have been removed, the cDNA can express proteins in a cell “which does *not* normally produce it”, has a completely different sequence to the template RNA from which it is constructed, has a completely different chemical structure to RNA” so that they “are the creation of man, made using biological tools and the naturally occurring mRNA as a template”.⁶⁰

Circuit Judge Moore then considered short DNA sequences and found they were patentable because they had a utility that was not available to native DNA, such as primers and probes (molecular tools).⁶¹ As such “[i]t is not the chemical change alone, but that change combined with the different and beneficial utility” that made the short DNA sequences patent eligible.⁶² In contrast the longer DNA sequences were not so clearly patentable:⁶³

All of the same structural arguments apply to any length of isolated DNA so, like the shorter strands, an isolated DNA coding for a gene does have a literal chemical difference from the gene as it appears on the chromosome. Unlike the shorter strands of isolated DNA, the chemical and structural differences in the isolated gene do not clearly lead to an “enlargement of the range of ... utility” as compared to nature ... For example, the full length gene is too large to be used as a probe ... (a probe is a DNA molecule usually 100-1,000 bases long). Likewise, an entire isolated gene appears unsuitable for use as a primer in genetic screening for mutations in that same gene ... (Primers “are complementary to an exact location of a much larger target DNA molecule”). The isolated full length gene does not clearly have a new utility and appears to simply serve the same ends devised by nature, namely to act as a gene encoding a protein sequence.⁶⁴

⁵⁹ *Ibid.* at 1337.

⁶⁰ *Ibid.* at 1340-1341.

⁶¹ *Ibid.* at 1341-1342.

⁶² *Ibid.* at 1342.

⁶³ Notably Circuit Judge Moore accepts that a long DNA sequence in the form of a whole chromosome is not patentable subject matter: *ibid.* at 1343.

⁶⁴ *Ibid.* at 1343.

The determinative factor for Circuit Judge Moore was that “Congress has, for centuries, authorized an expansive scope of patentable subject matter”, the United States Patent and Trademark Office has “allowed patents on isolated DNA sequences for decades, and, more generally, has allowed patents on purified natural products for centuries”, and “we must be particularly wary of expanding the judicial exception to patentable subject matter where both settled expectations and extensive property rights are involved”.⁶⁵ Significantly Circuit Judge Moore expressed some concern that given the long practice of patenting isolated DNA any change would likely disrupt settled expectations in the inventing communities and risked undermining inventors and their property.⁶⁶ The result for Circuit Judge Moore was that isolated DNA was patent eligible and if this was to be change then this was a matter for Congress – “I will not strip an entire industry of the property rights it has invested in, earned, and owned for decades unchallenged under the facts of this case”.⁶⁷

Circuit Judge Bryson concurred with the other judges about the patentability of cDNA claims,⁶⁸ but dissented on the patentability of native DNA and DNA fragment claims.⁶⁹ For Circuit Judge Bryson the dividing line between the natural product and the non-natural “manufacture” or “composition” in the isolated DNA was not sufficient to pass the patentability threshold.⁷⁰

In the case of the BRCA genes, by contrast, nature has defined the genes as independent entities by virtue of their capacity for protein synthesis and, ultimately, trait inheritance. Biochemists extract the target genes along lines defined by nature so as to preserve the structure and function that the gene possessed in its natural environment. In such a case, the extraction of a product in a manner that retains the character and function of the product as found in nature does not result in the creation of a human invention.⁷¹

⁶⁵ *Ibid.* at 1343.

⁶⁶ *Ibid.* at 1344 citing *Festo Corp v. Shoketsu Kinzoku Kogyo Kabushiki Co*, 535 U.S. 722, 739 (2002).

⁶⁷ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *ibid.* at 1348.

⁶⁸ *Ibid.* at 1355-1356.

⁶⁹ *Ibid.* at 1348.

⁷⁰ *Ibid.* at 1353 citing *Diamond v. Chakrabarty*, *op. cit.* note 2 at 309-310 (and citing, in part, *Hartranft v. Wiegmann*, *op. cit.* note 16) “a hitherto unknown natural phenomenon, but to a non-naturally occurring manufacture or composition of matter ‘having a distinctive name, character [and] use’”.

⁷¹ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *ibid.* at 1353.

Put slightly differently, Circuit Judge Bryson considers both the structure and function in assessing the creation of a human invention:

In sum, the test employed by the Supreme Court in *Chakrabarty* requires us to focus on two things: (1) the similarity in structure between what is claimed and what is found in nature and (2) the similarity in utility between what is claimed and what is found in nature. What is claimed in the BRCA genes is the genetic coding material; that material is the same, structurally and functionally, in both the native gene and the isolated form of the gene.⁷²

The significance of Circuit Judge Bryson was his regard to the informational content of the DNA and that through the isolation processes that information content remained the same – “structural similarity dwarfs the significance of the structural differences between isolated DNA and naturally occurring DNA”.⁷³ In contrast, Circuit Judge Bryson considered that the cDNA was patentable because there were distinct structural changes with removing the introns compared to the native DNA and a particular utility “because cDNA can be attached to a promoter and inserted into a non-human cell to drive protein expression”.⁷⁴ The claims to the short DNA fragments (ranging from the 15-mers up to the full length sequence isolates), however, was not so clear and foundered because it claimed some naturally occurring DNA:

That claim encompasses each BRCA1 exon, even though each exon is naturally defined by transcription. Moreover, because small sequences of DNA are repeated throughout the three billion nucleotides of the human genome, the claim covers portions of the cDNA of more than 4% of human genes. It also covers portions of the DNA of nearly all human genes. Accordingly, efforts to sequence almost any gene could infringe claim 6 even though Myriad’s specification has contributed nothing to human understanding of other genes. Myriad is not entitled to such broad protection ... The problem with [the 15-mers up to the full length sequence isolates claim] is that it is so broad that it includes products of nature (the BRCA1 exons) and portions of other genes; its validity is not salvaged because it includes some species that are not natural.⁷⁵

⁷² *Ibid.* at 1354.

⁷³ *Ibid.* at 1355.

⁷⁴ *Ibid.* at 1356.

⁷⁵ *Ibid.* at 1356. Notably this quotation refers to claim 6 and the same concerns applied to claims 1 and 5 (1356-1357).

The outcome for Circuit Judge Bryson was to find these DNA fragment claims not patent eligible, while noting that they could well have been patent eligible had they been more narrowly cast and confined to a subset of possible fragments.⁷⁶

The Supreme Court's decision

The analysis, so far, details the ultimate decision of the Supreme Court to find that “a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated” (covering both the naturally occurring DNA and fragments of the naturally occurring DNA) and that “cDNA is patent eligible because it is not naturally occurring” (covering both full length cDNAs and cDNA fragments) (see Table 1).⁷⁷ In summary, the Supreme Court's decision concluded:

- (a) *cDNAs* – Affirms the patent eligibility of cDNA found by the Federal Circuit (Circuit Judges Lourie, Bryson and Moore)⁷⁸ and contradicts the District Court decision (District Judge Sweet) that addressed cDNA in the same way as the other DNA claims.⁷⁹
- (b) *Naturally occurring DNA* – Affirms Circuit Judge Bryson in the Federal Circuit and District Judge Sweet in the District Court that “a naturally occurring DNA segment” is not patent eligible,⁸⁰ and contradicts Circuit Judges Lourie and Moore in the Federal Circuit.⁸¹

⁷⁶ *Ibid.* at 1356.

⁷⁷ *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2111.

⁷⁸ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 10 at 1309 (Circuit Judge Lourie), 1337 (Circuit Judge Moore) and 1356 (Circuit Judge Bryson).

⁷⁹ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 7 at 232.

⁸⁰ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 10 at 1309, 1348 and 1355; *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 7 at 232.

⁸¹ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *ibid.* at 1333 (Circuit Judge Lourie) and 1342-1343 (Circuit Judge Moore).

- (c) *Naturally occurring DNA fragments* – Affirms Circuit Judge Bryson in the Federal Circuit and District Judge Sweet in the District Court that “a naturally occurring DNA segment” is not patent eligible,⁸² and contradicts Circuit Judges Lourie and Moore in the Federal Circuit.⁸³

The question to be addressed now is whether the Supreme Court’s decision establishes any important limitations on DNA sequence patenting? The following sections deconstruct and critique the various elements of the Supreme Court’s decision.

“Composition of matter” and not “manufactures”

The Supreme Court’s decision is carefully crafted by expressly identifying that the relevant part of 35 U.S.C. § 101 in dispute as only the “composition of matter” element and not the element of “manufactures”.⁸⁴ This is significant as the Supreme Court cited *Diamond v Chakrabarty* for the proposition that a modified bacterium was patentable because the patent claim was “not to a hitherto unknown natural phenomenon, but to a non-naturally occurring manufacture or composition of matter – a product of human ingenuity ‘having a distinctive name, character [and] use’”.⁸⁵ By only addressing “composition of matter” the Supreme Court effectively excluded any consideration of whether Myriad’s claimed compositions were “manufactures”. This confines the decision to only the narrower question of whether the claims are to “composition of matter”.

⁸² *Ibid.* at 1309, 1348 and 1355; *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 7 at 232.

⁸³ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *ibid.* at 1333 (Circuit Judge Lourie) and 1342-1343 (Circuit Judge Moore).

⁸⁴ *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2116. A similar approach was adopted in the lower courts: *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 10 at 1325 (Circuit Judge Lourie), 1340 (Circuit Judge Moore) and 1352 (Circuit Judge Bryson); *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 7 at 220.

⁸⁵ *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2116 citing *Diamond v. Chakrabarty*, *op. cit.* note 2 at 309-310 citing *Hartranft v. Wiegmann*, *op. cit.* note 16.

This distinction between “composition of matter” and “manufactures” is interesting because the USPTO has previously dealt with isolated DNA as both:

An isolated and purified DNA molecule that has the same sequence as a naturally occurring gene is eligible for a patent because ... an excised gene is eligible for a patent as a composition of matter or as an article of manufacture because that DNA molecule does not occur in that isolated form in nature.⁸⁶

The significance, if any, of the Supreme Court dealing with *Myriad*’s claims as a “composition of matter” is that the claims (such as “[t]he isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1” (the ‘282 patent, claim 2)) were framed as claims to the “genetic information encoded in the BRCA1 and BRCA2 genes”.⁸⁷ This perhaps suggests that a claim in a different form, directed to the chemical composition of the DNA sequence as a “manufacture”, might be distinguishable and patentable, consistent with the standards established in earlier authority. For example, *Diamond v Chakrabarty* established that “[i]n choosing such expansive terms as ‘manufacture’ and ‘composition of matter,’ modified by the comprehensive ‘any’, Congress plainly contemplated that the patent laws would be given wide scope”,⁸⁸ and that:

Guided by these canons of construction, this Court has read the term “manufacture” in § 101 in accordance with its dictionary definition to mean “the production of articles for use from raw materials prepared by giving to these materials new forms, qualities, properties, or combinations whether by hand labour or by machinery”.⁸⁹

Earlier in *American Fruit Growers Inc v Brogdex Co* a similarly wide standard was established:

Manufacture implies a change, but every change is not manufacture, and yet every change in an article is the result of treatment, labor, and manipulation. But something more is necessary ... There

⁸⁶ United States Patent and Trademark Office, *Utility Examination Guidelines*, 66 Fed. Reg. 1092, 1093 (2001).

⁸⁷ *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2118.

⁸⁸ *Op. cit.* note 2 at 308.

⁸⁹ *Op. cit.* note 2 at 308.

must be transformation; a new and different article must emerge having a distinctive name, character, or use.⁹⁰

The outcome of the Supreme Court's decision appears to be narrowed by confining it to the "composition of matter" head of invention or discovery. Conceivably there are good arguments to be made about claims to DNA as a chemical (noting that Myriad's claims were "simply not expressed in terms of chemical compositions"⁹¹ addressed further below).

Deference to Patent Office practice

In the District Court and Federal Circuit the judgements addressed the concern that patents over DNA had been granted for a long time by the USPTO and that changing the patentability of DNA would be, for example, "contrary to the settled expectations of the inventing and investing communities".⁹² The Supreme Court rejected the entitlement to deference to USPTO practice.⁹³ Importantly, however, an United States government *amicus curiae* (submitted by the Department of Justice rather than the USPTO)⁹⁴ had asserted that the USPTO's practice was not "a sufficient reason to hold that isolated DNA is patent-eligible" and for the Supreme Court "[t]hese concessions weigh against deferring to the [USPTO's] determination".⁹⁵ While the internal governmental arrangements, and why the USPTO was not providing the *amicus curiae*, remain unclear, this was a clear governmental statement undermining the long term USPTO practice.

⁹⁰ *American Fruit Growers Inc v. Brogdex Co*, *op. cit.* note 29 at 12-13 citing *Anheuser-Busch Brewing Association v. United States*, 207 U.S. 556, 562 (1908).

⁹¹ *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2118.

⁹² *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 10 at 1333 (Circuit Judge Lourie). See also 1343-1347 (Circuit Judge Moore) and 1357-1358 (Circuit Judge Bryson); *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 7 at 220-221.

⁹³ *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2118.

⁹⁴ This was also surprising because the Department of Justice also submitted an *amicus curiae* in the Federal Circuit where the USPTO was the lead defendant.

⁹⁵ *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2119.

Interestingly, the Supreme Court did not consider that Congress had sufficiently endorsed patenting isolated DNA in legislation.⁹⁶ In the Federal Circuit, Circuit Judge Moore had considered that Congress had at least “implicitly” accepted the USPTO practice noting that Congress had explicitly declined to implement legislation affecting current DNA patents, declined to pass proposed laws limiting DNA patents and exempted the non-commercial uses of DNA patents.⁹⁷ While there was certainly no explicit congressional endorsement of the USPTO practice⁹⁸ this is a matter that might easily have been persuasive. As Circuit Judge Moore pointed out, “[t]he Supreme Court has earlier warned that ‘courts must be cautious before adopting changes that disrupt the settled expectations of the inventing community’”.⁹⁹ This perhaps suggests that deference to the USPTO practice can be significant, and would almost certainly have been in this matter given the long standing practice and its evolved complexity¹⁰⁰ *but for* the United States government *amicus curiae* (submitted by the Department of Justice). The decision does not, therefore, stand as a strong authority for there being no deference to USPTO practice.

DNA sequences

The relevant legal propositions from the Supreme Court’s precedents for 35 U.S.C. § 101 identified as applying to the present case was that “[l]aws of nature, natural phenomena, and abstract ideas are not patentable”.¹⁰¹ This was then framed within a broader policy context:

⁹⁶ *Ibid.* at 2118.

⁹⁷ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 10 at 1346.

⁹⁸ The Supreme Court pointing out that Circuit Judge Moore’s view pointing to appropriation laws “does not even mention genes, much less isolated DNA”: *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2118-2119.

⁹⁹ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 10 at 1344 citing *Festo Corporation v. Shoketsu Kinzoku Kogyo Kabushiki Co*, *op. cit.* note 66 at 739.

¹⁰⁰ As a measure of the USPTO practice addressing DNA and amino acid sequences see United States Patent and Trademark Office, *Manual of Patent Examining Procedure* (USPTO, 2012) [2420]-[2426].

¹⁰¹ *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2116 citing *Mayo Collaborative Services v. Prometheus Laboratories Inc*, *op. cit.* note 5 at 1293 that had cited *Bilski v. Kappos*, *op. cit.* note 4 at 3233-3234; *Diamond v. Diehr*, *op. cit.* note 5 at 185; *Diamond v. Chakrabarty*, *op. cit.* note 2 at 309.

The rule against patents on naturally occurring things is not without limits, however, for “all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas”, and “too broad an interpretation of this exclusionary principle could eviscerate patent law” ... As we have recognized before, patent protection strikes a delicate balance between creating “incentives that lead to creation, invention, and discovery” and “imped[ing] the flow of information that might permit, indeed spur, invention” ... We must apply this well-established standard to determine whether Myriad’s patents claim any “new and useful ... composition of matter” ... or instead claim naturally occurring phenomena (citations omitted).¹⁰²

The Supreme Court’s approach was to look for Myriad’s contribution¹⁰³ framed in the context of “genetic information” – “It is undisputed that Myriad did not create or alter any of the genetic information encoded in the BRCA1 and BRCA2 genes”.¹⁰⁴ According to the decision this contrasted with the earlier Supremes Court’s decision in *Diamond v Chakrabarty* where the inventors added plasmids that enabled the bacteria to degrade oils was patent eligible¹⁰⁵ – “Myriad did not create anything ... it found an important and useful gene, but separating that gene from its surrounding genetic material is not an act of invention”.¹⁰⁶ And was consistent with the earlier Supreme Court’s decision in *Funk Brothers Seed Co v Kalo Inoculant Co* where a mixture of naturally occurring bacteria combined as an inoculant was merely an unpatentable discovery¹⁰⁷ – “Myriad found the location of the BRCA1 and BRCA2 genes, but that discovery, by itself, does not render the BRCA genes ... patent eligible”.¹⁰⁸ According to this framing of the isolated DNA sequence, Myriad merely identified the location and content of the sequence information, and the isolated BRCA1 and BRCA2 sequences in their vectors separated out from the remaining parts of the chromosome molecule, were merely the physical medium for this “genetic information”.

¹⁰² *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2116.

¹⁰³ *Ibid.* at 2116-2119.

¹⁰⁴ *Ibid.* at 2116.

¹⁰⁵ *Diamond v. Chakrabarty*, *op. cit.* note 2 at 309-310.

¹⁰⁶ *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2117.

¹⁰⁷ *Funk Brothers Seed Co v. Kalo Inoculant Co*, *op. cit.* note 14 at 130-132.

¹⁰⁸ *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2117.

The Supreme Court also dismissed isolating DNA as creating a non-naturally occurring molecule.¹⁰⁹ From their perspective the claims “focus on the genetic information encoded in the BRCA1 and BRCA 2 genes”.¹¹⁰ As such the claims were not “expressed in terms of chemical compositions” or the chemical changes associated with isolation – “its claim is concerned primarily with the information contained in the genetic *sequence*, not with the specific chemical composition of a particular molecule” (emphasis in original).¹¹¹ This was significant as the District Court and the Federal Circuit had focussed on isolating the DNA composition and whether the act of isolating the DNA composition was a sufficiently inventive act to be patentable. Essentially District Judge Sweet considered whether the isolated DNA was “markedly different” from the naturally occurring DNA and found that the similar “physical embodiment of information” in DNA (including both cDNA and naturally occurring DNA) both naturally and isolated trumped any structural or functional differences.¹¹² Circuit Judge Lourie characterised the act of isolating DNA as breaking covalent bonds to make “a free-standing portion of a larger, natural DNA molecule” that was structurally and functionally distinct with the information content being “irrelevant”.¹¹³ Circuit Judge Bryson (dissenting) characterised the nucleotide sequence of the isolated DNA finding that “structural similarity dwarfs the significance of the structural differences between isolated DNA and naturally occurring DNA”.¹¹⁴ And Circuit Judge Moore was more nuanced characterising a functional difference that enabled cDNA and short naturally occurring DNA fragments patents because cDNAs and short sequences are “[u]nlike the isolated DNA, naturally occurring DNA simply does not have the requisite chemical and

¹⁰⁹ *Ibid.* at 2118.

¹¹⁰ *Ibid.*

¹¹¹ *Ibid.*

¹¹² *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 7 at 229.

¹¹³ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 10 at 1328 and 1330.

¹¹⁴ *Ibid.* at 1355.

physical properties needed to perform these functions” as “primers in a diagnostic screening process to detect gene mutations” and “probes”.¹¹⁵

The significance of the Supreme Court’s decision is that DNA in the form of the claims in this matter is treated as exceptional with the special qualities of “genetic information”. Importantly, and in contrast to the approach in the District Court whose focus was on “function”,¹¹⁶ the Supreme Court focussed on the “location and order” of the DNA nucleotides and that “Myriad did not create or alter any of the genetic information”.¹¹⁷ The degree to which a naturally occurring DNA isolate needs to be modified to be patent eligible, however, was expressly *not* addressed:

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 endeavours. 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.¹¹⁸

As such, any part of an isolated DNA (including the whole molecule (chromosome)) claimed according to its sequence that has the same sequence in the naturally occurring state will not be patent eligible. The problem with the Supreme Court’s decision is that there is no indication how much “alteration” is sufficient for a sequence to become patent eligible?

Chemical compositions

What is perhaps surprising is that the Supreme Court did not directly address the controversy in the lower courts about the patenting of isolated chemicals. Myriad relied on the earlier decision of the United States District Court for the Southern

¹¹⁵ *Ibid.* at 1341. Notably the Supreme Court decision did not characterize Circuit Judge Moore’s decision like this: *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2115.

¹¹⁶ See *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 7 at 228-229.

¹¹⁷ *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2116.

¹¹⁸ *Ibid.* at 2120.

District of New York in *Parke-Davis & Co v HK Mulford Co*¹¹⁹ (that was affirmed on appeal¹²⁰ and the similar cases *In re Bergstrom* (prostaglandins)¹²¹ and *Merck & Co v Olin Mathieson Chemical Corporation* (Vitamin B12))¹²² about the patenting of isolated adrenaline ((R)-4-(1-hydroxy-2-(methylamino)ethyl)benzene-1,2-diol) molecules from suprarenal glands.¹²³ The adrenaline had been purified from the glands removing most of the detritus and leaving a molecule that could then be used in therapeutic preparations.¹²⁴ This *Parke-Davis & Co v HK Mulford Co* decision (and *In re Bergstrom*) also featured in the USPTO's *Utility Examination Guidelines* and founded their position that an "isolated and purified DNA molecule that has the same sequence as a naturally occurring gene is eligible for a patent ... because that DNA molecule does not occur in isolated form in nature".¹²⁵

In the District Court District Judge Sweet had rejected this authority as unsupported by subsequent Supreme Court authority and the more recent *Diamond v Chakrabarty* and *Funk Brothers Seed Co v Kalo Inoculant Co* requirement for "markedly different characteristics".¹²⁶ In the Federal Circuit, Circuit Judge Lourie distinguished the case because he considered *Parke-Davis & Co v HK Mulford Co* concerned an "identical

¹¹⁹ 189 F.95 (C.C.S.D.N.Y.1911).

¹²⁰ See *Parke-Davis & Co v. HK Mulford Co*, 196 F.496 (2nd Cir. 1912).

¹²¹ *In re Bergstrom*, 427 F.2d 1394, 1401 (C.C.P.A.1970) for the proposition that "what appellants claim – pure PGE2 and PGE3 – is not 'naturally occurring'. Those compounds, as far as the record establishes, do not exist in nature in pure form, and appellants have neither merely discovered, nor claimed sufficiently broadly to encompass, what has previously existed in fact in nature's storehouse, albeit unknown, or what has previously been known to exist".

¹²² *Merck & Co v. Olin Mathieson Chemical Corporation*, 253 F.2d 156, 162-163 (4th Cir.1958) for the proposition that "[u]ntil the patentees produced them, there were no such B12 active compositions. No one had produced even a comparable product. The active substance was unidentified and unknown. The new product, not just the method, had such advantageous characteristics as to replace the liver products. What was produced was, in no sense, an old product".

¹²³ See *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 7 at 224-226.

¹²⁴ See *Parke-Davis & Co v. HK Mulford Co*, 189 F.95, 97-98 (C.C.S.D.N.Y.1911).

¹²⁵ *Utility Examination Guidelines*, *op. cit.* note 86 at 1093.

¹²⁶ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 7 at 226 citing *Diamond v. Chakrabarty*, *op. cit.* note 2 at 310 and *Funk Brothers Seed Co v. Kalo Inoculant Co*, *op. cit.* note 14 at 130-132.

molecule, albeit being ‘for every practical purpose a new thing commercially and therapeutically’”.¹²⁷ Circuit Judge Moore accepted *Parke-Davis & Co v HK Mulford Co* (and *Merck & Co v Olin Mathieson Chemical Corporation*) as “[t]he settled expectations of the inventing community with respect to isolated DNA claims ... built upon the broad language of the statute, judicial precedent [citing both cases] and the Patent Office’s longstanding policy and practice”.¹²⁸ Meanwhile Circuit Judge Bryson appears to accept the proposition from *Parke-Davis & Co v HK Mulford Co* (and *Merck & Co v Olin Mathieson Chemical Corporation*) but concludes that the “structural similarity dwarfs the significance of the structural differences between isolated DNA and naturally occurring DNA”.¹²⁹ The Supreme Court decision then sidesteps the isolated DNA as chemical arguments *altogether* by finding:¹³⁰

Nor are Myriad’s claims saved by the fact that isolating DNA from the human genome severs chemical bonds and thereby creates a non-naturally occurring molecule. Myriad’s claims are simply not expressed in terms of chemical composition, nor do they rely in any way on the chemical changes that result from the isolation of a particular section of DNA. Instead, the claims understandably focus on the genetic information encoded in the BRCA1 and BRCA2 genes ... [Myriad’s] claim is concerned primarily with the information contained in the genetic sequence, not with the specific chemical composition of a particular molecule.¹³¹

The Supreme Court appears to be distinguishing between particular kinds of claims to DNA sequences and other chemical compositions. This perhaps suggests that if the Myriad claims had been in the form of chemical composition claims then they might have been patent eligible. Whether a claim to a DNA sequence in the form of a claim to a chemical composition would be successful remains unclear.¹³² The problem,

¹²⁷ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 10 at 1328 citing *Parke-Davis & Co v. HK Mulford Co*, *op. cit.* note 124.

¹²⁸ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *ibid.* at 1344.

¹²⁹ *Ibid.* at 1355.

¹³⁰ Noting, of course, that the authority of *Parke-Davis & Co v. HK Mulford Co*, *op. cit.* note 124 is open to significant criticism: see Jon Harkness, “Dicta on Adrenalin(e): Myriad Problems with Learned Hand’s Product-of-Nature – Pronouncements in *Parke-Davis v. Mulford*” (2011) 93 *Journal of the Patent and Trademark Office Society* 363.

¹³¹ *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2118.

¹³² The lower court decisions seems to suggest that there are credible arguments to be made and that judges have different perspectives about the veracity of such arguments about DNA: compare

however, is that DNA is a chemical and that its representation as a sequence (as a listing of As, Ts, Gs and Cs) is a convenient convention for representing the chemical.¹³³ The listing of As, Ts, Gs and Cs is itself a convenient convention for a more detailed representation Adenine, Thymine, Guanine and Cytosine, that are themselves a convenient conventions for $C_5H_5N_5$, $C_5H_6N_2O_2$, $C_5H_5N_5O$ and $C_4H_5N_3O$ respectively. Similarly a claim to an amino acid (or polypeptide) sequence and the corresponding nucleotide sequences are in essence also claims to the chemical composition using conventions to describe the ultimate chemicals. The same may be said of claims to almost all polymers with repeating elements.

Framed as a chemical “composition of matter” and/or a “manufacture” a DNA molecule isolated from its naturally occurring state in a chromosome can be characterised as a “process [that] technically creates new molecules with unique chemical compositions”.¹³⁴ The Supreme Court’s decision leaves open the very real prospect that claiming DNA sequences as chemicals might make them patent eligible. And it is hard to conceive that the Supreme Court will overturn the existing authority that establishes isolated and purified chemicals as patent eligible, such as the decisions finding vitamin B12 compositions¹³⁵ and prostaglandins¹³⁶ eminently patentable. Notably the Supreme Court expressly did not adopt District Judge Sweet’s perspective that DNA was exceptional with “unique qualities as a physical embodiment of information” so that the structural and functional differences were not “markedly different”,¹³⁷ or expressly reject the Circuit Judge Lourie’s perspective that

Association for Molecular Pathology v. United States Patent and Trademark Office, *op. cit.* note 10 at 1327-1331 (Circuit Judge Lourie) and *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 7 at 227-232 (District Judge Sweet).

¹³³ Noting that the USPTO has been accepting claims relying on conventions that represent the claimed chemicals, such as the ‘Markush claim or structure’ for a very long time: see, for example, *Ex parte Markush*, 1925 *Decisions of the Commissioner of Patents* 126, 128 (1924).

¹³⁴ *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2115 paraphrasing *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 10 at 1328 (Circuit Judge Lourie).

¹³⁵ *Merck & Co v. Olin Mathieson Chemical Corporation*, *op. cit.* note 122.

¹³⁶ *In re Bergstrom*, *op. cit.* note 124.

¹³⁷ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 7 at 229 and 232.

an isolated DNA was “markedly different chemical structure compared to native DNAs”.¹³⁸ It’s conclusion that Myriad’s claims were “not expressed in terms of chemical composition” and “do they rely in any way on the chemical changes that result from the isolation of a particular section of DNA” means that the Supreme Court’s decision appears to be very narrowly confined to the particular form of Myriad’s claims, and not more broadly to claiming DNA as a chemical. What this probably means, and this is perhaps surprising, is that a DNA molecule claimed as a chemical will be consistent with the existing USPTO practice:

The genetic sequence data represented by strings of the letters A, T, C and G alone is raw, fundamental sequence data, i.e., non-functional descriptive information. While descriptive sequence information alone is not patentable subject matter, a new and useful purified and isolated DNA compound described by the sequence is eligible for patenting, subject to satisfying the other criteria for patentability.¹³⁹

What appears to matter is that it is the “isolated DNA compound described by the sequence” is a chemical description rather than an information description.

Conclusions

The Supreme Court’s decision has undoubtedly clarified the un-patentability of claims to naturally occurring DNA in the form of “[t]he isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1” (the ‘282 patent, claim 2) and “[a]n isolated DNA having at least 15 nucleotides of the DNA of [the nucleotide sequence set forth in SEQ ID NO:1]” (the ‘282 patent, claim 6). The same is the likely fate of other broad claims to naturally occurring DNA such as hybridisation, homology, similarity, and so on, claims that identify the naturally occurring composition according to sequence identity. Whether this will have a significant impact on DNA patenting activity remains unclear,¹⁴⁰ albeit the Supreme Court’s decision leaves open considerable scope for creative claiming.

¹³⁸ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 10 at 1331.

¹³⁹ *Utility Examination Guidelines*, *op. cit.* note 86 at 1093.

¹⁴⁰ See, for example, Editorial, “Myriad Diagnostic Concerns” (2013) 31 *Nature Biotechnology* 571.

Perhaps the main point is that the Supreme Court's decision is limited to just naturally occurring DNA sequence claims. There is no limitation on sequence claims to DNA if it is not naturally occurring, and this will include cDNA (as expressly approved by the Supreme Court's decision), substitutions and all the other possibilities. How different the DNA has to be from the naturally occurring state is unclear, although more than mere cosmetic differences (such as base changes without an amino acid change) might be required. So, for example, sited directed mutagenesis, codon preference changes, cassette constructs, additional codons, significant deletions, and so on, all seem likely to be patentable. The standard seems likely to be that the claimed sequence conveys different information to the naturally occurring sequence in the same way that intron-free cDNA conveys different information to the intron-incorporating naturally occurring DNA. This appears to have been the particular concern of the Supreme Court as Myriad's claims gave "it the exclusive right to isolate an individual's BRCA 1 and BRCA 2 genes (or any strand of 15 or more nucleotides within the genes)".¹⁴¹ As a matter of practice many of the naturally occurring DNA sequences can probably be claimed through skilful claim drafting emphasising the artificial (chemical) and synthetic over the natural.

The practical effect of the Supreme Court's decision is also likely to be limited with claims to naturally occurring DNA in the form of "[t]he isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1" (the '282 patent, claim 2) declining in recent years.¹⁴² Perhaps the significant and limiting factor about the Supreme Court's decision was the disputed diagnostic method claims that were not considered by the Supreme Court¹⁴³ but were considered by the Federal Circuit and rejected.¹⁴⁴ The significance of the diagnostic method claims was that they concerned "comparing" and "analysing" DNA sequences. Essentially they were about comparing a DNA sequence against reference sequences to determine the presence of mutations and predispositions to cancer.¹⁴⁵ The District Court had rejected these

¹⁴¹ *Association for Molecular Pathology v. Myriad Genetics Inc*, *op. cit.* note 10 at 2113.

¹⁴² See *Graff et. al.*, *op. cit.* note 12 at 406 (Figure 2a).

¹⁴³ See *Association for Molecular Pathology v. Myriad Genetics Inc*, 133 S.Ct. 694 (2012).

¹⁴⁴ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 10 at 1335 (Circuit Judge Lourie), 1337 (Circuit Judge Moore) and 1348 (Circuit Judge Bryson).

¹⁴⁵ See *ibid.* at 1303, 1334.

claims on the basis that they were merely abstract mental processes comparing gene sequences as information.¹⁴⁶ The Federal Circuit agreed saying “Myriad’s claims do not apply the step of comparing two nucleotide sequences in a process. Rather, the step of comparing two DNA sequences is the entire process that is claimed”.¹⁴⁷ This is consistent with the recent Supreme Court decision in *Mayo Collaborative Services v Prometheus Laboratories Inc* (and following *Bilski v Kappos*)¹⁴⁸ that concluded a method using scientifically routine procedures to determine metabolite levels in blood and then work out the correct dosage rates was patent ineligible as adding a routine activity to a “law of nature” does not make it patent eligible:

to transform an un-patentable 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” ... The case before us ... concerns patent claims covering processes that help doctors who use thiopurine drugs to treat patients with autoimmune diseases determine whether a given dosage level is too low or too high. The claims purport to apply natural laws describing the relationships between the concentration in the blood of certain thiopurine metabolites and the likelihood that the drug dosage will be ineffective or induce harmful side-effects. We must determine whether the claimed processes have transformed these un-patentable natural laws into patent-eligible applications of those laws. We conclude that they have not done so and that therefore the processes are not patentable ... the steps in the claimed processes (apart from the natural laws themselves) involve well-understood, routine, conventional activity previously engaged in by researchers in the field. At the same time, upholding the patents would risk disproportionately tying up the use of the underlying natural laws, inhibiting their use in the making of further discoveries.¹⁴⁹

This decision is likely to curtail many of the applications of DNA sequences.¹⁵⁰ How this will happen, and whether the Supreme Court’s decision about DNA sequences

¹⁴⁶ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 7 at 234-237. See also *Association for Molecular Pathology v. United States Patent and Trademark Office*, *ibid.* at 1334.

¹⁴⁷ *Association for Molecular Pathology v. United States Patent and Trademark Office*, *ibid.* at 133-1335.

¹⁴⁸ 130 S.Ct. 3218 (2010).

¹⁴⁹ *Mayo Collaborative Services v. Prometheus Laboratories Inc*, *op. cit.* note 5 at 1294.

¹⁵⁰ See also *Association for Molecular Pathology v. United States Patent and Trademark Office*, *op. cit.* note 10 at 1333-1335.

was just the latest in this ongoing debate about DNA sequence patenting, remain to be seen.¹⁵¹

¹⁵¹ The next round of litigation has already started with Myriad joining in suing Ambry Genetics Corporation in Utah: see *University of Utah v. Ambry Genetics Corporation*, Case No 2:13-cv-00640-RJS.

Table 1: Myriad's patent claims in dispute before the Supreme Court

Patent	Claim	Description of claim
'282 patent	1 An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2.	Naturally occurring DNA that includes the BRCA gene
	2 The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1.	cDNA of the BRCA gene
	5 An isolated DNA having at least 15 nucleotides of the DNA of claim 1.	15-mers up to the full length sequence of naturally occurring DNA that includes the BRCA gene
	6 An isolated DNA having at least 15 nucleotides of the DNA of claim 2.	15-mers up to the full length sequence of cDNA of the BRCA gene
	7 An isolated DNA selected from the group consisting of: (a) a DNA having the nucleotide sequence set forth in SEQ ID NO:1 having T at nucleotide position 4056; (b) a DNA having the nucleotide sequence set forth in SEQ ID NO:1 having an extra C at nucleotide position 5385; (c) a DNA having the nucleotide sequence set forth in SEQ ID NO:1 having G at nucleotide position 5443; and, (d) a DNA having the nucleotide sequence set forth in SEQ ID NO:1 having 11 base pairs at nucleotide positions 189-199 deleted.	Variations (mutations) of the naturally occurring DNA that includes the BRCA gene
'473 patent	1 An isolated DNA comprising an altered BRCA1 DNA having at least one of the alterations set forth in Tables 12A, 14, 18 or 19 with the proviso that the alteration is not a deletion of four nucleotides corresponding to base numbers 4184-4187 in SEQ. ID. NO:1.	Variations (mutations) of the naturally occurring DNA that includes the BRCA gene
'492 patent	1 An isolated DNA molecule coding for a BRCA2 polypeptide, said DNA molecule comprising a nucleic acid sequence encoding the amino acid sequence set forth in SEQ ID NO:2.	Variations (mutations) of the naturally occurring DNA that includes the BRCA gene
	6 An isolated DNA molecule coding for a mutated form of the BRCA2 polypeptide set forth in SEQ ID NO:2, wherein said mutated form of the BRCA2 polypeptide is associated with susceptibility to cancer.	Variations (mutations) of the naturally occurring DNA that includes the BRCA gene
	7 The isolated DNA molecule of claim 6, wherein the DNA molecule comprises a mutated nucleotide sequence set forth in SEQ ID cNO:1.	Variations (mutations) of the naturally occurring DNA that includes the BRCA gene