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 OF *AMICUS CURIAE* DR. ANANDA MOHAN CHAKRABARTY IN SUPPORT OF THE PETITIONER

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INTEREST OF AMICUS CURIAE[1]

Ananda Mohan Chakrabarty, Ph.D., is an Indian American microbiologist, scientist, and researcher, most notable for his work at General Electric in relation to directed evolution and his role in developing a genetically engineered organism using plasmid transfer, the patent for which (U.S. Patent No. 4,259,444) led to landmark Supreme Court case, *Diamond v. Chakrabarty*, 447 U.S. 303 (1980).

Dr. Chakrabarty is currently a Distinguished University Professor in the Department of Microbiology and Immunology of the University of Illinois at Chicago College of Medicine. Apart from being an eminent scientist, Dr. Chakrabarty has been an advisor to judges, governments, and the United Nations in relation to various scientific matters. As one of the founding members of a UNIDO Committee that proposed the establishment of the International Centre for Genetic Engineering & Biotechnology (ICGEB), he has been a member of its Council of Scientific Advisors ever since. He has also served the U.S. Government as a member of NIH Study Sections, as a member of the Board on Biology of the National Academy of Science, and on

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[1] No counsel for a party authored this brief in whole or in part, and no party directly or indirectly made monetary contribution to the preparation or submission of this brief. The parties in this case have mutually agreed to the filing of Amicus briefs.

the Committee on Biotechnology of the National Research Council. Also, he has served as a Scientific Advisor for meetings organized by the Supreme Court of Canada.

Still further, Dr. Chakrabarty has served on the Scientific Advisory Board of many academic institutions such as the Michigan Biotechnology Institute, the Montana State University Center for Biofilm Engineering, the Center for Microbial Ecology at the Michigan State University, and the Canadian Bacterial Diseases Network based in Calgary, Canada. Dr. Chakrabarty has also served as a member of NIAG, the NATO Industrial Advisory Group based in Brussels, Belgium. He was a member of the Board of Directors of Einstein Institute for Science, Health and the Courts, where he participated in judicial education.

From his lifelong focus on scientific research and its impact on human existence to his experiences that instilled an awareness of how the patent system acts to incentivize and to dis-incentivize scientific research, Dr. Chakrabarty holds an abiding and keen interest in this Court's handling of the issues in this case.

SUMMARY OF THE ARGUMENT

What constitutes patentable subject matter under U.S. patent law has been an issue for almost 200 years. *Evans v. Eaton*, 20 U.S. 356 (1822). But, the problem became more pronounced in the late 1970s and early 1980s as biological sciences and digital technologies gave rise to increasingly sophisticated inventions that could not be recognized or understood from a normal human point-of-reference. Now in the new millennium, the problem has reached a fever pitch as the pace of change has accelerated, the social awareness of inventions and patent protection has expanded, the mechanisms to pursue litigation have proliferated, and the impact of breakthrough inventions has reached more deeply into life and living.

However, the current direction for addressing the issue, represented by the Mayo/Myriad/Alice framework of analysis, has failed and will continue to fail all stakeholders in the United States patent system. For that reason, this Court should reconsider the basic issue of how to handle the judicial exceptions to § 101, particularly as relates to the judicial exception categories of "natural phenomena" and "law of nature." This current case offers an excellent opportunity to do so.

As shown below, the Mayo/Myriad/Alice framework of analysis has created confusion and harm to the purpose of § 101, as well as the judicially recognized exceptions thereto. The framework has turned § 101 into a needle's eye that

must be traversed, rather than the broad open archway it was intended to be. The proper role of the judicial exceptions to § 101 should be *de minimis*, not primary, as they have become.

In this case, the lower court erred in not determining *a priori* that the claimed subject matter of the Sequenom patent falls within the "process" category of §101. *See e.g., Diamond v. Chakrabarty*, 447 U.S. 303, 307 (1980). But the problem is not simply that the Federal Circuit improperly implemented the Mayo/Myriad/Alice framework. The problem is that the basic framework directed the court into the trees and the weeds of "inventive concept" and "conventional steps," rather than viewing the forest from above.

The notions of "inventive concept" and "conventional steps" are the province of §§ 102-103 and 112, not of § 101. The province of § 101 is simply whether the subject of the patent application is new and useful and made by mankind, recognizing that natural phenomena and laws of nature are not truly new and are not made by mankind.

In defence of the Mayo/Myriad/Alice framework, this Court noted that the lower courts should exercise caution lest "th[e] exclusionary principle … swallow all of patent law." *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2354 (2014). However, mere cautionary dictum was not and is not adequate instruction to the lower courts when the basic holding and definitions of the decision pointed in a different direction.

The more appropriate approach starts by not trying to do too much. In this instance, that means recognizing that dealing with the judicial exception categories of "natural phenomena" and "laws of nature" requires different thinking than dealing with the more ambiguous category of "abstract concept." The legal problems involving "natural phenomena" and "laws of nature" focus on physical things, whereas the legal problems involving "abstract concepts" do not, really. These differences warrant different thinking and different instruction to the lower courts.

For the judicial exception categories of "natural phenomena" and "laws of nature," the proper analysis should focus on determining whether the thing covered by the patent claims involves an alteration or manipulation by the hand of man and, if so, whether that alteration or manipulation has created useful qualities or characteristics that did not exist in the thing's natural state. If so, then the claimed invention is worthy of being considered for analysis under the other provisions of U.S. patent law. In this context, the "thing covered by the claimed invention" refers to the natural product, which comprises the starting point of the alleged invention.

This present case, owing to the outstanding nature of the underlying discovery and its acknowledged novelty and inventive character, provides an appropriate vehicle for review and reformulation of the standard for §101 eligibility.

ARGUMENT

A. A Scientist's View

In this case, the Federal Circuit's adherence to *Mayo*[2], rather than following its own conviction that Sequenom's significant invention is worthy of patent protection, was exceptionally disappointing to scientists. This was because scientists knew that nobody had ever conceived of the possibility – much less shown any specific way – of using maternal blood, serum, or plasma to amplify selectively the paternally-inherited sequences in fetal DNA. Such an accomplishment embodies the very definition of 'ingenuity' that the framers of the U.S. Constitution urged the government and the nation to encourage.

As compared to the Sequenom invention, the procedure of the *Mayo* patent was much less technology-oriented with less significant novel ideas, albeit with lot of common sense. Speaking as a scientist, it was not surprising that the *Mayo* patent was held invalid. But the Sequenom technology is altogether different, involving innovative and novel ideas for a technology that no longer requires the isolation of rare whole fetal cells. Instead, this brilliant and insightful procedure allows millions of pregnant women to avoid the use of invasive procedures with long needles to draw samples from the amniotic sac for detection of gender, genetic

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[2] *Mayo Collaborative Services v. Prometheus Laboratories, Inc.,* 132 S. Ct. 1289 (2012).

defects, or other possible characteristics that can endanger the baby's life and health. Sequenom's '540 patent covering the MaterniT21 test is vastly different in both scope and use of specific DNA techniques to recognize paternally inherited sequences that differentiate between fetal and maternal DNA. These are highly technical activities. *See* Fig. A below. Such sophisticated technical procedures clearly distinguish the Sequenom patent from the realm of natural law or phenomenon as applicable to the drug dosing procedure in *Mayo*.

B. Legal Argument

It is beyond dispute that 35 U.S.C. § 101 includes "anything under the sun that is made by man." *Diamond v. Chakrabarty,* 447 U.S. 303, 309 (1980), citing S. Rep. No. 1979, 82d Cong., 2d Sess., 5 (1952); H. R. Rep. No. 1923, 82d Cong., 2d Sess., 6 (1952). This principle is fully consistent with the judicially created exceptions of natural phenomena and laws of nature because those items – properly interpreted – are not new and not made by man.

The problem inherent in this case is not simply that the Federal Circuit failed to properly implement the Mayo/Myriad/Alice framework. The problem lay in the Mayo/Myriad/Alice framework itself, and the problem is being manifest in systemic happenings nationwide. Challenges under § 101 alleging unpatentable subject matter have become the option *de jour* in patent litigation, resulting in frequent motion practice, delays, expense, and inconsistent results. As recently reported by IP Law360:

> "Two judges with the nation's busiest patent dockets said at a conference Monday [April, 11, 2016] that the sweeping changes of the U.S. Supreme Court's Alice ruling and the advent of America Invents Act Proceedings have reshaped their workload, resulting in many complex new motions…. 'Alice has been a sea change at the district court level,' [Judge Gilstrap] said. 'Every case has a 101 issue now. It's a box on every good lawyer's

> checklist.'…. Judge Stark, who was assigned 126 patent cases last year, the fourth most of any judge nationwide, said that he likewise sees 101 motions in 'almost every case,' apart from Hatch-Waxman cases over generic drugs …."

See IP Law360, *Gilstrap, Stark Say Alice, AIA 'Sea Change' Means More Work* (April 12, 2016). Further, as separately reported by IP Law 360:

> The former director of the U.S. Patent and Trademark Office [David Kappos] on Monday [April 11, 2016] called for the abolition of Section 101 of the Patent Act, which sets limits on patent-eligible subject matter, saying decisions like Alice on the issue are a 'real mess' and threaten patent protection for key U.S. industries."

See IP Law360, *Kappos Calls for Abolition of Section 101 of Patent Act* (April 13, 2016). This Court should view these comments as cries for help, not from individual lawyers representing individual clients, but from knowledgeable authorities trying to deal with a "real mess" created by the Mayo/Myriad/Alice framework of analysis.

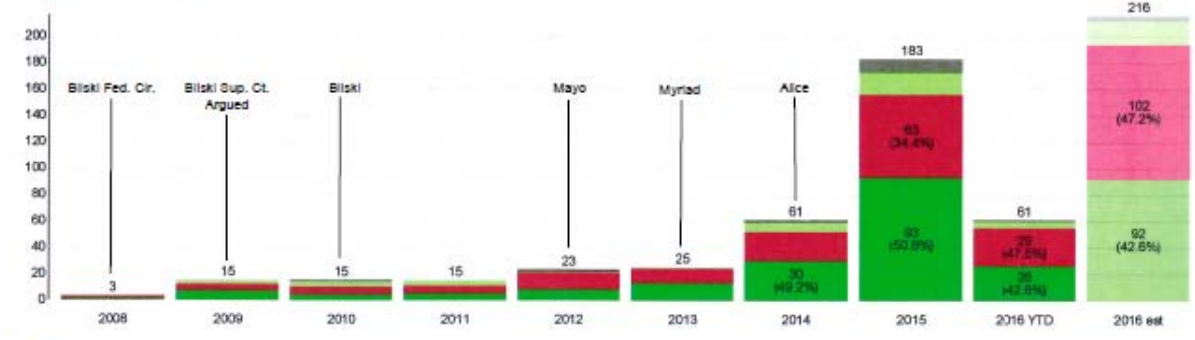
Lest these commentators be viewed as boys crying "wolf," hard core litigation statistics confirm the problem. Consider, for example, the following statistics from the commercial litigation data base, Docket Navigator®, showing the pattern of motions challenging § 101 unpatentable subject matter:

Docket Navigator

Search Criteria

Court/Agency	U.S. District Courts (and all courts)
Order filed date	on or before March 31, 2016
Legal issue	Unpatentable Subject Matter (35 USC § 101) (and all subcategories)

Motion Success by Year



Table

Percentages

	2008	2009	2010	2011	2012	2013	2014	2015	2016 YTD	2016 est
Granted	33.3%	46.7%	26.7%	33.3%	34.8%	52.0%	49.2%	50.8%	42.6%	42.6%
Denied	66.7%	33.3%	40.0%	40.0%	56.5%	44.0%	36.1%	34.4%	47.5%	47.2%

As everyone now recognizes, my U.S. Patent No. 4,259,444 ("Genetically Engineered Microorganism Harbouring Multiple Hydrocarbon Degradative Plasmids") is unequivocally proper and valid. However, it is easy to realize that the outcome might have been different under the Mayo/Myriad/Alice framework of analysis. Indeed, in that altered world of analysis, my patent would have been attacked as merely applying the basics of the genetic code, extracting a known natural DNA sequence from point A and inserting it into another known natural DNA sequence at point B using previously established (read "conventional") techniques. The same can be said over and over for many, if not most, of the breakthrough biotech patents that laid the foundation for the biotech industry in the United States in the early 1980s. *See e.g.*, Amgen's seminal U.S. Patent 4,703,008, which discloses Dr. Fu Quen Lin's discovery of the DNA sequence for making recombinant erythropoietin.

It seems likely that many, but not necessarily all, of the problematic scenarios tossed around during arguments about § 101 arise because speakers are not incorporating the entire framework of United States patent law. Apart from § 101, the rest of Title 35, United States Code, imposes tough, stringent controls that protect the public interest before any inventor receives the quid pro quo of a patent. In particular, regardless of how fantastic the underlying invention may be:

- No patent will extend beyond 20 years from its filing date, absent circumstances such as Patent Term Extension. After 20-years, the subject matter disclosed in a patent specification goes into the public domain;

- No patent will prevent the public from practicing technology that has passed into the public domain; and

- No patent will cover subject matter that is not made by the hand of man and described in the specification, thereby assuring that the discovery goes into the public domain after the patent expires.

These are the primary restraints on patent grants. The only proper role of § 101 is to make sure that patent claims rely upon an alteration or manipulation that is made by the hand of man. If so, then the rest of the patent prosecution process should determine whether the patent claims recite novel, and nonobvious (read "inventive") concepts that are properly described in the specification.

The destructive impact of the current situation goes far beyond any individual inventor and any individual patent. The time when a patent was important because it rewarded an individual inventor has passed long ago. It remains true that the public recognition of achievement is important to all inventors, and the financial benefit of a patent to the stock of a small start-up company is hard to overstate. But the most far-reaching role of patentability in the modern life of a technical economy is to incentivize the formation of capital

which leads to invention. The sophistication of current science requires large amounts of capital to fuel the fire of invention. The process takes *years*. And unless the Mayo/Myriad/Alice framework is revised significantly and soon, its disastrous effect will harm the U.S. (and world) economies for a long time.

Step 1 of the Mayo/Myriad/Alice framework, directing the lower court to "consider whether the claimed invention is directed to an abstract idea, law of nature, or natural phenomena" is distinctly unhelpful. It provides no guidance on what that statement means or how to do it. Moreover, as framed, the real question becomes not "whether" the patent is directed to such a topic, but rather "what is" the unpatentable topic to which the invention is directed. Any good trial lawyer can easily articulate an underlying "abstract concept, law of nature, or natural phenomena" for almost any invention, and certainly this is true for any important breakthrough invention in the life sciences. As a result, absent meaningful guidance from this Court on Step 1, the lower courts are almost automatically pushed into Step 2.

Step 2 of the Mayo/Myriad/Alice framework, *i.e.*, directing the lower court to consider whether the claimed invention has additional non-conventional steps so as to recite an inventive concept, is no better. This framework inherently conflates § 101 with §§ 102-103, if for no other reason than that terms such as "inventive concept" and "conventional steps" have a 200 year history of use in the context of

distinguishing claimed inventions from the prior art. It is essentially impossible to use those terms without importing the associated contexts of §§ 102-103, and the attempt to do so gives rise to at least two deeply troubling realities.

First, any good trial attorney, defending a charge of patent infringement, will consider the Mayo/Myriad/Alice framework as a whole. If smart, she starts her thinking by isolating all aspects of the claimed invention which can fairly be characterized as old, well-known, and conventional. She then figures out how best to articulate the remaining "natural phenomena" or "law of nature" which comprises the rest of the claim. The result gives a direct path through both steps 1 and 2, providing a plausible challenge of unpatentable subject matter, which has resulted in the filing of motions to dismiss in a shocking number of cases. *See* the Docket Navigator table on page 10 above.

Second, regardless of how much verbiage is given to the notion that the analysis of unpatentable subject matter under § 101 is separate and distinct from the analysis of validity under §§ 102-103 and 112, the existing framework forces the lower court to opine on the presence of non-conventional steps and inventive concept in the context of a legal issue raised in a pleading motion, typically near the outset of the case. As a result, the judge is inevitably forced to make a "gut call" without the benefit of fully examining all the pertinent evidence, which is normally introduced through extensive §§ 102-103 analysis. The situation puts the trial judge into a

relatively subjective, "I know it when I see it," framework, much more so than would be the situation at the end of trial. Although "I know it when I see it" may have seemed comfortable to Justice Stewart when discussing obscenity, *Jacobellis v. Ohio*, 378 U.S. 184 (1964), that result is far too ephemeral for addressing patent rights in the 21st century.

The pragmatic real-world situation is exemplified by the fact that district court decisions, relying on the Mayo/Myriad/Alice framework of analysis, now find all too often that the patent has claimed unpatentable subject matter. Yet, the proper issue should not be whether a claim encompasses unpatentable subject matter or whether the claim "locks up" a natural phenomenon or law of nature to some degree. Every patent does that to some degree. That is the statutorily established quid pro quo that the inventor gets for disclosing the invention to the world; the public's return quid pro quo lies in the benefits that flow from having the disclosure that becomes free and open for all to use after the patent expires, as well as by the immediate stimulation of new ideas and new design arounds even before the patent has expired. The proper issue is whether the patent claim relies upon actions or things made by mankind.

Moreover, pre-emption – or rather the scope of pre-emption – is not properly the realm of § 101. At least when dealing with natural phenomena and laws of nature, the proper § 101 issue should focus on (i) determining whether the thing covered by the

claimed invention involves any alteration or manipulation by the hand of man and, if so, (ii) whether that alteration or manipulation has resulted in useful qualities or characteristics that did not exist in the thing's natural state. If the answer to both questions is "yes," then the inventor is entitled to pursue a patent application that encompasses the alteration or manipulation made by his hand, providing the alteration or manipulation is properly disclosed in the patent application.

The concern about whether the patent claim has unduly pre-empted unpatentable subject matter is more properly dealt with under § 112 (*i.e.*, considering whether the patent claims are properly commensurate in scope with the disclosure of what "the hand of man" did in altering or manipulating the claimed subject matter) and also with §§ 102-103 (*i.e.*, considering whether and how the claimed subject matter differs from the prior art.)

The proper application of § 101 should be formulated in a manner that is separate and independent from §§ 101-103 and 112, just as those sections should be left free to do their jobs separate and independent from § 101. Thus, as long as the patent claims are properly confined to the alteration or manipulation that was actually performed by "the hand of man," the inventor should be allowed to pursue the application. If the alteration or manipulation is properly disclosed and recited in accord with § 112, and if the recited alteration or manipulation gives rise to a result that is new and nonobvious over the prior art as provided by §§102-103, then there is no justified concern about undue

pre-emption, at least insofar as products of nature are concerned. Given those starting assumptions, the resulting degree of pre-emption is the statutory quid pro quo established by Congress and the Constitution.

Consider the alternative. If the inventors and investors of the Sequenom patent had previously known the impact of the Mayo/Myriad/Alice framework of analysis, they would never have disclosed anything about their work to the rest of the world. Instead, they would have kept all the information about their work a trade secret. Using the trade secret framework, Sequenom could still have commercialized the invention; Sequenom would have advertised, "send us a blood sample, and we will tell you the sex of your fetus and whether your fetus is at risk for certain genetic conditions. Competitors would not have had any clues about how Sequenom was able to do such a miracle and, instead, would have had to recreate the inventions from scratch. In addition, without the quality control checkpoint of proven science, snake oil salesmen would have played on unsuspecting customers.

The patent system, administered properly, creates the protective foundation that allows scientists to disclose their work, not just in patent applications, but in *all publications*. This protective foundation is why companies, universities, and other institutions routinely require a patent application to be filed *before* a scientist is allowed to present his work publically at conferences or in scientific journals. Such public disclosure does not happen if

the owner feels the need to rely upon trade secret law. That is another reason why Congress drafted § 101 to encompass everything under the sun made by man. And that is why this Court should vacate the Mayo/Myriad/Alice framework of analysis and provide better guidance, at least for the life science technologies involving natural phenomena and laws of nature.

Lawyers can argue forever how commercially successful the trade secret strategy would be, but there can be no doubt that it offers an attractive alternative path to avoid the type of competition that comes from copying an invention without much hard work or investment. Dis-incentivizing the trade secret route is why the inventor's quid pro quo of a patent requires full disclosure of the invention. The public gets the benefit of that disclosure only if the inventor can get a patent on his invention. And that trade-off is why every industrialized country since the dark ages has had a patent system. Yet, the trade secret route is precisely the option that the Mayo/Myriad/Alice framework of analysis is suggesting (some might say "forcing") inventors – and investors – to consider, instead of relying upon patents, at least in respect to inventions in the life science arena.

The present petition for certiorari is a perfect vehicle to re-define the proper framework of analysis of § 101, at least for the area of life sciences. And, the correct result, focused on the wording of § 101, can be elegant without being complicated. Namely,

the proper § 101 analysis should provide that, if the inventor claims a material – or a process using a material – that has been altered or manipulated by the hand of man and, if as a result of that alteration or manipulation, the claimed subject matter is shown to have qualities, characteristics, or properties that did not exist in the natural material, then that claimed subject matter passes muster under § 101 and is worthy of being considered under §§ 102-103 and 112. Under those latter sections, the claimed subject matter will be examined in order to determine whether it has truly never been previously disclosed to the public and whether it is adequately disclosed to the public in the current specification.

If the analysis and examination under §§ 102-103 and 112 shows that the inventor's work (*i.e.*, the alteration or manipulation of the natural product) is novel, nonobvious, and properly disclosed, then it is fair and just that the inventor receives the exclusive right to use the invention for a limited period of time. That is the fundamental nature of the quid pro quo that the inventor gets for fully disclosing how to perform the alteration or manipulation and to obtain the resulting benefits. The public gets full and unfettered right to use the invention after the limited period of exclusivity has expired and, in the meantime, the inventor's disclosure will stimulate whole new areas of investigation, both using and designing around the claimed invention.

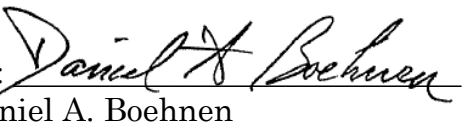
As to the Sequenom invention specifically, the starting point is a sample of maternal blood (claim 21), serum (claim 1), or plasma (claim 1). The sample is altered and manipulated, as disclosed in the patent, with the result of yielding information about sex and genetic deformities of a fetus. This is like turning lead into gold. There is no dispute in this record that this manipulation by the hand of man is novel, nonobvious, and properly disclosed in the specification. How can that not be patentable?

Ariosa may argue that the cffDNA was always present in the maternal sample and that the steps to purify and isolate the cffDNA were conventional. But, that is not the proper starting point. Using that starting point relies upon hindsight reasoning as well as starting in the middle of the process, not the beginning. Before the Sequenom invention, nobody knew that cffDNA was present in the maternal sample. The proper starting point of analysis is the maternal sample. Also, there can be no genuine dispute that the maternal sample was altered and manipulated by the hand of man, with the result of providing qualities and characteristics that reflect valuable, previously unknown information about the sex and potential genetic defects of the fetus.

CONCLUSION

For the reasons stated above, the judgment of the Federal Circuit should be reversed and the Mayo/Myriad/Alice framework of analysis should be reconsidered.

Respectfully submitted



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