**Nos. 2014-1139, 2014-1144**

# In the United States Court of Appeals for the Federal Circuit

ARIOSA DIAGNOSTICS, INC. and NATERA, INC.,

*Plaintiffs-Appellees,*

and

DNA DIAGNOSTICS CENTER, INC.,

*Counterclaim Defendant-Appellee,*

v.

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

*Defendants-Appellants,*

and

ISIS INNOVATION LIMITED,

*Defendant.*

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Appeals from the United States District Court for the Northern District of California, Case Nos. 3:11-cv-06391-SI, 3:12-cv-00132-SI. The Honorable **Susan Illston**, Judge Presiding.

## BRIEF OF *AMICUS CURIAE* PAUL GILBERT COLE IN SUPPORT OF APPELLANTS' PETITION FOR REHEARING *EN BANC*

DONALD L. ZUHN, JR.
MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 South Wacker Drive, Suite 3100
Chicago, IL 60606-6709
Tel: (312) 913-0001

*Counsel of Record for Amicus Curiae, Paul Gilbert Cole*

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# CERTIFICATE OF INTEREST

Pursuant to Federal Circuit Rules 28(a)(1) and 47.4(a), counsel for the *Amicus Curiae*, Paul Gilbert Cole, certifies the following:

1. The full name of every party or *amicus* represented by me is:

Paul Gilbert Cole

2. The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by me is:

None.

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or *amicus curiae* represented by me are:

None.

4. The names of all law firms and the partners or associates that appeared for the party or *amicus* now represented by me in the trial court or agency or in a prior proceeding in this case or are expected to appear in this Court are:

Donald L. Zuhn, Jr., McDonnell Boehnen Hulbert & Berghoff LLP

August 27, 2015

/s/ Donald L. Zuhn, Jr.
Donald L. Zuhn, Jr.
McDonnell Boehnen
Hulbert & Berghoff LLP
300 South Wacker Drive
Chicago, IL 60606-6709
Tel: (312) 913-0001

*Counsel of Record for Amicus Curiae, Paul Gilbert Cole*

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## INTEREST OF *AMICUS CURIAE*[1]

Paul Gilbert Cole is a practising UK and European patent attorney, is a visiting professor in IP Law at Bournemouth University in the UK and has been writing about and teaching patent law for over 35 years. He is concerned with the integrity of the legal system and the correctness of the consequential guidance that is given to patent examiners in the USPTO. It is his professional opinion that this court should grant rehearing *en banc* because the panel decision's application of § 101 exceeds the scope of the Supreme Court's § 101 jurisprudence and the scope of Article 27 of the TRIPS agreement[2], with consequential harm to future U.S. patent applicants and to harmonious development of the patent system internationally. He authored this brief in its entirety, is authorised to file this brief by his firm, Lucas & Co., Warlingham, UK, and has no stake in the parties or in the outcome of this case.

## OPENING STATEMENT

The decision in this case is contrary to cases concerning: (a) phenomena of

[1] No party's counsel authored this brief in whole or part; no party or party's counsel contributed money intended to fund preparing or submitting the brief; and no person other than *amicus* or counsel contributed money intended to fund preparing or submitting the brief. Fed. R. App. P. 29(c)(5). The authority under which this brief is filed comes from the contemporaneously filed motion for leave to file this brief in support of Appellants' Petition For Rehearing *En Banc*.

[2] Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), art. 27, Uruguay Round Agreements Act, Pub.L. No. 103–465, 108 Stat. 4809 (1994).

nature and natural products, including *Hartranft v. Wiegmann*, 121 U.S. 609 (1887); *Diamond v. Chakrabarty*, 447 U.S. 303 (1980); *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S. Ct. 1289 (2012); and *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013); (b) isolation, purification or concentration of substances, especially those naturally occurring, including *Kuehmsted v. Farbenfabriken of Elberfeld Co*., 179 F. 701 (7th Cir. 1910) (aspirin); *Parke-Davis & Co. v. H.K. Mulford Co.,* 189 F. 95 (C.C.S.D.N.Y. 1911) (adrenalin); and *Merck & Co. v. Olin Mathieson Chem. Corp*., 253 F.2d 156 (4th Cir. 1958) (vitamin $B_{12}$); and (c) new and beneficial results as evidence of invention, including *Webster Loom Co. v. Higgins* 105 U.S. 580 (1881); *Washburn & Moen Mfg. Co. v. Beat-'Em All Barbed Wire Co.*, 143 U.S. 275 (1892); *Carnegie Steel Co. v. Cambria Iron Co.,* 185 U.S. 403 (1902); *United States v. Adams,* 383 U.S. 39 (1966); and *KSR Int'l Co. v. Teleflex, Inc.,* 550 U.S. 398 (2007). It is based on a legally incomplete and a legally and factually incorrect interpretation of the invention described and claimed in U.S. Patent No. 6,258,540. In addition to the question contained in the Petition, it raises the following precedent-setting questions of exceptional importance:

(1) Should the context in which a claimed method that involves a newly discovered natural phenomenon be disregarded for the second part of the test in *Mayo*, so that steps that are known but only in different contexts do not count

towards eligibility?

(2) How relevant to the natural phenomenon exclusion of § 101 is a new and beneficial result never attained before and evidencing inventive step under § 103?

(3) Is the second part of the *Mayo* test applied in the breadth of the Panel Opinion incompatible with the obligations of the United States under Article 27 of TRIPS?

## BACKGROUND AND HOLDING

Although the Panel Opinion[3] acknowledged that methods are generally eligible subject matter, it held that the claimed method was ineligible. Its holding was based on its conclusion that the method started with cffDNA taken from a sample of maternal plasma or serum, which it acknowledged other researchers had discarded as medical waste but which it held was a natural phenomenon, that the method ended with paternally inherited cffDNA, which it also held to be a natural phenomenon, and that the method steps did not transform the natural phenomenon of cffDNA into a patentable invention because they did not add significantly more, being well-understood, routine and conventional activity specified at a high level of generality.

## REASONS FOR GRANTING REHEARING EN BANC

### I. This decision is likely to be followed by the USPTO for its examination guidance and if wrongly decided may adversely affect many pharmaceutical

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

**and biotechnology applicants.**

In this controversial field of natural product and process patent eligibility this court should exercise care and restraint in its holdings and in its dicta. In its natural product eligibility guidance to examiners, the USPTO has a history of over-broad interpretation of Supreme Court and other decisions, which has created widespread difficulty for patent applicants and hence widespread adverse comment from both individuals and organizations[4]. The present author has commented extensively to the USPTO on this guidance and his March 2015 comments[5] cover a number of issues concerning the TRIPS agreement, which are also mentioned in this brief.

## II. The amplification product was misclassified as a natural phenomenon and not as a non-natural composition of matter contributing to eligibility as a manufacture under § 101.

The end point of amplification is not cffDNA but instead is a synthetic

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[4] *Public Comments on Guidance For Determining Subject Matter Eligibility Of Claims Reciting Or Involving Laws of Nature, Natural Phenomena, & Natural Products* (visited Aug. 26, 2015) <http://www.uspto.gov/patent/laws-and-regulations/comments-public/public-comments-guidance-determining-subject-matter>; Comments on 2014 Interim Guidance on Patent Subject Matter Eligibility (visited Aug. 26, 2015) <http://www.uspto.gov/patent/laws-and-regulations/comments-public/comments-2014-interim-guidance-patent-subject-matter.html>.

[5] Paul Cole, *Comments on the 2014 Interim Guidance on Patent Subject-Matter Eligibility and on the Accompanying Nature Based Product Examples* (16 March 2015) <http://www.uspto.gov/sites/default/files/documents/2014ig_f_cole_2015mar16.pdf>.

product made from nucleotide monomers and resulting in isolated oligonucleotides of length determined by the primers used for amplification, *e.g.*, in Example 1 of length 198 base pairs. The isolated oligonucleotides are not within the definition in the Panel Opinion since they are derived from the supplied nucleotide monomers, not from the fetal DNA and since isolated oligonucleotides do not circulate freely in the maternal bloodstream. The fact pattern here diverges materially from that in *Myriad* where neither wild-type BRCA1 nor the corresponding cDNA were reported as having been isolated as real and tangible molecules. That was recognised by Judges Moore and Bryson[6], and also, it is submitted, by the Justices of the Supreme Court[7].

In addition to the change in chemical nature, the isolated oligomers at the end point of amplification are increased in concentration by a factor of 1,000 to 1,000,000 and to a point where they can be detected, *e.g.*, by ethidium bromide and fluorescent light, whereas the unamplified cffDNA is not. Following the language of Judge Learned Hand in *Parke-Davis*, the real and tangible oligomer sequences in their amplified form have become for every practical purpose a new thing commercially and analytically, *see also Kuehmsted* and *Merck*. In *Mayo*, it is

[6] *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 689 F.3d 1303 (Fed. Cir. 2012).

[7] Paul Cole, *The Unacknowledged Role of Section 112 in the Myriad Decisions* (30 November 2013) <http://www.patents4life.com/2013/11/the-unacknowledged-role-of-section-112-in-the-myriad-decisions/>.

implicit that the Court did not intend to overrule established case law about new drugs or new ways of using existing drugs, and the same reasoning applies to the amplified oligomers here. Moreover, these short sequences satisfy the criteria in *Hartranft*, which was approved in both *Chakrabarty* and *Myriad*. In *Hartranft*, a change of form accompanied by new utility is the hallmark of a manufacture, and hence also implicitly patent-eligibility consistent with reference to utility in § 101.

The amplification step in the claimed process produces DNA in the new form of oligomeric sequences in vastly higher concentration than before and is accompanied by new utility since it can act as a substrate for analysis whereas cffDNA cannot. The amplified sequences are the product of human ingenuity being a non-naturally occurring composition of matter having (following the wording in *Chakrabarty* and *Myriad*) a distinctive name (amplified maternal plasma sequences), character (short oligomer sequences in high and analyzable concentration) and use (analytical detectability) not possessed by maternal cffDNA. Accordingly, these sequences in the context of maternal serum and plasma testing meet the eligibility requirements of novelty and new utility set out in *Hartranft* and contribute to § 101 eligibility for the method claimed herein.

**III. Contrary to *Mayo* the Panel Opinion provides precedent for establishing ineligibility by considering features merely individually and ignoring or giving insufficient weight to their "ordered combination".**

Although the Panel Opinion acknowledges a requirement derived from

*Mayo* to consider the elements of each claim both individually and as an "ordered combination", the required "ordered combination" comparison was omitted, and the claim was held ineligible for appending routine, conventional steps to a natural phenomenon, specified at a high level of generality. That should not, in itself be conclusive since in the words of Chief Judge Markey[8]: "Only God works from nothing. Man must work with old elements". If the panel had considered the "ordered combination" as required, it should have held that the starting point for the claimed method is not cffDNA but instead is a maternal serum or plasma sample, the selection of that material defining the context of all subsequent steps and setting the claimed method apart from the prior art, *see United States v. Adams,* 383 U.S. 39 (1966). It should have continued through the amplification step and ended with the amplified synthetically-created paternally inherited sequences in 1,000-1,000,000-fold concentration having utility as explained above and subject to a detection procedure, *e.g*., with agarose gel and ethidium bromide. It should also have considered the result of the ordered combination claimed, which is a hitherto unavailable test of high sensitivity for a range of medical conditions that can be applied early in pregnancy and avoids the risks to the fetus inherent in amniocentesis and that revolutionized prenatal care.

**IV. The Panel Opinion disregarded the acknowledged new and beneficial**

[8] Howard T. Markey, *Why Not the Statute* 65 J. PAT. OFF. SOC'Y 331, 334 (1983).

**results of the ordered combination as evidence of invention and hence relevant to § 101 eligibility.**

The principle is aptly summarised by Justice Bradley in *Webster Loom Co. v. Higgins*, 105 U.S. at 591: "It may be laid down as a general rule, though perhaps not an invariable one, that if a new combination and arrangement of known elements produce a new and beneficial result, never attained before, it is evidence of invention." That opinion was cited with approval by Justice Brown in *Washburn* and in *Carnegie Steel*. Similarly, in *KSR*, 550 U.S. at 416, the Court observed of the *Adams* invention: "The fact that the elements worked together in an unexpected and fruitful manner supported the conclusion that Adams's design was not obvious to those skilled in the art." That the claimed combination of starting material and method steps here produced a new and beneficial test for fetal abnormalities and the like is affirmative evidence of invention, which evidence could not and should not have been disregarded when considering eligibility of the "ordered combination" under § 101.

## V. When broadly interpreted the two-part test raises issues of compliance with TRIPS.

Acts of Congress including § 101, where fairly possible, ought to be construed so as not to conflict with international law or with an international agreement with the U.S., particularly where, as with TRIPS, the U.S. was the

moving spirit behind the Treaty[9]. Over-broad interpretation of the *Myriad* and *Mayo* decisions in USPTO Guidance gave rise to adverse comment, *e.g.*, from the *Japan Intellectual Property Association*[10], which complained that the U.S. was introducing special eligibility criteria contrary to the international trend of intellectual property protection.

Article 27.1 of TRIPs entitled "Patentable Subject Matter" provides a complete code for patent-eligibility which WTO member countries including the U.S. are required to respect. It requires patents to be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application, and that patent rights should be enjoyable without discrimination as to the field of technology. Note 5 to Article 27 equates "capable of industrial application", *e.g.*, under the EPC with "utility", *e.g.*, under § 101. The Case Law of the Boards of Appeal of the European Patent Office, 7th Ed. 2013, explains at page 15 that discoveries, scientific theories and mathematical methods excluded under art. 52(2)(a)-(d) EPC share the common feature that they do not aim at any direct

[9] *Murray v. Schooner Charming Betsy*, 6 U.S. (2 Cranch) 64, 118 (1804).
[10] Hiroshi Morita, *JIPA Comments on the "Guidance for Determining Subject matter Eligibility of Claims Reciting or Involving Laws of Nature, Natural Phenomena, & Natural Products"* (9 May 2014) <http://www.uspto.gov/sites/default/files/patents/law/comments/mm-a-jipa20140509.pdf>.

technical result but are rather of an abstract and intellectual character and that:

> If a new property of a known material or article is found out, that is mere discovery and unpatentable because discovery as such has no technical effect and is therefore not an invention within the meaning of *Art. 52(1) EPC*. If, however, that property is put to practical use, then this constitutes an invention which may be patentable. To find a previously unrecognised substance occurring in nature is also mere discovery and therefore unpatentable. However, if a substance found in nature can be shown to produce a technical effect, it may be patentable…."

It is submitted that this statement encapsulates the proper bounds of the exclusion under TRIPS Art 27 and any conflict with U.S. law rises from over-expansive interpretation of *Mayo* and in *Myriad*, whose narrow interpretation consistent with TRIPS was urged on the USPTO by the American Bar Association[11].

This case is an example of an internationally discordant, not harmonious, result, contrary to the eligibility requirements of TRIPS Article 27. Eligibility of the corresponding European patent was never disputed and it was held unobvious for solving the technical problem of detecting fetal nucleic acid with higher sensitivity, *see* EPO Appeal decision T 0146/07 *Prenatal diagnosis/ISIS*. It is wrong that a patent that survived obviousness challenge in Europe should be held ineligible in the U.S.

[11] Robert. O. Lindefjeld, *Comments of the American Bar Association* (30 July 2014) <http://www.uspto.gov/sites/default/files/patents/law/comments/mm-a-abaipl20140731.pdf>.

August 27, 2015

/s/ Donald L. Zuhn, Jr.
Donald L. Zuhn, Jr.
McDonnell Boehnen
Hulbert & Berghoff LLP
300 South Wacker Drive
Chicago, IL 60606-6709
Tel: (312) 913-0001

*Counsel of Record for Amicus Curiae, Paul Gilbert Cole*

## CERTIFICATE OF COMPLIANCE

1. This brief complies with the page limit set forth in Federal Circuit Rule 35(g).

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August 27, 2015

/s/ Donald L. Zuhn, Jr.
Donald L. Zuhn, Jr.
McDonnell Boehnen
Hulbert & Berghoff LLP
300 South Wacker Drive
Chicago, IL 60606-6709
Tel: (312) 913-0001

*Counsel of Record for Amicus Curiae, Paul Gilbert Cole*

## CERTIFICATE OF SERVICE

I, Gary Y. Chyi, being duly sworn according to law and being over the age of 18, upon my oath deposes and states that:

Counsel Press was retained by Donald L. Zuhn, Jr., McDonnell Boehnen Hulbert & Berghoff LLP, Attorney for *Amicus Curiae* Paul Gilbert Cole, to print this document. I am an employee of Counsel Press.

On August 27, 2015, Mr. Zuhn authorized me to electronically file the foregoing Brief of *Amicus Curiae* Paul Gilbert Cole In Support of Appellants' Petition for Rehearing *En* Banc with the Clerk of the Federal Circuit using the CM/ECF System, which will serve e-mail notice of such filing on the following:

David I. Gindler
(*Principal Counsel*)
Andrei Iancu
Amir Naini
Irell & Manella LLP
1800 Avenue of the Stars, Suite 900
Los Angeles, CA 90067
310-277-1010
dgindler@irell.com
aiancu@irell.com
anaini@raklaw.com
*Counsel for Appellee*
*Ariosa Diagnostics, Inc.*

William P. Schuck
(*Principal Counsel*)
Bartko, Zankel, Bunzel & Miller
One Embarcadero Center
Suite 800
San Francisco, CA 94111
415-956-1900
pschuck@bzbm.com
*Counsel for Appellees*
*Natera, Inc., et al.*

Thomas C. Goldstein
Eric F. Citron
GOLDSTEIN & RUSSELL, PC
7475 Wisconsin Avenue, Suite 850
Bethesda, MD 20814
(202) 362-0636
tg@goldsteinrussell.com
ecitron@goldsteinrussell.com
*Counsel for Appellants Sequenom, Inc. et al.*

Additionally, paper copies will also be mailed to the above counsel for the parties at the time paper copies are sent to the Court.

Sixteen paper copies will be filed with the Court within the time provided in the Court's rules.

/s/ Gary Y. Chyi
Gary Y. Chyi

August 27, 2015