No. 15-1182

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

BRIEF FOR *AMICI CURIAE* WISCONSIN ALUMNI RESEARCH FOUNDATION, INDIANA UNIVERSITY RESEARCH AND TECHNOLOGY CORPORATION, AND SAN DIEGO INTELLECTUAL PROPERTY LAW ASSOCIATION IN SUPPORT OF PETITIONER

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IDENTITY AND INTEREST OF THE *AMICI CURIAE*[1]

The Wisconsin Alumni Research Foundation ("WARF"), Indiana University Research and Technology Corporation ("IURTC"), and San Diego Intellectual Property Law Association ("SDIPLA") (hereafter collectively, "*amici*") submit this brief in support of Petitioner.

WARF is a non-profit organization supporting and promoting scientific research at the University of Wisconsin-Madison by patenting, licensing, and commercializing inventions and discoveries by university researchers and scientists. IURTC is a non-profit organization that assists Indiana University researchers and scientists in protecting and commercializing university based research. WARF and IURTC function to protect research-based innovations, and to support, aid and encourage research by protecting its discoveries and licensing them to commercial partners for beneficial use in the real world.

SDIPLA is an association of corporate, university, government and private attorneys that practice in all areas of intellectual property law in and around the San Diego region. SDIPLA is interested in the advancement of intellectual property laws that

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[1] The parties have consented to the filing of this brief. No counsel for a party authored this brief in whole or in part, and no such counsel or party made a monetary contribution intended to fund the preparation of submission of this brief. No persons other than *amici curiae* or their counsel made a monetary contribution to its preparation or submission. Counsel for each of the parties received timely notice of the intent to file this brief.

provide reasonable certainty and clarity for member patent stakeholders.

The *amici* are concerned with the far reaching effect of the Federal Circuit's decision on the diagnostic industry and related research efforts. The court incorrectly focused on conventionality of certain techniques used in the underlying invention, and overlooked the novel application of those techniques. Absent review by this Court, the Federal Circuit's decision will leave an uncertain and inconsistent basis for determining patent eligible subject matter when inventive applications involve a novel and practical application of natural phenomena, laws of nature, or abstract ideas. The result will upend the advancement of new and useful diagnostic tools and methods, and may stall the progression of scientific discovery through inevitable uncertainty over patent eligibility.

The participants of this brief have no stake in this litigation or the specific outcome, other than an interest in seeking a correct and consistent interpretation of the laws involved in this case.

SUMMARY OF ARGUMENT

The Federal Circuit's decision below is erroneous for three principal reasons.

First, the Federal Circuit misconstrued the meaning of the term "conventional" used in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S. Ct. 1289 (2012). In *Mayo*, the Court reviewed the patent eligibility of claims reciting a method of optimizing therapeutic efficiency comprising "administering" a drug providing 6-thioguanine (6-TG) to a subject, and "determining" the level of 6-TG in the subject. Both of these steps

were known in the prior art. The point of novelty lay in a "wherein" clause that set forth a correlation between levels of 6-TG in a subject and need to increase or decrease the amount of drug subsequently administered. The Court held that the claims were not statutory because, other than the correlation, which is a law of nature, the method only involved well-understood, routine, *conventional activity previously engaged by the scientific community*. As such, the claimed method steps were "conventional," i.e., already known in the prior art. The Court expressly declined to decide whether "*less* conventional" steps would have led to a different result. *See Mayo*, 132 S. Ct. at 1302.

Unlike *Mayo*, this case involves claims that recite *unconventional* steps. Prior to the invention, researchers separated blood samples from pregnant women into cellular and non-cellular fractions, and discarded the non-cellular portion. The present inventors, however, surprisingly discovered that fetal DNA was contained in the cell-free maternal serum and plasma, and applied known amplification and detection techniques to a subset of this DNA (i.e., paternally inherited DNA). Since the presence of cell-free fetal DNA in maternal serum and plasma was unknown, it was not "conventional" to amplify and detect such DNA. Accordingly, in stark contrast to *Mayo, none* of the instantly claimed method steps had ever been performed, let alone suggested by the prior art.

The Federal Circuit, relying on *Mayo*, held that the claims were non-statutory because methods of "amplifying" and "detecting" DNA were known in the art and thus conventional. The court is wrong. The proper inquiry under *Mayo* is whether the

specifically claimed steps—amplifying and detecting a *paternally inherited* nucleic acid *from maternal serum or plasma*—were conventional. They were not. Indeed, while the general techniques of amplifying and detecting DNA were known in the art, there is no dispute that such techniques had never been applied to paternally inherited nucleic acids from maternal serum or plasma. In fact, the court agreed that the inventors "combined and utilized man-made tools of biotechnology *in a new way* that revolutionized prenatal care." *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1379 (Fed. Cir. 2015) (emphasis added). Accordingly, the Federal Circuit erred by improperly expanding *Mayo*'s definition of "conventional" to encompass novel, i.e., unconventional, steps.

Second, the Federal Circuit ignored the Court's precedent that the application of an obvious and well-known natural phenomenon to solve a problem, whose root cause was unknown, is a "new and useful" discovery deserving patent protection. In *Eibel Process Co. v. Minn. & Ontario Paper Co.*, 261 U.S. 45 (1923), the Court reviewed the patent eligibility of paper making machines that used gravity to increase the flow of paper stock. Eibel discovered that existing paper machines produced defective paper because the paper stock and wire traveled at different speeds in the prior art machines. To solve this problem, Eibel simply increased the pitch of the wire so that, through gravity, the paper stock traveled at a faster speed corresponding to the wire's speed. The Court of Appeals ruled against Eibel, holding that the invention was no more than a combination of the prior art and the "obvious" application of a natural

principle. *Id.* at 52. The issue presented by this Court was "whether Eibel's discovery was invention rather than the mere obvious and simple application of known natural forces." *Id.* at 62. The Court held that "[t]he invention was not the mere use of a high or substantial pitch to remedy a known source of trouble," but rather "the discovery of the source not before known, and the application of the remedy, for which Eibel was entitled to be rewarded in his patent." *Id.* at 68.

Similarly here, the invention is not merely the amplification and detection of a "known source" of fetal DNA. Rather, it is "the discovery of the source not before known," i.e., maternal plasma and serum containing paternally inherited DNA, and "the application of the remedy," for which the inventors are entitled to a patent. *Id.* at 68. The inventors surprisingly discovered that fetal DNA was present in maternal plasma and serum—previously discarded as medical waste—and applied known techniques to the newly identified DNA. While it may have been obvious to perform these techniques once *cell-free fetal DNA was discovered*, *Eibel* confirms that the solution to an unknown problem is patent eligible even if the technique used in the solution was well known. Accordingly, under *Eibel*, the instant claims are statutory.

Third, the Federal Circuit erred in failing to conduct a meaningful preemption analysis. This Court has made clear that preemption is "the concern that drives" the exclusion of natural phenomena from patent eligibility. *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2354 (2014). The Federal Circuit concluded that any such "concerns" are moot because the claims failed the

two-part *Mayo* test. The court is wrong. The claims do not merely recite the natural phenomena of cell-free fetal nucleic acids, or a general application of the phenomena. Rather, the claims are limited to methods that, at a minimum, amplify a *paternally inherited* nucleic acid from maternal serum or plasma. To perform this step, one must first identify paternal nucleic acids by, for example, genotyping the father and mother, selecting a mutation or allele present in the father but absent in the mother, and preparing primers for amplifying the selected mutation or allele. *See* U.S. Patent No. 6,258,540 ("'540 patent") at 3:6–24. As such, the claimed steps limit the invention to a practical application of the discovery and necessarily excludes the possibility of preempting the whole field. Accordingly, because the claims amount to "more than a drafting effort designed to monopolize the [natural phenomena]," the claims are patent eligible. *See Mayo*, 132 S. Ct. at 1297.

In sum, the Federal Circuit misapplied and ignored this Court's precedent by expanding the ineligibility doctrine to encompass unconventional methods. In doing so, it has unnecessarily excluded from patent protection a practical application of an important discovery, and threatens to eviscerate protection for other novel and potentially lifesaving applications of newly discovered scientific principles. Here, the invention provides physicians with the ability to diagnose fetal DNA using non-invasive techniques—a goal long sought by the scientific community. Tomorrow, it may be the discovery of a marker that enables early detection and treatment for a rare cancer. Without reasonable certainty of patent protection, biotechnology companies and

research universities have little incentive to continue their valuable research. The Federal Circuit's overly broad and inconsistent approach with this Court's precedent, if left unchanged, will have a chilling effect on research and adversely affect the current and future state of healthcare in this country.

Accordingly, the Court should take this opportunity to (1) address the issue left unresolved by *Mayo*—whether claims that recite the application of "*less* conventional" and/or "unconventional" steps to a natural phenomenon or law of nature are patent eligible; (2) reaffirm the principle in *Eibel* that the application of an obvious step to an unknown problem is patent eligible; and/or (3) clarify the relationship between *Mayo*'s two-step test and preemption.

ARGUMENT

I. THE FEDERAL CIRCUIT MISINTERPRETED THIS COURT'S PRECEDENT.

In *Mayo*, the Court held that a claim reciting "conventional" steps—steps already performed in the prior art—and a law of nature or natural phenomenon, is patent ineligible. The Federal Circuit misconstrued and misapplied the meaning of the term "conventional." The court analyzed whether the underlying invention uses a conventional technique rather than whether the claimed steps themselves were known in the prior art. As a result, the Federal Circuit has expanded the scope of patent ineligible subject matter far beyond what the Court contemplated in *Mayo*.

A. "Conventional" activities are "steps" that have already been performed in the prior art.

In *Mayo*, the Court set forth a two-step framework for analyzing claims involving patent ineligible concepts, such as natural phenomena. *See Mayo*, 132 S. Ct. at 1296–97. First, a court must determine whether the claims are directed to a patent ineligible concept. *Id*. at 1297. If so, then a court must consider the claim elements individually and "as an ordered combination" and determine whether the additional elements "transform the nature of the claim" into a patent-eligible application. *Id*. at 1298. The second step of this analysis is 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*.

The *Mayo* Court considered the patent eligibility of a method of optimizing therapeutic efficiency. The method recited the steps of "administering" a drug that provides 6-TG to a subject, and "determining" the level of 6-TG in the subject. The claim concluded with "wherein" clauses providing that certain levels of 6-TG indicated the need to increase or decrease the amount of drug subsequently administered. The "wherein" clauses set forth laws of nature—i.e., relationships between concentrations of 6-TG and the likelihood that a dosage of a thiopurine drug would be ineffective or cause harm. *Id*. at 1296. Accordingly, the Court considered whether the claims added "significantly more" than the law of nature.

The Court explained that the "administering" step had been performed "long before anyone asserted these claims." *Mayo*, 132 S. Ct. at 1297. Likewise, "scientists routinely measured" thiopurine metabolites, such as 6-TG, and thus the "determining" step "tells doctors to engage in well-understood, routine, conventional activity *previously engaged* in by scientists who work in the field." *Id*. at 1298 (emphasis added). Moreover, "scientists *already* understood" that levels of 6-TG 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*. at 1295 (emphasis added). Accordingly, the *only* novel aspects of the claims were the precise correlations.

The Court held that the claims were invalid because, other than the natural law, the method steps had already been performed in the prior art. *See, e.g.*, *Mayo*, 132 S. Ct. at 1294 ("[T]he *steps* in the claimed processes (apart from the natural laws themselves) involve well-understood, routine, conventional activity *previously engaged* in by researchers in the field." (emphasis added)); *id*. at 1298 (the "*steps* consist of well-understood, routine, conventional activity *already engaged* by the scientific community" (emphasis added)); *id*. at 1299–300 ("These instructions 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 1305 ("the patent claims at issue here effectively claim the underlying laws of nature themselves.").

The Court relied on its precedent to reinforce its decision. In *Diamond v. Diehr*, 450 U.S. 175 (1981), the Court held that a method for molding raw,

uncured rubber into cured, molded rubber using a known mathematical equation was patent eligible because of the manner in which the equation was integrated into the process as a whole. *Id*. at 192. "Nowhere" did the *Diehr* court suggest that "all of these steps, or at least the combination of those steps were in context obvious, *already in use*, or *purely conventional*." *Mayo*, 132 S. Ct. at 1299 (emphasis added).

On the other hand, in *Parker v. Flook*, 437 U.S. 584, 585–86, 588 (1978), the Court held that a method of updating alarm limits using a mathematical formula was not patent eligible because the "only difference" between the prior art methods and the claimed method was the mathematical formula, i.e., a law of nature. *Id*. at 586 (concluding that, other than the formula, the claimed steps were "well known"). Accordingly, the Court's precedent, relied on in *Mayo*, confirms that when a method claim recites conventional steps—i.e., steps already performed in the prior art—and the only novel aspect of the claim is a law of nature or natural phenomenon, the claimed method is patent ineligible.[2]

B. None of the claimed steps had ever been performed and thus are not "conventional."

Prior to the '540 patent, "[c]onventional prenatal screening methods" for detecting fetal abnormalities,

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[2] The Court's post-*Mayo* precedent is consistent with this principle. *See Alice*, 134 S. Ct. at 2359 ("[A]ll of these computer functions are 'well understood, routine, conventional activities' *previously known to the industry*." (emphasis added)).

such as amniocentesis, presented "a degree of risk to the mother and to the pregnancy." '540 patent at 1:12–17. As such, researchers sought non-invasive methods for prenatal diagnoses, including analyzing the *cellular* portion of a maternal blood sample for fetal DNA. *Id*. at 1:26–36. These methods proved ineffective. *Id*. at 9:10–14.

The inventors of the '540 patent surprisingly and unexpectedly discovered that fetal DNA is found in maternal serum or plasma—the *non*-cellular portion of a maternal blood sample that was "routinely discarded" by investigators studying fetal cells in maternal blood. *Id*. at 1:50–55. With this newfound knowledge, the inventors developed a method of amplifying and detecting *paternally inherited* nucleic acids of fetal origin, i.e., fetal DNA inherited from the father and not shared by the mother. For example, the '540 patent explains that, in order to amplify paternally inherited nucleic acids, one can genotype the father and mother, select a mutation or allele present in the father but absent in the mother, and prepare primers for amplifying the selected mutation or allele. *See* '540 patent at 3:6–24. Accordingly, the '540 patent claims are directed to non-invasive, diagnostic methods that amplify and detect a subset of cell-free fetal DNA—paternally inherited nucleic acids.

The Federal Circuit cited the *Mayo* two-part test in analyzing the claims. The court determined that the existence of cell-free fetal DNA in maternal blood is a natural phenomenon, and moved to the second step of the inquiry. The court concluded that "[b]ecause the method *steps* were well-understood, conventional and routine, the method of detecting paternally inherited cffDNA is not new and useful."

Ariosa, 788 F. 3d at 1377 (emphasis added).

The court is wrong. While amplifying and detecting DNA were generally known techniques, the *claimed* "amplifying" and "detecting" steps had *never* been performed, let alone contemplated in the prior art. *See, e.g.*, *Ariosa*, 788 F.3d at 1379 (court agreeing that the method "combined and utilized man-made tools of biotechnology *in a new way* that revolutionized prenatal care." (emphasis added)); *id*. at 1381 (Linn, J., concurring) ("*[N]o one* was amplifying and detecting paternally-inherited cffDNA using the plasma or serum of pregnant mothers."); *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, Nos. 2014-1139, 2014-1144, slip op. at 6 (Fed. Cir. Dec. 2, 2015) (denying en banc review) (Lourie & Moore, JJ., concurring) ("[I]t is undisputed that before this invention, the *amplification and detection of cffDNA* from maternal blood . . . *were not routine and conventional*." (emphasis added)); *id*. at 2 (Newman, J., dissenting) ("*the claimed method was not previously known*" (emphasis added)). Accordingly, because the claimed *steps* were not "well-understood, routine, conventional activity *previously engaged* in by researchers in the field," the claims satisfy the second part of the *Mayo* test. *Mayo*, 132 S. Ct. at 1294 (emphasis added).

The Federal Circuit erred in applying *Mayo*. In *Mayo*, the Court concluded that the claimed methods were patent ineligible because all of the claimed steps were known in the prior art and the only novel aspect was a law of nature. As such, the proper inquiry under *Mayo* is whether amplifying and detecting a *paternally inherited* nucleic acid *from maternal serum or plasma* was conventional, i.e., "previously engaged in" by skilled artisans. Instead,

the court considered whether the *techniques* used in the claimed methods were conventional. For example, the court relied on the '540 patent specification and the prosecution history to conclude that amplification and detection of DNA, in general, was "well-understood, routine, and conventional." *Ariosa*, 788 F.3d at 1377–78. There is no dispute that these general methods were well known at the time of the invention. The issue is whether these techniques had been applied in a new and useful manner. The court acknowledged that the claimed methods "combined and utilized man-made tools of biotechnology *in a new way* that revolutionized prenatal care," but nonetheless concluded that "the method steps" were conventional. This conclusion is wrong and inconsistent with *Mayo*. *See Mayo*, 132 S. Ct. at 1302 ("a new way of using an existing drug" is patent eligible).[3]

The compelling need for this Court's review has become more urgent because the Federal Circuit continues to misapply *Mayo*. In *Genetic Technologies Ltd. v. Merial L.L.C.*, the court invalidated a claim for detecting genetic variations that includes a step of amplifying *non*-coding DNA genetically linked with coding DNA. Nos. 2015-1202, 2015-1203, 2016 WL 1393573, at *10 (Fed. Cir. Apr. 8, 2016). Non-coding DNA, referred to as "junk DNA," historically "appeared to serve no function." *Id*. at *1. The inventor, however, "discovered that

[3] *See also Ass'n for Molecular Pathology v. Myriad*, 133 S. Ct. 2107, 2120 (2013) ("Judge Bryson aptly noted 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.'").

certain DNA sequences in coding regions (exons) of certain genes are correlated with non-coding regions (introns)," and can be used to diagnose genetic diseases, such as cystic fibrosis. *Id*. at *1, *4. The court acknowledged that "no one was 'using the non-coding sequence as a surrogate marker for the coding region allele,'" and that the U.S. Patent & Trademark Office found the claims "novel." *Id*. at *10. The court, citing *Mayo,* concluded that the claims were patent ineligible, in part because the general technique of amplifying DNA was known. *Id*. at *9–10. Accordingly, like the instant case, the court disregarded the fact that the *claimed* step of amplifying specific genetic material had never been performed in the prior art.

In sum, the Federal Circuit has and continues to misapply *Mayo*. The court's analysis improperly focuses on whether a conventional technique is used in a claimed method involving a natural phenomenon or law, and not whether the method steps themselves are conventional. Taken to its logical end, the Federal Circuit is on course to invalidate *any* method that applies a conventional technique to a newly discovered natural phenomenon or law even when the method steps are novel. This Court has correctly observed that "all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas," and thus the Federal Circuit's decision extends far beyond, and is inconsistent with, this Court's precedent. *Mayo*, 132 S. Ct. at 1293. In addition, the court's decision will prove detrimental to the biotechnology industry and research universities. For example, diagnostic methods typically apply a conventional technique to

a natural phenomenon and are directly impacted by the Federal Circuit's recent jurisprudence. The court's current approach effectively denies patent protection for all diagnostic inventions, and, as a result, will lead to reduced investment in valuable, lifesaving research. Accordingly, the Federal Circuit misapplied this Court's precedent and, if left unchecked, the court will continue to invalidate vitally important inventions.

II. THE FEDERAL CIRCUIT IGNORED THIS COURT'S PRECEDENT.

This Court has held that a claim is patent eligible when an inventor discovers the source of a problem, and solves the problem using an obvious method. The Federal Circuit acknowledges that the inventors were the first to discover cell-free fetal DNA from maternal plasma or serum, but nonetheless concludes that amplifying and detecting this unknown DNA would have been routine, well-understood, and conventional. The court's rationale is inconsistent with, and ignores, this Court's precedent.

In *Eibel Process Co. v. Minn. & Ontario Paper Co.*, 261 U.S. 45 (1923), the Court considered whether the application of gravity, i.e., a natural phenomenon, to a known paper making machine was patent eligible. The "Fourdrinier" paper making machine introduces paper stock onto a wire (or screen) that moves continuously. Before Eibel's invention, it was known that moving the wire at high speeds resulted in defective paper. Eibel discovered that the paper stock moved more slowly than the wire and caused ripples in the paper stock. Once he identified the cause of the problem, he

simply increased the pitch (or angle) of the wire such that the paper stock moved faster by gravity. Eibel's invention revolutionized the paper making industry by enabling faster production of paper. *See Eibel*, 261 U.S. at 55 (Eibel's invention "surprised and startled the paper-making trade"; "[i]t spread . . . like wildfire."); *id.* at 68 ("[A]ll adopted his remedy . . . .").

The Court of Appeals invalidated Eibel's patent, concluding that "[t]he prior art and the obvious application of the principle that water will run downhill" "robbed it of novelty or discovery." *Id.* at 52. The Supreme Court granted certiorari and considered "whether Eibel's discovery was invention rather than the mere obvious and simple application of known natural forces." *Id.* at 62.

The Court held that "[t]he invention was not the mere use of a high or substantial pitch to remedy a known source of trouble," but rather "the discovery of the source not before known, and the application of the remedy, for which Eibel was entitled to be rewarded in his patent." *Id.* at 68. The Court acknowledged that Eibel's solution was "obvious" once the problem had been identified, and thus Eibel would not have been entitled to a patent had the prior art identified the cause of the problem. *Id.* at 56, 68. However, since no one had discovered that the paper stock moved slower than the wire nor applied Eibel's solution, what Eibel "saw and did was not obvious, and did involve discovery and invention." *Id.* at 56; *see also id.* ("what he discovered and invented was new and useful"); *id.* at 63 ("Eibel made a very useful discovery, which has substantially advanced the art."). Accordingly, *Eibel* stands for the proposition that the application of an

obvious step to solve a problem, the cause of which was previously unknown, is patent eligible.

In this case, it is undisputed that the inventors discovered cell-free fetal DNA in maternal plasma and serum—material that was "routinely discarded" by researchers. *See Ariosa*, 788 F.3d at 1376, 1380–81. Following their discovery, the inventors employed known techniques to amplify and detect this previously unknown DNA. Had the existence of cell-free fetal DNA been known before the invention, it is doubtful that the amplification and detection of the DNA would be patentable. *Accord Eibel*, 261 U.S. at 68. However, since no one had discovered cell-free fetal DNA in maternal plasma or serum, nor amplified and detected this DNA, what the inventors "did was not obvious, and involved discovery and invention." *Id*. at 56; *see also Ariosa*, 788 F.3d at 1379 (court agreeing that the inventors "combined and utilized man-made tools of biotechnology in a new way that revolutionized prenatal care"); *id* at 1381 (describing discovery as "groundbreaking" and "a paradigm shift in noninvasive prenatal diagnosis"). Accordingly, under *Eibel*, the claims at issue are patent eligible.

The claims in *Eibel* and the present claims both involve a natural phenomenon combined with novel method steps. Although *Eibel* combined a natural phenomenon with a known process, whereas the instant invention combines a novel application of known techniques with a natural phenomenon, the principle is the same: combining a natural phenomenon and known techniques *in a novel process* is patent eligible.

The Federal Circuit acknowledges "the discovery

of the presence of cffDNA in maternal plasma or serum" was "new and useful," but held that "the method of detecting paternally inherited cffDNA is not new and useful" because it used conventional techniques. *Ariosa*, 788 F.3d at 1377. This presents a simple question: if the discovery of cffDNA in maternal plasma or serum is "new and useful," then how can a method that amplifies and detects paternally inherited cffDNA—steps never performed in the prior art—*not* be "new and useful"? The Federal Circuit does not answer this question. *Eibel* does. Indeed, *Eibel* makes clear that when a natural phenomenon is used in conjunction with an established process, the resultant process is patent eligible if it solves a problem, the cause of which was unknown or misunderstood. Accordingly, the Federal Circuit ignored this Court's precedent, and, as a result, incorrectly held that the claims are not patent eligible.

The Federal Circuit's decision is also inconsistent with its own precedent. For example, in *In re Sponnoble*, 405 F.2d 578, 585 (C.C.P.A. 1969), the court considered the patentability of an improved center seal plug that prevented water transmission between two compartments in a vial. Sponnoble discovered the cause of the moisture transmission was the passage of moisture *through*, rather than around, the center plug. *Id.* at 586. The court framed the issue as "whether the prior art recognized the *cause* of the problem," and concluded that "[t]here is no teaching in the prior art which would suggest the necessity of selecting a center seal plug material which is more impervious to *liquid* water." *Id.* In reaching its decision, the court explained that "[i]t should not be necessary for this

court to point out that a patentable invention may lie in the discovery of the source of a problem even though the remedy may be obvious once the source of the problem is identified." *Id*. at 585.

The court was correct then and wrong now. In the instant case, researchers had investigated the possibility of using fetal cells in maternal blood for determination of fetal RhD status. *See* '540 patent at 9:8–17. The "main problem" of this approach was, due to extremely low concentrations of fetal DNA in cells, these methods resulted in false-positives and false-negatives. *Id*. The inventors discovered that the concentration of fetal DNA in maternal plasma and serum was significantly higher than in fetal cells and thus offered "a new approach for non-invasive prenatal diagnosis." *Id*. at 9:18–20. As such, the inventors discovered the source of the problem—fetal DNA was more concentrated in maternal plasma and serum and not in cellular fractions—and proposed a solution using known techniques. Accordingly, under *Sponnoble*, the instant claims are patent eligible.

III. THE FEDERAL CIRCUIT FAILED TO PROPERLY CONSIDER PREEMPTION.

A natural phenomenon is a "building block" of technology and excluded from patent eligibility. *See Mayo*, 132 S. Ct at 1303; *Alice*, 134 S. Ct. at 2354. This Court has explained that preemption is "the concern that drives" the exclusion of natural phenomena from patent eligibility. *Alice*, 134 S. Ct. at 2354; *see also Mayo*, 132 S. Ct. at 1301 ("The Court has repeatedly emphasized . . . a concern that patent law not inhibit further discovery by improperly tying up the future use of these building

blocks of human ingenuity.") (citation omitted). For example, a claim that states a natural phenomenon and simply adds the words "apply it" is "not enough for patent eligibility." *Alice*, 134 S. Ct. at 2358. Accordingly, a court must analyze the claim language to determine whether the breadth of the claims subsumes all possible uses of the natural phenomena. *See Mayo*, 132 S. Ct. at 1302 (concluding that the "determining" step covered "all processes that make use of the correlations").

In this case, the Federal Circuit did not conduct a preemption analysis. Rather, the court simply concluded that "preemption concerns are fully addressed and made moot" by the *Mayo* two-part test. *Ariosa*, 788 F.3d at 1379. But *Mayo* itself suggests that a preemption analysis follows or, at a minimum, is an independent aspect of the two-part test. Indeed, *after* analyzing the claims using its two-step framework, the *Mayo* Court addressed preemption concerns. The Court considered the law of nature implicated by the claims and the scope of the claimed steps, concluding that "the patent claims do not confine their reach to particular applications of those laws." *Mayo*, 132 S. Ct. at 1302. The Court contrasted the claims with a "typical" patent on "a new way of using an existing drug," which is patent eligible, and found that the claims "tie[d] up too much future use of laws of nature." *Id*. Accordingly, by simply dismissing the issue of preemption as "moot," the Federal Circuit erred by failing to properly complete or augment the *Mayo* two-part analysis.

Had the Federal Circuit carried out a proper preemption analysis, it would have confirmed that the claims at issue are patent eligible. The claims

recite methods that comprise amplifying a *paternally inherited* nucleic acid *from a maternal serum or plasma* sample from a pregnant female, and detecting the presence of a paternally inherited nucleic acid of fetal origin. Paternally inherited nucleic acids—i.e., genetic material distinguishable from maternally inherited nucleic acids—are a subset of cell-free fetal nucleic acids. Amplification of a paternally inherited nucleic acid requires nucleic acid primers that hybridize to a nucleic acid sequence indicative of the father. *See, e.g.*, '540 patent at 3:4–10 ("the paternal mutation can be used as an amplification target on maternal plasma and serum" to assess the risk that a fetus may be affected by disease); *id*. at 5:10–14 (describing the amplification of a Y sequence (DYS 14) using primers Y1.7 and Y1.8). For example, to determine whether a fetus is at risk for a paternally inherited genetic disease, the analysis would require "the prior genotyping of the father and mother using a panel of polymorphic markers," and selecting an allele for detection "present in the father, but is absent in the mother." *Id*. at 3:10–24. Accordingly, the claims are limited to amplifying a subset of specific cell-free nucleic acids and thus do not tie up the use of all cell-free nucleic acids.

The dependent claims of the '540 patent further confine the natural phenomena and their use. For example, several claims require that a specific sequence is detected. *See, e.g.*, '540 patent at claims 6 ("sequence is from the DYS14 locus"), 7 ("sequence is from the SRY gene"), 8 ("nucleic acid from a paternally-inherited non-Y chromosome is detected"), and 9 ("sequence is a blood group antigen gene"). Other claims recite specific conditions or

diseases are detected. *See, e.g.*, *id*. at claims 17 ("for detection of pre-eclampsia") and 18 ("for detection of a foetal chromosomal aneuploidy"). The Court has suggested that specific applications of natural phenomena, such as genetic material, may be patent eligible. *See Myriad*, 133 S. Ct. at 2120. Accordingly, the Court should consider whether such specific applications are patent eligible even beyond the eligibility of the process set forth in the independent claim.

In sum, the Federal Circuit failed to properly conduct the preemption analysis required by this Court. Had it done so, the court would have concluded that the claims do not tie up all future uses of cell-free fetal nucleic acids.

CONCLUSION

For the foregoing reasons, the Court should grant certiorari.

Respectfully submitted,

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Dated: April 20, 2016