No. 15-1182

IN THE

Supreme Court of the United States

SEQUENOM, INC.,

Petitioner,

v.

ARIOSA DIAGNOSTICS, INC., *et al.*,

Respondents.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

BRIEF FOR *AMICI CURIAE* BIOTECHNOLOGY INNOVATION ORGANIZATION, PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA AND THE ASSOCIATION OF UNIVERSITY TECHNOLOGY MANAGERS IN SUPPORT OF PETITION FOR A WRIT OF CERTIORARI

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STATEMENT OF INTEREST OF *AMICI CURIAE*

The **Biotechnology Innovation Organization** (BIO, formerly "Biotechnology Industry Organization") is the world's largest biotechnology trade association, with over 1,100 members worldwide involved in the research and development of innovative healthcare, agricultural, industrial, and environmental biotechnology products.

The **Pharmaceutical Research and Manufacturers of America** (PhRMA) is a voluntary, nonprofit association representing the nation's leading research-based pharmaceutical and biotechnology companies. PhRMA's mission is to advocate in support of public policies that encourage the discovery of life-saving and life-enhancing new medicines. A complete list of PhRMA members is available at http://www.phrma.org/about/member-companies.

The **Association of University Technology Managers** (AUTM) is a nonprofit organization dedicated to bringing research to life by supporting and enhancing the global academic technology transfer profession through education, professional development, partnering, and advocacy. AUTM's more than 3,200 members represent managers of intellectual property from more than 300 universities, research institutions, and teaching hospitals around the world, as well as numerous businesses and government organizations.

Amici have no direct stake in the result of this appeal.[1] This brief is solely the work of amici and amici's counsel;

1. No counsel for a party authored this brief in whole or in part, and no such counsel or party, nor any person or entity other than the amici curiae or its counsel, made a monetary contribution intended to fund the preparation or submission of this brief.

it reflects the consensus view of amici's members, but not necessarily the view of any individual member.[2]

SUMMARY OF THE ARGUMENT

Amici are concerned that the development and commercialization of life-improving biotechnologies will be impeded and the United States' premier status in this sector will be lost if this Court does not address the mounting uncertainty of patent-eligible subject matter. Biotechnology research and development is expensive and time consuming, and therefore relies heavily on the economic incentives afforded by patent protection. Absent such incentives, research findings may remain idle textbook curiosities, or may be concealed as trade secrets. Neither situation is healthy for innovation.

Biotechnology inventions fit the broad statutory definition in 35 U.S.C. §101 of patent-eligible subject matter, but courts are rapidly shrinking this definition through regular invocation of judicial exceptions. Copiers of today's technologies benefit, but the future innovation that drives U.S. economic growth loses.

Biotechnology research investigates the natural world, and biotechnology inventors develop practical applications–including new products and processes–based on what is learned. Invoking a judicial exception framework discerned from the Court's recent *Mayo* and *Alice* decisions, the United States Patent and Trademark Office ("Patent Office") and lower courts currently dissect

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2. Counsel of record received timely notice of the intent to file this brief under Supreme Court Rule 37. On March 28, 30, and 31, 2016, Petitioner and Respondents filed letters with the Clerk of the Court consenting to the filing of any and all *amicus curiae* briefs.

biotechnology inventions into ineligible laws/phenomena of nature reflecting the fruits of research and additional elements added by the inventor to create a practical application of the research. Even though the combined elements define a new and useful invention, the Patent Office and courts analyze these elements separately under the *Mayo/Alice* framework, ignore the laws/phenomena of nature, and label the other elements "routine and conventional." The inventions are held ineligible for patenting – even when the invention is a groundbreaking practical application that improves healthcare, like the invention at issue in this case.

This case affords an important opportunity for the Court to reaffirm the importance of the patent statute as an incentive for innovation and sharpen the contours of the judicial exception analysis, including this Court's requirement that claims be viewed as a whole. Numerous Federal Circuit judges praised the involved invention in this case–a non-invasive prenatal diagnostic–as patent-worthy, but saw no basis under this Court's recent decisions to evaluate the claims as a whole or sustain the patent's validity.

This case also presents an opportunity to discuss the interplay between the judicial exceptions analysis and the preemption concerns that underlie it. The patent claims at issue are directed to a process that uses human DNA and/or knowledge about it in a practical application, but does not claim the DNA itself. In its *Myriad* opinion, this Court suggested that new applications involving DNA may be patent-eligible. The invention in this proceeding is defined by process claims that require a series of laboratory actions. This case affords an opportunity for this Court to articulate the circumstances under which process claims can pre-empt DNA that occurs in nature.

That clearly was not the case here: the record shows several alternative sources of the same DNA, and even shows alternative methods for using the same DNA from the same source.

Amici urge the Court to grant review and invite briefing on these issues.

ARGUMENT

I. APPLICABLE LAW & BACKGROUND

A. The claimed invention

Petitioner Sequenom is the licensee under U.S. Patent No. 6,258,540 (the '540 patent) that describes and claims a novel application for human serum. Previously, doctors had used serum for transfusions and for countless "blood tests" to evaluate patients.

The inventors here revolutionized prenatal care by inventing another previously unknown and unrecognized use for serum: a method that enabled genetic testing of an unborn fetus without amniocentesis or other invasive surgical procedure, by amplifying (making synthetic copies of) paternally inherited *fetal* DNA (cell-free fetal DNA, or "cffDNA") that is present in minute quantities in serum from a pregnant woman, and then analyzing these copies. The '540 patent was obtained on that claimed genetic testing method and was licensed by the patentee to Petitioner Sequenom.

Several Federal Circuit judges concluded that the claimed method is precisely the type of meritorious invention that patents are designed to protect. Judges

Reyna and Wallach "agreed" with Sequenom that "the method reflects a significant human contribution in that [the inventors] combined and utilized man-made tools of biotechnology in a new way that revolutionized prenatal care."[3] Judge Linn characterized the invention as follows:

> It is hard to deny that Sequenom's invention is truly meritorious.... 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 ... 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.... [T]he '540 patent claims a new method that should be patent eligible.... The new use of the previously discarded maternal plasma to achieve such an advantageous result is deserving of patent protection.... I see no reason, in policy or statute, why this breakthrough invention should be deemed patent ineligible.[4]

Despite the judges' expressions of patent-worthiness, the Federal Circuit panel concluded that this Court's judicial exceptions to 35 U.S.C. §101 mandated invalidation of the '540 patent's process claims. The Federal Circuit

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3. *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1379 (Fed. Cir. 2015).

4. *Id.* at 1381 (Linn, J., concurring.)

subsequently denied *en banc* review.[5] Petition to this Court for review followed.

B. The patent statute

Pursuant to its constitutional authority,[6] Congress defined patent-eligible inventions in 35 U.S.C. §101: "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor," so long as other provisions of the patent statutes are met. "The term 'process' means process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material." 35 USC §100(b). As noted by this Court, "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*, 447 U. S. 303, 308 (1980).

Section 101 begins, "Whoever invents or discovers," and §100(a) similarly states, "The term 'invention' means invention or discovery." The inclusion of "discovers/discovery" in the statute reflects a deliberate expression by Congress that both "invents" and "discovers" are relevant to patent-eligibility analysis: an inventor's discovery is within and part of an eligible "invention."

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5. *Ariosa Diagnostics, Inc. v. Sequenom, Inc.,* 809 F.3d 1282 (Fed. Cir. 2015).

6. Constitution, Article I, Section 8, Clause 8.

C. Judicial exceptions to §101

This Court generally characterizes its role as limited to legislative interpretation. *See Marbury v. Madison*, 1 Cranch 137, 177, 2 L.Ed. 60 (1803). Nonetheless, the Court created three exceptions to §101: "The laws of nature, physical [or natural] phenomena, and abstract ideas have been held not patentable." *Chakrabarty*, 447 U.S. at 309 (1980) (citing decisions from 1853-1978).

This Court first addressed patent-eligibility of a biotechnology patent under §101 in *Chakrabarty*. Observing that "[t]he subject-matter provisions of the patent law have been cast in broad terms to fulfill the constitutional and statutory goal of promoting 'the Progress of Science and the useful Arts' with all that means for the social and economic benefits envisioned by Jefferson,"[7] the Court held that a genetically engineered bacterium was patent-eligible. In the ensuing 30 years, the Court did not invalidate any patents under its §101 judicial exceptions. During the same time, the United States became the undisputed world leader in biotechnology by virtually any measure.[8]

But beginning in 2010, the scope of patent-eligible subject matter has become one of the most frequently debated and litigated topics of substantive patent law, and a source of uncertainty for inventors, businesses, patent examiners, and courts.

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7. *Id.* at 315.

8. *See* Ernst & Young, "Biotechnology Industry Report 2015" at page 5 (http://www.ey.com/Publication/vwLUAssets/EY-beyond-borders-2015/$FILE/EY-beyond-borders-2015.pdf).

In *Bilski v. Kappos*, 561 U.S. 593 (2010), the Court deemed ineligible patent claims to a business method, and the Court rejected a relatively bright-line test, known as the "Machine-or-Transformation test," for distinguishing patent-eligible processes from ineligible judicial exceptions, explaining that "categorical rules that might have wide-ranging and unforeseen impacts," would impose limits on eligible processes not justifiable by the plain language of §101.[9]

Mayo Collaborative Services v. Prometheus Laboratories, 132 S. Ct. 1289 (2012), involved a medical process that entailed administering a thiopurine drug to a patient and measuring a drug metabolite in the patient's blood to indicate safety/efficacy of the drug dose. This Court concluded that Prometheus' claim *involved* a patent-ineligible "law of nature"–the correlation between the drug metabolite measurement and drug safety/efficacy–and asked, "[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?"[10] This Court concluded that the "administering" and "determining" steps of the claims, while "not themselves natural laws," were insufficient "to transform the nature of the claim" to an eligible invention.[11]

Prometheus' patent in *Mayo* is a poor standard-bearer for modeling important Supreme Court §101 precedent, because the combination of active steps in the claim was

9. *Bilski*, 561 U.S. at 607-609.

10. *Mayo,* 132 S.Ct. at 1297.

11. *Id.*

old: the drug administration and metabolite measurement had already been practiced, together and for the same purpose, by scientists in the medical field.[12] The Solicitor General had advised the Court that "the claims are likely invalid" under the novelty and nonobviousness requirements of 35 U.S.C. §§102 and 103–issues not then before the Court.[13] It was in this unusual factual context–a patent covering a process largely in the public domain, with appended "statements" of correlations–that this Court in *Mayo* issued an opinion that appears to have expanded judicial notions of "laws of nature" while, at the same time, diminishing the importance placed upon the Machine-or-Transformation test for identifying patent-eligible subject matter.

In *Myriad*, this Court concluded that Myriad's patent claims to isolated human DNA (BRCA genes) were not directed to an eligible "new and useful ... composition of matter," but were instead directed to ineligible "naturally occurring phenomena," though claims to non-naturally occurring cDNA were deemed eligible. *Association for Molecular Pathology v. Myriad*, 133 S. Ct. 2107, 2117-19 (2013). The Court admonished that it was "important to note" that process claims, including claims directed to new applications of the knowledge about the isolated DNA, were not before the Court and not implicated by its holding.[14]

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12. *Id.* at 1295.

13. Brief for the United States as Amicus Curiae Supporting Neither Party at 8-9, *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S. Ct. 1289 (2012) (No. 10-1150).

14. *Myriad,* 133 S.Ct. at 2119-20.

Most recently, the Court in *Alice Corp. Pty. Ltd. v. CLS Bank Intern.*, 134 S.Ct. 2347 (2014), invalidated claims to a computer-implemented scheme for mitigating settlement risk in a financial transaction, using a "framework" discerned from *Mayo* ("*Mayo/Alice* 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 one of those patent-ineligible concepts.… If so, we then ask, "[w]hat else is there in the claims before us?" … [W]e consider the elements of each claim both individually and as an ordered combination to determine whether the additional elements "transform the nature of the claim" into a patent-eligible application.... We have described step two … 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.[15]

In the wake of these cases, the Patent Office and lower courts have interpreted the *Mayo/Alice* framework to encompass many situations in which the peculiar fact scenario of *Mayo* was not present. Eligibility questions have been raised about a wide range of biotechnology and other life sciences patents, including patents to antibiotic

15. *Alice,* 134 S.Ct. at 2355 (internal quotations and citations omitted).

compositions[16] and biomarker diagnostic processes. The Federal Circuit (in *Sequenom* and other cases) construes the *Mayo/Alice* framework as an expansive two-part *test*[17] for patent-eligibility.

Amici urge this Court to grant Sequenom's petition to consider whether the *Mayo/Alice* framework has become over-inclusive in invalidating patents on meritorious inventions involving breakthrough biomedical discoveries that satisfy the terms of §101. As currently interpreted by lower courts and the Patent Office, this framework is ineffective for distinguishing meritorious inventions from unmeritorious ones.

II. AN INVENTOR'S DISCOVERY OF A NEW LAW OF NATURE OR NATURAL PHENOMENON SHOULD BE CONSIDERED AS PART OF THE "CLAIM AS A WHOLE" ANALYSIS

This case affords this Court an opportunity to clarify the boundaries of its judicial exceptions to the patent statute and address an issue of fundamental importance to the life sciences: whether a previously unknown law of nature or natural phenomenon–discovered by inventors–

16. Amici believe that strong reasons exist for limiting the *Myriad* judicial exception to DNA compositions, as distinct from compositions of other biomolecules that may have a counterpart in nature, but Sequenom's facts do not present that issue for consideration.

17. See, *e.g.*, *Genetic Technologies Ltd. v. Merial LLC*, Docket Nos. 2015-1202, 2015-1203, slip op. at 7(Fed. Cir. April 8, 2016)("[I]n its *Mayo* and *Alice* decisions, the Supreme Court has articulated a now well-established two-step test for patent eligibility….")

should be considered as part of the "claim-as-a-whole" analysis for patent-eligibility, for claimed processes involving practical applications of that newly discovered law or phenomenon.

This issue troubled Federal Circuit judges, who concluded that the invention of the '540 patent deserved patent protection, yet was invalid under the mandatory *Mayo/Alice* framework analysis. Although other fetal DNA tests existed, the inventors of the '540 patent fundamentally transformed pre-natal diagnostics through their discovery and insight that maternal serum contains minute amounts of cell-free fetal DNA, and their ability to adapt existing biotechnology techniques, such as polymerase chain reaction (PCR), to amplify portions of that fetal DNA inherited from the father for a new approach to prenatal diagnosis.

Having concluded that the claimed method failed step one of the eligibility inquiry because it "begins and ends with a natural phenomenon" of cffDNA, the Federal Circuit understood step two of the *Mayo/Alice* framework to require it to (i) dissect the claims, (ii) disregard elements relating to the cffDNA (the judicial exception), and (iii) find something innovative in the remaining dissected process elements of the claims, which they failed to do. "Because the method steps were well-understood, conventional and routine, the method of detecting paternally inherited cffDNA is not new and useful." *Ariosa*, 788 F.2d at 1377. Since *Mayo*, other personalized medicine method patents have met the same fate as the '540 patent in district courts and the Federal Circuit.[18]

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18. *See, e.g., In re BRCA1- & BRCA2-Based Hereditary Cancer Test*, 774 F.3d 755 (Fed. Cir. 2014); *PerkinElmer, Inc. v.*

Federal Circuit judges are troubled that they see no discretion in the *Mayo/Alice* framework for a "claim-as-a-whole" analysis as it relates to the underlying "discovery" that led to and is integrated into specific steps recited in the claimed method. "[I]t 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."[19]

"*Mayo* states that the inventive concept necessary for eligibility must come in the application analyzed at step two [of the framework], rather than from the discovery of the law of nature itself."[20] Judge Dyk identified a fundamental shortcoming of the *Mayo/Alice* framework when applying it to facts that were not before this Court in *Mayo*:

> 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.... But ... there is a problem with *Mayo* insofar as it concludes that

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Intima Ltd., 496 Fed. Appx. 65 (2012), *cert. denied, Intema Ltd. v. PerkinElmer, Inc.*, 2013 U.S. LEXIS 5248 (U.S., Oct. 7, 2013); *Genetic Technologies*, *supra*.

19. *Ariosa*, 809 F.3d at 1286 (Lourie, J., concurring in denial of rehearing *en banc*.)

20. *Id.* at 1287 (Dyk, J., concurring.)

> inventive concept cannot come from discovering something new in nature—*e.g.*, identification of a previously unknown natural relationship or property.... *Mayo* did not fully take into account the fact that an inventive 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.[21]

Lower courts have been uncertain how to reconcile *Mayo* with this Court's subsequent statement in Section III of *Myriad,* which suggested that, while the isolated DNA in *Myriad* was ineligible, "new applications of knowledge about the [isolated DNA] could generally be eligible.... *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."[22]

Unfortunately, current application of the *Mayo*/*Alice* framework by lower courts risks prohibition of patents on innovative, meritorious process inventions, such as biomarker-based prognostic and diagnostic inventions. Biomarker diagnostics shift the emphasis on medicine from reaction/treatment to prevention; improve diagnoses; optimize therapy selection and reduce side-effects; improve quality of life; and can reduce healthcare

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21. *Id.* at 1289.

22. *Id.* at 1290 (internal citations and quotation marks omitted).

costs. Such inventions often are built upon biomedical "discoveries" and heavily reliant upon patent protection for development.

The decentralized, market-driven nature of the U.S. healthcare system amplifies the importance of patent protection to drive biomarker diagnostic innovation, including the cffDNA detection methods in the current case. Economic incentives, like patent protection, incentivize the development of new devices and drugs, especially when useful to treat diagnosed diseases and conditions. By contrast, the same incentives may be weaker or non-existent for important facets of biomarker diagnostics and personalized medicine, particularly where the diagnostic addresses long-term health. For instance, payors (*e.g.*, health-care insurers with rapid customer turn-over) may have short-term cost incentives to pay for a diagnostic test to determine which of three expensive cancer treatments will be effective for a breast cancer patient, but little or no economic incentive to pay for a test designed to identify a healthy subject's ten- or twenty-year risk of developing breast cancer.

The economic risks, combined with a denial of patent protection through current application of the *Mayo/Alice* framework, may discourage investment to develop many classes of biomarker diagnostics, including those with great potential to improve early diagnosis and long-term health. This Court's judicial exception doctrine, through unguided implementation of the *Mayo/Alice* framework in the lower courts and the Patent Office, may result in a system in which the only biomarker diagnostics with commercial incentives for development are "companion diagnostics" to assist in the development of new drugs, these incentives coming from any investor belief that the

new drugs themselves enjoy better prospects of patent protection.

In Europe and many other industrialized regions of the world, patent protection for innovative diagnostic processes is available under predictable rules. That was historically true in the United States before this Court created the *Mayo/Alice* framework and suggested in *Alice* that it applied to all judicial exception analysis. That framework now is applied rigidly and expansively to deny patent protection for innovative diagnostic inventions.

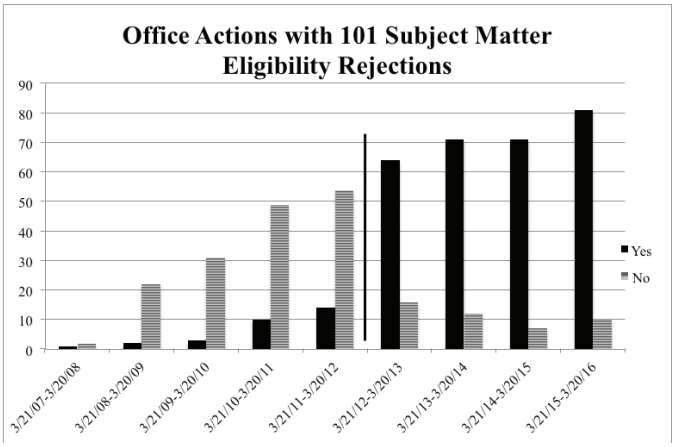
Applying step one of the framework, the Patent Office and the lower courts find judicial exceptions in patent claims directed to diagnostics: a natural substance being measured is labeled a "natural phenomenon," and/or the correlation between the measurement and a medical condition is labeled a "law of nature." Even though the claimed diagnostic method is not directed to either the substance *per se* or the correlation *per se*, the claimed method is held to be "directed to" the judicial exception(s). Under step two of the framework, if inventors have created their new diagnostic process by adapting/modifying proven existing laboratory techniques–laudable for a medical invention[23]–then the Patent Office and courts hold that the claims fail the second step of the *Mayo/Alice* framework, and are ineligible.

As Judge Dyk wrote, "a too restrictive test for patent eligibility … with respect to laws of nature (reflected in some of the language in *Mayo*) may discourage

23. Regulatory approval, industry acceptance, and user proficiency may be quicker for innovations employing trusted technologies.

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."[24] Amici share Judge Dyk's concern, and believe it is worthy of this Court's consideration.

Judge Lourie commented, "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."[25] Patent Office statistics support Judge Lourie's observation. According to one recent sampling, the frequency of Section 101-based rejections of personalized medicine patent applications abruptly rose from 15.9% in the few years before Mayo to a remarkable 86.4% after Mayo, with the frequency steadily increasing.[26]



24. *Ariosa*, 809 F.3d at 1287 (Dyk, J., concurring).

25. *Id.* at 1285 (Lourie, J., concurring.)

26. Chao and Mapes, "An Early Look at Mayo's Impact on Personalized Medicine," 2016 Patently-O Patent Law Journal 10 (http://patentlyo.com/media/2016/04/Chao.2016.PersonalizedMedicine.pdf).

This Court "has repeatedly emphasized" that its judicial exceptions arose from "a concern that patent law not inhibit future discovery by improperly tying up the use of laws of nature…. [B]ecause those laws and principles are 'the basic tools of scientific and technological work,' there is a danger that granting patents that tie up their use will inhibit future innovation."[27] Ironically, lower courts' application of the *Mayo/Alice* framework is having an effect that the judicial exceptions were designed to avoid: it dis-incentivizes the expenditure of private capital to perform basic biomarker research. And whereas patents require disclosure, the *Mayo/Alice* framework currently incentivizes biomarker researchers to maintain their discoveries as a trade secret, hidden indefinitely from both competitors and other researchers.

When a biomarker-disease relationship remains undiscovered or hidden as a trade secret, the loss to future discovery and innovation is not limited to the loss of a new diagnostic, which is often the first, but rarely the only, practical application that can be developed from such a discovery. When an innovator determines that a biomarker is useful for a particular disease state and discloses this work in a patent application directed to a diagnostic invention, the disclosure inevitably spurs other biomedical innovation. Biologists will conduct research to discover why the biomarker is correlated with the disease, and perhaps discover an underlying cause of the disease. Medicinal chemists will try to develop new therapeutic or prophylactic drugs to treat

27. *Mayo*, 132.S.Ct. at 1292.

affected populations identified by the biomarker. Clinical researchers can re-evaluate existing drugs to determine which, if any, are more effective for diseased individuals who have the biomarker, and which drugs are more effective for diseased individuals who don't, improving individual patient outcomes and reducing healthcare costs by reducing the number of prescriptions for ineffective drugs. Other diagnostic researchers will develop a panel of biomarkers that include the first marker and improve upon its performance, or be incentivized to look for a completely different marker that is easier to measure or more informative.

Patents that disclose new biomarkers and disease correlations and claim biomarker diagnostics incentivize and promote all of these areas of research, moving "trial-and-error" medicine into precision medicine. As Judge Newman observed, "Nor does patenting of [Sequenom's] 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."[28]

Congress recognized more than 60 years ago that new applications of technologies often are implemented using combinations of known technologies in new ways, and legislated that new uses of a known process, machine, manufacture, composition of matter, or material constituted patent-eligible processes. See 35 U.S.C. §100(b). Likewise, this Court recognized more than 35 years ago:

28. *Ariosa*, 809 F.3d at 1294 (Newman, J., dissenting).

> 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. The "novelty" of any element or steps in a process, or even of the process itself, is of no relevance in determining whether the subject matter of a claim falls within the §101 categories of possibly patentable subject matter.

Diamond v. Diehr, 450 U.S. 175, 188-9 (1981).

By clarifying that a newly discovered law or phenomenon of nature is an integral part of this Court's "claim-as-a-whole" patent-eligibility analysis, the Court can restore, in the United States, the patent-eligibility of practical and innovative biotechnology inventions that are currently protectable in Europe and other jurisdictions. When all claim elements (old, new, and those involving a judicial exception) are considered as a combination, a decision-maker can correctly identify inventive applications of the judicial exceptions.

III. IF THE *MAYO*/*ALICE* FRAMEWORK IS APPLICABLE, THIS CASE AFFORDS AN OPPORTUNITY TO REQUIRE A DETAILED, OBJECTIVE ANALYSIS OF THE FRAMEWORK ELEMENTS.

To date, this Court has never articulated how to identify and frame its three "judicial exceptions" for the first step of the *Mayo/Alice* framework. This case

demonstrates how subjective, yet influential, this first step can be. The "judicial exception" analysis of the first step often determines whether the second step need be performed at all, and how.

A. Methods of using natural phenomena are not "directed to" the phenomena *per se*.

This case presents an opportunity for this Court to examine whether and how the *Mayo/Alice* framework applies to a circumstance that was foreseen in *Myriad* but not presented by *Chakrabarty*, *Mayo*, or *Myriad*: a claim to a process of using a newly discovered biological material that exists in nature.

To frame this issue, one must recognize that process claims comprise process steps defining actions to be undertaken. A series of actions is neither directed to, nor preemptive of, a physical substance. In particular, the action steps of the claims of the '540 patent, *e.g.*, fractionating, amplifying, and/or analyzing, do not remove from the public domain the maternal serum or the fetal DNA as it exists in nature–they simply define a method of applying or using it. "The claims rely on …, but do not recite, a natural phenomenon or law."[29]

Viewed through this lens, the present case represents precisely the type of patent claims that this Court in *Myriad* suggested would be appropriate for a first discoverer to protect innovations involving the natural phenomenon of human DNA: claims directed to a method of using the DNA.[30]

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29. *Ariosa*, 809 F.3d at 1286 (Lourie, J., concurring.)

30. *See Myriad*, 133 S.Ct. at 2119-20.

B. For claims "directed to" a judicial exception, the framing of the exception can prejudice the patentability analysis.

Litigators understand that framing of a judicial exception currently is highly subjective and can be leveraged under the *Mayo/Alice* framework to disqualify key elements of a patent claim, including the significance of the "discovery" on which an invention is based. In practice, a patent's specification can be searched for particular elements or steps of the claim that distinguish it over the prior art; and a statement of a natural law or phenomenon is then articulated around those features. By framing a "judicial exception" to which the claim is "directed" in this manner, a claim is simultaneously fitted to the first step of the *Mayo/Alice* framework, and doomed under the second step, because the remainder of the claim can be characterized as routine or conventional.

The subjectivity of the first step of the *Mayo/Alice* framework is apparent in this case. Of many possible ways of framing the '540 patent's invention, the panel below viewed the claims as directed to the "natural phenomenon" of cffDNA, even though the claimed method neither starts nor ends[31] with cffDNA. In the current case, the lower courts correctly understood that the previously unknown existence of cffDNA in maternal serum was an important discovery that the inventors used to develop their claimed process. However, without the artful position advanced by Ariosa,[32] it is questionable whether cffDNA would have

31. The amplification reaction creates synthetic copies of tiny fragments of the naturally occurring cffDNA.

32. *Ariosa*, 788 F.3d at 1375 ("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….")

been selected as a "judicial exception" to which the process claims were "directed."

As explained above, the lower courts could have concluded that the claimed process was not directed to any phenomenon of nature per se, because the claim was directed to a series of actions.

If the courts had wanted to focus on starting materials, each independent claim calls for the performance of laboratory analysis on a sample of a pregnant woman's serum, plasma or blood. Had maternal serum/plasma/blood been selected as the "judicial exception," the analysis might have proceeded differently. Doctors use blood or serum donations for transfusions. Laboratories assay numerous components of patients' blood/serum to help doctors evaluate patients. For example, serum/blood is analyzed for glucose or Hb1Ac to evaluate diabetes; for numerous salts, chemicals, and enzymes to evaluate organs' functions; for antigens or antibodies to identify infection or evaluate immune system function; and for hormones to determine fertility and pregnancy. Surely Ariosa could not have persuaded any court that the '540 patent threatened to pre-empt these many pre-existing medical uses for human serum, or prevented researchers from studying human serum. However, courts might be persuaded that the '540 patent represents an inventive new use for serum.

Nor should a court have concluded that Sequenom's claims monopolized fetal DNA or the detection of fetal DNA, as fetal DNA was sourced through conventional amniocentesis or chorionic villus sampling and detected. Nor was the detection of fetal DNA *in maternal blood* preempted, as the test could be done on fetal *cells* known to circulate in the mother's bloodstream. In fact, the record

showed that not even the detection of cffDNA in maternal blood was preempted by the '540 patent.[33]

These observations underscore several reasons to grant Sequenom's petition. First, the way the "judicial exception" was selected and framed contributed to a misapplication of the *Mayo/Alice* framework to the '540 patent by the lower courts. Second, these judicial exceptions are malleable to being tailored by those who seek to invalidate an otherwise meritorious patent claim. Third, and more fundamentally, the two-step *Mayo/Alice* framework requires modification, so that eligibility of claimed methods, like those of the '540 patent, can be determined more objectively, rather than through subjective "judicial exception" attacks. The identification of a "judicial exception" can be result-determinative in the *Mayo/Alice* framework, yet little guidance exists from this Court to elucidate how to properly frame a judicial exception or objectively choose between conflicting judicial exception narratives.

C. Step two of *Mayo/Alice* should focus on the details of the claims, not the "gist" of the claims.

Amici are concerned about the lack of scientific scrutiny that patent claims currently receive under step two of the *Mayo/Alice* framework. In the current case, the lower courts repeatedly failed to focus their "routine and conventional" analyses on the details of the eleven claims

33. Sequenom presented evidence of non-infringing alternatives which should be accepted as true under the summary judgment posture of the case.

at issue, or even on the details of the three independent claims. Instead, the lower courts focused on the most general elements of them–the "gist."[34] To read the district court's opinion, the only material limitations of the claims, apart from cffDNA, were preparing human serum and amplifying and detecting DNA sequences. The claims contain more substance.

For example, the first step of claim 1 does not simply say "amplifying DNA sequences." Rather, claim 1 specifies "amplifying a paternally inherited nucleic acid from the serum or plasma sample [from a pregnant female]." Several sections of the '540 patent describe such analysis in detail. While Ariosa may have presented evidence that amplifying DNA was routine, the lower court opinions do not appear to address whether the technical details of amplifying *paternal* nucleic acid from *maternal* serum was routine and conventional at the filing date.

If challengers, courts, and patent examiners are permitted to distill claim steps down to their "gist" and ignore specific claim limitations, then all process patents may be more vulnerable to a well-crafted §101 challenge under current application of the *Mayo/Alice* framework. As the Court has repeatedly noted, "At some level, all inventions embody, use, reflect, rest upon, or apply laws

34. Motion practice appears to encourage this phenomenon. A disturbing trend exists of courts invalidating patents under § 101 on the pleadings, before claim construction hearings or significant fact discovery that can be critical for understanding inventions. See Marshall, "The Alice-Effect: An Empirical Study of Section 101 Motion Practice," (March 9, 2015) http://www.fr.com/fish-litigation/the-alice-effect-an-empirical-study-of-section-101-motion-practice/

of nature, natural phenomena, or abstract ideas." By implication, without more guidance from the Court, it will always be possible to identify an applicable judicial exception to meet the *Mayo/Alice* framework step one. Likewise, if the technical details of remaining claim elements can be ignored in favor of their "gist," then it will be far easier to assert that the remaining elements are routine and conventional to meet step two. This case affords the Court an opportunity to re-emphasize the importance of evaluating the details, rather than just the "gist," of claims.

CONCLUSION

For the foregoing reasons, amici respectfully request that this Court grant the Writ of Certiorari.

Respectfully submitted,

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