Patent Eligibility of Medical Diagnostic Claims – In Search of "Significantly More"

Ariosa Diagnostics, Inc. v. Sequenom, Inc.
(Fed. Cir. June 12, 2015)

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Ariosa v. Sequenom Discussion

I. Background and the US 6,258,540 ('540) Patent
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Medical Diagnostics

- Diagnostic test
  - "A generic term for any test used to determine the nature or severity of a particular condition."
    - Segen's Medical Dictionary, 2012
- Personalized medicine
  - "The study of an individual's unique biochemical and genetic makeup, in order to determine his susceptibility to disease or potential responses to treatment."
    - Medical Dictionary, 2009

Economics of Medical Diagnostics

- "The economics of innovative diagnostic tests reflect exactly the economic justification for the patent system: the cost of applying a genetic diagnostic test is relatively low, but the *ex ante* R&D cost is enormous and is not reflected in the marginal cost of the medical test itself" (Amicus Brief by Mossoff et al. for *Ariosa v. Sequenom*).
- Without patent protection, there is either little incentive for research or incentive to maintain a trade secret.

The Parties

- Plaintiffs – Appellee (declaratory judgement)
  - Ariosa makes and sells the Harmony Test that uses cell-free fetal DNA (cffDNA)
  - DNA Diagnostics Center is a licensee of Naderra (which makes and sells the Non-Invasive Paternity Test that uses cffDNA)
- Defendants - Appellants
  - Sequenom commercializes the MaterniT21 test for cffDNA based on an exclusive license of the '540 patent from Isis Innovation Limited
  - ISIS is the assignee of the '540 patent

The First Trial and First Appeal

- District Court (N.D. Cal 2012)
  - Denied Sequenom's motion for a preliminary injunction.
  - substantial question over whether the subject matter of the asserted claims was directed to eligible subject matter.
- Fed. Cir. (2013)
  - vacated and remanded the case, holding that the district court erred in certain respects of claim construction.
  - offered no opinion "as to whether there is or is not a substantial question regarding the subject matter eligibility of the asserted claims" of the '540 patent, but remanded "for the district court to examine subject matter eligibility . . . . in light of [*Myriad* (2013)]."

Independent Claims in the '540 Patent

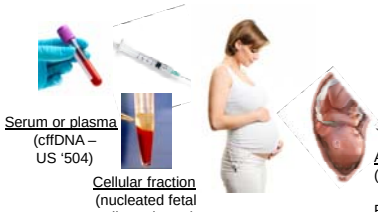
1. A method for detecting a paternally inherited nucleic acid of fetal origin performed on a maternal serum or plasma sample from a pregnant female, which method comprises

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.

(Independent claims 24 and 25 are analogous)

Prenatal Diagnostics



Serum or plasma (cffDNA – US '504)

Cellular fraction (nucleated fetal cells - prior art)

cffDNA = cell-free fetal DNA

Amniotic sac fluid (Amniocentesis – prior art)

Placental tissue (Chorionic villus sampling – prior art)

Prenatal Diagnostic Tests using cffDNA

- Advantages
  - Eliminate complications to mother and fetus of amniocentesis and chorionic villus sampling
  - Less invasive than amniocentesis and chorionic villus sampling
  - Detection rate is much higher than using fetal cells in maternal blood
  - Less time-consuming and less expensive than using fetal cells in maternal blood
- Examples
  - Predicting complications in pregnancy
  - Predicting abnormalities in the fetus
  - Sex determination of fetus

Patent Eligible Subject Matter 35 U.S.C. § 101

- "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."

Patent Eligible Subject Matter Exceptions

- Exceptions: Laws of nature, natural phenomena, and abstract ideas. *Alice Corp. v. CLS Bank Int'l.* (2014)
- BUT patentable subject matter if an "inventive concept" is present — i.e., an element or combination of elements that is "sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself." *Mayo Collaborative Services v. Prometheus Laboratories, Inc. (2012)*
- (Intermediate step for nature-based products) "markedly different characteristics from any found in nature". *Chakrabarty.* (USPTO: A process claim is not subject to the markedly different analysis for nature-based products used in the process.)

Comparing Recent Supreme Court Cases on Subject Matter Eligibility of Utility Inventions

Case	Claims	Judicial Exception	Holding
Alice Corp (2014)	Process (mitigating settlement risk)	Abstract idea (settlement risk)	Ineligible
Myriad (2013)	Product (BRCA genes)	Natural phenomenon (DNA)	Ineligible
Mayo (2012)	**Process (thiopurine dosages)**	**Law of nature (metabolite relationships)**	**Ineligible**
Bilski (2010)	Process (hedging risk)	Abstract idea (hedging)	Ineligible
Diehr (1981)	**Process (molding rubber)**	**Abstract idea (Arrhenius eq.)**	**Eligible**
Chakrabarty (1980)	Product (genetically modified bacteria)	Natural phenomenon (bacteria)	Eligible
Flook (1978)	Process (alarm limits)	Abstract idea (algorithm)	Ineligible
Gottschalk (1972)	Process (numeral conversion)	Abstract idea (mathematical formula)	Ineligible
Funk Bros (1948)	Product (packaged bacteria)	Natural phenomenon (bacteria)	Ineligible

Mayo v. Prometheus (2012)

- The courts considered this case the most directly on point to *Ariosa*
- Method to identify correlations between metabolite levels of thiopurine drugs and likely harm or ineffectiveness with precision in treating autoimmune diseases.
  - 1. "administering" step of a thiopurine drug
  - 2. "determining" step of measuring metabolite levels of the thiopurine drug in blood
  - 3. "wherein" step describing critical metabolite thresholds may "indicate a need" to decrease or increase dosage of thiopurine drug

Mayo v. Prometheus (2012)

- Prometheus' process is not patent eligible.
- Law of nature – "the relationships between concentrations of certain metabolites in the blood and the likelihood that a thiopurine drug dosage will prove ineffective or cause harm"
- The three additional steps in the claimed processes are insufficient to transform the nature of the claims.
  - (1) Administering step, (2) determining step, (3) wherein step

Mayo v. Prometheus (2012)

- (1) Administering step: "Doctors had been using these [thiopurine] drugs for this purpose long before these patents existed."
- (2) Determining step: "methods for making such determinations were well known in the art, this step simply tells doctors to engage in well-understood, routine, conventional activity previously engaged in by scientists in the field."
- (3) Wherein step: "about the relevant natural laws, adding, at most, a suggestion that they should consider the test results when making their treatment decisions." (point of novelty = precisely defining the correlation between metabolite levels and harm)
- No synergy when steps are combined

Mayo v. Prometheus (2012)

- "The three steps add nothing specific to the laws of nature other than what is well-understood, routine, conventional activity, previously engaged in by those in the field."
- "simply appending conventional steps, specified at a high level of generality, to laws of nature, natural phenomena, and abstract ideas cannot make those laws, phenomena, and ideas patentable"
- "forecloses more future invention than the underlying discovery could reasonably justify."

Comparing the Claims in *Mayo* and *Ariosa*

- Method claims are at issue in both cases.
- BUT the judicial exception in *Mayo* was a law of nature, while the judicial exception in *Ariosa* was a natural phenomenon and the additional steps in Mayo were clearly obvious.
- How should we analyze subject matter eligibility of a claimed process reciting a natural phenomenon?

2014 Interim Guidance on Patent Subject Matter Eligibility - USPTO

- Limitations that may qualify as "significantly more"
  - "Improvements to another technology or technical field
  - Improvements to the functioning of the computer itself
  - Applying the judicial exception with, or by use of, a particular machine
  - Effecting a transformation or reduction of a particular article to a different state or thing
  - Adding a specific limitation other than what is well-understood, routine and conventional in the field, or adding unconventional steps that confine the claim to a particular useful application
  - Other meaningful limitations beyond generally linking the use of the judicial exception to a particular technological environment."

2014 Interim Guidance on Patent Subject Matter Eligibility - USPTO

- Limitations that were found out not to be enough to qualify as "significantly more"
  - Adding the words ''apply it'' (or an equivalent) with the judicial exception
  - Simply appending well-understood, routine and conventional activities
  - Adding insignificant extrasolution activity to the judicial exception,
  - Generally linking the use of the judicial exception to a particular technological environment or field of use.

Ariosa Diagnostics v. Sequenom (N.D. Cal. 2013)

- District Court Opinion
- cffDNA in maternal plasma or serum is a natural phenomenon.
- BUT the '540 patent claims are directed to a method of using cffDNA, not the cffDNA itself.

Ariosa Diagnostics v. Sequenom (N.D. Cal. 2013)

- The method steps contained in the claims of the '540 patent "do not add enough to the natural phenomenon of paternally inherited cffDNA to make these claims patentable under § 101." (i.e. not "significantly more")
- Specifically, "the additional limitations in the claims either apply well-understood, routine, and conventional activity to the natural phenomenon or limit the natural phenomenon to specific types of the natural phenomenon, which are also unpatentable."
  - sample preparation, amplification and detection of DNA in plasma or serum was well known

Ariosa Diagnostics v. Sequenom (N.D. Cal. 2013)

- "Sequenom argues that its use of cffDNA is inventive because prior to the invention, no one had started with the mother's plasma or serum to detect paternally inherited fetal DNA." (Significantly more?)
- "The Court similarly concludes that paternally inherited cffDNA is not patentable simply because the claims contain steps indicating that it may be detected using existing DNA detection methods." (but this is a method claim)

Ariosa Diagnostics v. Sequenom (N.D. Cal. 2013)

- Preemption is a consideration in a § 101 analysis: "a court should consider whether the claim poses a risk of preempting a law of nature, natural phenomenon, or abstract idea." *See CLS Bank Int'l v. Alice Corp.* (Fed. Cir. 2013).
  - Burden on Sequenom do demonstrate alternate methods that are commercially viable.
- "it appears that the effect of issuing the '540 patent was to wholly preempt all known methods of detecting cffDNA."
- **Summary Judgement for Ariosa**

Ariosa Diagnostics v. Sequenom (Fed. Cir. 2015)

- Majority Opinion: Circuit Judges Reyna and Wallach
  - Invalidity of claim under § 101 is reviewed *de novo*.
- "It is undisputed that the existence of cffDNA in maternal blood is a natural phenomenon."
- "Thus, the claims are directed to matter that is naturally occurring."
- BUT the '540 patent claims are directed to a method of using cffDNA, not the cffDNA itself.

Ariosa Diagnostics v. Sequenom (Fed. Cir. 2015)

- "Because the method steps were well-understood, conventional and routine, the method of detecting paternally inherited cffDNA is not new and useful."
  - sample preparation, amplification and detection of DNA generally in plasma or serum was well known
- "We conclude 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." (i.e. not "significantly more")

Ariosa Diagnostics v. Sequenom (Fed. Cir. 2015)

- "Sequenom argues that "before the '540 patent, *no one* was using the plasma or serum of pregnant mothers to amplify and detect paternally-inherited cffDNA." (Significantly more?)
- "This argument implies that the inventive concept lies in the discovery of cffDNA in plasma or serum. Even if so, this is not the invention claimed by the '540 patent." (???)

Ariosa Diagnostics v. Sequenom (Fed. Cir. 2015)

- "significant contribution to the medical field" and "revolutionized prenatal care"
- "publication has been cited over a thousand times."
- "Groundbreaking, innovative, or even brilliant discovery does not by itself satisfy the § 101 inquiry." *Myriad*
- "But even such valuable contributions can fall short of statutory patentable subject matter, as it does here."

Ariosa Diagnostics v. Sequenom (Fed. Cir. 2015)

- "questions on preemption are inherent in and resolved by the § 101 analysis."
- "Where a patent's claims are deemed only to disclose patent ineligible subject matter under the *Mayo* framework, as they are in this case, preemption concerns are fully addressed and made moot."
- **Affirmed**

Ariosa Diagnostics v. Sequenom (Fed. Cir. 2015)

- Concurring Opinion: Circuit Judge Linn
- "Unlike in *Mayo*, the '540 patent claims a new method that should be patent eligible." "Sequenom 'effectuate[d] a practical result and benefit not previously attained'"
- "I see no reason, in policy or statute, why this breakthrough invention should be deemed patent ineligible."
- (Dissent?)

Ariosa Diagnostics v. Sequenom (Fed. Cir. 2015)

- "the Supreme Court in *Mayo* discounted, seemingly without qualification, any '[p]ost-solution activity that is purely conventional or obvious'"
- "I join the court's opinion invalidating the claims of the '540 patent only because I am bound by the sweeping language of the test set out in *Mayo".*
- (Now it becomes a concurring opinion)

Ariosa Diagnostics v. Sequenom (Petition for en banc rehearing)

- Sequenom has requested the Federal Circuit for a rehearing of this case *en banc*.
- "Is a novel method patent-eligible under §101 where: (1) a researcher is the first to discover a natural phenomenon; (2) that unique knowledge motivates her to apply a new combination of previously known techniques to the phenomenon; and (3) she thereby achieves a previously unknown and impossible result?"
- "The panel's apparent rationale was that because the *motivation* for the new combination of techniques in the '540 method lay in the discovery of cffDNA in maternal"

Ariosa Diagnostics v. Sequenom (Petition for en banc rehearing)

- "The panel's core error lies in ignoring *Diehr* and so misunderstanding what it means for a method's steps to be 'routine,' 'conventional,' or 'well-understood.'" (Significantly More)
- *"Diehr* thus emphasized that the patent there did 'not seek to pre-empt the use of th[e] [unpatentable] equation,' but 'only to foreclose from others the use of that equation in conjunction with *all of the other steps* in their claimed process.'"
- "To that end, *Diehr* was emphatic that '[i]n determining the eligibility of respondents' claimed process … under §101, their claims must be considered as a whole.'"

Ariosa Diagnostics v. Sequenom (Petition for en banc rehearing)

- "just like that in *Diehr*, and not at all like that in *Mayo*: The natural phenomenon Drs. Lo and Wainscoat discovered motivated them to teach a new method that *no one* was practicing, and whose combined steps were in fact the opposite of the 'conventional' approach, even if each individual technique involved was 'well-understood' on its own."
- "That is why, *per Diehr*, a method's 'inventive concept' inheres in the novelty of its combined steps, *not* the discovery that motivates them."

Ariosa Diagnostics v. Sequenom

- Did the claim as a whole amount to "significantly more"? (Sequenom Petition)
- Was amplifying cffDNA from maternal blood serum or plasma "significantly more"?
- Has the Federal Circuit in *Ariosa* analyzed the judicial exception as a law of nature instead of a natural phenomenon?
  - cffDNA is a natural phenomenon in maternal blood, or
  - cffDNA being in maternal blood is a natural phenomenon
- Questions?