No. 15-___

IN THE

Supreme Court of the United States

SEQUENOM, INC.,

Petitioner,

v.

ARIOSA DIAGNOSTICS, INC., NATERA, INC., AND DNA DIAGNOSTICS CENTER, INC.

Respondents.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

PETITION FOR A WRIT OF CERTIORARI

Michael J. Malecek
Robert Barnes
KAYE SCHOLER LLP
Two Palo Alto Square
Suite 400
3000 El Camino Real
Palo Alto, CA 94306
(650) 319-4500

Thomas C. Goldstein
Counsel of Record
Eric F. Citron
GOLDSTEIN & RUSSELL, P.C.
7475 Wisconsin Ave.
Suite 850
Bethesda, MD 20814
(202) 362-0636
tg@goldsteinrussell.com

QUESTION PRESENTED

In 1996, two doctors discovered cell-free fetal DNA (cffDNA) circulating in maternal plasma. They used that discovery to invent a test for detecting fetal genetic conditions in early pregnancy that avoided dangerous, invasive techniques. Their patent teaches technicians to take a maternal blood sample, keep the non-cellular portion (which was "previously discarded as medical waste"), amplify the genetic material within (which they alone knew about), and identify paternally inherited sequences as a means of distinguishing fetal and maternal DNA. Notably, this method does not preempt other demonstrated uses of cffDNA.

The Federal Circuit "agree[d]" that this invention "combined and utilized man-made tools of biotechnology in a new way that revolutionized prenatal care." Pet.App. 18a. But it still held that *Mayo Collaborative Servs. v. Prometheus Labs.*, 132 S. Ct. 1289 (2012), makes all such inventions patent-ineligible as a matter of law if their new combination involves only a "natural phenomenon" and techniques that were "routine" or "conventional" on their own. Multiple judges wrote separately below to explain that while this result was probably not intended by *Mayo*, it controlled, and only this Court could now "clarify" *Mayo*'s reach to prevent a "crisis" in life-science innovation.

The Question Presented is:

Whether a novel method is patent-eligible where: (1) a researcher is the first to discover a natural phenomenon; (2) that unique knowledge motivates him to apply a new combination of known techniques to that discovery; and (3) he thereby achieves a previously impossible result without preempting other uses of the discovery?

CORPORATE DISCLOSURE STATEMENT

Pursuant to Rule 29.6 of this Court's Rules, petitioner Sequenom, Inc. states that it has no parent company, and no publicly held corporation owns 10% or more of its stock.

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

Constitution and Statutes

Other Authorities

PETITION FOR A WRIT OF CERTIORARI

Petitioner respectfully seeks a writ of certiorari to review the judgment of the United States Court of Appeals for the Federal Circuit.

OPINIONS BELOW

The opinions below (Pet.App. 1a) are published at 788 F.3d 1371. The opinions respecting rehearing *en banc* (Pet.App. 70a) are published at 809 F.3d 1282. The district court's opinion (Pet.App. 25a) is published at 19 F. Supp. 3d 938.

JURISDICTION

The Federal Circuit entered judgment on June 12, 2015 and denied rehearing on December 2, 2015. Pet.App. 74a. The Chief Justice extended this petition's filing date to April 1, 2016, No. 15A871. The Court has jurisdiction under 28 U.S.C. §1254(1).

STATEMENT

1. In the 1990s, researchers were searching for non-invasive tests that might detect fetal genetic features early in pregnancy—including, most importantly, substantial abnormalities—without using dangerous techniques like amniocentesis. They knew some "nucleated cells" (that is, cells with their DNA core intact) passed from fetus to mother, and believed that finding even one such cell might permit diagnoses through analysis of the fetal DNA inside. *See* U.S. Patent No. 6,258,540 at 1:26-31. Researchers were thus meticulously combing the *cellular* portion of maternal blood for fetal cells, and routinely discarded the rest of their maternal blood samples—the plasma and serum—as waste. Pet.App. 3a; Patent 1:51-55.

Drs. Dennis Lo and James Wainscoat revolutionized this field. Pet.App. 18a. They discovered that "cell-free" fetal DNA (cffDNA) was circulating in pregnant women's plasma in surprising concentrations. *Id.* 13a. Their experiments further determined that relatively new genetic-research tools like "polymerase chain reaction" (PCR) would allow them to reliably detect that cffDNA in a sample otherwise dominated by nearly identical maternal DNA. This was a profound breakthrough; their *Lancet* article describing it has since been cited over a thousand times. *Id*. 18a.

This discovery, however, replaced one scientific problem with another. Researchers had been searching for a fetal-cell-shaped needle in a billions-of-maternal-cells-sized haystack, because that cell could yield a pure fetal sample. Lo and Wainscoat now had a ready source of fetal DNA, but it was "cell-free" fetal DNA mixed up with cell-free maternal DNA that would confound their diagnostic testing.

Lo and Wainscoat devised a solution that turned their discovery into a practical, non-invasive, early-prenatal test. Pet.App. 3a. They realized that, by identifying genetic fragments containing *paternally inherited* sequences the mother did not share, they could reliably identify fetal DNA, which would in turn allow them to diagnose certain fetal genetic conditions. For example, they recognized that fetal aneuploidies like Down Syndrome would cause predictable variations in the amount of identifiably fetal DNA associated with certain chromosomes in a given

maternal blood sample. Pet.App. 4a; Pet.App. 23a (Linn, J.); Patent 3:44-52.[1] In sum, these inventors had devised an early-prenatal genetic test whose key steps—never previously combined in this way—were to take a maternal blood sample, keep only the long-discarded *non*-cellular fraction, amplify the cell-free DNA only they had discovered therein, and search for paternally inherited sequences whose presence or quantity indicated diagnostically relevant conditions.

The '540 patent teaches this invention. Claim 1 teaches that the critical steps are amplification and detection of "paternally inherited nucleic acid[s] of fetal origin" in a "maternal serum or plasma sample." Patent 23:60-67. Claim 21 situates these steps within a larger diagnostic method that up-ended conventional practice:

> 21. A method of performing a prenatal diagnosis, which method comprises the steps of:
>
> (i) providing a maternal blood sample;
>
> (ii) separating the sample into a cellular and non-cellular fraction;
>
> (iii) detecting the presence of nucleic acid of fetal origin in the non-cellular fraction according to the method of claim 1 [that is, by (i) amplifying and (ii) detecting paternally inherited nucleic acids, and];

---

[1] "Aneuploidies" are disorders involving the wrong *number* of chromosomes, and they affect the expected amount of cffDNA from those chromosomes in a given sample by altering the relative amount of source material.

(iv) providing a diagnosis based on the presence and/or quantity and/or sequence of the fetal nucleic acid.

Patent 26:4-14.

Beyond this particularized method, the patent discloses several even-more-concrete diagnostic tests. For example, in addition to the aneuploidy-detection case above, it explains how to use the method to determine fetal gender by searching for Y-chromosome material in maternal plasma (a "particularly useful" application, because mothers necessarily lack Y-chromosomes). *See* Patent 2:49-51. This test, separately claimed through dependent Claims 5 and 12, Patent 25:1-3, 25:18-20, is now often used to determine fetal gender using nothing more than a blood sample from a ten-week-pregnant mother.

The patent also describes how to use its method to achieve a breakthrough in avoiding RhD hemolytic disease. Briefly, when RhD-negative women carry RhD-positive fetuses (who inherit the RhD blood-antigen gene from their fathers), the mother's antibodies can attack the fetus's blood, leading to fetal illness, and even death. Despite possible complications, the main previous option was indiscriminately treating RhD-negative women just in case the fetus was positive. But because (like the Y-chromosome) the RhD gene is necessarily absent in the RhD-negative mother, the patent's method works perfectly for testing the fetus's RhD status. Patent 2:62-3:3. This test is separately claimed through dependent Claims 8 and 11; Claim 9 covers using the same method for other blood-antigen tests. Patent 25:8-12, 25:16-17.

In the Federal Circuit's words, this "invention, commercialized by [petitioner] Sequenom as its MaterniT21 test, created an alternative for prenatal diagnosis of fetal DNA that avoids the risks of widely-used techniques." Pet.App. 3a. This, if anything, undersells the benefit: Previously, accurate early-prenatal diagnosis of such conditions required dangerous techniques like amniocentesis, carrying a material risk of heartbreaking miscarriage or fetal injuries. These inventors replaced a long needle invading the amniotic sac—and a terrifying moment for expecting parents—with a simple and safe blood draw, solving a problem that frustrated their field for years.

Notably, Lo and Wainscoat did not try to patent cffDNA itself, nor preempt all uses of it by others. *Id.* In fact, peer-reviewed research in the record below has demonstrated practical uses for cffDNA that do not (i) fractionate maternal blood, (ii) amplify DNA in the sample; or (iii) detect paternally inherited DNA at all. Pet.App. 55a-56a. And the patent does not preempt such practices because it nowhere claims the use of the cffDNA itself. Instead, it is infringed only if *all* its steps are practiced in combination.

Indeed, what was so novel about the '540 patent was precisely that combination of techniques it first disclosed. Researchers in the 1990s surely knew how to fractionate blood, amplify DNA, look for genetic sequences, and make diagnoses from them. But it is undisputed that no one was previously practicing these steps in the '540 patent's combination because, evocatively, they were discarding the relevant materials as waste. Pet.App. 3a. In short, the '540 patent's *combined* steps were anything but "conventional" because the "convention" was the opposite.

2. Petitioner Sequenom exclusively licensed the '540 patent and invested enormously in bringing it to market as a viable medical test. As the pioneer, Sequenom spent heavily on clinically validating the method, obtaining regulatory approvals, and educating clinicians. *See* N.D. Cal. #11-6391, Dkt. 36, ¶¶15-21, 36-43. When MateriT21 launched in late 2011, Sequenom had already spent about $70 million developing it, *id.* ¶41, and expected to double that in 2012. And, of course, it committed substantial royalties to license the technology.

Respondents launched their price-competing products shortly thereafter, targeting the same markets and affirmatively trying to free-ride on Sequenom's investment. *Id.* ¶¶45, 54. Respondent Ariosa candidly told its investors that it would "draft on Sequenom's efforts to go after the same geographies," N.D. Cal. #11-6391, Dkt. 114, Ex. 16, and its Chairman testified about Ariosa's "strategies of being a fast follower and letting your competitor educate the market around advantages to cell-free DNA," Dkt. 114, Ex. 3, pp.117-18. This predictably caused "price and market erosion," *Aria Diagnostics v. Sequenom*, 726 F.3d 1296, 1304-05 (Fed. Cir. 2013), and so Sequenom has yet to achieve profitability on its investment.

3. As a heavily-invested practicing entity, Sequenom refused to license competitors. Respondents sued petitioner seeking a declaratory judgment; Sequenom counterclaimed and sought a preliminary injunction. After construing the '540 patent's claims, the district court denied the injunction. But, in an initial appeal, the Federal Circuit corrected the district court's claim constructions, found significant

risks of irreparable harm to Sequenom's patent-protected product, and so vacated and remanded "with additional guidance" regarding an injunction. *See id.* On remand, however, the district court invalidated the patent under Section 101. Pet.App. 68a.

This time, a different Federal Circuit panel affirmed (with a remarkable concurrence from Judge Linn, *see infra* p.8-9). The majority concluded that the '540 patent fails the two-step test this Court first developed in *Mayo* for when a method patent impermissibly claims a natural law or phenomenon. First, it said, the claims "are directed to a patent-ineligible concept" because the "method begins and ends with a natural phenomenon" (*i.e.*, cffDNA). Pet.App. 9a-11a. Second, it said, the claimed method did not "'transform' the claimed naturally occurring phenomenon into a patent-eligible application." *Id.* 12a. The core reasoning was that, "[f]or process claims that encompass natural phenomen[a], the process steps … must be new and useful." *Id.* And because researchers already knew how to accomplish the *individual* steps of (1) fractionating blood; (2) amplifying DNA; and (3) detecting characteristics in amplified DNA, the combined method impermissibly added only "well-understood, routine, and conventional activity" to the natural phenomenon Lo and Wainscoat had discovered—rendering it patent-ineligible as a matter of law. *Id.* 13a.

The majority then rejected "Sequenom's remaining argument[]" that "before the '540 patent, *no one* was using the plasma or serum of pregnant mothers to amplify and detect paternally-inherited cffDNA." Pet.App. 18a. This argument, it said, "implies that the inventive concept lies in the discovery of cffDNA

in plasma or serum." *Id.* The majority's evident rationale was that, because the discovery of cffDNA in maternal plasma directly motivated the '540 patent's new combination of known techniques, that invention merely reflected that patent-ineligible discovery itself. According to the majority, that rendered the patent ineligible under Section 101 as a matter of law, even though it "agree[d]" that the patent "*combined* and utilized man-made tools of biotechnology *in a new way* that revolutionized prenatal care." *Id.* (emphasis added).

Finally, without disputing that alternative inventions not preempted by the '540 patent had put cffDNA to practical use, *supra* p.5, the majority simply waived this critical fact away. Pet.App. 17a. It acknowledged that, under longstanding Section 101 precedent, "the principle of preemption is the basis for the judicial exceptions to patentability." *Id.* But it regarded preemption as a one-way ratchet: It "may signal patent ineligible subject matter," but "the absence of complete preemption does not demonstrate patent eligibility." *Id.* Indeed, the panel held that, once a court concludes that the claims involve only natural phenomena and "conventional" techniques, "preemption concerns are fully addressed and made moot." *Id.*

Judge Linn wrote separately, explaining in very direct terms that he joined "only because [he was] bound by the sweeping language of the test set out in *Mayo*." Pet.App. 20a. In his view, "[t]his case represents the consequence—perhaps unintended—of that broad language in excluding a meritorious invention from the patent protection it deserves and should have been entitled to retain." *Id*. 20a-21a. He noted

that the patent appeared eligible under *Diamond v. Diehr*, 450 U.S. 175, 188 (1981), which *Mayo* reaffirmed and the majority did not discuss. Pet.App. 21a-22a. Nonetheless, he concluded that certain language in *Mayo*, though unnecessary to its holding, seemed to compel a finding of ineligibility, *id.* 22a—even though "Sequenom's invention is nothing like the invention at issue in *Mayo*," and there was "no reason, in policy or statute" to invalidate it. *Id.* 24a.

Petitioner sought rehearing *en banc*, supported by twelve *amicus* briefs, but it was denied with three further opinions. Building on Judge Linn's concurrence, their basic thrust was that, despite this patent's inventive merit, the case would have to be resolved in this Court because *Mayo* tied the Federal Circuit's hands. For example, Judge Lourie, joined by Judge Moore, explained that the patent's claims merely "rely on or operate by, but do not recite, a natural phenomenon," Pet.App. 79a, and that barring such inventions under Section 101 would mean that "nothing in the physical universe would be patent-eligible," *id.* 77a. He emphasized that this patent claimed "innovative and practical *uses* for" cffDNA through methods that, as a whole, were "*not* routine and conventional," and did not foreclose "other methods of prenatal diagnostic testing using cffDNA." *Id.* 81a. He thus concluded that it was "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." *Id.* 82a. But because, "applying *Mayo*, we are unfortunately obliged to divorce the additional steps from the asserted natural phenomenon," he agreed the court was bound to affirm. *Id.* 81a.

Judge Dyk made similar points. He highlighted "a problem with *Mayo* insofar as it concludes that inventive concept cannot come from discovering something new in nature," especially "in the life sciences, where development of useful new diagnostic and therapeutic methods is driven by investigation of complex biological systems." Pet.App. 89a-90a. He worried that "*Mayo* may not be entirely consistent with the Supreme Court's decision in" *Association for Molecular Pathology v. Myriad Genetics*, 133 S. Ct. 2107, 2112-13 (2013). Pet.App. 90a. And, critically, while he emphasized his belief that "some further illumination as to the scope of *Mayo* would be beneficial," he concluded that, given "the language of *Mayo* … any further guidance *must come from the Supreme Court*, not this court." *Id*. 84a (emphasis added).

Judge Newman would have granted rehearing. She noted that her colleagues all seemed to "agree … that this case is wrongly decided," Pet.App. 100a, because the "diagnostic method here is novel and unforeseen, and is of profound public benefit." *Id.* 102a. But she did not "share the view that this incorrect decision is required by Supreme Court precedent," *id.* 100a, reasoning that the distinction between patenting "new applications" of knowledge and patenting knowledge itself could have allowed the Federal Circuit to save this meritorious invention. *Id.*

REASONS FOR GRANTING THE WRIT

This is as straightforward a certiorari candidate as any patent case can be. It is manifestly important: A host of judges and *amici* have stressed that the result below is untenable—invalidating previously irreproachable inventions and precipitating what Judge Lourie called "a crisis of patent law and medi-

cal innovation." Pet.App. 78a. Those judges have likewise emphasized that the only clarifications that can avoid such results "must come from the Supreme Court." Pet.App. 84a (Dyk, J.); Pet.App. 20a-21a (Linn, J.). And this is the vehicle this Court needs to provide that clarification: Every opinion below agrees that this case tests *Mayo*'s uncertain limits by invalidating an otherwise *plainly* meritorious invention. As *Mayo*'s author has acknowledged, that case could only "sketch an outer shell" of its test, Arg. Tr. 28, *Alice v. CLS Bank Int'l*, 134 S. Ct. 2347 (2014) (No. 13-298) (Breyer, J.), partly because it was hard to "figure out much … to go beyond … an obvious case." *Id.* 10-11. Here, unlike *Mayo*, every intuition points towards patent-eligibility. And yet the Federal Circuit felt compelled by *Mayo* to condemn this meritorious patent—and, *a fortiori*, the patents underlying an entire, vital field of American healthcare innovation. If, as several judges below observed, that cannot be what *Mayo* intended, this is precisely the case in which this Court needs to say so.

The case itself shows why. Sequenom invested enormously in developing and validating a recognized "breakthrough" for clinical use, only to see that investment radically undermined by fast-following competitors trading on an uncertain legal doctrine. As several judges below explained, even they find it hard to reconcile *Mayo*'s test with other language in the opinion, Pet.App. 23a-24a (Linn, J.), let alone other language in other opinions, Pet.App. 90a-91a (Dyk, J.). It is infinitely harder for businesses to decipher where the doctrine now stands, especially because it (now) seems divorced from intuitions about patent-eligibility for "revolutionary" inventions like

this one. Right now, Section 101 doctrine lacks any discernable limits, and so no company can trust in the patent system when deciding whether to invest in bringing an invention to market. This issue has become particularly life-threatening to life-science innovators. Pet.App. 77a-78a (Lourie, J.); Pet.App. 90a (Dyk, J.). And so unless this Court clarifies some limits on Section 101, a doctrine that was meant to be a narrow exception will become the rule by default in at least this industry, and likely beyond.

This is a perfect case in which to provide that clarification; here, the Court can confirm the eligibility of inventions like the '540 patent by merely making explicit a distinction the cases already contain. In particular, the Court can brighten the line between a method that merely adds a new discovery to what practitioners were already doing, *see Mayo*, 132 S. Ct. at 1299, and one that, by the Federal Circuit's own description, "*combine[s]* … man-made tools … *in a new way*" to achieve a revolutionary result. Pet.App. 18a (emphasis added). Put otherwise, this case allows the Court to emphasize that a *new combination* of otherwise conventional techniques is patent-eligible even if it is straightforwardly motivated by a patentee's unique discovery of a natural law or phenomenon. That is precisely why, in *Mayo* itself, this Court said that discovering a "new way of using an existing drug" should remain patent-eligible, even though such an invention only combines a newly discovered natural phenomenon with otherwise known substances and techniques. 132 S. Ct. at 1302. And it is why, in *Myriad*, this Court endorsed Judge Bryson's view that "the first party with knowledge of [a natural phenomenon]" should be "in an excellent

position to claim applications of that knowledge." 133 S. Ct. 2120. That, of course, is an excellent description of these inventors: They were "the first parties with knowledge of" cffDNA, and should have been "in an excellent position to claim applications of that knowledge"—like previously impossible blood tests for fetal gender or Down Syndrome—by teaching others the new combination of available techniques that would enable such revolutionary results.

Unfortunately, the Federal Circuit reached the opposite conclusion by adopting a reading of *Mayo* so broad that it demands this Court's intervention. Indeed, the rote version of *Mayo*'s two-part test endorsed below invalidates any method patent combining a natural discovery with "conventional" techniques—even if those techniques are admittedly "new" in combination and that new combination admittedly does not preempt all uses of the discovered phenomenon. Pet.App. 13a. Recognizing that "all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas," *Mayo* promises that its test is not meant to "eviscerate patent law." 132 S. Ct. at 1293. But the Federal Circuit's version of *Mayo*'s test does exactly that—gutting protections for a host of meritorious inventions, especially in the life-sciences, where almost all inventions come from combining existing techniques in new ways to capitalize on new insights from basic research. Pet.App. 84a (Dyk, J.).

Indeed, the Federal Circuit's version of *Mayo* undermines just about any biomedical breakthrough you can conceive. Vaccines? They combine the natural fact of immune response with known methods of drug administration. Even for previously unstudied

diseases like Zika? Yes. Aspirin—perhaps the world's most successful patented medicine? It combined a natural plant product with basic chemistry techniques. Gene amplification by PCR—the Nobel-winning method that respondent Ariosa's parent (Roche) has earned billions licensing? By its inventor's description, a simple idea that "lay unrecognized for more than 15 years after *all the elements for its implementation were available*." Mullis, *The Unusual Origin of the Polymerase Chain Reaction,* SCIENTIFIC AMERICAN, Apr. 1990, at 56 (emphasis added). If combining a new insight about the natural world with "available elements" to achieve extraordinary new results is unpatentable subject matter—as is now U.S. law absent this Court's intervention—no such breakthroughs are patent-eligible. That means anyone who would invest in making, validating, or commercializing inventions like these for human medical use must invite others along for the free ride, with predictably unfortunate results.

Even worse, the decision below exacerbates this confusion by jettisoning the one reliable compass this Court had identified for Section 101 cases—the patent's "preemptive" scope. As *Alice* made clear, preemption is "the concern that drives" the Section 101 exceptions, 134 S. Ct. at 2354-55, and so the way to identify patents that claim an impermissible natural law or abstract idea is to determine whether they preempt *all* uses of the law or idea, or rather only particular applications. But the Federal Circuit expressly held below that such concerns are "made moot" whenever a legalistic application of *Mayo*'s test identifies only "routine" or "conventional" techniques in a patent that builds on a natural phenomenon or

law. Pet.App. 17a. That unbounded application of *Mayo*'s "outer shell" leads directly to untenable and unintended results like those below. It is undisputed here that the '540 patent does not preempt *multiple*, demonstrated uses of cffDNA. An approach to Section 101 that reduces such a critical fact to a "moot" afterthought is too badly broken to let lie. And this case is a perfect vehicle for fixing it.

Ultimately, it is clear that the Federal Circuit has turned *Mayo*'s somewhat ambiguous language into a "crisis of patent law and medical innovation," Pet.App. 78a (Lourie, J.), while affirmatively disclaiming any ability to stop it. This case thus requires this Court's review, while also providing an ideal vehicle through which to provide some clarity in an area of law that badly needs it.

I. The Decision Below Has Dangerously Overextended *Mayo*.

A. This Court now needs to clarify that its precedents permit patenting meritorious inventions like this one.

This Court's Section 101 cases recognize a deep jurisprudential tension. On the one hand, patents should not preempt the fundamental building-blocks of human ingenuity. Thus, abstract ideas (like "hedging risk"), natural phenomena (like actual human DNA), and natural laws (like $E=mc^2$) are ineligible for patenting. On the other hand, as this Court has recognized, all inventions at bottom "reflect, rest upon, or apply" those kinds of discoveries, *Mayo*, 132 S. Ct. at 1293. Accordingly, the law must distinguish between eligible *applications* of fundamental discov-

eries, and ineligible patents on discoveries themselves. *Id.* at 1294.

That limitation on Section 101 jurisprudence is critical because the categories above are exceptions to a broad statute that, on its face, allows patents on "anything under the sun that is made by man." *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980). The Patent Act provides that "[w]hoever invents *or discovers* any new and useful process … may obtain a patent." 35 U.S.C. §101 (emphasis added). Accordingly, as the Court has acknowledged, the Section 101 exceptions are judicial carve-outs whose only purpose is to ensure that patents do not "tend to impede innovation more than [they] would tend to promote it." *Mayo*, 132 S. Ct. at 1293. The Court should thus be very skeptical about using Section 101 precedents to invalidate patents on apparently meritorious inventions—especially where those patents serve the Act's policies by encouraging those who achieve previously impossible results to invest in bringing them to market. Put otherwise, those who (like respondents here) invoke Section 101 against a recognized "breakthrough" that solved long-standing practical problems in their field should have a very steep hill to climb. *See Microsoft Corp. v. i4i Ltd.*, 131 S. Ct. 2238, 2242 (2011) (statute presumes patents valid, puts burden on challenger, and requires clear evidence for invalidation).

But while practical applications like the invention here should be easily eligible, this Court has struggled to articulate a pragmatic legal rule that allows it to distinguish this invention and others like it from far-less-meritorious patents. That is because, as the Court recognized in *Mayo*, it cannot allow cre-

ative drafters to circumvent Section 101 by "simply stat[ing] the law of nature while adding the words 'apply it.'" 132 S. Ct. at 1294. The Court in *Mayo* and *Alice* thus sketched a two-part test that first asks if the patent incorporates one of the excepted categories (like a natural law) and, if so, whether the "patent claims add *enough* … to allow the processes they describe to qualify as patent-eligible processes that *apply* natural laws." *Id.* at 1297. If the "additional steps consist of well-understood, routine, conventional activity already engaged in by the scientific community," both individually and "as an ordered combination," the method is patent-ineligible. *Id.* at 1298.

It should be obvious that—as *Mayo*'s author has acknowledged—this two-part "test" was not intended to serve as a fully developed legal rule that could be easily or mechanistically applied to all future cases. Instead, *Mayo* had merely "sketched the outer shell of the content" for its test in an "obvious case," requiring careful elucidation through further examples. *See supra* p.11. That is partly why it is so critical to review cases like this one, which test *Mayo*'s uncertain boundaries with seemingly meritorious inventions (rather than "obviously" problematic patents like the one in *Mayo* itself). But it also recommends looking to the several concrete examples this Court has invoked—in and after *Mayo*—to see why an invention like this one need not be found ineligible.

1. This Court's cases already demonstrate why this and similar inventions are patent-eligible.

As explained below, principles and examples described in this Court's precedents disclose an im-

portant limitation on *Mayo* that the Federal Circuit missed and this Court should reinforce through this vehicle. That limitation is that even if the techniques in a method motivated by a natural law are known separately, they can be unconventional "as an ordered *combination*"—that is, the method might not involve "conventional activity already engaged in by the scientific community … when viewed *as a whole*." 132 S. Ct. at 1298 (emphases added).

Begin with *Diehr*, which *Mayo* reaffirmed but the panel below ignored. *Diehr* considered a patent for a method of curing rubber that relied on an unpatentable mathematical equation and a computer to constantly measure the temperature inside a rubber mold and recalculate curing time using that equation. Each separate technique was already known and practiced, but not the combination. Critically, *Diehr* explained that "[i]t is inappropriate to dissect the claims into old and new elements and then to ignore the presence of the old elements," and that "[t]his is particularly true in a process claim because a new combination of steps in a process may be patentable even though all the constituents of the combination were well known and in common use before the combination was made." 450 U.S. at 188.

Diehr emphasized that the patent at issue did "not seek to pre-empt the use of th[e] [unpatentable] equation," but "[r]ather … only to foreclose from others the use of that equation in conjunction with all of the other steps in the[] claimed process." *Id.* at 187. This emphasis that, "[i]n determining the eligibility of respondents' claim[s] … under §101, their claims must be considered as a whole," *id.* at 188, is what the Federal Circuit missed below. Indeed, the Feder-

al Circuit's (mis)reading of this Court's decisions does in fact "dissect the claims into old and new elements" and then ignore both the new discovery and any old elements, thereby invalidating the kind of "new combination of steps" that *Diehr* specifically holds patent-eligible.

Mayo reaffirmed *Diehr* on this very point. In holding that the claims in *Mayo* were unlike those in *Diehr*, the Court stressed that the three method steps involved, considered together, merely specified "well-understood, routine, conventional activity *previously engaged in by those in the field*," 132 S. Ct. at 1299 (emphasis added), and that "[t]he process in *Diehr* was not so characterized," *id.* As Judge Linn explained, the "'conventional activities' in *Mayo* were the very steps that doctors were already doing [in combination]—administering the drug at issue, measuring metabolite levels, and adjusting dosing based on the[m]." Pet.App. 22a; *see* Pet.App. 89a-90a (Dyk, J.). Accordingly, the addition of the unpatentable natural law in *Mayo* did not change anything beyond informing doctors of the law itself.

By contrast, the '540 patent's method is just like *Diehr*'s and not at all like *Mayo*'s: The phenomenon 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 a "conventional" approach that had previously treated the key materials as waste. Pet.App. 3a; *see id.* 18a (agreeing patent "combined" existing "tools of biotechnology in a new way").

A second, no-less-critical example comes from *Mayo* itself. There, the Court intimated that "a new way of using an existing drug" would be patent-

eligible. Pet.App. 24a (Linn, J.) (quoting *Mayo*, 132 S. Ct. at 1302). But that can be true only if patent-eligibility extends to new combinations of routine steps that would be self-evident to researchers who knew about a new discovery: After all, the drug is known, the means of administering it are known, and the only new insight is the natural law that the drug treats a disease no one previously knew it treated. So, unless the "inventive concept" that *Mayo* requires can be found in combining existing techniques in a new way to capitalize on a newly discovered natural phenomenon, *Mayo* itself is wrong about the patent-eligibility of new uses for existing drugs. Conversely, if *Mayo* (like *Diehr*) is better understood to permit patenting unconventional *combinations* of known techniques and materials to accomplish new results that capitalize on newly discovered natural phenomena, the invention at issue here is patent-eligible, because that description fits it to a T.

Finally, there is this Court's endorsement of Judge Bryson's view in *Myriad* that, "as the first party with knowledge of [a natural phenomenon], Myriad was in an excellent position to claim applications of that knowledge," even though it could not claim the knowledge or phenomenon itself. 133 S. Ct. 2120. Again, this proposition would be false if the law forecloses patenting new combinations of already-known steps motivated by a patentee's unique discovery, as the Federal Circuit believed. In that case, the "first party with knowledge" of a natural phenomenon would be in no better position to claim applications of their knowledge, because, before claiming anything at all, they would have to invent a second, entirely

new technique to incorporate into their methods for applying their discovery.

This case is thus a perfect vehicle to clarify *Mayo* and its limits. Correctly understood, *Mayo* does not prohibit claiming new methods assembled by combining previously known techniques even when those methods are motivated by or incorporate new insights into nature and its laws. Instead, it prohibits taking a series of steps "already engaged in by the scientific community" and claiming them for oneself by merely adding new *knowledge* of a natural law (like the correct correlations between thiopurine metabolite levels and drug dosages). *See* 132 S. Ct. at 1298-99. The Court should take this opportunity to make this distinction clear.

2. A proper preemption analysis confirms this patent's eligibility.

The Court should also take this unique opportunity to reiterate the centrality of preemption to Section 101 analysis. Drawing on 150 years of authority, *Alice* affirmed that preemption is "the concern that drives" the Section 101 exceptions. 134 S. Ct. at 2354-55. The very reason we distinguish "patents that claim the building blocks of human ingenuity" from "those that integrate the building blocks into something more," is that the "latter pose no comparable risk of pre-emption." *Id.* Section 101 thus forecloses claims that preempt essentially *all* uses of a natural phenomenon—not claims foreclosing only *particular* methods of using them that the inventor has disclosed. *Id.*

In this case, however, we know the inventors made only the latter kinds of claims, because re-

searchers have undisputedly identified practical uses for cffDNA *not preempted* by the patent. Demonstrated methods show that cffDNA may be used without practicing each of the patent's core steps: One need not fractionate the sample; one may forego amplification; and one can use cffDNA without distinguishing paternally inherited sequences at all. These non-preempted innovations are conclusive evidence that petitioner's patent does not claim the natural phenomenon itself—instead claiming merely one set of applications then known only to the inventors. This should have strongly signaled to the Federal Circuit that its analysis was amiss.

The Federal Circuit missed that signal, however, because it reduced preemption to a one-sided afterthought. On its view, "[w]hile preemption may signal patent ineligible subject matter, the absence of complete preemption does not demonstrate patent eligibility." Pet.App. 17a. Instead, once a formalistic application of *Mayo*'s two-part test suggests that the claims combine an unpatentable discovery with conventional techniques, "preemption concerns are fully addressed and made moot." *Id.* This kind of rote legalism is not what this Court envisioned when it "sketched" out *Mayo*'s rationale: A patent's preemptive scope is not just some dispensable consideration; it is this Court's best-tested way of knowing when a patent claims only an application of a newly discovered phenomenon, rather than the whole phenomenon itself.

Indeed, if preemption is a one-way ratchet (as the Federal Circuit evidently believed), it should ratchet the other way. Sometimes, a meritorious patent will appear to preempt all currently-known ways

of using a revolutionary insight, especially at the moment of the invention itself. That's because, as *Myriad* recognizes, the first person with knowledge of a newly discovered phenomenon is in an excellent position to claim its applications. At that moment, she (alone) can claim every straightforward application she (alone) can teach the world, 133 S. Ct. at 2120, and that is exactly what you would expect her to do.

In other words, the preemption concern is not that the patent covers all the immediately useful ways in which an insight known only to the inventor can be harnessed *right now*. As this Court explicitly recognized in *The Telephone Cases*, 126 U.S. 1, 535 (1888), that fact may "show more clearly the great importance of [a] discovery, but it will not invalidate [a] patent."[2] Instead, the concern is that a patent covers all the ways a natural discovery might *ever* be put to use, including highly innovative ones the patentee does not know and cannot teach. *See* Pet.App. 93a (Dyk, J.) (endorsing alternative Section 101 approach limiting patentees to applications of natural laws they fully reduce to practice and disclose). That is precisely why this Court allowed Samuel Morse to patent the telegraph, but not "the use of the motive power of the electric or galvanic current … *however developed*, for making or printing intelligible charac-

---

[2] The district court thus erred by discounting the evidence of non-preemption here on the ground that the other, undisputed uses of cffDNA arose only after the patent was granted. Pet.App. 57a. Not even the Federal Circuit endorsed this reasoning, which is incoherent: If non-preempted uses of a natural discovery are *ever* created, then—by simple logic—the patent had *never* claimed the ineligible discovery itself.

ters." *Mayo*, 132 S. Ct. at 1301 (quoting *O'Reilly v. Morse*, 56 U.S. 62, 86 (1853)).

To be sure, even the clarifications outlined above cannot render Section 101 jurisprudence into an exact science, and *Mayo* may remain a barrier to even some seemingly meritorious inventions. But whatever the outcome might be for the '540 patent, this case remains an indispensable vehicle for clarifying *Mayo*'s breadth, so that at least the biomedical community and its investors will know which breakthrough inventions—many of which are already patented—provide no actual guarantee of exclusivity to those who would bring them to market. The Court needs now to reconcile the analytic tensions in its case law, and provide some semblance of predictability in an area of law that depends vitally upon it. This alone recommends review.

B. The Federal Circuit's contrary reading of *Mayo* poses far-reaching dangers.

The need for this Court's intervention multiplies, however, when one considers the breadth the Federal Circuit gave *Mayo* below. It agreed that the '540 patent was a "breakthrough"; that it "combined and utilized man-made tools of biotechnology in a new way that revolutionized prenatal care"; and that "no one was using" its method in combination before because they were in fact discarding the relevant material as waste. Pet.App. 18a. But it still held the patent ineligible because it interpreted *Mayo* to require invalidating patents whenever they incorporate a natural law or phenomenon and recite techniques that are separately "well-known," "conventional," or "routine." As explained, *Mayo* need not be read that way, and

that confusion merits clarification. But the Federal Circuit has now unambiguously adopted that reading, and it has thereby "eviscerate[d] patent law" in the very way this Court and the Solicitor General warned against in *Mayo* itself. *See Mayo*, 132 S. Ct. at 1293; Brief of U.S., *Mayo*, No. 10-1150, at 31-32.

To begin, the Federal Circuit's version of *Mayo* plainly swallows all three examples above. *Supra* pp.18-21. *Diehr*'s invention combined an unpatentable law of nature and otherwise conventional techniques like "measuring" temperature and "recalculating" curing time. A new use for a known drug combines a natural law (that the drug treats a new disease), a known substance (by hypothesis), and conventional methods of administration (like taking a pill). And the only way someone with unique knowledge of a new discovery would be in an "excellent position" to claim new applications of that discovery is if using that discovery to motivate new combinations of known techniques suffices for eligibility. The Federal Circuit's approach to *Mayo*'s test is thus irreconcilable with principles and examples this Court has already recognized, and—as in the case of new drug applications—have long been critical to biomedical research.

It gets worse. The Federal Circuit's version of *Mayo* would invalidate even the very first patent, signed by George Washington on July 31, 1790, after a review headed by Thomas Jefferson. That patent was granted to Samuel Hopkins for an improved method of making potash, whose innovation involved burning the ashes in a furnace before undertaking the conventional steps of dissolving and boiling them in water, drawing off the lye, and boiling it down into

salts. *See* U.S. Patent X1, https://goo.gl/fIFfsg. Of course, burning ashes in a furnace and boiling water were not, themselves, unknown techniques—even in 1790. But combining these ancient steps led to an improved result, and so a patentable invention.

Hopkins's patent—like all inventive methods—relied on an insight about the natural world that motivated him to combine available tools in new ways to do something previously impossible. Hopkins discovered that you get purer potash if you first burn ashes in a furnace, just like Lo and Wainscoat discovered that you get detectable paternally inherited sequences if you amplify the DNA in maternal plasma. To be sure, any trained artisan who knew what these inventors had discovered might also have known how to put those discoveries to practical use, because the necessary techniques were readily available. But that didn't stop the Founders who wrote Section 101's precursor from granting Hopkins his patent on his new combination of routine techniques (literally, "burning," "boiling" and "drawing off"), and it shouldn't have stopped the Federal Circuit here.

Indeed, only arbitrary distinctions can prevent the Federal Circuit's version of *Mayo* from eventually swallowing all of patent law. As *Mayo* notes, almost every patent can be expressed as an unpatentable idea combined with conventional techniques. The light bulb is a natural law—that electrified filament glows without burning in an oxygen-free environment—plus glass, gas, and wire. And this is why discovering practical natural phenomena must be allowed to contribute to taking the "inventive step" that *Mayo* requires. *See* Pet.App. 89a (Dyk, J.). The point is that, while Edison could not patent the *fact* that a

filament will glow without burning in an oxygen-free environment, he could patent all the applications that were obvious (only to him) after that discovery, even if others might easily have done the same things if they knew what he knew. *See Myriad*, 133 S. Ct. at 2120. And yet, as academic commentators have observed, Edison and several other famous inventors would likely have been denied their iconic patents under the Federal Circuit's version of *Mayo*'s test. *See* Risch, *Nothing Is Patentable,* 67 Fla. L. Rev. 45, 51-53 (2015) (because each invention applied previously-known techniques to newly-discovered natural phenomena, current law would invalidate patents for cotton gin, electric motor, telegraph, telephone, airplane, and radio antenna, many of which this Court itself had approved).

Indeed, it would be exhausting to list all the world-altering inventions the courts would have invalidated under the Federal Circuit's new regime. As the first-patent example indicates, industrial processes would fare poorly. But, as this case even-more-vividly shows, biomedical innovations are uniquely vulnerable to the Federal Circuit's interpretation of *Mayo* because of their inherent connection to basic biological research, *see* Pet.App. 90a (Dyk, J.). And that is ironic, because these kinds of inventions also uniquely depend on investments that are readily susceptible to free-riding, and that no first-mover will make without an assurance of patent protection—among them, clinical validation, regulatory approval, and (of course) the invention itself.

Consider vaccines. Inoculation is, quite simply, a natural phenomenon involving the body's inherent immune response to pathogens. For every new vac-

cine, the hard part is discovering the natural law—that a particular protein or attenuated germ will provoke immunity without serious illness. Edward Jenner invented smallpox vaccine after discovering that cowpox exposure led to smallpox immunity. Apart from that discovery, creating a smallpox inoculant involved no unknown or unconventional techniques. This is true for essentially every vaccine subsequently produced, no matter the massive private outlay that may be required to research and clinically validate it for widespread human use. But under the rule of this case, all are patent-ineligible because all rely on known techniques and natural phenomena—even if those techniques and phenomena had never been combined in this life-saving way before.

Or consider PCR—the Nobel-winning invention that birthed almost all modern genetic medicine. As its inventor Kary Mullis has acknowledged, PCR is just the application of a "simple idea" to a set of chemical reagents that had been in conventional use for years. All Mullis realized was a natural law whereby combining those reagents in a repeated procedure would exponentially redouble a particular genetic sequence in a sample. The only techniques involved were heating, cooling, adding reagents, and starting over. The separate steps were thus "well-understood"; Mullis's genius lay in an insight into the natural world he had on a moonlit drive, which motivated him to combine these long-available materials and techniques. *See* Mullis, *supra*, at 56.

Moreover, the most important (and valuably patented) improvement to PCR occurred when Mullis and his coworkers realized that using DNA polymerase from a *naturally-occurring*, heat-resistant bacte-

ria (called Taq) would make the process more efficient, because you would no longer need to add fresh enzyme after every cycle. *See Hoffman-La Roche v. Promega Corp.,* 323 F.3d 1354, 1358 (Fed. Cir. 2003). Natural phenomenon; known techniques; new combination; massive practical improvement. Before this case, everyone understood that these were patent-eligible inventions (on which Ariosa's parent reaped incalculable returns). But as *amici* attest, this decision turns those settled expectations upside-down.

Finally, the Federal Circuit's reading of *Mayo* leads to two ironic and unacceptable results.

First, it inexplicably punishes the most valuable inventions—namely, those that recombine only "well-understood" and readily available techniques to achieve breakthrough results. It is far more valuable to devise a way of turning lead to gold with a high-school chemistry set than with a redesigned particle accelerator. No intelligible patent policy supports deeming only the former method patent-ineligible.

Second, the Federal Circuit's rule punishes inventors for understanding how their inventions work. Imagine that, instead of discovering and understanding the diagnostic relevance of cffDNA, Lo and Wainscoat had serendipitously discovered that running maternal serum through a sequencer and looking for certain outputs predicted fetal gender or Down Syndrome, but they didn't know why. They plainly have a patentable method in hand—they have a new set of steps that leads to a new practical result, and mentions no natural law or phenomenon. But once they explain why this method works, and the Federal Circuit determines that it involves a set of available techniques others would have performed if they too

had understood the existence of cffDNA, their patent disappears. Plainly, this rule does not "promote the Progress of Science," U.S. Const. art. I, § 8, cl. 8.

Ultimately, the Federal Circuit's interpretation of *Mayo* is not only erroneous but unacceptably dangerous—discarding patented inventions recognized by everyone from the Founders to this Court to the Nobel Committee, and treating the most useful inventions as suspect only because of the profound scientific understanding and breakthroughs of their inventors. This error will fatally undermine the biomedical field and this entire area of law, making this Court's immediate intervention to clarify *Mayo* all the more necessary and appropriate.

II. This Issue is Vitally Important.

Were anything more required, we add three simple indicia of this case's importance.

First is the overwhelming support of trustworthy *amici*. Twelve different briefs supported rehearing below and more are expected here. The *amici* encompass the largest biotech and pharmaceutical associations, companies, professors, practitioners, universities, international interests, and more. The Solicitor General sounded a similar alarm about unintended consequences as an *amicus* in *Mayo*. *See* Brief of U.S., *Mayo*, at 31-32. And these varied voices only join the chorus of judges who warned below that only this Court can clarify *Mayo* and prevent it from swallowing the field of life-science innovation.

Indeed, there is widespread agreement that the concerns above are real, including in the relevant press. *See, e.g.*, Marandett, *Ariosa v. Sequenom Signals Trouble Ahead For Life Sciences*, LAW360 LIFE

SCIENCES, Nov. 3, 2015 ("*Ariosa* portends ominous consequences for patents … in the life sciences. … [It] puts at risk such inventions as immunodiagnostics, molecular diagnostics, and method patents directed to therapeutic uses of antibodies, vaccines, gene therapy, and biologics and biosimilars[.]"). And, as *amici* attest, this public perception alone has already changed market realities, along with the practices of their companies and university researchers.

Second, the decision below threatens to destroy the predictability and certainty the patent system needs to do its job. At a minimum, the biomedical community is now adrift in determining whether or not patents will ever be available in these or related fields. And that's essentially the ballgame, because once you must seriously question the availability of patent protection, you cannot: (1) confidently invest in research; (2) confidently invest in clinical validation and commercialization of existing patents; or (3) confidently predict that it is better to disclose your discoveries through the patent system than it is to keep them a trade secret.

That last result is a deeply ironic place for this area of law to end up. While regulatory approval processes may preclude absolute secrecy forever, the current regime now affirmatively encourages researchers to keep as secret as possible those very "basic tools of scientific and technological work" that Section 101 doctrine is designed to render into a public good for the benefit of scientific progress. *Mayo*, 132 S. Ct. at 2193. Before, those engaged in such research could freely disclose their findings, secure in the knowledge that—as *Myriad* put it—they remained in an excellent position to claim practical ap-

plications of that knowledge. 133 S. Ct. at 2120. Now, secrets look much more valuable than patents. And that benefits no one, especially in fields like these, where sharing research is so fundamental to the timely development of life-saving interventions.

The realistic consequence is that the bottom may well fall out of life-science innovation. *See* Pet.App. 78a (Lourie, J.) ("It is said that the whole category of diagnostic claims is at risk. It is also said that a crisis of patent law and medical innovation may be upon us, and there seems to be some truth in that concern."). After the decision below, those seeking new vaccines, new uses for existing drugs, and even holy-grail insights like early, non-invasive cancer screens, may conclude that the game isn't worth the candle. And who could blame them: They could revolutionize their field, teach their colleagues a method that is the diametric opposite of conventional wisdom, create a practical, non-invasive test that confers enormous medical benefits on society, have their research cited a thousand times, and yet still lose their patent (after incurring a huge expense in reliance on its protection) because their previously unknown method relies on too fundamental an insight *they alone had* into the natural world. If this is the permanent reality, neither aspiring scientists nor venture capitalists may see much to gain in developing or commercializing biomedical research.

Finally, the decision below places the United States out of step with the international community regarding the patent-eligibility of biomedical methods—perhaps even breaching our treaty obligations. Other authorities, including the European Patent Office, have bars on patenting natural laws. But none

has invalidated an invention anything like this one; indeed, the EPO upheld this very patent. *See* Technical Board of Appeal Decision, No. T0146/07, ¶35 (Dec. 13, 2011). As various *amici* explain, the now-governing U.S. approach to eligibility is far more restrictive than the rest of the world's, runs afoul of international treaties that oblige us to conform our patent rules to international standards, and can impermissibly place international applicants at a unilateral disadvantage. In addition to the factors above, this kind of international legal tension strongly recommends this Court's review.

III. This Case Is An Ideal Vehicle.

Many of this case's vehicle strengths appear above, including—most critically—the intuitive patent-eligibility of this "breakthrough" invention, and the many opinions below holding that *only* this Court can save it by clarifying *Mayo*. *Supra* p.9-12. Moreover, this is the exceptionally rare case in which the Federal Circuit will have expressly "agree[d]" that the patent "*combined* and utilized man-made tools … in a *new way* that revolutionized" a field. Pet.App. 18a (emphasis added). No future case could frame the question presented more precisely than that.

To this, we add three final points.

First, this is an extremely well-ventilated patent, with a far-more-developed record than is usual for Section 101 cases. Because of the preliminary-injunction appeal, the Federal Circuit already construed the '540 patent's claims. *See* 726 F.3d at 1300-04. There is also a well-established factual record based on peer-reviewed scientific publications conclusively establishing that the patent has not preempted

all uses of cffDNA. Pet.App. 55a-56a. And because respondents have already challenged the '540 patent in *inter partes* review, there's no real question whether, for example, Claim 21 is novel and non-obvious,[3] which is rarely true of patents with alleged 101 infirmities. The EPO has even upheld this patent against allegations that it lacked an "inventive step" and did not enable testing for Down Syndrome and other conditions. *Supra* p.33. Its meaning and background are thus uniquely clear.

Second, this patent involves not only broader independent claims, but also narrower dependent claims. The independent claims (like Claim 21) describe one particular diagnostic application of cffDNA, where fractionation, amplification, and detection of paternally inherited sequences enable fetal diagnoses. But the dependent claims refine that down to the level of *individual tests*, like using the method to detect Down Syndrome, RhD status, or gender. And, notably, respondents' infringing tests are for precisely those conditions.

This is a pertinent detail, because one judge below suggested a novel doctrine under which the inde-

---

[3] *See* Final Written Decision, IPR2012-00022, at 46 (upholding Claim 21, among others). This decision did hold that Claim 1 was "inherently" anticipated by a Russian paper, even though that paper failed to detect (or even express any awareness of) paternally inherited cffDNA. *Id.* at 36. But that is immaterial here both because Claim 21 covers all the products at issue, and because that holding depends on the very district court decision this petition seeks to reverse, *see id.* at 50-52; CAFed. #15-01691, Order (July 22, 2015) (granting stipulated stay of IPR appeal pending this petition).

pendent claims here might fail for being too broad, even though they are "inventive" in the sense Section 101 jurisprudence had previously required. *See* Pet.App. 98a (Dyk, J.). Were the Court interested in such a test, this patent would allow it to draw a line between broader and narrower claims actually presented in the case.

Finally, while this issue is important in numerous cases,[4] this may be the Court's last good chance to clarify this aspect of *Mayo*, because the decision below will incentivize behaviors precluding future vehicles. The press reactions and *amicus* briefs demonstrate that the entire biomedical field (and even those beyond it) have gotten the message. Unless this Court intervenes now, many companies will decline to patent, exclusively license, or commercialize similar inventions in a way that would permit a suit to reach this Court. Moreover, given the threat of invalidation the decision hangs over every diagnostic method patent, patentees will just settle or grant cheap licenses to avoid risking a catastrophic loss.

In sum, this is the perfect case for this Court to clarify *Mayo* and articulate a principled line in this now-severely-muddied area of law. That line can embrace existing precedent and continue to reject patents that purport to claim natural phenomena, while still protecting meritorious patents (like petitioner's) from being collateral damage in what is properly a war on overbroad claims on facially dubious inven-

---

[4] For example, a similar question is presented in another pending petition, *see Hemopet v. Hill's Pet Nutrition, Inc.*, No. 15-1062 (filed Nov. 10, 2015).

tions often brought by abusive, non-practicing entities. This Court should take this opportunity to provide the guidance the Federal Circuit is openly seeking, and avoid a result neither it nor Congress could have intended.

CONCLUSION

This Court should grant certiorari.

Respectfully submitted,

Thomas C. Goldstein
Counsel of Record
Eric F. Citron
GOLDSTEIN & RUSSELL, P.C.
7475 Wisconsin Ave.
Suite 850
Bethesda, MD 20814
(202) 362-0636
tg@goldsteinrussell.com

Michael J. Malecek
Robert Barnes
KAYE SCHOLER LLP
Two Palo Alto Square
Suite 400
3000 El Camino Real
Palo Alto, CA 94306
(650) 319-4500

APPENDIX A

United States Court of Appeals
for the Federal Circuit.

ARIOSA DIAGNOSTICS, INC., NATERA, INC.,

Plaintiffs-Appellees

DNA DIAGNOSTICS CENTER, INC.,

Counterclaim Defendant-Appellee

v.

SEQUENOM, INC., SEQUENOM CENTER FOR MOLECULAR MEDICINE, LLC,

Defendants-Appellants

ISIS INNOVATION LIMITED,

Defendant

2014-1139, 2014-1144

Appeals from the United States District Court for the Northern District of California in Nos. 3:11-cv-06391-SI, 3:12-cv-00132-SI, Judge Susan Y. Illston.

Decided: June 12, 2015

DAVID ISAAC GINDLER, Irell & Manella LLP, Los Angeles, CA, argued for plaintiff-appellee Ariosa

Diagnostics, Inc. Also represented by ANDREI IANCU; AMIR NAINI, Russ August & Kabat, Los Angeles, CA.

WILLIAM PAUL SCHUCK, Bartko, Zankel, Bunzel & Miller, San Francisco, CA, for plaintiff-appellee Natera, Inc., counterclaim defendant-appellee DNA Diagnostics Center, Inc.

MICHAEL J. MALECEK, Kaye Scholer LLP, Palo Alto, CA, argued for defendants-appellants. Also represented by PETER E. ROOT, Menlo Park, CA; ATON ARBISSER, Los Angeles, CA.

RICHARD L. BLAYLOCK, Pillsbury Winthrop Shaw Pittman LLP, San Diego, CA, for amicus curiae Invitae Corporation. Also represented by KIRKE M. HASSON, COLIN TRAVERS KEMP, San Francisco, CA.

KEVIN EDWARD NOONAN, McDonnell, Boehnen Hulbert & Berghoff, LLP, Chicago, IL, for amicus curiae Biotechnology Industry Organization.

WILLIAM LARRY RESPESS, I, Sheppard, Mullin, Richter, & Hampton LLP, San Diego, CA, for amicus curiae The San Diego Intellectual Property Law Association.

Before REYNA, LINN, and WALLACH, *Circuit Judges.*

Opinion for the court filed by *Circuit Judge REYNA.*

Concurring Opinion filed by *Circuit Judge LINN.*

REYNA, Circuit Judge.

This appeal is from a grant of summary judgment of invalidity of the asserted claims of U.S. Patent No. 6,258,540 ("the '540 patent"). The United States District Court for the Northern District of California found that the asserted claims of the '540 patent are not directed to patent eligible subject matter and are therefore invalid under 35 U.S.C. § 101. For the reasons explained below, we *affirm*.

I

In 1996, Drs. Dennis Lo and James Wainscoat discovered cell-free fetal DNA ("cffDNA") in maternal plasma and serum, the portion of maternal blood samples that other researchers had previously discarded as medical waste. cffDNA is non-cellular fetal DNA that circulates freely in the blood stream of a pregnant woman. Applying a combination of known laboratory techniques to their discovery, Drs. Lo and Wainscoat implemented a method for detecting the small fraction of paternally inherited cffDNA in maternal plasma or serum to determine fetal characteristics, such as gender. The invention, commercialized by Sequenom as its MaterniT21 test, created an alternative for prenatal diagnosis of fetal DNA that avoids the risks of widely-used techniques that took samples from the fetus or placenta. In 2001, Drs. Lo and Wainscoat obtained the '540 patent, which relates to this discovery.

The parties agree that the patent does not claim cffDNA or paternally inherited cffDNA. Instead, the '540 patent claims certain methods of using cffDNA. The steps of the method of claim 1 of the '540 patent include amplifying the cffDNA contained in a sample

of a plasma or serum from a pregnant female and detecting the paternally inherited cffDNA. Amplifying cffDNA results in a single copy, or a few copies, of a piece of cffDNA being multiplied across several orders of magnitude, generating thousands to millions of copies of that particular DNA sequence. In the amplification step, DNA is extracted from the serum or plasma samples and amplified by polymerase chain reaction ("PCR") or another method. PCR exponentially amplifies the cffDNA sample to detectable levels.

In the detecting step, the lab technician adds the amplified cffDNA to an agarose gel containing ethidiumbromide to stain and visualize the paternally inherited cffDNA.

The '540 patent also provides for making a diagnosis of certain fetal characteristics based on the detection of paternally inherited cffDNA. The specification explains that analysis of cffDNA permits more efficient determination of genetic defects and that a pregnant woman carrying a fetus with certain genetic defects will have more cffDNA in her blood than will a woman with a normal fetus. '540 patent col. 3 ll. 30-43.

Claims 1, 2, 4, 5, 8, 19-22, 24, and 25 of the '540 patent are at issue in this appeal.[1] Independent claim 1 requires:

---

1 The parties have stipulated that for the purposes of this appeal claims 1, 2, 4, 5, 8, 9-22, 24 and

> 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.
>
> '540 patent col. 23 l. 61-67.

For comparison, independent claims 24 and 25 require:

> 24. A method for detecting a paternally inherited nucleic acid on a maternal blood sample, which method comprises:
>
> removing all or substantially all nucleated and
>
> anucleated cell populations from the blood sample,
>
> amplifying a paternally inherited nucleic acid from the remaining fluid and subjecting the amplified nucleic acid to a test for the Paternally [sic] inherited fetal nucleic acid.
>
> 25. A method for performing a prenatal diagnosis on a maternal blood sample, which method comprises

---

25 are representative of claims 6, 7, 12, 13, 15, and 18 of the '540 patent. J.A. 24-25, 30-31.

> obtaining a non-cellular fraction of the blood sample
>
> amplifying a paternally inherited nucleic acid
>
> from the non-cellular fraction
>
> and performing nucleic acid analysis on the amplified nucleic acid to detect paternally inherited fetal nucleic acid.

Id. at 26 ll. 20-36.

The remaining claims explain how the method of detection occurs or how it can be used. For example, claim 2 depends from claim 1 and claims amplification by polymerase chain reaction. *Id.* at col. 24 ll. 60-61. Claim 4 similarly depends from claim 1 and claims detection via a sequence specific probe. *Id.* col. 24 ll. 65-67. Claim 21 also depends from claim 1, but instead of focusing solely on a method for detecting, it focuses on a method for performing a prenatal diagnosis, using claim 1's method for detecting. *Id.* col. 26 ll. 4-14.

II

Appellee Ariosa Diagnostics, Inc. (formerly known as "Aria Diagnostics, Inc.") makes and sells the Harmony Test, a non-invasive test used for prenatal diagnosis of certain fetal characteristics. Natera, Inc. makes and sells the Non-Invasive Paternity Test, which is intended to confirm the paternity or non-paternity of a gestating fetus from genetic information in fetal DNA available in the blood of the pregnant female. Diagnostics Center, Inc. is a licensee of Natera.

In response to letters threatening claims of infringement, Ariosa Diagnostics, Inc., Natera, Inc.

and Diagnostics Center, Inc. each filed separate declaratory judgment actions from December 2011 through early 2012 against Sequenom alleging that they did not infringe the '540 patent. Sequenom counterclaimed alleging infringement in each case. The district court related the three actions for pretrial purposes.

In the *Ariosa* action, Sequenom filed a motion seeking to preliminarily enjoin Ariosa from selling the accused Harmony Prenatal Test. In July 2012, the district court issued an order denying Sequenom's motion for a preliminary injunction. In the context of doing so, the district court found that there was a substantial question over whether the subject matter of the asserted claims was directed to eligible subject matter. Sequenom appealed to this court.

On August 9, 2013, this court vacated and remanded the case, holding that the district court erred in certain respects not relevant to this appeal. *Aria Diagnostics, Inc. v. Sequenom, Inc.*, 726 F.3d 1296, 1305 (Fed. Cir. 2013). In addition, this Court noted that it 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 *[Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. ___, 133 S. Ct. 2107, 2117 (2013)]." *Id.* at 1304.

After remand, the parties filed cross motions for summary judgment regarding invalidity under 35 U.S.C. § 101. The district court agreed with Ariosa's argument that the claims of the '540 patent were

directed to the natural phenomenon of paternally inherited cffDNA and that the claims did not add enough to the natural phenomenon to make the claims patent eligible under § 101. The district court determined that the steps of amplifying and detecting were well-understood, routine, or conventional activity in 1997, when the application for the '540 patent was filed. The district court concluded that the '540 patent was not directed to patentable subject matter because "the only inventive component of the processes of the '540 patent is to apply those well-understood, routine processes to paternally inherited cffDNA, a natural phenomenon." J.A. 18. The district court also found that the claimed processes posed a risk of preempting a natural phenomenon. Sequenom appeals.

We have jurisdiction under 28 U.S.C. § 1295(a)(1).

III

We review the grant of summary judgment under the law of the regional circuit, in this case the Ninth Circuit. *Charles Mach. Works, Inc. v. Vermeer Mfg. Co.*, 723 F.3d 1376, 1378 (Fed. Cir. 2013). The Ninth Circuit reviews the grant or denial of summary judgment de novo. *Leever v. Carson City*, 360 F.3d 1014, 1017 (9th Cir. 2004). We also review de novo the question of whether a claim is invalid under section 101. *In re BRCA1- and BRCA2- Based Hereditary Cancer Test Patent Litig.*, 774 F.3d. 755, 759 (Fed. Cir. 2014).

Section 101 of the Patent Act defines patent eligible subject matter:

> 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.

35 U.S.C. § 101. The Supreme Court has long held that there are certain exceptions to this provision: laws of nature, natural phenomena, and abstract ideas. *Alice Corp. v. CLS Bank Int'l*, ___ U.S. ___, 134 S. Ct. 2347, 2354 (2014) (collecting cases).

In Mayo Collaborative Services v. Prometheus Laboratories, Inc., 566 U.S. ___, 132 S. Ct. 1289 (2012), the Supreme Court set forth a framework for distinguishing patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts. First, we determine whether the claims at issue are directed to a patent-ineligible concept. Id. at 1297. If the answer is yes, then we next 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. Id. at 1298. The Supreme Court has described the second step of this analysis as a search for an "inventive concept"—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." Id. at 1294; see also Digitech Image Techs., LLC v. Elecs. For Imaging, Inc., 758 F.3d 1344, 1351 (Fed. Cir. 2014) ("Without additional limitations, a process

that employs mathematical algorithms to manipulate existing information to generate additional information is not patent eligible.").

The claims of the '540 patent that are at issue in this appeal are method claims. Methods are generally eligible subject matter. In this case, the asserted claims of the '540 patent are directed to a multistep method that starts with cffDNA taken from a sample of maternal plasma or serum—a naturally occurring non-cellular fetal DNA that circulates freely in the blood stream of a pregnant woman. *See, e.g.*, '540 patent claims 1, 24, 25. It is undisputed that the existence of cffDNA in maternal blood is a natural phenomenon. Sequenom does not contend that Drs. Lo and Wainscoat created or altered any of the genetic information encoded in the cffDNA, and it is undisputed that the location of the nucleic acids existed in nature before Drs. Lo and Wainscoat found them. The method ends with paternally inherited cffDNA, which is also a natural phenomenon. The method therefore begins and ends with a natural phenomenon. Thus, the claims are directed to matter that is naturally occurring.

The written description supports the conclusion that the claims of the '540 patent are directed to a naturally occurring thing or natural phenomenon. In the Summary and Objects of the Invention section of the '540 patent, the patent states that "[i]t has now been discovered that foetal DNA is detectable in

maternal serum or plasma samples."[2] '540 patent col. 1 ll. 50-51. The patent goes on to state that "[t]his is a surprising and unexpected finding; maternal plasma is the very material that is routinely discarded by investigators studying noninvasive prenatal diagnosis using foetal cells in maternal blood." *Id.* col. 1 ll. 51-55. In the discussion, the patent notes:

> In this study we have demonstrated the feasibility of performing non-invasive foetal RhD genotyping from maternal plasma. This represents the first description of single gene diagnosis from maternal plasma.

Id. col. 10 ll. 53-58. Further, the description of the invention notes: "[w]e have demonstrated that foetal DNA is present in maternal plasma and serum," *id.* col. 13 ll. 6-7, and "[t]hese observations indicate that maternal plasma/ serum DNA may be a useful source of material for the non-invasive prenatal diagnosis of certain genetic disorders," *id.* col. 13 ll. 11-13. The patent also states: "[t]he most important observation in this study is the very high concentration of foetal DNA in maternal plasma and serum." *Id.* col. 16 ll. 12-14. Thus, the claims at issue, as informed by the specification, are generally directed to detecting the presence of a naturally occurring thing or a natural phenomenon, cffDNA in maternal plasma or serum. As we noted above, the claimed method begins and ends with a naturally occurring phenomenon.

---

2 The term "fetal" and "foetal" are used interchangeably in the '540 patent and by the parties.

Because the claims at issue are directed to naturally occurring phenomena, we turn to the second step of *Mayo*'s framework. In the second step, we examine the elements of the claim to determine whether the claim contains an inventive concept sufficient to "transform" the claimed naturally occurring phenomenon into a patent-eligible application. 132 S. Ct. at 1294. 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.

Mayo made clear that transformation into a patent-eligible application requires "more than simply stat[ing] the law of nature while adding the words 'apply it.'" *Id.* at 1294. A claim that recites an abstract idea, law of nature, or natural phenomenon must include "additional features" to ensure "that the [claim] is more than a drafting effort designed to monopolize the [abstract idea, law of nature, or natural phenomenon]." *Id.* at 1297. For process claims that encompass natural phenomenon, the process steps are the additional features that must be new and useful. *See Parker v. Flook*, 437 U.S. 584, 591 (1978) ("The process itself, not merely the mathematical algorithm, must be new and useful.").

In *Mayo*, the patents at issue claimed a method for measuring metabolites in the bloodstream in order to calibrate the appropriate dosage of thiopurine drugs in the treatment of autoimmune diseases. 132 S. Ct. at 1294. The respondent contended that the claimed method was a patent eligible application of a natural law that described the relationship between the

concentration of certain metabolites and the likelihood that the drug dosage will be harmful or ineffective. Methods for determining metabolite levels, however, were already "well known in the art." *Id.* at 1298. Further, the process at issue amounted to "nothing significantly more than an instruction to doctors to apply the applicable laws when treating their patients." *Id.* In that case, "[s]imply appending conventional steps, specified at a high level of generality," was not enough to supply an inventive concept. *Id*. at 1300.

Like the patentee in *Mayo*, Sequenom contends that the claimed methods are patent eligible applications of a natural phenomenon, specifically a method for detecting paternally inherited cffDNA. Using methods like PCR to amplify and detect cffDNA was well-understood, routine, and conventional activity in 1997. The method at issue here amounts to a general instruction to doctors to apply routine, conventional techniques when seeking to detect cffDNA. Because the method steps were well-understood, conventional and routine, the method of detecting paternally inherited cffDNA is not new and useful. 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.

The specification of the '540 patent confirms that the preparation and amplification of DNA sequences in plasma or serum were well-understood, routine, conventional activities performed by doctors in 1997. The '540 patent provides that "[t]he preparation of serum or plasma from the maternal blood sample is

carried out by standard techniques." '540 patent col. 2 ll. 27-28. It also provides that "[s]tandard nucleic acid amplification systems can be used, including PCR, the ligase chain reaction, nucleic acid sequence based amplification (NASBA), branched DNA methods, and so on." *Id.* col. 2 ll. 44-47.

Other evidence supports this conclusion. For example, Sequenom's expert, Dr. Evans, testified at deposition that PCR and other methodologies for amplifying DNA were "already well known in science [in 1997]." J.A. 1092- 93, 1995-96. Similarly, in a declaration filed during prosecution of the '540 patent, Dr. Lo testified that "[s]uitable amplification techniques can be ordinary PCR or more sophisticated developments thereof, but these techniques were all known in the literature before the date of my invention." J.A. 1109.

The detecting step was similarly well-understood, routine, and conventional. During prosecution of the application that became the '540 patent, the applicant stated:

> [O]ne skilled in the art is aware of a variety of techniques which might be used to detect different nucleic acid species. For example, there are numerous techniques which might be used to detect repeat expansions, single gene mutations, deletions or translocations. These techniques are a matter of routine for one skilled in the art for the analysis of DNA.

J.A. 1052. The applicant went on to note:

> [O]ne skilled in the art is readily able to apply the teachings of the present application to any

> one of the well-known techniques for detection of DNA with a view to analysis of foetal DNA in paternal [sic] plasma or serum.

J.A. 1055. Similarly, the applicant later added that "[t]he person skilled in the art has a broad range of techniques available for the detection of DNA in a sample." J.A. 1057.

The dependent claims are broad examples of how to detect cffDNA in maternal plasma. The dependent claims are focused on the use of the natural phenomenon in combination with well-understood, routine, and conventional activity. For example, claim 2 identifies the polymerase chain reaction as the amplification technique to be used in the detection method of claim 1. As noted above, this technique was well-understood, routine, and conventional in 1997, as specified by the patent itself. Like claim 1, claims 5 and 8 focus on detecting a specific chromosome within the cffDNA—a natural phenomenon— again, adding no inventive concept to the limitations of claim 1. None of the remaining asserted dependent or independent claims differ substantially from these claims. Thus, in this case, appending routine, conventional steps to a natural phenomenon, specified at a high level of generality, is not enough to supply an inventive concept. 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. The claims of the '540 patent at issue in this appeal are not directed to

patent eligible subject matter and are, therefore, invalid.

IV

In its opinion, the district court addressed the principle of preemption. The district court noted:

> It is important to note that the '540 patent does not merely claim uses or applications of cffDNA, it claims methods for detecting the natural phenomenon. Because generally one must be able to find a natural phenomenon to use it and apply it, claims covering the only commercially viable way of detecting that phenomenon do carry a substantial risk of preempting all practical uses of it.
>
> J.A. 19.

Sequenom argues that there are numerous other uses of cffDNA aside from those claimed in the '540 patent, and thus, the '540 patent does not preempt all uses of cffDNA, as shown by evidence in the record before the district court. Sequenom also argues that "a method applying or using a natural phenomenon in a manner that does not preclude alternative methods in the same field is non-preemptive, and, by definition, patent-eligible under Section 101." Appellants' Br. 30. Similarly, Sequenom and amici argue that because the particular application of the natural phenomena that the '540 patent claims embody are narrow and specific, the claims should be upheld. Ariosa argues that the principle of preemption does not alter the analysis. Ariosa argues that the claimed methods are not, as Sequenom asserts, limited and specific.

The Supreme Court has made clear that the principle of preemption is the basis for the judicial exceptions to patentability. Alice, 134 S. Ct at 2354 ("We have described the concern that drives this exclusionary principal as one of pre-emption"). For this reason, questions on preemption are inherent in and resolved by the § 101 analysis. The concern is that "patent law not inhibit further discovery by improperly tying up the future use of these building blocks of human ingenuity." Id. (internal quotations omitted). In other words, patent claims should not prevent the use of the basic building blocks of technology— abstract ideas, naturally occurring phenomena, and natural laws. While preemption may signal patent ineligible subject matter, the absence of complete preemption does not demonstrate patent eligibility. In this case, Sequenom's attempt to limit the breadth of the claims by showing alternative uses of cffDNA outside of the scope of the claims does not change the conclusion that the claims are directed to patent ineligible subject matter. 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.

Sequenom and amici encourage us to draw distinctions among natural phenomena based on whether or not they will interfere significantly with innovation in other fields now or in the future. The Supreme Court cases, however, have not distinguished among different laws of nature or natural phenomenon according to whether or not the principles they embody are sufficiently narrow. See, e.g., Parker v. Flook, 437 U.S. 584 (1978) (holding narrow mathematical formula

unpatentable). In Parker v. Flook, the Supreme Court stated the issue in the case as follows: "The question in this case is whether the identification of a limited category of useful, though conventional, post-solution applications of such a formula makes respondent's method eligible for patent protection." Id. at 585. The answer to that question was "no" because granting exclusive rights to the mathematical formula would be exempting it from any future use.

V

For completeness, we address Sequenom's remaining arguments. 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." Appellants' Br. 49 (emphasis original). 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.

Sequenom further argues that "[o]ne simple measure of [Drs.] Lo and Wainscoat's contribution is that their 1997 Lancet publication has been cited over a thousand times." Appellants' Br. 25. Sequenom also notes that "the method reflects a significant human contribution in that [Drs.] Lo and Wainscoat combined and utilized man-made tools of biotechnology in a new way that revolutionized prenatal care." *Id.* We agree but note that the Supreme Court instructs that "[g]roundbreaking, innovative, or even brilliant discovery does not by itself satisfy the § 101 inquiry." *Myriad Genetics, Inc.*, 133 S. Ct. at 2117. The discovery of the BRCA1 and BRCA2 genes was a

significant contribution to the medical field, but it was not patentable. *Id.* at 2117. While Drs. Lo and Wainscoat's discovery regarding cffDNA may have been a significant contribution to the medical field, that alone does not make it patentable. We do not disagree that detecting cffDNA in maternal plasma or serum that before was discarded as waste material is a positive and valuable contribution to science. But even such valuable contributions can fall short of statutory patentable subject matter, as it does here.

VI

For each of the reasons stated above, we affirm the district court's summary judgment ruling.

AFFIRMED

COSTS

No costs.

United States Court of Appeals
for the Federal Circuit.

ARIOSA DIAGNOSTICS, INC., NATERA, INC.,

Plaintiffs-Appellees

DNA DIAGNOSTICS CENTER, INC.,

Counterclaim Defendant-Appellee

v.

SEQUENOM, INC., SEQUENOM CENTER FOR MOLECULAR MEDICINE, LLC,

Defendants-Appellants

ISIS INNOVATION LIMITED,

Defendant

2014-1139, 2014-1144

Appeals from the United States District Court for the Northern District of California in Nos. 3:11-cv-06391-SI, 3:12-cv-00132-SI, Judge Susan Y. Illston.

LINN, *Circuit Judge*, concurring.

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 Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. ___, 132 S. Ct. 1289 (2012). In my view, the breadth of the second part of the test was unnecessary to the decision reached in *Mayo*. This case

represents the consequence—perhaps unintended—of that broad language in excluding a meritorious invention from the patent protection it deserves and should have been entitled to retain.

It has long been established that "[l]aws of nature, natural phenomena, and abstract ideas are not patentable." *Alice Corp. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2354 (2014) (citations omitted). In *Mayo*, the Supreme Court set forth a two-step framework for distinguishing patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts. The first step looks to determine whether claims are directed to a patent-ineligible concept. *Mayo*, 132 S. Ct. at 1297. If they are, the second step is to consider whether the additional elements recited in the claim "transform the nature of the claim" into a patent-eligible application by reciting an "inventive concept" that is "sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself." *Id.* at 1294.

In applying the second part of the test, the Supreme Court in *Mayo* discounted, seemingly without qualification, any "[p]ost-solution activity that is purely conventional or obvious," *id.* at 1299 (original alterations omitted). This was unnecessary in *Mayo*, because doctors were already performing in combination all of the claimed steps of administering the drug at issue, measuring metabolite levels, and adjusting dosing based on the metabolite levels, *id*.

In *Diamond v. Diehr,* the Supreme Court held that "a new combination of steps in a process may be

patentable even though all the constituents of the combination were well-known and in common use before the combination was made." 450 U.S. 175, 188 (1981). As *Mayo* explained: *Diehr* "pointed out that the basic mathematical equation, like a law of nature, was not patentable. But [*Diehr*] found the overall process patent eligible because of the way the additional steps of the process integrated the equation into the process as a whole." *Mayo* 132 S. Ct. at 1298. Despite that recognition, *Mayo* discounted entirely the "conventional activity" recited in the claims in that case because the 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." *Id.* at 1299. While that conclusion might have been warranted in that case, given the fact that the "conventional activities" in *Mayo* were the very steps that doctors were already doing—administering the drug at issue, measuring metabolite levels, and adjusting dosing based on the metabolite levels—the Supreme Court did not limit its ruling to those particular facts and circumstances.

The Supreme Court's blanket dismissal of conventional post-solution steps leaves no room to distinguish *Mayo* from this case, even though here *no one* was amplifying and detecting paternally-inherited cffDNA using the plasma or serum of pregnant mothers. Indeed, the maternal plasma used to be "routinely discarded," '540 patent col.1 ll.50–53, because, as Dr. Evans testified, "nobody thought that fetal cell-free DNA would be present."

It is hard to deny that Sequenom's invention is truly meritorious. Prior to the '540 patent, prenatal diagnoses required invasive methods, which "present[ed] a degree of risk to the mother and to the pregnancy." *Id.* at col.1 ll.16–17. The available "techniques [we]re time-consuming or require[d] expensive equipment." *Id.* at col.1 ll.17–37. Dr. Mark Evans testified that "despite years of trying by multiple methods, no one was ever able to achieve acceptable success and accuracy." In a groundbreaking invention, Drs. Lo and Wainscoat discovered that there was cell-free fetal DNA in the maternal plasma. The Royal Society lauded this discovery as "a paradigm shift in non-invasive prenatal diagnosis," and the inventors' article describing this invention has been cited well over a thousand times. The commercial embodiment of the invention, the MaterniT21 test, was the first marketed non-invasive prenatal diagnostic test for fetal aneuploidies, such as Down's syndrome, and presented fewer risks and a more dependable rate of abnormality detection than other tests. Unlike in *Mayo*, the '540 patent claims a new method that should be patent eligible. While the instructions in the claims at issue in *Mayo* had been widely used by doctors—they had been measuring metabolites and recalculating dosages based on toxicity/ inefficacy limits for years—here, the amplification and detection of cffDNA had never before been done. The new use of the previously discarded maternal plasma to achieve such an advantageous result is deserving of patent protection. *Cf.* Rebecca S. Eisenberg, *Prometheus Rebound: Diagnostics, Nature, and Mathematical Algorithms*, 122 Yale L.J. Online

341, 343–44 (2013) (noting that despite *Mayo*'s declaration that a claim to "a new way of using an existing drug" is patentable, *Mayo*, 132 S. Ct. at 1302, it is unclear how a claim to new uses for existing drugs would survive *Mayo*'s sweeping test).

In short, Sequenom's invention is nothing like the invention at issue in *Mayo*. Sequenom "effectuate[d] a practical result and benefit not previously attained," so its patent would traditionally have been valid. *Le Roy v. Tatham*, 63 U.S. 132, 135–36 (1859) (quoting *Househill Coal & Iron Co. v. Neilson*, Webster's Patent Case 673, 683 (House of Lords 1843)); *Le Roy v. Tatham*, 55 U.S. 156, 175 (1852) (same); *see generally* Jeffrey A. Lefstin, *Inventive Application: a History*, 67 Fla. L. Rev. (forthcoming 2015), *available at* http://ssrn.com/abstract=2398696 (last visited June 10, 2015) (analyzing traditional notions of patent eligibility of newly discovered laws of nature). 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.

APPENDIX B

IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA

ARIOSA DIAGNOSTICS, INC.,
Plaintiff/Counterdefendant
v.
SEQUENOM, INC.,
Defendant/Counterclaimant
_____/

No. C 11-06391 SI

ORDER GRANTING PLAINTIFF'S MOTION FOR SUMMARY JUDGMENT AND DENYING DEFENDANT'S MOTION FOR SUMMARY JUDGMENT

Cross-motions for summary judgment by plaintiff/counterdefendant Ariosa Diagnostics, Inc. and defendant/counterclaimant Sequenom, Inc. came on for oral argument on October 11, 2013. Having considered the parties' motion papers, pleadings and arguments, and for good cause shown, the Court GRANTS Ariosa's motion for summary judgment and DENIES Sequenom's motion for summary judgment.

BACKGROUND

In this declaratory judgment action, plaintiff Ariosa, formerly known as Aria Diagnostics, Inc., seeks a declaration that its non-invasive prenatal test, the Harmony test, using cell-free fetal DNA circulating

in the blood of a pregnant woman does not directly infringe or contribute to the infringement of U.S. Patent No. 6,258,540 ("the '540 patent"), licensed by defendant Sequenom.

1. The '540 Patent

Sequenom is the exclusive licensee of the '540 patent, which Sequenom licensed from Isis Innovation Limited ("Isis"). *See* DocketNo. 37, Tatman Decl. ¶¶ 3-4. The '540 patent is entitled "Non- Invasive Prenatal Diagnosis," and was issued to inventors Yuk-Ming Dennis Lo and James Stephen Wainscoat on July 10, 2001 and assigned to Isis. U.S. Patent No. 6,258,540 The '540 patent relates to prenatal detection methods performed on a maternal serum or plasma sample from a pregnant female, which methods comprise detecting the presence of a paternally inherited nucleic acid of fetal origin in the sample. *Id.* at 2:1-4. "This invention enables non-invasive prenatal diagnosis, including for example sex determination, blood typing and other genotyping, and detection of pre-eclampsia in the mother." *Id.* (Abstract).

According to the patent, conventional pre-natal diagnostic DNAtests such as amniocentesis and chorionic villus sampling involved invasive procedures with risks to the mother and the pregnancy. '540 Patent at 1:12-17; *see also* Docket No. 35, Evans Decl. ¶¶ 34-37. Therefore, non-invasive techniques began to be developed that used maternal blood or serum. '540 Patent at 1:18-20. Prior noninvasive DNA research had focused on detecting fetal cells in a mother's bloodstream, because the presence of cell-free fetal DNA was not known. *Id.* at 1:28-36; *see also* Docket

No. 35, Evans Decl. ¶ 21. However, these techniques were time-consuming or required expensive equipment. '540 Patent at 1:36-37; *see also* Docket No. 35, Evans Decl. ¶¶ 39-41 ("Ultimately, neither approach, using fetal cells or the other noninvasive screening measurements described above, has proved sufficiently successful or reliable to replace invasive testing.").

"The '540 patent is based on the discovery in 1996-1997 by Drs. Lo and Wainscoat that cell-free fetal DNA (sometimes referred to as "cffDNA") is detectable in maternal serum or plasma samples.[1] '540 Patent at 1:50-51; *see also* Docket No. 35, Evans Decl. ¶ 45. This discovery was important because according to the patent, "[t]he detection rate is much higher using serum or plasma than using nucleated blood cell DNA extracted from a comparable volume of whole blood,

---

1 "Nucleic acid" is the overall name for the class of molecules that includes DNA (deoxyribonucleic acid) and RNA (ribonucleic acid). The significance of the discovery is that the process of isolating fetal cells was not necessary because fetal DNA was present outside of cells, as "extracellular" or "cell-free DNA" suspended in the maternal bloodstream. Docket No. 35, Evans Decl. ¶¶ 53, 57. Blood is made up of cells and plasma (the fluid containing proteins and other molecules in which cells are suspended). *Id.* ¶ 44. Serum is plasma without the clotting proteins (platelets), *i.e.*, blood minus the cells and the clotting factors. *Id.*

suggesting there is enrichment of foetal DNA in maternal plasma and serum." '540 Patent at 1:55-58.

The three independent claims of the '540 patent are as follows:

> **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.
>
> **24.** A method for detecting a paternally inherited nucleic acid on a maternal blood sample, which method comprises:
>
> removing all or substantially all nucleated and a nucleated cell populations from the blood sample,
>
> amplifying a paternally inherited nucleic acid from the remaining fluid and subjecting the amplified nucleic acid to a test for the Paternally [sic] inherited fetal nucleic acid.
>
> **25.** A method for performing a prenatal diagnosis on a maternal blood sample, which method comprises
>
> obtaining a non-cellular fraction of the blood sample
>
> amplifying a paternally inherited nucleic acid from the non-cellular fraction and performing nucleic acid analysis on the amplified nucleic

acid to detect paternally inherited fetal nucleic acid.

'540 Patent at 23:60-67; 26:20-36.

2. Procedural Background

Ariosa filed this declaratory relief action against Sequenom on December 19, 2011, seeking a declaration that its Harmony Test does not infringe any claims of the '540 patent.[2] Docket No. 1, Compl. On March 8, 2012, Sequenom filed an answer against Ariosa and a counterclaim for infringement of the '540 patent. Docket No. 33. On March 8, 2012, Sequenom also filed a motion for a preliminary injunction, seeking to enjoin Ariosa from making, using, selling, offering for sale, or importing into the United States the Harmony Prenatal Test. Docket No. 34.

On July 5, 2012, the Court denied Sequenom's motion for a preliminary injunction. Docket No. 121. In the order, the Court found that Ariosa had raised a substantial question with regard to the validity of the '540 patent based on Ariosa's argument that the '540 patent does not cover patent eligible subject matter.

---

2 Two other cases have been filed in the Northern District of California which also seek declaratory judgments that specific products do not infringe the '540 patent and that the '540 patent is invalid. *See Natera, Inc. v. Sequenom, Inc.*, Case No. 12-cv-00132-SI (filed Jan. 6, 2012); *Verinata Health, Inc. v. Sequenom, Inc.*, Case No. 12-cv-865-SI (filed Feb. 22, 2012).

Id. at 16-19. Sequenom appealed the Court's denial of its motion for a preliminary injunction. Docket No. 123.

On August 9, 2013, the Federal Circuit vacated the Court's order denying the preliminary injunction and remanded the case for further proceedings. *AriaDiagnostics, Inc. v. Sequenom, Inc.*, 726 F.3d 1296, 2013 U.S. App. LEXIS 16506 (Fed. Cir. 2013). In vacating the order, the Federal Circuit rejected this Court's initial claim construction, but 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. *Id.* at *16-17. Rather, the Federal Circuit remanded with directions that this Court examine subject matter eligibility of the asserted claims in the first instance in light of the Supreme Court's recent decision in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013) and the Federal Circuit's claim construction holdings. *Id.* at *16.

By the present cross-motions for summary judgment, the parties move for summary adjudication of whether claims 1, 2, 4, 5, 8, 19-22, 24, and 25 of '540 patent are drawn to patent-eligible subject matter.

LEGAL STANDARD

1. Summary Judgment

Summary judgment is proper "if the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). The moving party bears the initial burden of demonstrating the

absence of a genuine issue of material fact. *Celotex Corp. v. Catrett*, 477 U.S. 317, 323 (1986). The moving party, however, has no burden to disprove matters on which the non-moving party will have the burden of proof at trial. The moving party need only demonstrate to the Court that there is an absence of evidence to support the non-moving party's case. *Id.* at 325.

Once the moving party has met its burden, the burden shifts to the nonmoving party to "set forth, by affidavit or as otherwise provided in Rule 56, 'specific facts showing that there is a genuine issue for trial.'" *T.W. Elec. Service, Inc. v. Pacific Elec. Contractors Ass'n*, 809 F.2d 626, 630 (9th Cir. 1987) (citing *Celotex*, 477 U.S. at 324). To carry this burden, the non-moving party must "do more than simply show that there is some metaphysical doubt as to the material facts." *Matsushita Elec. Indus. Co., Ltd. v. Zenith Radio Corp.*, 475 U.S. 574, 586 (1986). "The mere existence of a scintilla of evidence . . . will be insufficient; there must be evidence on which the jury could reasonably find for the [non-moving party]." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 252 (1986).

In deciding a summary judgment motion, the Court must view the evidence in the light most favorable to the non-moving party and draw all justifiable inferences in its favor. *Id.* at 255. "Credibility determinations, the weighing of the evidence, and the drawing of legitimate inferences from the facts are jury functions, not those of a judge . . . ruling on a motion for summary judgment." *Id.* However, conclusory, speculative testimony in affidavits and moving papers is insufficient to raise

genuine issues of fact and defeat summary judgment. *Thornhill Publ'gCo., Inc. v. GTE Corp.*, 594 F.2d 730, 738 (9th Cir. 1979). The evidence the parties present must be admissible. Fed. R. Civ. P. 56(c)(2).

2. Subject Matter Eligibility Under § 101

Under § 101 of the Patent Act, "[w]hoever 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." 35 U.S.C. § 101. "In choosing such expansive terms . . . modified by the comprehensive 'any,' Congress plainly contemplated that the patent laws would be given wide scope." *Diamond v. Chakrabarty*, 447U.S. 303, 308 (1980).

However, the Supreme Court has long held that there is an important exception to § 101: "'[L]aws of nature, natural phenomena, and abstract ideas' are not patentable." *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1293 (2012); *see also id.* ("[T]he [Supreme] Court has written that a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that E=mc2; nor could Newton have patented the law of gravity. Such discoveries are manifestations of . . . nature, free to all men and reserved exclusively to none." (internal quotation marks omitted)). The Federal Circuit has explained that these exceptions should be applied narrowly. *Ultramercial, Inc. v. Hulu, LLC*, 722 F.3d 1335, 1342 (Fed. Cir. 2013); *see also Prometheus*, 132 S. Ct. at 1293 ("The Court has

recognized . . . that too broad an interpretation of this exclusionary principle could eviscerate patent law. For all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas.").

Patent eligibility under § 101 is an issue of law that may involve underlying factual issues. *Accenture Global Servs. v. Guidewire Software, Inc.*, 2013 U.S. App. LEXIS 18446, at *10 (Fed. Cir. Sept. 5, 2013). Moreover, under 35 U.S.C. § 282, patents are presumed to be valid. Therefore, an alleged infringer must prove invalidity by clear and convincing evidence. *See Microsoft Corp. v. i4i L.P.*, 131 S. Ct. 2238, 2242 (2011); *see also Ultramercial*, 722 F.3d at 1339 (explaining that an accused infringer must prove ineligible subject matter under § 101 by clear and convincing evidence). In this connection, it is the factual evidence itself which must be clear and convincing. *See Buildex, Inc. v. Kason Indus., Inc.,* 849 F.2d 1461, 1463 (Fed. Cir. 1988) (clear and convincing evidence is evidence "which produces in the mind of the trier of fact an abiding conviction that the truth of [the] factual contentions are highly probable" (alteration in original) (citation and internal quotation marks omitted)).

3. Supreme Court Case Law on Subject Matter Eligibility

The Supreme Court has issued several recent decisions articulating standards for the subject matter eligibility, building on cases decided over the last half-century. Several of these cases are briefly reviewed below.

A. *Funk Brothers*

The patent in *Funk Brothers* claimed an inoculant for leguminous plants comprising a plurality of selected mutually non-inhibitive strains of different species of bacteria of the genus Rhizobium, where the strains are unaffected by each other in respect to their ability to fix nitrogen in the leguminous plant for which they are specific.[3] *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 129 n.3 (1948). The Supreme Court noted that prior to the invention, the general practice was to manufacture and sell inoculants containing only one of the six species of the Rhizobium bacteria, meaning that the inoculant could only be used successfully in plants that belonged to that specific species' inoculation group. *Id.* at 129. The inventors of the patent discovered that there are strains of each species of bacteria which do not exert a mutually inhibitive effect on each other, and,

---

3 Leguminous plants take nitrogen from the air and fix it in the plant for conversion to organic nitrogenous compounds. *Funk Bros.*, 333 U.S. at 129. The ability of these plants to fix nitrogen from the air depends on the presence of bacteria of the genus Rhizobium in the plant. *Id.* Bacteria of the genus Rhizobium fall into at least six species. *Id.* "No one species will infect the roots of all species of leguminous plants. But each will infect well-defined groups of those plants." *Id.*

therefore, could be isolated and used in mixed cultures. *Id.* at 130. "Thus [the invention] provided a mixed culture of Rhizobia capable of inoculating the seeds of plants belonging to several cross-inoculation groups." *Id.*

The Supreme Court held that the claims were not patentable because "patents cannot issue for the discovery of the phenomena of nature." *Id.* at 130. The Supreme Court explained that discovery of the fact that certain strains of each species of these bacteria can be mixed without harmful effect to the properties of either is no more than the discovery of some of the handiwork of nature and hence is not patentable. *Id.* at 131. "If there is to be invention from such a discovery, it must come from the application of the law of nature to a new and useful end." *Id.* at 130. The Court recognized that the aggregation of select strains of the species of bacteria into one product is an application of a newly-discovered natural principle, but explained that the application of that principle "is hardly more than an advance in the packaging of the inoculants." *Id.* at 131; *see also id.* at 132 ("[O]nce nature's secret of the non-inhibitive quality of certain strains of the species of Rhizobium was discovered, the state of the art made the production of a mixed inoculant a simple step.").

B. *Gottschalk v. Benson*

The patent application in *Benson* "claimed a method for converting binary-coded decimal (BCD) numerals into pure binary numerals." *Gottschalk v. Benson*, 409 U.S. 63, 64 (1972). The Supreme Court noted that "[t]he claims were not limited to any

particular art or technology, to any particular apparatus or machinery, or to any particular end use," and "[t]hey purported to cover any use of the claimed method in a general-purpose digital computer of any type." *Id.*; *see also id.* at 68 ("Here the 'process' claim is so abstract and sweeping as to cover both known and unknown uses of the BCD to pure binary conversion").

The Supreme Court held that the claims were ineligible subject matter because the formula for converting BCD numerals to pure binary numerals was an abstract idea. *See id.* at 71. The Court explained: "The mathematical formula involved here has no substantial practical application except in connection with a digital computer, which means that if the judgment below is affirmed, the patent would wholly pre-empt the mathematical formula and in practical effect would be a patent on the algorithm itself." *Id.* at 71-72.

C. *Parker v. Flook*

The patent application in *Flook* claimed a method of updating alarm limits,[4] consisting of three steps: "an

---

4 "An 'alarm limit' is a number." *Parker v. Flook*, 437 U.S. 584, 585 (1978). During catalytic conversion processes (various processes used in the petrochemical and oil-refining industries), operating conditions such as temperature, pressure and flow rates are constantly monitored. *Id.* "When any of these 'process variables' exceeds a predetermined 'alarm limit,' an alarm may signal the presence of an abnormal condition

initial step which merely measures the present value of the process variable (e.g., the temperature); an intermediate step which uses an algorithm to calculate an updated alarm-limit value; and a final step in which the actual alarm limit is adjusted to the updated value." *Parker v. Flook*, 437 U.S. 584, 585 (1978). The Court noted that "[t]he only difference between the conventional methods of changing alarm limits" and the claimed method "rests in the second step – the mathematical algorithm or formula." *Id.* at 585-86; *see also id.* at 588 (stating that because the patentee did not challenge the examiner's finding, the Court assumed that "the formula is the only novel feature of respondent's method").

The Supreme Court held that the application did not claim a patentable invention. *Id.* at 594.

The Supreme Court explained that "[t]he only novel feature of the method is a mathematical formula," *id.* at 585, and the discovery of a phenomenon of nature or mathematical formula "cannot support a patent unless there is some other inventive concept in its application." *Id.* at 594. In addition, the Supreme Court rejected the patentee's argument that his invention was patentable because,

---

indicating either inefficiency or perhaps danger. Fixed alarm limits may be appropriate for a steady operation, but during transient operating situations, such as start-up, it may be necessary to 'update' the alarm limits periodically." *Id.*

unlike the patent in *Benson*, his invention did not wholly preempt the use of a mathematical formula. *See id.* at 589-95. The Court recognized that the invention did not wholly preempt the formula, but explained that "'if a claim is directed essentially to a method of calculating, using a mathematical formula, even if the solution is for a specific purpose, the claimed method is nonstatutory.'" *Id.* at 595 (quoting *In re Richman*, 563 F.2d 1026, 1030 (CCPA 1977)); *see also id.* at 590 ("The notion that post-solution activity, no matter how conventional or obvious in itself, can transform an unpatentable principle into a patentable process exalts form over substance. A competent draftsman could attach some form of post-solution activity to almost any mathematical formula; the Pythagorean theorem would not have been patentable, or partially patentable, because a patent application contained a final step indicating that the formula, when solved, could be usefully applied to existing surveying techniques.").

D. *Diamond v. Diehr*

The patent application in *Diehr* claimed "a process for molding raw, uncured synthetic rubber into cured precision products." *Diamond v. Diehr*, 450 U.S. 175, 177 (1981). The process involved constantly determining the actual temperature inside the mold, then automatically feeding the temperatures into a computer which would repetitively calculate the necessary cure time using a mathematical formula known as the Arrhenius equation, and opening the press whenever the elapsed cure time equaled the calculated necessary cure time. *See id.* at 178-79 & n.5.

The Supreme Court found the invention to be patentable. The Court held that "a physical and chemical process for molding precision synthetic rubber products falls within the § 101 categories of possibly patentable subject matter." *Id.* at 184. The Court distinguished the invention at issue from the inventions found unpatentable in *Benson* and *Flook*. *See id.* at 185-88, 191-92 & n.14. The Court recognized that "the process admittedly employs a well-known mathematical equation, but [the patentees] do not seek to pre-empt the use of that equation. Rather, they seek only to foreclose from others the use of that equation in conjunction with all of the other steps in their claimed process." *Id.* at 187. "[W]hen a claim containing a mathematical formula implements or applies that formula in a structure or process which, when considered as a whole, is performing a function which the patent laws were designed to protect (e. g., transforming or reducing an article to a different state or thing), then the claim satisfies the requirements of § 101." *Id.* at 192. In addition, unlike in *Flook*, the patentees contended that there were novel aspects of the invention other than the use of the mathematical formula.

E. *Bilski v. Kappos*

The patent application in *Bilski* claimed a procedure for instructing buyers and sellers of commodities in the energy market how to protect against the risk of price fluctuations in those commodities. *Bilski v. Kappos*, 130 S. Ct. 3218, 3223 (2010). "Claim 1 describes a series of steps instructing how to hedge risk. Claim 4 puts the concept

articulated in claim 1 into a simple mathematical formula. . . . The remaining claims explain how claims 1 and 4 can be applied to allow energy suppliers and consumers to minimize the risks resulting from fluctuations in market demand for energy." *Id.* at 3223-24.

The Supreme Court held that the claims were unpatentable under *Benson*, *Flook*, and *Diehr* because the claims "are attempts to patent abstract ideas." *Id.* at 3230. The Court explained that claims 1 and 4 in the patentees' application explain the basic concept of hedging, or protecting against risk, and the concept of hedging is an unpatentable abstract idea. *Id.* at 3231. "Allowing petitioners to patent risk hedging would preempt use of this approach in all fields, and would effectively grant a monopoly over an abstract idea." *Id.* The Court also rejected the remaining claims of the application because they were "broad examples of how hedging can be used in commodities and energy markets." *Id.* "*Flook* established that limiting an abstract idea to one field of use or adding token postsolution components d[o] not make the concept patentable." *Id.*

F. *Mayo v. Prometheus*

The patents in *Prometheus* claimed processes that help doctors using thiopurine drugs to treat patients with autoimmune diseases determine whether a given dosage level is too low or too high. *Prometheus*, 132 S. Ct. at 1294. Too high a dosage would risk harmful side effects, but too low a dosage might be ineffective. *Id.* at 1295. At the time of the invention, scientists already understood that the levels of certain metabolites in a

patient's blood were correlated with the likelihood that a particular dosage of a thiopurine drug could cause harm or prove ineffective. *Id.* The patents' claims set forth processes embodying researchers' findings that identified the precise correlations between metabolite levels and likely harm or ineffectiveness. *Id.*

The Supreme Court held that the claims were invalid under § 101. *Id.* at 1305. The Court explained that "Prometheus' patents set forth laws of nature – namely, relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm." *Id.* at 1296. "If a law of nature is not patentable, then neither is a process reciting a law of nature, unless that process has additional features that provide practical assurance that the process is more than a drafting effort designed to monopolize the law of nature itself. A patent, for example, could not simply recite a law of nature and then add the instruction 'apply the law.'" *Id.* at 1297. Therefore, the Court concluded that although the patents recited additional steps in addition to the law of nature, the additional steps were insufficient to transform the character of the claims. *See id.* at 1297-98 ("[T]he claims inform a relevant audience about certain laws of nature; any additional steps consist of well understood, routine, conventional activity already engaged in by the scientific community; and those steps, when viewed as a whole, add nothing significant beyond the sum of their parts taken separately.").

G. *Ass'n for Molecular Pathology v. Myriad*

The patentees in *Myriad* discovered the precise location and sequence of two human genes, the BRCA1 andBRCA2 genes, mutations of which can substantially increase the risks of breast and ovarian cancer, and obtained several patents based on that discovery. *Myriad*, 133 S. Ct. at 2110-11. The claims at issue gave Myriad "the exclusive right to isolate an individual's BRCA1 and BRCA2 genes . . . by breaking the covalent bonds that connect the DNA to the rest of the individual's genome. The patents [also gave]Myriad the exclusive right to synthetically create BRCA cDNA[("complementary DNA")]." *Id.* at 2113.

The Supreme Court 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." *Id.* at 2111. The Court noted that Myriad did not create or alter any of the genetic information encoded in the BRCA1 and BRCA2 genes and did not create or alter the genetic structure of DNA. *Id.* at 2116. "Instead, Myriad's principal contribution was uncovering the precise location and genetic sequence of the BRCA1 and BRCA2 genes within chromosomes 17 and 13." *Id.* "To be sure, [Myriad] found an important and useful gene, but separating that gene from its surrounding genetic material is not an act of invention." *Id.* at 2117. In contrast, the Court found that cDNA is not a "product of nature" and, therefore, is patent eligible under § 101. *Id.* at 2119.

DISCUSSION

Ariosa argues that claims 1, 2, 4, 5, 8, 19-22, 24, and 25 of the '540 patent are not drawn to patent

eligible subject matter because paternally inherited cffDNA is a natural phenomenon and the claims of the '540 patent merely add well-understood, routine, conventional activity in the field to that natural phenomenon. Docket No. 219 at 7-20. In response, Sequenom argues that the claimed methods are patentable because they are novel uses of a natural phenomenon, rather than a patent on the natural phenomenon itself. Docket No. 223 at 7-18. In addition, Sequenom argues that the claims are patentable because the claims do not preempt all uses of cffDNA. *Id.* at 18-22.

The parties agree that neither cffDNA nor the discovery of cffDNA in maternal plasma or serum is patentable, because the presence of cffDNA in maternal plasma or serum is a natural phenomenon. Docket No. 219 at 1-2; Docket No. 223 at 1, 8; *see Myriad*, 133 S. Ct. at 2116; *Prometheus*, 132 S. Ct. at 1293; *see also Funk Bros.*, 333 U.S. at 130 ("He who discovers a hitherto unknown phenomenon of nature has no claim to a monopoly of it which the law recognizes."). This is true even if the discovery of cffDNA in maternal plasma or serum was considered groundbreaking, innovative, and brilliant. *See Myriad*, 133 S. Ct. at 2117. However, the '540 patent does not claim as an invention the discovery of cffDNA in maternal plasma or serum. The '540 patent claims methods of detecting paternally inherited cffDNA in maternal plasma or serum. *See* '540 Patent at 2:1-5, 23:60-26:40. Therefore, the issue before the Court is whether the steps of the claimed methods in the '540 patent, applied to that natural phenomenon, are sufficient to render the claims patentable. *See*

Prometheus, 132 S. Ct. at 1297 ("[D]o the patent claims add enough to their statements of the correlations to allow the processes they describe to qualify as patent eligible processes that apply natural laws").

A process or method is not unpatentable simply because it contains a law of nature, a natural phenomenon, or an abstract idea. *Prometheus*, 132 S. Ct. at 1293; *Flook*, 437 U.S. at 590. But, to be patentable, a process that focuses upon the use of a natural law, a natural phenomenon, or an abstract idea must contain other elements or a combination of elements, sometimes referred to as an "inventive concept," sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the natural law, natural phenomenon, or abstract idea itself. *Prometheus*, 132 S. Ct. at 1294; *see also Flook*, 437 U.S. at 594 ("[T]he discovery of such a phenomenon cannot support a patent unless there is some other inventive concept in its application."). In other words, the claimed process – apart from the natural law, natural phenomenon, or abstract idea – must involve more than "well-understood, routine, conventional activity," previously engaged in by those in the field. *Prometheus*, 132 S. Ct. at 1294, 1299; *see also id.* at 1300 ("[S]imply 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."); *Myriad*, 133 S. Ct. at 2119-20 (explaining that an innovative method of manipulating a natural phenomenon – as opposed to applying a well-understood process in the field – would be patentable).

Here, Ariosa argues that the method steps contained in claims 1, 2, 4, 5, 8, 19-22, 24, and 25 of the '540 patent do not add enough to the natural phenomenon of paternally inherited cffDNA to make these claims patentable under § 101. Docket No. 219 at 10-20. Specifically, Ariosa argues that 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. *See id.* The Court agrees. For example, claim 1 of the '540 patent claims a method for detecting cffDNA, comprising the following two steps: "amplifying a paternally inherited nucleic acid from the serum or plasma sample [from a pregnant female] and detecting the presence of a paternally inherited nucleic acid of fetal origin in the sample." '540 Patent at 23:64-67. Ariosa has presented the Court with evidence, including the specification and prosecution history of the '540 patent and testimony by Sequenom's own expert, Dr. Evans, stating that the amplification and detection of DNA sequences in plasma or serum was well known by 1997. Docket No. 219 at 10-14 (citing evidence); Docket No. 238 at 6-7 (citing evidence). For example, the specification of the '540 patent states that "[t]he preparation of serum of plasma from the maternal blood sample is carried out by standard techniques" and also states "[s]tandard nucleic acid amplification systems can be used." '540 Patent at 2:26-27, 2:44-45; *see also* Docket No. 219-7, Gindler Decl. Ex. 5 ¶ 7. In addition, the inventors during the prosecution history stated that any of the well-known, routine techniques for detection of DNA

could be used to detect fetal DNA in maternal serum or plasma. Docket No. 219-4, Gindler Decl. Ex. 2 at 5, 7-8, 10, 12; *see also* '540 Patent at 1:38-43. Sequenom's expert Dr. Evans acknowledged that traditional DNA diagnostics, prior to the invention, commonly involved sample preparation, amplification, and detection. Docket No. 219-6, Gindler Decl. Ex. 4 at 188:5-13; *see also id.* at 150:18-151:7, 152:4-15. Dr. Evans also acknowledged that others before the inventors had amplified and detected nucleic acid in plasma or serum. *Id.* at 188:15-17; Docket No. 35, Evans Decl. ¶ 58; *see also* Docket No. 238-7, Gindler Decl. Ex. 16 at 485 ("There has been much interest in the use of DNA derived from plasma or serum for molecular diagnosis."). Sequenom does not contest that these steps and other steps in the patent[5] were well-

---

5 Dependent Claims 2 and 4 respectively add the limitations of requiring the use of the polymerase chain reaction ("PCR") and the use of a sequence specific probe. *See* '540 Patent at 24:60- 61, 24:65-67. Ariosa has presented the Court with evidence that these two techniques were well-understood, routine, conventional activity engaged in by those in the field at the time of the invention. *See id.* at 2:44-45, 5:7-10, 6:42-7:10, 9:62-63, 10:5-7; Docket No. 35, Evans Decl. ¶ 42.

Dependent Claims 5, 8, 19, and 20 merely limit the natural phenomenon of paternally inherited cffDNA to specific types of that natural phenomenon, such as requiring that the cffDNA is from a Y

understood, routine, and conventional activity by those in the field at the time of the invention. Indeed, in its reply brief and at oral argument, Sequenom acknowledges that the claims of the '540 patent merely apply "conventional techniques" to the newly discovered natural phenomenon of cffDNA. DocketNo. 240 at 7 ("Just like Myriad's claim21, the '540 patent's claims apply conventional techniques to use a newly-isolated natural phenomenon for diagnostic purposes."); Docket No. 253 at 19:7-10 ("The inventive concept was to take a known method and to look at [it] in a place where people were – where the Federal

---

chromosome or requiring that the cffDNA is at least a certain percentage of the total DNA. *See* '540 Patent at 25:1-3, 25:8-10, 25:39-26:3. A specific type of a natural phenomenon is still a natural phenomenon and, thus, is not patentable. *See Myriad*, 133 S. Ct. at 2116; *Prometheus*, 132 S. Ct. at 1293.

Dependent claims 21 and 22 add the limitations of fractionating the blood sample and providing a diagnosis based on the cffDNA. *See id.* at 26:4-26:16. Independent claims 24 and 25 contain – in addition to the limitations in claim 1 – limitations related to fractionating a blood sample. *See id.* at 26:20-36. Ariosa has presented the Court with evidence that fractionating blood and providing a diagnosis based on fetal DNA were well-understood, routine, conventional activity engaged in by those in the field at the time of the invention. *See id.* at 2:26-27; Docket No. 219-2, Gindler Decl. Ex. 3 at 6, Ex. 4 at 152:4-15, Ex. 5 ¶ 7.

Circuit and all the experts agree were throwing waste away, to look there . . ."), 21:19-21 ("I don't disagree that if you go through all the elements in the claim you could put a check as either a conventional item or a natural phenomenon.), 37:20-22, 38:25-39:1 ("They used conventional tools to make it useful to other people."). Because the claimed processes at issue – apart from the natural phenomenon of paternally inherited cffDNA – involve no more than well-understood, routine, conventional activity, previously engaged in by those in the field, they are not drawn to patent eligible subject matter and are invalid under § 101. *See Prometheus*, 132 S. Ct. at 1294, 1299-1300; *Myriad*, 133 S. Ct. at 2119-20.

Sequenom argues that the claims are patentable because although cffDNA is not patentable, the use of cffDNA is patent eligible. Docket No. 223 at 7-10. The Court disagrees. The Supreme Court has never stated that any use of a natural phenomenon is patentable. To the contrary, the Supreme Court has held that "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." *Prometheus*, 132 S. Ct. at 1300. It is only an innovative or inventive use of a natural phenomenon that is afforded patent protection. *See Myriad*, 133 S. Ct. at 2119 ("Had Myriad created an innovative method of manipulating genes while searching for theBRCA1 andBRCA2 genes, it could possibly have sought a method patent."); *Flook*, 437 U.S. at 594 ("[A]n inventive application of the principle may be patented."). Sequenom attempts to argue that its patent claims an

inventive method of using cffDNA. But, based on the undisputed facts before the Court, the only inventive part of the patent is that the conventional techniques of DNA detection known at the time of the invention are applied to paternally inherited cffDNA as opposed to other types of DNA. Thus, the only inventive concept contained in the patent is the discovery of cffDNA, which is not patentable.

The Court's conclusion conforms with the relevant Supreme Court case law, in particular *Flook* and *Myriad*. The patent in *Flook,* like the present patent, claimed methods that utilized an abstract idea or a natural phenomenon – a mathematical algorithm in *Flook*, paternally inherited cffDNA in the present case.[6] *See* 437 U.S. at 585. In *Flook*, as in here, the use of the abstract idea or the natural phenomenon is the only inventive feature of the claims. *See id.* at 588. In

---

6 The Court recognizes that the claims in Flook utilized an abstract idea, while the present claims utilize a natural phenomenon. However, the Supreme Court has never drawn a distinction between natural phenomena, laws of nature, and abstract ideas in determining patent eligibility. To the contrary, the Supreme Court has applied its § 101 jurisprudence uniformly regardless of whether the claims at issue involved a natural phenomenon, law of nature, or abstract idea. See, e.g., Myriad, 133 S. Ct. 2116- 20 (natural phenomenon); Prometheus, 132 S. Ct. at 1293-1302 (law of nature); Bilski, 130 S. Ct. at 3229-31 (abstract idea).

Flook, the Supreme Court noted "the only difference between the conventional methods of changing alarm limits and that described in respondent's application rests in the second step – the mathematical algorithm or formula." *Id.* at 585-86. Similarly, based on the undisputed facts, the only difference between the conventional methods of DNA detection and that described in the '540 patent rests in the application of the methods to paternally inherited cffDNA, a natural phenomenon. 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. Docket No. 223 at 7, 16. Even assuming this true, the same argument could be made for the claims in *Flook*. Prior to the invention in *Flook*, no one had used that particular mathematical formula to update alarm limits. Despite this, the Supreme Court held that the claims in *Flook* were not drawn to patent eligible subject matter. Thus, use of a newly discovered natural phenomenon, law of nature, or abstract idea will not render a claim patentable if the use of that natural phenomenon, law of nature or abstract idea is the only innovation contained in the patent. *See Flook*, 437 U.S. at 594 ("[T]he discovery of such a phenomenon cannot support a patent unless there is some other inventive concept in its application."); *Prometheus*, 132 S.Ct. at 1294, 1299 (requiring that claims – apart from the natural phenomenon – contain more than well-understood, routine, conventional activity); *Funk Bros.*, 333U.S. at 131 ("[H]owever ingenious the discovery of that natural principle may have been, the application of it is hardly more than an advance in the

packaging of the inoculants."). As explained in *Flook*, "the Pythagorean theorem would not have been patentable, or partially patentable, because a patent application contained a final step indicating that the formula, when solved, could be usefully applied to existing surveying techniques." 437 U.S. at 590. 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.

Further, even though *Myriad* involved composition claims rather than method claims, that decision also supports the Court's conclusion. The claims in *Myriad* gave the patentees the exclusive right to isolate the BRCA1 and BCRA2 genes. *See* 133 S. Ct. at 2113. Although the Supreme Court was not presented with method claims, the Court explained "[h]ad Myriad created an innovative method of manipulating genes while searching for the BRCA1 and BRCA2 genes, it could possibly have sought a method patent. But the processes used by Myriad to isolate DNA were well understood by geneticists at the time of Myriad's patents . . . ."[7] *Id.* at 2119-20.

---

[7] The Supreme Court drew this distinction even though Myriad was the first to use those well understood processes to isolate the BRCA1 and BRCA2 genes. *See Myriad*, 133 S. Ct. at 2112-13. Therefore, *Myriad* also supports the principle that the use of a newly discovered natural phenomenon, law of nature, or abstract idea will not render a claim

Similarly, had the inventors of the '540 patent created an innovative method of performing DNA detection while searching for paternally inherited cffDNA, such as a new method of amplification or fractionation, those claims would be patentable. But, the claims presently before the Court simply rely on processes to detect DNA that – as Sequenom concedes – were conventional techniques by those in the field at the time of the invention. Docket No. 240 at 7; Docket No. 253 at 19:7-10, 21:19-121, 37:20-22, 38:25-39:1.[8]

---

patentable if the use of that natural phenomenon, law of nature or abstract idea is the only innovation contained in the patent.

8 The Court rejects Sequenom's argument that Myriad supports the patentability of the '540 patent's claims because the Supreme Court implicitly approved of claim 21 of Myriad's patent. See Docket No. 223 at 12; Docket No. 240 at 6-7. In Myriad, the Supreme Court endorsed the statement in Judge Bryson's Federal Circuit dissent that "'[a]s the first party with knowledge of the [BRCA1 and BRCA2] sequences, Myriad was in an excellent position to claim applications of that knowledge. Many of its unchallenged claims are limited to such applications.'" 133 S. Ct. at 2120. In his dissent, Judge Bryson cited to claim 21 as an example of such an application. However, the Supreme Court did not refer to claim 21, or any other method claims, as an example of that principle. See id. Moreover, although Sequenom argues that claim 21 merely applied the conventional

Sequenom cautions that the Court should not engage in a step-by-step dismantling of the claims. Docket No. 223 at 22-24 (citing *Diehr*, 450 U.S. at 188 ("In determining the eligibility of respondents' claimed process for patent protection under § 101, their claims must be considered as a whole. It is inappropriate to dissect the claims into old and new elements and then to ignore the presence of the old elements in the analysis. This is particularly true in a process claim because a new combination of steps in a process may be patentable even though all the constituents of the combination were well known and in common use before the combination was made."); *Ultramercial*, 722

---

steps of hybridizing and detecting with probes the BRCA1 gene, Docket No. 223 at 12, Sequenom has not presented this Court with any evidence showing that hybridizing and detecting a gene with probes was conventional activity at the time of that invention.

In addition, the Court rejects Sequenom's argument that Myriad's holding that cDNA is patent eligible supports the patentability of the claims of the '540 patent. Docket No. 223 at 11; Docket No. 240 at 5. In Myriad, the Supreme Court held that cDNA was patent eligible because it was not a naturally occurring phenomenon. 133 S. Ct. at 2119. Here, Sequenom has failed to provide any evidence or argument stating that the methods claimed in the '540 patent produce a non-naturally occurring phenomenon. To the contrary, Sequenom concedes that cffDNA is a naturally occurring phenomenon. See Docket No. 223 at 1, 8.

F.3d at 1344)). In evaluating the patentability of the claims, the Court has not dissected the claims into their individual limitations and then determined whether the individual elements are old or new. Rather, the Court has considered the claimed processes as a whole. The unrebutted evidence does not merely show that the individual steps of fractionation, amplification and detection were well-understood, routine, and conventional activity at the time of the invention. The evidence shows that its was well-understood, routine, and conventional activity to combine these steps to detect DNA in serum or plasma. *See* '540 Patent at 1:19- 43; Docket No. 35, Evans Decl. ¶ 58; Docket No. 219-6, Gindler Decl. Ex. 4 at 188:5-13, 188:15-17; Docket No. 238-7, Gindler Decl. Ex. 16 at 485. Therefore, looking at the claimed processes as a whole, the only inventive component of the processes in the '540 patent is to apply those well-understood, routine processes to paternally inherited cffDNA, a natural phenomenon.

In addition, in determining whether a claim is patentable, a court should consider whether the claim poses a risk of preempting a law of nature, natural phenomenon, or abstract idea.[9] *See Accenture*, 2013

---

9 Although the Court agrees that preemption is a consideration when performing a § 101 analysis, the Court disagrees with Sequenom that whether the claims preempt all uses of the natural phenomenon is dispositive of the analysis. *See* Docket No. 223 at 2, 20. In *Flook*, the Supreme Court held that the claims were

U.S. App. LEXIS 18446, at *10-11; *CLS Bank Int'l v. Alice Corp. Pty*, 717 F.3d 1269, 1280-82 (Fed. Cir. 2013) (en banc) (Lourie, J., concurring); *see also Prometheus*, 132 S. Ct. at 1294 (Supreme Court case law "warn[s] against upholding patents that claim processes that too broadly preempt the use of a natural law."); *Diehr*, 450 U.S. at 187 (noting that the claims did not preempt use of the equation). Sequenom argues that the claims of the '540 patent do not preempt all other uses of cffDNA. Docket No. 223 at 20. In support of this argument, Sequenom has presented the Court with scientific articles describing

---

drawn to ineligible subject matter even though the Supreme Court conceded that the claims did not wholly preempt the mathematical formula at issue. *See* 437 U.S. at 589-90. In *Bilski*, the Supreme Court held that the dependent claims at issue were drawn to ineligible subject matter even though they were limited to how the abstract idea of hedging could be used in commodities and energy markets and, thus, would not preempt use of the abstract idea in other fields. *See* 130 S. Ct. at 3231. *Flook* and *Bilski* have not been overruled and remain good precedent. *See also Ultramercial*, 722 F.3d at 1346 ("[T]he Supreme Court has stated that, even if a claim does not wholly pre-empt an abstract idea, it still will not be limited meaningfully if it contains only insignificant or token pre- or post-solution activity – such as identifying a relevant audience, a category of use, field of use, or technological environment.").

methods for detecting cffDNA. Docket No. 223-1, Root Decl. Ex. A at A1875, A2011-12, A2102-05, A2273-80, Ex. F. Ariosa argues that even if these articles disclose alternative methods of detecting cffDNA, Sequenom has failed to present any evidence showing that any of these alternative methods are practical and commercially viable. Docket No. 238 at 17 n.3. In response, Sequenom argues that it is only relevant that the alternative methods can be practiced, not that they are commercially viable alternatives. Docket No. 240 at 14-15. The Court disagrees. If the alternative methods are not commercially viable, then the effect of the patent in practice would be to preempt all uses of the natural phenomenon. It is important to note that the '540 patent does not merely claim uses or applications of cffDNA, it claims methods for detecting the natural phenomenon. Because generally one must be able to find a natural phenomenon to use it and apply it, claims covering the only commercially viable way of detecting that phenomenon do carry a substantial risk of preempting all practical uses of it. It is also important to note the age of the patent. The '540 patent was issued in July 2001. That twelve years have passed since the issuance of the patent but Sequenom does not present the Court with any evidence of a commercially viable alternative method of detecting cffDNA reflects the broad scope of the '540 patent's claims and the great risk that the patent could preempt the use of cffDNA. Indeed, Sequenom itself has acknowledged the preemptive effect of its patent. *See* Docket No. 238-1, Gindler Decl Ex. 11 at 2 ("'[M]anagement believes that the in-licensed '540 patent . . . will block all non-invasive cell-free DNA-

based approaches.'"), Ex. 12 at 6 ("[W]e believe [the '540 patent] is the underpinnings of this whole field, and potentially believe anybody whose [*sic*] developing, an approach that interrogates the circulating cell [free] DNA is infringing this key patent in the field.")

Further, the articles cited by Sequenom were published after the issuance of the patent and well after the date of the invention. *See* Docket No. 223-1, Root Decl. Ex. A at A2102-05 (2003), A2273-80 (2012), Ex. F (2002). Therefore, even assuming that the articles disclose alternative methods of detecting cffDNA, Sequenom has failed to show that any alternative methods existed at the time of the invention or at the time of issuance of the patent. Thus, it appears that the effect of issuing the '540 patent was to wholly preempt all known methods of detecting cffDNA at that time. Accordingly, the Court concludes that the claims at issue pose a substantial risk of preempting the natural phenomenon of paternally inherited cffDNA and that the preemption inquiry supports the Court's conclusion that the claims are not drawn to patent eligible subject matter.

In sum, the Court concludes that, based on the undisputed facts before the Court, Ariosa has met its burden of proving by clear and convincing evidence that claims 1, 2, 4, 5, 8, 19-22, 24, and 25 of the '540 patent are not drawn to patent eligible subject matter and are invalid under 35 U.S.C. § 101.

CONCLUSION

For the foregoing reasons, the Court GRANTS Ariosa's motion for summary judgment and DENIES

Sequenom's motion for summary judgment. Docket Nos. 219, 223.

IT IS SO ORDERED.

/s/ Susan Illston
SUSAN ILLSTON
United States District Judge
Dated: October 30, 2013

UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA

ARIOSA DIAGNOSTICS, INC.,
Plaintiff,
v.
SEQUENOM, INC.,
Defendant/
Counterclaim-Plaintiff,
v.
ARIOSA DIAGNOSTICS, INC.,
Counterclaim-Defendant,
and
ISIS INNOVATION LIMITED,
Nominal Counterclaim-Defendant.

Case No. 3:11-cv-06391-SI

[~~PROPOSED~~] FINAL JUDGMENT

Pursuant to Federal Rule of Civil Procedure 58, the Court hereby enters Final Judgment in this action as follows:

1. For the reasons stated in the Court's October 30, 2013 Order Granting Plaintiffs Motion for

Summary Judgment and Denying Defendant's Motion for Summary Judgment, judgment is hereby entered in favor of Plaintiff Ariosa Diagnostics, Inc. (" Ariosa") and against Defendant Sequenom, Inc. ("Sequenom") on Sequenom's counterclaim for infringement.

2. Ariosa's claim for a declaration of noninfringement is hereby dismissed without prejudice as moot.

IT IS SO ORDERED AND ADJUDGED:

/s/ Susan Illston

The Honorable Susan Illston

United States District Court Judge

Dated: November 20, 2013

KAYE SCHOLER LLP
Michael J. Malecek (171034)
michael.malecek@kayescholer.com
Peter E. Root (142348)
peter.root@kayescholer.com
Two Palo Alto Square, Suite 400
3000 El Camino Real
Palo Alto, California 94306
Telephone: (650) 319-4500
Facsimile: (650) 319-4700
Attorneys for Defendants and
Counterclaim-Plaintiffs
SEQUENOM, INC. and
SEQUENOM CENTER FOR
MOLECULAR MEDICINE, LLC

BARTKO, ZANKEL, BUNZEL & MILLER
W. Paul Schuck (203717)
pschuck@bzbm.com
Sony B. Barari (243379)
sbarari@bzbm.com
One Embarcadero Center, Suite 800
San Francisco, California 94111
Telephone: (415) 956-1900
Facsimile: (415) 956-1152

Attorneys for Plaintiff and Counterclaim-Defendant NATERA, INC. and

Counterclaim-Defendant

DNA DIAGNOSTICS CENTER, INC.

UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

NATERA, INC.,

Plaintiff,

v.

SEQUENOM, INC. and

ISIS INNOVATION LIMITED,

Defendants,

SEQUENOM INC.,

Counterclaim-Plaintiff,

v.

NATERA, INC. and

DNA DIAGNOSTICS CENTER, INC.

Counterclaim- Defendants,

and

ISIS INNOVATION LIMITED,

Nominal Counterclaim-

Defendant.

Case No. 3: 12-cv-00132-SI

[~~PROPOSED~~] FINAL JUDGMENT OF INVALIDITY OF ASSERTED CLAIMS OF U.S. PATENT NO. 6,258,540

Natera, Inc. ("Natera"), DNA Diagnostics Center, Inc. ("DDC"), Sequenom, Inc., and Isis Innovation, Limited ("Isis") (collectively, the "Parties"), by and through their respective counsel of record, hereby stipulate as follows:

WHEREAS Natera filed this declaratory judgment action against Sequenom and Isis seeking a declaration of non-infringement and invalidity of U.S. Patent No. 6,258,540 ("the '540 patent");

WHEREAS Sequenom counterclaimed against Natera and DDC for infringement of the '540 patent; WHEREAS on October 30, 2013, in the related case *Ariosa Diagnostics, Inc.* v. *Sequenom, Inc.* (Case No. C 11-06391 SI) *("Ariosa"),* this Court granted the motion for summary judgment made by Ariosa Diagnostics, Inc., based on this Court's determination that claims 1, 2, 4, 5, 8, 19, 20, 21, 22, 24, and 25 of the '540 patent are not drawn to patent eligible matter and are invalid under 35 U.S.C. § 101, as set forth in this Court's Order Granting Plaintiffs Motion For Summary Judgment And Denying Defendant's Motion For Summary Judgment (Docket No. 254 in Case No. C 11-06391 SI) ("Summary Judgment Order");

WHEREAS Sequenom asserts two additional claims of the '540 patent (claims 13 and 18) in its counterclaim for infringement against Natera and DDC in the present case;

WHEREAS the Parties agree, without prejudice to Sequenom' s right to appeal, that this Court's rationale and reasoning in its Summary Judgment Order in the *Ariosa* case that claims 1, 2, 4, 5, 8, 19, 20, 21, 22, 24, and 25 of the '540 patent are invalid under 35 U.S.C. § 101 applies equally in the present case;

WHEREAS, in order to conserve judicial and party resources and allow for immediate appeal, the Parties agree that this Court should further grant summary judgment with respect to the additional claims of the '540 patent - claims 13 and 18 - asserted against Natera and DDC on the basis that the claims that were the subject of the Summary Judgment Order in the *Ariosa* case are representative of these two additional claims.

NOW, THEREFORE, IT IS STIPULATED by and among the Parties, through their respective counsel, as follows:

1. The Court's Summary Judgment Order in the *Ariosa* case applies with equal force to the present case with respect to the claims of the '540 patent asserted in both the *Ariosa* case and the present case (claims 1, 2, 5, 8, 21, 22, 24, and 25). These claims are deemed invalid under 35 U.S.C. § 101 pending appeal.

2. For purposes of patent eligibility under 35 U.S.C. § 101, claims 1, 2, 4, 5, 8, 19, 20, 21, 22, 24, and

25 of the '540 patent are deemed representative of claims 13 and 18 of the '540 patent.

3. The dependent claims-in-suit in the present case (claims 13 and 18) not addressed by the Court's Summary Judgment Order in the *Ariosa* case are deemed invalid under 35 U.S.C. § 101 pending appeal, and the claims of the '540 patent addressed in the Court's Summary Judgment Order in the *Ariosa* case will be treated on appeal as representative claims of these two dependent claims.

4. Insofar as the United States Court of Appeals for the Federal Circuit (the Federal Circuit") vacates the summary judgment as to any of claims 1, 2, 4, 5, 8, 19, 20, 21, 22, 24, and 25, any claims that depend from a claim for which summary judgment was vacated and are asserted against Natera or DDC shall be treated as revived like such claims for which summary judgment was vacated.

5. By stipulating in the present case that this Court's Summary Judgment Order in the *Ariosa* case applies with equal force to the present case with respect to the claims of the '540 patent that are asserted in both the *Ariosa* case and the present case (claims 1, 2, 5, 8, 21, 22, 24, and 25) and by treating these claims as representative of the non-overlapping dependent claims of the '540 patent in suit in the present case, Sequenom retains the right to challenge this Court's Summary Judgment Order on appeal of the present judgment (as well as appeal of judgment in the *Ariosa* case or judgment in any other related case).

6. Natera stipulates to dismissal without prejudice of its claims for declaratory judgment relating to the

'540 patent that are not subject to the following judgment, and reserves its right to reinstate these claims for declaratory judgment in the present action if the Federal Circuit vacates this judgment of invalidity under 35 U.S.C. § 101.

IT IS SO STIPULATED, THROUGH COUNSEL OF RECORD.

Dated: November 18, 2013 BARTKO, ZANKEL, BUNZEL, & MILLER

By: /s/ W. Paul Schuck

W. Paul Schuck

Attorneys for Plaintiff and Counterclaim-Defendant NATERA, INC. and Counterclaim-Defendant DNA DIAGNOSTICS CENTER, INC.

Dated: November 18, 2013 KAYE SCHOLER LLP

By: /s/ Peter E. Root

Peter E. Root

Attorneys for Defendants and

Counterclaim Plaintiffs SEQUENOM, INC.

and SEQUENOM CENTER FOR MOLECULAR MEDICINE LLC

Dated: November 18, 2013 SATTERLEE STEPHENS BURKE & BURKE LLP

By: /s/ Mario Aieta

Mario Aieta

Attorneys for Nominal Defendant

ISIS INNOVATION LIMITED

I, Peter E. Root, am the ECF User whose ID and password are being used to file this [Proposed] Final Judgment Of lnvalidity Of Asserted Claims Of U.S. Patent No. 6,258,540. I compliance with General Order 45, X.B, I hereby attest that the above counsel have concurred in this filing.

Dated: November 18, 2013 /s/ Peter E. Root

Peter E. Root

[PROPOSED] FINAL JUDGMENT OF INVALIDITY UNDER 35 U.S.C. § 101 AS TO SEQUENOM'S COUNTERCLAIM FOR INFRINGEMENT

THE COURT, having considered the foregoing stipulations of the Parties, and expressly adopting these stipulations, hereby ORDERS AND ADJUDGES:

1. Based on this Court's reasoning and rationale stated in this Court's Summary Judgment Order in the *Ariosa* case, the Court hereby enters final judgment under Rule 58 of the Federal Rules of Civil Procedure in favor of Natera as to Natera's claim for a declaratory judgment of patent invalidity pursuant to 35 U.S.C. § 101 as to claims l, 2, 4, 5, 8, 13, 18, 19, 21, 22, 24 and 25 of the '540 Patent, which are hereby adjudged as invalid under 35 U.S.C. § 101, without prejudice to Sequenom's right to appeal;

2. Based upon this Court's finding that all '540 Patent claims asserted against Natera and DDC are invalid under 35 U.S.C. § 101, the Court hereby enters final judgment under Rule 58 of the Federal Rules of Civil Procedure in favor of Natera and DDC as to Sequenom's counterclaim for infringement of the '540 patent in the present case and Natera's declaratory judgment claims for non-infringement, without prejudice to Sequenom's right to appeal;

3. Natera's declaratory judgment claims for invalidity and non-infringement of all other claims of the '540 patent are dismissed without prejudice; and

4. All issues relating to fees and costs are reserved pending the outcome of any appeals, and the deadlines for filing such motions shall be set by the Court, upon application by the Parties, after a ruling by the United States Court of Appeals for the Federal Circuit.

IT IS SO ORDERED AND ADJUDGED:

/s/ Susan Illston
Honorable Susan Illston
United States District Court Judge

Dated: November 20, 2013

APPENDIX C

United States Court of Appeals
for the Federal Circuit.

ARIOSA DIAGNOSTICS, INC., NATERA, INC.,

Plaintiffs-Appellees

DNA DIAGNOSTICS CENTER, INC.,

Counterclaim Defendant-Appellee

v.

SEQUENOM, INC., SEQUENOM CENTER FOR MOLECULAR MEDICINE, LLC,

Defendants-Appellants

ISIS INNOVATION LIMITED,

Defendant

2014-1139, 2014-1144

Appeals from the United States District Court for the Northern District of California in Nos. 3:11-cv-06391-SI, 3:12-cv-00132-SI, Judge Susan Y. Illston.

ON PETITION FOR REHEARING EN BANC

MICHAEL J. MALECEK, Kaye Scholer LLP, Palo Alto, CA, filed a petition for rehearing en banc for defendants-appellants. Also represented by PETER E.

ROOT; ATON ARBISSER, Los Angeles, CA; THOMAS GOLDSTEIN, ERIC F. CITRON, Goldstein & Russell, P.C., Bethesda, MD.

DAVID ISAAC GINDLER, Irell & Manella LLP, Los Angeles, CA, filed a response to the petition for plaintiff-appellee Ariosa Diagnostics, Inc. Also represented by ANDREI IANCU, JOSHUA GORDON; AMIR NAINI, Russ August & Kabat, Los Angeles, CA.

MARK ANDREW PERRY, Gibson, Dunn & Crutcher LLP, Washington, DC, filed a response to the petition for plaintiff-appellee Natera, Inc. Also represented by TRACEY B. DAVIES, BRETT ROSENTHAL, MICHAEL A. VALEK, Dallas, TX.

WILLIAM PAUL SCHUCK, Bartko, Zankel, Bunzel & Miller, San Francisco, CA, for counterclaim defendant-appellee DNA Diagnostics Center, Inc.

GIDEON A. SCHOR, Wilson Sonsini Goodrich & Rosati, PC, New York, NY, for amici curiae Amarantus Bioscience Holdings, Inc., Personalis, Inc., Population Diagnostics, Inc. Also represented by MAYA SKUBATCH, Palo Alto, CA; RICHARD TORCZON, CHARLES J. ANDRES, JR., Washington, DC.

LANA GLADSTEIN, Nutter McClennen & Fish LLP, Boston, MA, for amicus curiae Bioindustry Association. Also represented by KONSTANTIN M. LINNIK, ISAAC A. HUBNER.

CHRISTOPHER MICHAEL HOLMAN, University of Missouri- Kansas City, Kansas City, MO, for amici curiae Biotechnology Industry Organization, Pharmaceutical Research and Manufacturers of America. Biotechnology Industry Organization also

represented by BRIAN P. BARRETT, Eli Lilly and Company, Indianapolis, IN; LI WESTERLUND, Bavarian Nordic, Inc., Redwood City, CA.

BENJAMIN JACKSON, Myriad Genetics, Inc., Salt Lake City, UT, for amicus curiae The Coalition for 21st Century Medicine. Also represented by DAVID CARTER HOFFMAN, Genomic Health, Inc., Redwood City, CA.

DONALD LOUIS ZUHN, JR., McDonnell Boehnen Hulbert & Berghoff LLP, Chicago, IL, for amicus curiae Paul Gilbert Cole. TEIGE P. SHEEHAN, Heslin, Rothenberg, Farley & Mesiti, P.C., Albany, NY, for amicus curiae Intellectual Property Owners Association. Also represented by PHILIP STATON JOHNSON, Johnson & Johnson, New Brunswick, NJ; KEVIN H. RHODES, 3M Innovative Properties Company, St. Paul, MN; HERBERT CLARE WAMSLEY, JR., Intellectual Property Owners Association, Washington, DC.

MATTHEW JAMES DOWD, Andrews Kurth LLP, Washington, DC, for amicus curiae JYANT Technologies, Inc. Also represented by ROBERT A. GUTKIN, SUSHILA CHANANA.

JEFFREY LEFSTIN, University of California Hastings College of Law, San Francisco, CA, for amici curiae Jeffrey Lefstin, Peter S. Menell. JOHN D. MURNANE, Fitzpatrick, Cella, Harper & Scinto, New York, NY, for amicus curiae New York Intellectual Property Law Association. Also represented by ALICIA ALEXANDRA ROSE RUSSO, ERIN AUSTIN; DOROTHY R. AUTH, Cadwalader, Wickersham & Taft LLP, New York, NY; IRENA ROYZMAN,

Patterson Belknap Webb & Tyler LLP, New York, NY; DAVID F. RYAN, Croton-on-Hudson, NY.

COREY A. SALSBERG, Novartis International AG, Basel, Switzerland, for amicus curiae Novartis AG.

KEVIN EDWARD NOONAN, McDonnell Boehnen Hulbert & Berghoff LLP, Chicago, IL, for amici curiae Twenty- Three Law Professors.

DAN L. BAGATELL, Perkins Coie LLP, Phoenix, AZ, for amici curiae Wisconsin Alumni Research Foundation, Marshfield Clinic, MCIS, Inc. Also represented by MICHELLE MARIE UMBERGER, Madison, WI; MICHAEL ROBERT OSTERHOFF, Chicago, IL.

Before PROST, *Chief Judge*, NEWMAN, LOURIE, DYK, MOORE, O'MALLEY, REYNA, WALLACH, TARANTO, CHEN, HUGHES, and STOLL, *Circuit Judges*.

LOURIE, *Circuit Judge*, with whom MOORE, *Circuit Judge*, joins, concurs with the denial of the petition for rehearing en banc.

DYK, *Circuit Judge*, concurs with the denial of the petition for rehearing en banc.

NEWMAN, *Circuit Judge*, dissents from the denial of the petition for rehearing en banc.

PER CURIAM.

O R D E R

A petition for rehearing en banc was filed by defendants-appellants Sequenom, Inc. and Sequenom Center for Molecular Medicine, LLC. The petition for

rehearing was first referred to the panel that heard the appeal, and thereafter, to the circuit judges who are in regular active service. A response was invited by the court and filed by plaintiffs-appellees Ariosa Diagnostics, Inc. and Natera, Inc. A poll was requested, taken, and failed.

Upon consideration thereof,

IT IS ORDERED THAT:

(1) The petition for rehearing en banc is denied.

(2) The mandate of the court will issue on December 9, 2015.

FOR THE COURT

December 2, 2015
Date

/s/ Daniel E. O'Toole
Daniel E. O'Toole
Clerk of Court

United States Court of Appeals
for the Federal Circuit.

ARIOSA DIAGNOSTICS, INC., NATERA, INC.,

Plaintiffs-Appellees

DNA DIAGNOSTICS CENTER, INC.,

Counterclaim Defendant-Appellee

v.

SEQUENOM, INC., SEQUENOM CENTER FOR MOLECULAR MEDICINE, LLC,

Defendants-Appellants

ISIS INNOVATION LIMITED,

Defendant

2014-1139, 2014-1144

Appeals from the United States District Court fo the Northern District of California in Nos. 3:11-cv-06391-SI, 3:12-cv-00132-SI, Judge Susan Y. Illston.

LOURIE, *Circuit Judge*, with whom MOORE, *Circuit Judge*, joins, concurring in the denial of the petition for rehearing en banc.

I concur in the court's denial of rehearing en banc in this case, based on the precedent of *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. __, 132 S. Ct. 1289 (2012). I do so

because I find no principled basis to distinguish this case from *Mayo*, by which we are bound. I write separately to express some thoughts concerning laws of nature and abstract ideas, which seem to be at the heart of patent-eligibility issues in the medical sciences.

Since the Supreme Court's decision in *Bilski v. Kappos*, 561 U.S. __, 130 S. Ct. 3218 (2010), the issue of patent eligibility under § 101 has been of key importance in the adjudication of patent cases, particularly in the field of software. The Court's decisions in *Mayo*, *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. __, 133 S. Ct. 2107 (2013), and *Alice Corp. v. CLS Bank International*, 573 U.S. __, 134 S. Ct. 2347 (2014), have further brought the focus onto the field of medical diagnostics.

The Supreme Court in *Mayo* determined that the claims in that patent "set forth laws of nature." It further held in *Mayo* that steps additional to those setting forth laws of nature in a claimed process must add something "that in terms of patent law's objectives ha[ve] significance" to the natural laws, such that those steps transform the process into an inventive application of those laws. *Mayo*, 132 S. Ct. at 1299. Moreover, the Court rejected "post-solution activity that is purely conventional or obvious" as not significant enough to bring a claimed invention within the realm of patent-eligible subject matter. *Id.* (internal quotation marks and alteration omitted).

Alice relates to the third specific exception to eligibility—abstract ideas—and its discussion also incorporates the requirement of an "inventive concept"

beyond "conventional steps." It held that claims that amount to nothing more than *instruction to apply* an abstract idea are not patent eligible, although *application of the abstract idea may be*. In my view, neither of the traditional preclusions of laws of nature or of abstract ideas ought to prohibit patenting of the subject matter in this case.

Laws of nature are *exact* statements of physical relationships, deduced from scientific observations of natural phenomena. They are often represented by equations, and include such laws as the relationship between energy and mass (E=mc2), the relationship between current and resistance (Ohm's Law), that between force, mass, and acceleration (F=ma), Maxwell's equations, Newton's laws of motion, and many more. Those laws, all agree, are not and should not be patent-eligible subject matter. But methods that utilize laws of nature do not set forth or claim laws of nature. All physical steps of human ingenuity utilize natural laws or involve natural phenomena. Thus, those steps cannot be patent-ineligible solely on that basis because, under that reasoning, nothing in the physical universe would be patent-eligible.

Abstract steps are, axiomatically, the opposite of tangible steps; that which is not tangible is abstract. But steps that involve machines, which are tangible, steps that involve transformation of tangible subject matter, or tangible implementations of ideas or abstractions should not be considered to be abstract ideas. In *Bilski*, the Supreme Court supported this proposition when it described our earlier machine-or-

transformation test as a useful clue, albeit not the only test, for eligibility.

Conversely, abstract ideas are essentially mental steps; they are not tangible even if they are written down or programmed into a physical machine. *Alice,* in affirming this court, held that claims that amount to nothing significantly more than *instruction to apply* an abstract idea are not patent eligible. But the fact that steps are well-known, although relevant to other statutory sections of the patent law, does not necessarily make them abstract.

The claims at issue in Sequenom's patent are directed to methods for detecting paternally-inherited fetal DNA in maternal blood samples, and performing a prenatal diagnosis based on such DNA. Following *Mayo*, which held that certain steps merely recite natural laws and that the remaining steps must be sufficiently innovative apart from the natural laws, the panel in this case held that the claims do not involve patent-eligible subject matter. Appellants and amici have argued before us in briefs that a broad range of claims of this sort appear to be in serious jeopardy. It is said that the whole category of diagnostic claims is at risk. It is also said that a crisis of patent law and medical innovation may be upon us, and there seems to be some truth in that concern.

The claims in this case perhaps should be in jeopardy, not because they recite natural laws or abstract ideas, but because they may be indefinite or too broad. But they should not be patent-ineligible on the ground that they set forth natural laws or are abstractions.

Claim 1 is directed to a method for detecting a paternally inherited nucleic acid of fetal origin from a pregnant female comprising amplifying a paternally inherited nucleic acid and detecting the presence of a paternally inherited nucleic acid. Claim 21 is directed to a method of performing a prenatal diagnosis comprising providing a maternal blood sample, separating the sample into a cellular and non-cellular fraction, detecting the presence of a nucleic acid, and providing a diagnosis. Both of these claims contain the nucleus of patent-eligible subject matter.

As the panel noted, the natural phenomenon here is the presence of cell-free fetal DNA ("cffDNA") in maternal plasma, which, when subjected to certain conventional steps, has led to an important new development: diagnosis of possible birth defects without using highly intrusive means. Applications of natural phenomena or laws to a known process "may well be deserving of patent protection." *Diehr*, 450 U.S. at 187. And it is not disputed that this scientific work on its own seems like an important discovery and a valuable contribution to the medical field, although no one asserts that a claim directed to the mere existence of cffDNA is patent-eligible. But neither of the representative claims here merely recites a law of nature, a natural phenomenon, or an abstract idea. The claims rely on or operate by, but do not recite, a natural phenomenon or law. The claimed invention involves taking maternal serum, separating it, amplifying the genetic material to detect cffDNA, and running tests to identify certain genes or genetic defects; these are all physical, and not insignificant, steps requiring human intervention.

The claims might be indefinite or too broad in that they do not specify how to amplify and detect, or how to separate, detect, and diagnose. Or they perhaps attempt to claim all known methods of carrying out those steps. But the finer filter of § 112 might be better suited to treating these as questions of patentability, rather than reviewing them under the less-defined eligibility rules.

It is not disputed that fractionating blood, amplifying DNA, and analyzing DNA to detect specific gene sequences are known techniques in the art. As all other steps in the claims are individually well-known, the innovative aspect of the claims appears to be the improvement in the method of determining fetal genetic characteristics or diagnosing abnormalities of fetal DNA, consisting of *use of the non-cellular fraction of fetal DNA* obtained from a maternal blood sample.

The claim to this invention, then, might have been better drafted as a so-called Jepson claim, which recites what is in the prior art and what is the improvement. Such a claim might read, perhaps with more details added: "In a method of performing a prenatal diagnosis using techniques of fractionation and amplification, the improvement consisting of using the non-cellular fraction of a maternal blood sample."

Regardless, we are not experts in drafting claims to protect new biological procedures and we are not in a position to rewrite claims or review a hypothetical claim. But against the accusation that such a claim to the invention might be considered mere draftsmanship and thus still ineligible under the seemingly expansive holding of *Mayo*, it must be said that a process,

composition of matter, article of manufacture, and machine are different implementations of ideas, and differentiating among them in claim drafting is a laudable professional skill, not necessarily a devious device for avoiding prohibitions. This is true despite the Supreme Court's affirmance of this court in *Alice*, where we had held, by a 7–3 vote, that method and media claims in inventions *of the type claimed there* were essentially the same.

But focusing on the claims we have rather than those we might have had, the claims here are directed to an actual use of the natural material of cffDNA. They recite innovative and practical *uses* for it, particularly for diagnostic testing: blood typing, sex typing, and screening for genetic abnormalities. And it is undisputed that before this invention, the amplification and detection *of cffDNA from maternal blood*, and use of these methods for prenatal diagnoses, were *not* routine and conventional. But applying *Mayo*, we are unfortunately obliged to divorce the additional steps from the asserted natural phenomenon to arrive at a conclusion that they add nothing innovative to the process.

Moreover, the claims here are not abstract. There is nothing abstract about performing actual physical steps on a physical material. And if the concern is preemption of a natural phenomenon, this is, apparently, a novel process and that is what patents are intended to incentivize and be awarded for. The panel here also noted that there were other uses for cffDNA and other methods of prenatal diagnostic testing using cffDNA that do not involve the steps

recited in the various claims. That fact should sufficiently address the concern of improperly tying up future use of natural phenomena and laws.

In sum, 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, or that they claim abstract concepts. But I agree that the panel did not err in its conclusion that under Supreme Court precedent it had no option other than to affirm the district court.

United States Court of Appeals
for the Federal Circuit.

ARIOSA DIAGNOSTICS, INC., NATERA, INC.,

Plaintiffs-Appellees

DNA DIAGNOSTICS CENTER, INC.,

Counterclaim Defendant-Appellee

v.

SEQUENOM, INC., SEQUENOM CENTER FOR MOLECULAR MEDICINE, LLC,

Defendants-Appellants

ISIS INNOVATION LIMITED,

Defendant

2014-1139, 2014-1144

Appeals from the United States District Court fo the Northern District of California in Nos. 3:11-cv-06391-SI, 3:12-cv-00132-SI, Judge Susan Y. Illston.

DYK, *Circuit Judge*, concurring in the denial of the petition for rehearing en banc.

I concur in the court's denial of rehearing en banc. In my view the framework of *Mayo* and *Alice* is an essential ingredient of a healthy patent system, allowing the invalidation of improperly issued and highly anticompetitive patents without the need for

protracted and expensive litigation. Yet I share the concerns of some of my colleagues that a too restrictive test for patent eligibility under 35 U.S.C. § 101 with respect to laws of nature (reflected in some of the language in *Mayo*) may 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. This leads me to think that some further illumination as to the scope of *Mayo* would be beneficial in one limited aspect. At the same time I think that we are bound by the language of *Mayo*, and any further guidance must come from the Supreme Court, not this court.

I

The language of *Mayo* is clear. The *Mayo* Court found that prior Supreme Court decisions "insist that a process that focuses upon the use of a natural law also contain other elements or a combination of elements, sometimes referred to as an 'inventive concept,' sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself." *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1294 (2012) (quoting *Parker v. Flook*, 437 U.S. 584, 594 (1978)). Patent claims directed to laws of nature are ineligible under 35 U.S.C. § 101 when, "(*apart* from the natural laws themselves) [they] involve well-understood, routine, conventional activity previously engaged in by researchers in the field." *Id.* (emphasis added). Reviewing the Court's earlier *Flook* decision, the *Mayo* Court determined that Flook's claim to a chemical process applying an "apparently novel mathematical

algorithm," *id.* at 1298, was ineligible under § 101 because the steps of the process "were all 'well known,' to the point where, *putting the formula to the side*, there was no 'inventive concept' in the claimed application of the formula," *id.* at 1299 (quoting *Flook*, 437 U.S. at 594) (emphasis added). "[S]imply 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." *Id.* at 1300. In other words, *Mayo* states that the inventive concept necessary for eligibility must come in the application analyzed at step two, rather than from the discovery of the law of nature itself.

Alice subsequently confirmed that the two-step framework articulated in *Mayo* is a unitary rule that applies equally "for distinguishing patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts." *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2355 (2014) (citing *Mayo*). *Alice* explained,

> First, we determine whether the claims at issue are directed to one of those patent-ineligible concepts. If so, we then ask, what else is there in the claims before us? . . . *We have described step two of this analysis as a search for an inventive concept— 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.

Id. (emphasis added) (alterations, citations, and quotation marks omitted). "*At Mayo step two*, we must examine the elements of the claim to determine whether it contains an 'inventive concept' sufficient to 'transform' the claimed abstract idea into a patent-eligible application." *Id.* at 2357 (emphasis added) (quotation marks omitted). Thus *Alice* also holds that inventive concept must be found at step two of the framework.

Mayo has unambiguously announced a generally applicable test for determining subject-matter eligibility under § 101 with respect to laws of nature, and we are bound to follow it. We cannot confine *Mayo* to its facts or otherwise cabin a clear statement from the Supreme Court. "[O]nce the Court has spoken, it is the duty of other courts to respect that understanding of the governing rule of law." *Rivers v. Roadway Express, Inc.*, 511 U.S. 298, 312 (1994). A court of appeals must not "confus[e] the factual contours of [a Supreme Court decision] for its unmistakable holding" to arrive at a "novel interpretation" of that decision. *Thurston Motor Lines, Inc. v. Jordan K. Rand, Ltd.*, 460 U.S. 533, 534–35 (1983) (per curiam). As we have recognized, "[a]s a subordinate federal court, we may not so easily dismiss [the Supreme Court's] statements as dicta but are bound to follow them." *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1347 (Fed. Cir. 2010) (en banc) (citing *Stone Container Corp. v. United States*, 229 F.3d 1345, 1349–50 (Fed. Cir. 2000)).

The panel thus held correctly that *Mayo* is controlling precedent that governs the outcome here. The panel's opinion aptly states and applies the two-

step framework of *Mayo*. "First, we determine whether the claims at issue are directed to a patent-ineligible concept." *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1375 (Fed. Cir. 2015) (citing *Mayo*, 566 U.S. at 1292). "[T]he claims at issue, as informed by the specification, are generally directed to detecting the presence of a naturally occurring thing or a natural phenomenon, cffDNA in maternal plasma or serum. . . . [T]he claimed method begins and ends with a naturally occurring phenomenon." *Id.* at 1376. At the second step of the *Mayo* framework, the panel determined that "[t]he method at issue here amounts to a general instruction to doctors to apply routine, conventional techniques when seeking to detect cffDNA." *Id.* at 1377. The panel therefore found that the claims were not patent eligible under § 101. *Id.* at 1378.

II

The *Mayo/Alice* framework works well when the abstract idea or law of nature in question is well known and longstanding, as was the situation in *Mayo* itself (as discussed below), earlier Supreme Court cases,[1] and in many of our own recent cases where we

---

1 See, e.g., Bilski v. Kappos, 561 U.S. 593, 611 (2010) ("Hedging is a fundamental economic practice long prevalent in our system of commerce and taught in any introductory finance class.") (quoting In re Bilski, 545 F.3d 943, 1013 (Fed. Cir. 2008) (Rader, J., dissenting)) (emphasis added); Diamond v. Diehr, 450 U.S. 175, 177 n.2 (1981) (noting that the Arrhenius

have found claims patent ineligible under § 101.[2] Where the abstract idea or law of nature is well known

---

equation "has long been used to calculate the cure time in rubber-molding processes") (emphasis added); Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 129 (1948) ("Methods of selecting the strong strains [of nitrogen-fixing root-nodule bacteria] and of producing a bacterial culture from them have long been known.") (emphasis added); see also the influential English patent case discussed in Mayo, 132 S. Ct. at 1300, Neilson v. Harford, Webster's Patent Cases 295, 371 (1841) ("We think the case must be considered as if the principle [that hot air promotes ignition better than cold air is] well known . . . .") (emphasis added).

2 See, e.g., Intellectual Ventures I LLC v. Capital One Bank, 792 F.3d 1363, 1369 (Fed. Cir. 2015) (invalidating claims that applied an abstract idea—tailoring of advertising to individual customers—which "had often been" used before); OIP Techs., Inc. v. Amazon.com, Inc., 788 F.3d 1359, 1362, 1364 (Fed. Cir. 2015) (invalidating claims to computerized methods of offer-based price optimization and noting that the abstract idea implicated was a "fundamental economic concept[]"); Ultramercial, Inc. v. Hulu, LLC, 772 F3d 709, 715 (Fed. Cir. 2014) (invalidating a claim to routine, conventional application of the abstract idea of "using advertising as an exchange or currency" and rejecting the patentee's argument that the idea was new); buySAFE, Inc. v. Google, Inc., 765 F.3d 1350, 1351, 1355 (Fed. Cir. 2014) (invalidating a claim

and longstanding, there is no basis for attributing novelty to that aspect of the claimed invention.

Also, it seems to me that the *Mayo/Alice* framework works well with respect to abstract ideas. In my view, claims to business methods and other processes that merely organize human activity should not be patent eligible under any circumstances. *See Alice*, 134 S. Ct. at 2360 (Sotomayor, J., concurring); *In re Bilski*, 545 F.3d 943, 972 (Fed. Cir. 2008) (en banc) (Dyk, J., concurring). In any event, departing from the *Mayo/Alice* framework with respect to abstract ideas (as opposed to discoveries of natural laws and phenomena) would create serious risks of undue preemption because of the difficulty in distinguishing between new and established abstract ideas.

But, as I see it, there is a problem with *Mayo* insofar as it concludes that inventive concept cannot come from discovering something new in nature—*e.g.*, identification of a previously unknown natural relationship or property. In my view, *Mayo* did not fully take into account the fact that an inventive

---

to a method of guaranteeing a party's performance in an online transaction and finding that the abstract idea implicated was "beyond question of ancient lineage"); SmartGene, Inc. v. Advanced Biological Labs., SA, 555 F. App'x 950 (Fed. Cir. 2014) (invalidating a claim to computerized application of a mental process for treating medical patients that "doctors do routinely").

concept can come not just from creative, unconventional application of a natural law, but also from the creativity and novelty of the discovery of the law itself. This is especially true in the life sciences, where development of useful new diagnostic and therapeutic methods is driven by investigation of complex biological systems. I worry that method claims that apply newly discovered natural laws and phenomena in somewhat conventional ways are screened out by the *Mayo* test. In this regard I think that *Mayo* may not be entirely consistent with the Supreme Court's decision in *Myriad*.[3]

In *Myriad* the patent applicant discovered a previously unknown natural phenomenon: the sequences of the BRCA1 and BRCA2 genes and their connection with cancer. *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2112–13 (2013). While the Court found ineligible Myriad's claims to naturally occurring gDNA sequences, it suggested that "new *applications* of knowledge about the BRCA1 and BRCA2 genes" could generally be eligible, with reference to claim 21 of U.S. Patent No.

---

3 Any tension between Mayo and Myriad does not, of course, change our obligation to respect the sweeping precedent of Mayo, as the panel did. Supreme Court "decisions remain binding precedent until [the Court] see[s] fit to reconsider them, regardless of whether subsequent cases have raised doubts about their continuing vitality." Hohn v. United States, 524 U.S. 236, 252–53 (1998) (citation omitted).

5,753,441 (discussed further below).[4] *Id.* at 2120. *Myriad* thus appeared to recognize that an inventive concept can sometimes come from discovery of an unknown natural phenomenon, not just from unconventional application of a phenomenon. As *Myriad* emphasized, the first party with knowledge of a law of nature, natural phenomenon, or abstract idea should be "in an excellent position to claim applications of that knowledge." *Id.* (quoting *Ass'n. for Molecular Pathology v. USPTO*, 689 F.3d 1303, 1349 (Fed. Cir. 2012) (Bryson, J., concurring in part and dissenting in part)).

III

Of course, I do not suggest that a newly discovered law of nature should be patent eligible in its entirety. Laws of nature are never patentable as such, even when first discovered by the patent applicant. As *Mayo* recognized, "Einstein could not patent his celebrated law that E=mc2." 132 U.S. at 1293 (quoting *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980)); *see also Flook*, 437 U.S. at 591; *Gottschalk v. Benson*, 409 U.S. 63, 72 (1972) (holding that claims to methods of using a new mathematical algorithm were unpatentable because they "in practical effect would be a patent on the algorithm itself"). *Myriad* itself reminded us that

---

4 The "new applications" referred to by the Court must have meant applications of the newly discovered genes rather than inventive concepts at step two of the Mayo/Alice framework.

"[g]roundbreaking, innovative, or even brilliant discovery does not by itself satisfy the § 101 inquiry." *Myriad*, 133 S. Ct. at 2117; *see also Ariosa*, 788 F.3d at 1379.

The primary concern with a patent on a law of nature is undue preemption—the fear that others' innovative future applications of the law will be foreclosed. *See O'Reilly v. Morse*, 56 U.S. 62, 113 (1853); *Mayo*, 132 S. Ct. at 1301. As *Mayo* emphasized, "there is a danger that the grant of patents that tie up the[] use [of laws of nature] will inhibit future innovation premised upon them . . . ." 132 S. Ct. at 1301; *see also id.* at 1304 (highlighting "the kind of risk that underlies the law of nature exception, namely the risk that a patent on the law would significantly impede future innovation").

As far back as *O'Reilly v. Morse*, the Supreme Court found unpatentable Morse's sweeping claim to all "marking or printing [of] intelligible characters, signs, or letters, at any distances" via "the use of the motive power of the electric or galvanic current, which I call electromagnetism," holding that "the claim is too broad, and not warranted by law." 56 U.S. at 112, 113. *Morse*, like *Mayo*, was concerned with undue preemption of the building blocks of human ingenuity. "[W]hile he shuts the door against inventions of other persons, the patentee would be able to avail himself of new discoveries in the properties and powers of electro-magnetism which scientific men might bring to light." *Id.* at 113.

Similarly, in an aspect of our original *Myriad* decision that was not reversed by the Supreme Court,

Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 694 (2012), and again in our court's recent *In re BRCA1- & BRCA2-Based Hereditary Cancer Test* decision, we found genetic testing claims that sought to capture "all comparisons between the patient's BRCA genes and the wild-type BRCA genes" to be overbroad and thus ineligible under § 101, noting that "[t]he covered comparisons are not restricted by the purpose of the comparison or the alteration being detected." 774 F.3d 755, 763, 765 (Fed. Cir. 2014).

However, if the breadth of the claim is sufficiently limited to a specific application of the new law of nature discovered by the patent applicant and reduced to practice, I think that the novelty of the discovery should be enough to supply the necessary inventive concept. My proposed approach would require that the claimed application be both narrow in scope and actually reduced to practice, not merely "constructively" reduced to practice by filing of a patent application replete with prophetic examples.

In my view, the breadth of the claim should be critical.

Even when a patent applicant has demonstrated some particular utility for a newly discovered law of nature and reduced it to practice, the claim should be invalid unless narrowly tailored to the particular application of the law that has been developed. Claims that extend far beyond the utility demonstrated by the patent applicant and reduced to practice should be invalid, as they "too broadly preempt the use" of the underlying idea by others. *Mayo*, 132 S. Ct. at 1294; *see also Diamond v. Diehr*, 450 U.S. 175, 191–92

(1981). But, so long as a claim is narrowly tailored to what the patent applicant has actually invented and reduced to practice, there is limited risk of undue preemption of the underlying idea. In *Myriad* the Court noted, 133 S. Ct. at 2120, that an example of a meritorious claim might be claim 21 of Myriad's U.S. Patent No. 5,753,441 ("the '441 patent"), which was not at issue in the case and which Judge Bryson discussed in his concurring opinion on our court's decision below, *Ass'n for Molecular Pathology*, 689 F.3d at 1348 (Bryson, J., concurring). Claim 21 of the '441 patent covers a method of detecting any of several specific mutations in the BRCA1 gene, newly discovered by the patent applicant and shown to increase a person's risk of developing particular cancers, using conventional methods. *See In re BRCA1 & BRCA2*, 774 F.3d at 765.

This approach appears also to be supported by *Morse*. The Supreme Court established in *Morse* that the extent to which a patentee can claim is the extent to which he has actually made some concrete use of the discovery and reduced it to practice. "The specification of this patentee describes his invention or discovery, and the manner and process of constructing and using it; and his patent . . . covers nothing more." *Morse*, 56 U.S. at 119. Limiting patentees to narrow applications they have actually developed and reduced to practice would be in keeping with *Mayo*'s commandment that "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." *Mayo*, 132 S. Ct. at 1300 (emphasis added).

This proposed approach, limiting the scope of patents based on new discoveries to narrow claims covering applications actually reduced to practice, would allow the inventor to enjoy an exclusive right to what he himself has invented and put into practice, but not to prevent new applications of the natural law by others.[5] This would ensure that the scope of the

---

5 It has been suggested that the requirements of enablement and written description will guard against the dangers of overclaiming a law of nature. Those doctrines, important as they are, generally require only that one or a handful of representative embodiments be described by the patentee. See, e.g., Donald S. Chisum, Chisum on Patents, § 7.03 at 7-15 (2015) ("An enabling disclosure is all that is required [for enablement]. The applicant need not describe actual embodiments or examples. Indeed, an applicant need not have reduced the invention to practice prior to filing."); Id. § 7.04[1][e] at 7-309–7-310.1 ("In Ariad Pharmaceuticals, Inc. v. Eli Lilly & Co. (2010), the Federal Circuit, sitting en banc, reaffirmed that written description of the invention is a requirement distinct from enablement . . . . [The court] declined to set forth 'bright-line rules,' including rules on the number of species needed to support a generic claim.") (citing and quoting Ariad, 598 F.3d at 1351–52). Therefore, the doctrines of enablement and written description would not entirely prevent claims that preempt future applications of the law of nature by others.

patent claims would not "foreclose[] more future invention than the underlying discovery could reasonably justify." *Id.* at 1301. Limiting the scope of the patent also would avoid the problem that "the more abstractly [a process patent's] claims are stated, the more difficult it is to determine precisely what they cover." *Mayo*, 132 S. Ct. at 1302 (quoting Christina Bohannan & Herbert Hovenkamp, *Creation without Restraint: Promoting Liberty and Rivalry in Innovation* 112 (2012)).

To be sure, determination of whether a claim applying a new law of nature is overbroad could present difficulties of definition and line drawing. But allowing narrow claims that have been actually reduced to practice when those claims embody an inventive, newly discovered law of nature would promote the fundamental policies underlying § 101. Requiring narrow claims and actual reduction to practice would be a reasonable accommodation in return for a more permissive inventive concept requirement. The approach would, I think, ensure that only diagnostic and therapeutic method patents limited in their claim scope would survive. These patents would provide the world with disclosure and useful applications of previously unknown natural laws, and the opportunity to obtain such patents would help to restore the incentive to make those discoveries that the patent system has historically provided.

IV

To be clear, I do not suggest that *Mayo* was incorrectly decided on its particular facts. The claims

at issue in *Mayo* contributed only routine application to a law of nature that was already well known. "At the time the discoveries embodied in the patents were made, scientists *already understood* that the levels in a patient's blood of certain metabolites, including, in particular, [the individual metabolites measured in the claimed methods], were correlated with the likelihood that a particular dosage of a thiopurine drug could cause harm or prove ineffective." 132 S. Ct. at 1295 (emphasis added). While "those in the field did not know the precise correlations between metabolite levels and likely harm or ineffectiveness," *id.*, "scientists *routinely* measured metabolites as part of their investigations into the relationships between metabolite levels and efficacy and toxicity of thiopurine compounds," *id.* at 1298 (emphasis added). In *Mayo*, the application of the natural law was merely routine optimization of drug dosage to maximize therapeutic effect.[6] As discussed above, *Mayo* thus forms part of a long line of Supreme Court decisions

---

6 Cf. Pfizer, Inc., v. Apotex, Inc., 480 F.3d 1348, 1368 (Fed. Cir. 2007) ("[D]iscovery of an optimum value of a variable in a known process is usually obvious."); In re Geisler, 116 F.3d 1465, 1470 (Fed. Cir. 1997) (noting that generally, in the context of obviousness, "it is not inventive to discover the optimum or workable ranges by routine experimentation") (quoting In re Aller, 220 F.2d 454, 456 (CCPA 1955)).

invalidating patent claims to conventional applications of well-known laws of nature.

V

Finally, it seems to me that the approach I suggest would not change the result in this case. Sequenom's challenged claims embody a newly discovered natural phenomenon, the presence of paternally inherited cell-free fetal DNA (cffDNA) in a mother's bloodstream. Judge Linn's concurrence notes that "the amplification and detection of cffDNA had never before been done." *Ariosa*, 788 F.3d at 1381 (Linn, J., concurring). But the major defect is not that the claims lack inventive concept but rather that they are overbroad. *See Mayo*, 132 S. Ct. at 1294.

For example, claim 1 of the '540 patent broadly covers any method of detecting paternally inherited cffDNA from maternal serum or plasma via amplification and detection of that cffDNA. '540 patent, col. 23, ll. 61–67. Even the somewhat narrower claim 21 of the '540 patent, which recites a method of performing a prenatal diagnosis based on the presence, quantity, or sequence of paternally inherited cffDNA detected by the method of claim 1, still broadly encompasses *any* diagnosis of *any* disease, disorder, or condition. '540 patent, col. 26, ll. 4–14. Such claims appear to be impermissible attempts to capture the entire natural phenomenon of cffDNA rather than any particular applications thereof developed and actually reduced to practice by the inventors.

A future case is likely to present a patent claim where the inventive concept resides in a newly discovered law of nature or natural phenomenon, but

the claim is narrowly drawn and actually reduced to practice. That case will, I hope, provide the Supreme Court with an opportunity to revisit the *Mayo/Alice* framework in this one limited aspect.

United States Court of Appeals
for the Federal Circuit.

ARIOSA DIAGNOSTICS, INC., NATERA, INC.,

Plaintiffs-Appellees

DNA DIAGNOSTICS CENTER, INC.,

Counterclaim Defendant-Appellee

v.

SEQUENOM, INC., SEQUENOM CENTER FOR MOLECULAR MEDICINE, LLC,

Defendants-Appellants

ISIS INNOVATION LIMITED,

Defendant

2014-1139, 2014-1144

Appeals from the United States District Court fo the Northern District of California in Nos. 3:11-cv-06391-SI, 3:12-cv-00132-SI, Judge Susan Y. Illston.

NEWMAN, *Circuit Judge*, dissenting from denial of the petition for rehearing en banc.

I agree with my colleagues that this case is wrongly decided. However, I do not share their view that this incorrect decision is required by Supreme Court precedent. The facts of this case diverge significantly from the facts and rulings in *Mayo*

Collaborative Services v. Prometheus Laboratories, Inc., 132 S. Ct. 1289 (2012), and in *Association for Molecular Pathology v. Myriad Genetics*, 133 S. Ct. 2107 (2013).

In *Mayo,* both the medicinal product and its metabolites were previously known, leaving sparse room for innovative advance in using this information as a diagnostic dosage tool. Nonetheless, the Court recognized the principle that patent eligibility is not disabled when science is put to practical use, stating that "a new way of using an existing drug" is patent-eligible under Section 101. 132 S. Ct. at 1302.

Whether or not *Mayo* drew an appropriate line in that case, particularly in view of the specificity of the diagnostic method that was developed, this decision does not require the drawing of a different line on quite different facts. In the case now before us, the claimed method was not previously known, nor the diagnostic knowledge and benefit implemented by the method.

Similar caveats accompanied the Court's decision in *Association for Molecular Pathology v. Myriad Genetics*, with the Court stating that "this case does not involve patents on new *applications* of knowledge about the BRCA1 and BRCA2 genes." 133 S. Ct. at 2120 (emphasis original). The Court further explained its holding, stating that: "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." *Id.*

In the case at bar, the inventors are not claiming the scientific fact of the discovery of paternal DNA in

the blood of a pregnant woman; they are claiming the discovery and development of a new diagnostic method of using this information. As the panel recognized, this is a "breakthrough," for this information can now be learned not only earlier in the gestation period than was previously available, but without the risks of the previously required invasive procedures of penetrating the amniotic sac.

Precedent does not require that all discoveries of natural phenomena or their application in new ways or for new uses are ineligible for patenting; the Court has cautioned against such generalizations. Such caution takes hold for the case at bar. The new diagnostic method here is novel and unforeseen, and is of profound public benefit—"a significant contribution to the medical field," Panel Maj. Op. at 16—a "breakthrough," Panel Conc. Op. at 5. The panel's decision to withhold access to patenting, now endorsed by the en banc court's refusal to rehear the case, is devoid of support.

Nor does patenting of this new diagnostic method preempt further study of this science, nor the development of additional applications. Patenting does, however, facilitate the public benefit of provision of this method through medical diagnostic commerce, rather than remaining a laboratory curiosity.

This subject matter is not ineligible under Section 101, but warrants standard legal analysis for compliance with the requirements of patentability, that is, novelty, unobviousness, specificity of written description, enablement, etc., and whether the claims are appropriately limited, as discussed many years ago

in *O'Reilly v. Morse*, 56 U.S. 62, 112 (1853) ("We perceive no well-founded objection to the description which is given of the whole invention and its separate parts, nor to his right to a patent for the first seven inventions set forth in the specification of his claims.").

I respectfully dissent from my colleagues' conclusion that Supreme Court precedent on Section 101 excludes this invention from eligibility for patenting. The subject matter should be reviewed for compliance with Sections 102, 103, and 112, and any other relevant provisions of the patent law.