PATENT FILE

Turning tide on diagnostic method claims


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After a wave of patent eligibility decisions on diagnostic method claims, **Keith A Zullow**, **Michael B Cottler** and **Alexandra D Valenti** consider whether it could be the start of a sea change

The Supreme Court of the US, in *Mayo Collaborative Services v Prometheus Laboratories* and *Alice Corporation v CLS Bank Intl,* enunciated a test for evaluating patent eligibility under 35 USC §101. Courts have since grappled with applying that test, often invalidating patents, including those relating to medical diagnostics. For example, the Federal Circuit panel in *Ariosa Diagnostics v Sequenom* invalidated claims directed to detecting fetal genetic conditions in early pregnancy. Despite 22 *amicus* briefs supporting a request for Supreme Court review, the review was denied. After *Ariosa,* more diagnostic claims met the same demise.

Various groups have raised concerns that such jurisprudence has chilled innovation in the biotech field and proposed amendments to Section 101 that would negate the *Mayo/Alice* test – but no amendments have made it into a bill. Now, 18 months after denying *certiorari* in *Ariosa*, the Supreme Court is again being asked to consider the eligibility of diagnostic claims in *The Cleveland Clinic Foundation v True Health Diagnostics.* Whether or not the Supreme Court grants review, diagnostics patentees have reason for hope; recent decisions suggest that at least some Federal Circuit judges support a higher bar for proving ineligibility under Section 101.

The Mayo/Alice test and Ariosa

In *Mayo*,[1] the Supreme Court invalidated under Section 101 claims directed to optimising the efficacy of drugs to treat autoimmune diseases by assessing levels of the drug in the patient's blood. The court applied a two-part test for evaluating patent eligibility in which, as described in *Alice*,[2] the court should first "determine whether the claims at issue are directed to [a] patent-ineligible concept[]."

> **"Section 101 jurisprudence is 'too restrictive on what is patentable' in the biopharmaceutical space."**

If so, the court should consider whether additional claim elements "transform" the claims into a patent-eligible invention.

Following *Mayo* and *Alice*, the Federal Circuit evaluated patent eligibility of a diagnostic test in *Ariosa*.[3] At issue were Sequenom's patented method of diagnosing certain fetal characteristics using maternal blood by "amplifying" paternally-inherited nucleic acid from a sample and "detecting" such nucleic acid of fetal origin. The Federal Circuit affirmed a summary judgment of invalidity under Section 101. Under the *Mayo/Alice* test, the panel found that the claims were directed to a natural relationship between fetal DNA and maternal blood samples, and that the additional "amplifying" and "detecting" steps applied well-known techniques that did not transform the claims into patent-eligible subject matter.

Sequenom's petition for rehearing *en banc* was denied.[4] In a concurrence, Judges Lourie and Moore acknowledged that *Mayo* was correctly applied but lamented that "it is unsound to have a rule that takes inventions of this nature out of the realm of patent-eligibility on grounds that they only claim a natural phenomenon plus conventional steps," which may put "the whole category of diagnostic claims at risk". Judge Dyk also concurred, noting he "share[d] the concerns of some of [his] colleagues that a too restrictive test for patent eligibility under 35 USC § 101… may discourage development and disclosure of new diagnostic and therapeutic methods in the life sciences."

Sequenom sought Supreme Court review, with the support of 22 *amicus* briefs. *Amici* argued that the Federal Circuit failed to consider the claimed subject matter as a whole and conflated the patent-eligibility standard with obviousness or anticipation. The Supreme Court denied Sequenom's petition.

Patent eligibility of diagnostic methods after Ariosa

Applying *Mayo* and *Ariosa*, courts have found that numerous diagnostic method claims are patent ineligible. For instance, in *Genetic Technologies v Merial,*[5] the patentee discovered a correlation between DNA coding regions and non-coding regions of genes, and claimed detecting genetic variations by amplifying and analysing these non-coding regions. The Federal Circuit affirmed a ruling of patent ineligibility because the patent was directed to a natural law and the amplifying and analysing steps were routine and conventional. The patentee's discovery regarding genetic sequences did not save the claims.

Other examples abound. For instance, in *Esoterix Genetic Laboratories v Quagen*, 133 F Supp 3d 349 (D Mass 2015), the district court held ineligible claims to a method of determining increased cancer treatment efficacy by obtaining tumour DNA and determining the presence or absence of certain genetic variations. The district court in *Endo Pharmaceuticals v Actavis*,[6] invalidated claims to a method of treating pain by administering a drug, measuring a creatinine clearance rate and determining if it is in a certain range, and adjusting dosage based on that determination. In both cases, the courts found that the claims were based on newly-discovered natural laws – correlations between drug efficacy and patient characteristics – but that the claimed method steps merely applied well-known, routine techniques. Interestingly, many cases, including *Genetic Technologies, Esoterix,* and *Endo*, resolve these issues at the pleading stage, without claim construction or a fully-developed record.

A resulting outcry

An outcry ensued. In response to a US Patent and Trademark Office (USPTO) request for comments regarding subject matter eligibility requirements, Pharmaceutical Research and Manufacturers of America highlighted the importance of precision medicine as a tool for targeted treatment, but argued that Section 101 jurisprudence is "too restrictive on what is patentable" in the biopharmaceutical space and "is causing the US to fall behind its competitor countries in terms of the breadth of patent protection that is available for innovation in the biopharmaceutical area". The Intellectual Property Owners Association similarly noted that the jurisprudence "might discourage development and disclosure of new diagnostic and therapeutic methods in the life sciences, which are often driven by discovery of new natural laws and phenomena." Validating these concerns, the US Chamber of Commerce recently downgraded the US with respect to patent rights, citing, *inter alia*, "relative weakness in patentability requirements". Comments submitted in response to the USPTO request also criticised the *Mayo/Alice* test, and proposed legislation to Section 101 negating the test and related jurisprudence.

Nevertheless, Section 101 has not changed. In June 2017, the stronger Patents Act (S 1390) was introduced in the US Senate. While the bill's stated purpose is to "strengthen the position of the US", the proposed amendments do not address Section 101. Neither does the House companion bill (HR 5340).

Cleveland Clinic

Nevertheless, the Supreme Court may have an opportunity to clarify Section 101 in *Cleveland Clinic*. Cleveland Clinic seeks review of the invalidation under Section 101 of three patents directed to methods of characterising a subject's cardiovascular disease ("CVD") risk by determining myeloperoxidase ("MPO") levels and comparing them with control group levels.

"It is unsound to have a rule that takes inventions of this nature out of the realm of patent eligibility on grounds that they only claim a natural phenomenon plus conventional steps."

In the district court,[7] True Health Diagnostics ("THD") moved to dismiss Cleveland Clinic's complaint under Section 101. The district court, employing the *Mayo/Alice* test, invalidated the claims as directed to a law of nature – the correlation between MPO levels and CVD risk – with no saving inventive concept.

On appeal,[8] Cleveland Clinic argued that the district court erred by invalidating its claims without claim construction or adequate record development. The Federal Circuit disagreed, stating that it has "repeatedly affirmed § 101 rejections at the motion to dismiss stage" and that Cleveland Clinic provided no proposed constructions or expert testimony that would have changed the analysis on a fuller record.

Assessing eligibility using the *Mayo/Alice* test, the Federal Circuit found that the MPO-testing claims were directed to a law of nature, analogising them to fetal DNA detection claims in *Ariosa:* Cleveland Clinic detects naturally-occurring MPO and employs a natural relationship to predict CVD risk. The Federal Circuit also distinguished *Rapid Litigation Management v CellzDirect*,[9] where it upheld the validity of claims under Section 101 that were directed to a new method of preparing (freezing and thawing) preserved liver cells. Despite concerning a known type of cell, the claims were patent eligible because they claimed a "new and useful laboratory technique". Unlike *CellzDirect*, the Federal Circuit found that the Cleveland Clinic claims were directed to the natural existence of MPO and its correlation to CVD risk, applying only well-known techniques. The court concluded that "[t]he claims, whether considered limitation-by-limitation or as a whole, do not sufficiently transform the natural existence of MPO in a bodily sample and its correlation to cardiovascular risk into a patentable invention."

After denial of rehearing, Cleveland Clinic filed a petition for a writ of *certiorari* presenting two questions: 1) whether the Federal Circuit erred in invalidating claims to known techniques that have been adapted for a new use and purpose not previously known in the art; and 2) whether *Mayo* allows for a decision on invalidity under Section 101 at the pleadings stage without a developed factual record, notwithstanding Seventh Amendment safeguards.

Cleveland Clinic argues that the panel decision conflicts with *Mayo*, *CellzDirect*, and other precedent by finding the claims patent ineligible because they apply a natural phenomenon by adapting known techniques – even though they do so in novel ways to create new and improved methods. Cleveland Clinic also argues that the decision improperly encourages district courts to analyse eligibility challenges on the pleadings without a developed record and that the decision, if permitted to stand, will chill innovation. THD's response was due 7 May 2018.

Footnotes

1. 566 US 66 (2012).
2. 134 S Ct 2347 (2014)
3. 788 F.3d 1371 (Fed Cir 2015).
4. (809 F.3d 1282 (Fed Cir 2015)).
5. 818 F.3d 1369 (Fed Cir 2016).
6. No 14-1381-RGA, 2015 WL 7253674 (D Del 17 Nov 2015).
7. No 1:15-cv-2331, 2016 WL 705244 (ND Ohio 23 Feb 2016).
8. 859 F.3d 1352 (Fed Cir 2017).
9. 827 F.3d 1042 (Fed Cir 2016).

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