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# Mayo Test Dooms Breakthrough Biotech Invention

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The Federal Circuit recently handed down a long-awaited Section 101 decision, one with potentially far-reaching consequences for biotech diagnostic patents. In Ariosa Diagnostics Inc. v. Sequenom Inc., No. 14-1139 (Fed. Cir. June 12, 2015), the Federal Circuit, applying the U.S. Supreme Court's test for patent eligibility set out in Mayo Collaborative Servs. v. Prometheus Labs. Inc., 132 S. Ct. 1289 (2012), invalidated Sequenom's breakthrough patent on noninvasive prenatal diagnosis through the amplification and detection of paternally inherited cell-free fetal DNA ("cffDNA") in the blood of pregnant women. According to the court, "even such valuable contributions can fall short of statutory subject matter" under the test set out in Mayo.[1]

In addition to its implications for other biotech patents and investment in diagnostics, the Federal Circuit's decision illustrates the potentially unintended consequences of Mayo and the need for a legislative solution so that breakthrough manmade inventions remain patent-eligible.

As the Federal Circuit acknowledged, Sequenom "combined and utilized man-made tools of biotechnology in a new way that revolutionized prenatal care."[2] Indeed, prior to Sequenom's "ground-breaking invention," prenatal diagnoses, such as the detection of chromosomal abnormalities, required invasive methods that involved obtaining DNA directly from the placenta or fetus.[3] Such methods posed a risk to the mother and the pregnancy. "[N]o one was amplifying and detecting paternally-inherited cffDNA from the plasma or serum of pregnant mothers."[4] The maternal plasma used to be discarded since "'nobody thought that [cffDNA] would be present.'"[5]

The Royal Society described Sequenom's discovery and use of cffDNA in maternal plasma as a "'a paradigm shift in non-noninvasive diagnosis.'"[6] In his concurring opinion, Judge Richard Linn stated that the "new use of the previously discarded maternal plasma to achieve such an advantageous result is deserving of patent protection."[7] He noted that "Sequenom 'effectuat[ed] a practical result and benefit not previously attained,'" and that therefore "its patent would traditionally have been valid."[8]

But as Judge Linn went on to explain, the Supreme Court's test in Mayo deprived "a meritorious invention from the patent protection it deserves and should have been entitled to retain."[9] Mayo established a two-step test for determining patent eligibility. At step one, a court must "determine whether the claims at issue are directed to a patent-ineligible concept," namely "laws of nature, natural phenomena, [or] abstract ideas."[10] If the answer is yes, then a court must proceed to step two and

"consider the elements of each claim both individually and 'as an ordered combination' to determine whether additional elements 'transform the nature of the claim' into a patent-eligible application."[11] In applying the second part of the test, Mayo discounts any "[p]ost solution activity that is purely conventional or obvious."[12]

According to the Federal Circuit, Sequenom's breakthrough invention is not patent-eligible under Mayo. Claim 1 of Sequenom's patent is representative:

1. A method for detecting a paternally inherited nucleic acid of fetal origin performed on a maternal serum or plasma sample from a pregnant female, which method comprises

amplifying a paternally inherited nucleic acid from the serum or plasma sample and

detecting the presence of a paternally inherited nucleic acid of fetal origin in the sample.

At Mayo step one, the Federal Circuit found that Sequenom's claims were "directed to matter that is naturally occurring" because the claimed method "begins and ends with a natural phenomenon," the presence of cffDNA in a pregnant woman's blood.[13] In reaching this conclusion, the court relied heavily on the specification of the patent, which, as scientific research papers often do, described its fundamental technological advancement as a discovery of how things work in nature:

- "It has now been discovered that foetal DNA is detectable in maternal serum or plasma samples."

- "We have demonstrated that foetal DNA is present in maternal plasma and serum."

- "The most important observation in this study is the very high concentration of foetal DNA in maternal plasma and serum."[14]

The Federal Circuit also noted that Sequenom did not "create[] or alter[] any of the genetic information encoded in the cffDNA."[15]

Moving to Mayo step two, the court — drawing an analogy to Mayo's methods of modifying a treatment regimen based on measurements of the drug's metabolites — concluded that the "practice of the method claims does not result in an inventive concept that transforms the natural phenomenon of cffDNA into a patentable invention."[16] According to the court, the steps of amplifying DNA and detecting it were "well-understood, routine, and conventional" at the time of the invention, such that the claimed method "amounts to a general instruction to doctors to apply routine, conventional techniques when seeking to detect cffDNA."[17]

The only subject matter new and useful as of the date of the application was the discovery of the presence of cffDNA in maternal plasma or serum. ...

Where claims of a method patent are directed to an application that starts and ends with a naturally

occurring phenomenon, the patent fails to disclose patent eligible subject matter if the methods themselves are conventional, routine and well understood applications in the art.[18]

The court's decision illustrates the potentially unintended consequences of the Mayo test and its limitations. Judge Linn noted in his concurring opinion that he joined the majority in invalidating the claims of Sequenom's patent "only because [he was] bound by the sweeping language" of the Mayo test.[19] He said: "But for the sweeping language in the Supreme Court's Mayo opinion, I see no reason, in policy or statute, why this breakthrough invention should be deemed patent ineligible."[20]

Notably, Sequenom's patent is not to naturally occurring cffDNA. It is to a method of detecting and using that previously discarded DNA to achieve an important, practical result and obtain a benefit not previously attained. "[T]he amplification and detection of cffDNA had never before been done."[21] The cffDNA in maternal plasma was not known and the maternal plasma was discarded. Sequenom discovered that it was there and how to put it to practical use. As Judge Linn recognized, such a discovery is worthy of patent protection: "[t]he new use of the previously discarded maternal plasma to achieve such an advantageous result is deserving of patent protection."[22]

Indeed, it is well settled that new uses of old products are patentable.[23] Why should a new use of previously discarded material that is now amplified and detected using manmade techniques be any different simply because the cffDNA has nucleotides that exist in the same order and location as they do in nature? While Sequenom's claimed method does not alter the identity and location of the nucleotides in the cffDNA — indeed, the method would not be useful if it did — it certainly represents the "discover[y]" of a "new and useful process" that makes use of previously discarded material.[24]

In addition, as the Federal Circuit applied Mayo, Sequenom's claimed process was not considered as a whole. Instead, the court ignored steps that are "well-understood, routine, and conventional."[25] This is so despite the undisputed fact that "no one was amplifying and detecting paternally-inherited cffDNA using the plasma or serum of pregnant mothers" until Sequenom's invention.[26] While certain steps may be "well-understood, routine, conventional activity already engaged in by the scientific community," "those steps, when viewed as a whole" add something "significant beyond the sum of their parts taken separately," as evidenced by the paradigm shift in prenatal diagnosis brought about by Sequenom's invention.[27]

It seems unlikely that the Supreme Court will grant cert in this important case. But the Federal Circuit's application of Mayo puts in stark relief the limitations of Mayo's reductionist approach. A ground-breaking invention somehow became patent-ineligible subject matter because the genetic information being detected exists in nature and that information was not altered in amplifying and detecting it by known techniques. The decision reflects the need for a legislative solution so that the threshold requirement for patentable subject matter does not "exclud[e] a meritorious invention from the patent protection it deserves"[28] and spurs on innovation instead.

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[1] Ariosa Diagnostics Inc. v. Sequenom Inc., No. 14-1139, slip op. at 16 (Fed. Cir. June 12, 2015), available at http://www.cafc.uscourts.gov/images/stories/opinions-orders/14-1139.Opinion.6-10-2015.1.PDF.

[2] Id. at 15.

[3] See id. at 3-4; id. at 3 (Linn, J., concurring).

[4] Id. at 3 (Linn, J., concurring).

[5] Id. at 3 (quoting Sequenom's expert).

[6] Id. at 3-4 (quoting the Royal Society).

[7] Id. at 4.

[8] Id. (quoting Le Roy v. Tatham, 63 U.S. 132, 135-36 (1859)).

[9] Id. at 1.

[10] Id. at 8 (majority opinion) (quoting Mayo, 134 S. Ct. at 1297, and Alice Corp. v. CLS Bank Int'l, 134 S. Ct. 2347, 2355 (2014)).

[11] Id. (quoting Mayo, 134 S. Ct. at 1298).

[12] Mayo, 134 S. Ct. at 1299.

[13] Ariosa, slip op. at 8-9.

[14] Id. at 9-10.

[15] Id. at 9.

[16] Id. at 10.

[17] Id. at 11-12.

[18] Id. at 11, 13.

[19] Id. at 1 (Linn, J., concurring).

[20] Id. at 4-5.

[21] Id. at 4.

[22] Id.

[23] See, e.g., Perricone v. Medicis Pharm. Corp., 432 F.3d 1368, 1378 (Fed. Cir. 2005).

[24] See 35 U.S.C. § 101 (“Whoever invents or discovers any new and useful process ... may obtain a patent therefor . . . .”).

[25] See Ariosa, slip op. at 11-12.

[26] Id. at 3 (Linn, J., concurring).

[27] See Mayo, 132 S. Ct. at 1298 (emphasis added).

[28] See Ariosa, slip op. at 2 (Linn, J., concurring).

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