Nos. 22-1027, -1028

United States Court of Appeals for the Federal Circuit

CAREDX, INC., THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY,

Plaintiffs-Appellants,

v.

NATERA, INC.,

Defendant-Appellee.

Appeal from the United States District Court for the District of Delaware in Nos. 1:19-cv-00567-CFC-CJB, 1:20-cv-00038-CFC-CJB, Judge Colm F. Connolly.

CAREDX, INC., THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY,

Plaintiffs-Appellants,

v.

EUROFINS VIRACOR, INC.,

Defendant-Appellee.

Appeal from the United States District Court for the District of Delaware in No. 1:19-cv-01804-CFC-CJB, Judge Colm F. Connolly.

APPELLEE NATERA, INC.'S RESPONSE TO THE COMBINED PETITION FOR PANEL REHEARING AND REHEARING EN BANC

Gabriel K. Bell
Ashley M. Fry
LATHAM & WATKINS LLP
555 Eleventh Street, NW
Suite 1000
Washington, DC 20004
(202) 637-2200

Counsel for Appellee Natera, Inc.

November 14, 2022

CERTIFICATE OF INTEREST

Case Numbers 22-1027, -1028

Short Case Caption *CareDx, Inc. v. Natera, Inc.*

Filing Party/Entity Natera, Inc., Appellee

I certify the following information is accurate and complete to the best of my knowledge.

Date: November 14, 2022 Signature: */s/ Gabriel K. Bell*
Name: Gabriel K. Bell

1. **Represented Entities**. Provide the full names of all entities represented by undersigned counsel in this case.

Natera, Inc.

2. **Real Party in Interest.** Provide the full names of all real parties in interest for the entities. Do not list the real parties if they are the same as the entities.

N/A.

3. **Parent Corporations and Stockholders.** Provide the full names of all parent corporations for the entities and all publicly held companies that own 10% or more stock in the entities.

N/A.

4. **Legal Representatives.** List all law firms, partners, and associates that (a) appeared for the entities in the originating court or agency or (b) are expected to appear in this court for the entities. Do not include those who have already entered an appearance in this court. Fed. Cir. R. 47.4(a)(4).

Quinn Emanuel Urquhart & Sullivan LLP: Andrew M. Holmes, Carl G. Anderson, Charles K. Verhoeven, Kevin P.B. Johnson, Sandra L. Haberney, Miles Freeman, Felipe Corredor.

Morris, Nichols, Arsht & Tunnell LLP: Jack B. Blumenfeld, Anthony David Raucci, Derek James Fahnestock.

5. Related Cases. Provide the case titles and numbers of any case known to be pending in this court or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal. Do not include the originating case number(s) for this case. Fed. Cir. R. 47.4(a)(5). See also Fed. Cir. R. 47.5(b).

CareDx, Inc. v. Eurofins Viracor, Inc., No. 22-1028 (docketed Oct. 8, 2021; consolidated Oct. 18, 2021).

6. Organizational Victims and Bankruptcy Cases. Provide any information required under Fed. R. App. P. 26.1(b) (organizational victims in criminal cases) and 26.1(c) (bankruptcy case debtors and trustees). Fed. Cir. R. 47.4(a)(6).

N/A.

TABLE OF CONTENTS

Page

TABLE OF AUTHORITIES

Page(s)

CASES

Page(s)

STATUTES

INTRODUCTION

The unanimous panel correctly held that Appellants' ("CareDx") diagnostic method claims for "detecting" and "quantifying" cell-free DNA ("cfDNA") are ineligible under 35 U.S.C. § 101 and the two-part test of *Alice Corp. Pty. Ltd. v. CLS Bank International*, 573 U.S. 208 (2014), and *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66 (2012). ECF No. 55 ("Op."). As the panel held, the claims lack eligible subject matter because they use admittedly conventional techniques to observe admittedly natural phenomena—the presence of an organ donor's cfDNA in a transplant recipient's blood and the correlation between elevated cfDNA levels and transplant rejection. The panel's analysis and holding is squarely controlled by *Mayo* and this Court's precedent, including *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1376 (Fed. Cir. 2015), and numerous other decisions. Nonetheless, in its petition, CareDx argues that the panel erred at both steps of the *Alice/Mayo* test and departed from precedent. Its arguments lack merit and do not warrant panel or en banc rehearing.

First, at *Alice/Mayo* step one, CareDx contends that the claims are eligible because they purportedly recite "a new and improved laboratory measurement method" using known natural phenomena and "human-made" techniques. ECF No. 62 ("Pet.") at 2. But as the panel recognized, CareDx's claims start and end with detecting the natural phenomena, and CareDx's common specification repeatedly

admits that all of the claimed techniques are conventional. Op. 11-17. Critically, nothing in the specification's lengthy description of commercially available technologies for performing the claimed techniques discusses any ways to *improve* or *modify* those existing technologies. CareDx does not even contend that it does. Thus, the panel rightly rejected CareDx's attempt to rewrite its claims—which merely use conventional tools to observe natural phenomena—as eligible technological improvements to a measurement technique. Op. 13. And, as it did in its briefing to the panel, CareDx improperly treats pre-emption as a requirement for (rather than evidence of) ineligibility and asks this Court to exclude any consideration from conventionality from step one. This Court's precedent forecloses both arguments.

Second, at *Alice/Mayo* step two, CareDx contends that the panel overlooked that the claimed methods are "new, different, and better than those conventional methods" for measuring the natural phenomena that are discussed in the specification. Pet. 3-4. CareDx attempts, but fails, to manufacture an inventive concept from the admittedly non-inventive devices and techniques recited in its claims. It also rehashes the same flawed arguments it made to the panel, which improperly substitute obviousness and novelty for patent eligibility and ignore the patents' own admissions of conventionality. The panel correctly held that the asserted claims add nothing inventive to the natural phenomena. Instead, they recite

detecting the natural phenomena using devices and techniques that the specification admits are conventional.

In short, the panel addressed (and rejected) CareDx's challenges and correctly held the asserted claims are ineligible under § 101 because they are directed to natural phenomena and include no inventive concept—like the diagnostic claims in *Mayo*, *Ariosa*, and numerous others decisions. *See, e.g.*, Op. 18. CareDx fails to identify any reason for the panel (much less the en banc Court) to revisit the panel's well-reasoned decision. CareDx's rehearing petition should be denied.

ARGUMENT

CareDx identifies two purported errors in the panel's opinion. Pet. v. First, CareDx argues that the panel at step one ignored the "claimed advance," which it contends is a "patent eligible improvement on existing measurement methods (which are human-made)." Pet. v; *see* Pet. 2-3, 12-14. Second, CareDx contends that the panel at step two overlooked that the claimed methods "depart[] from conventional methods for measuring" the natural phenomena and "instead appl[y] existing laboratory tools in a new context that evaded the prior art." Pet. v; *see* Pet. 3-4, 14-16. Those arguments are wrong and do not warrant panel or en banc rehearing.

I. THE PANEL CORRECTLY HELD THAT THE CLAIMS ARE DIRECTED TO THE DETECTION OF NATURAL PHENOMENA

At *Alice/Mayo* step one, the panel correctly held that CareDx's claims are directed to detecting the natural phenomena of cfDNA in a transplant recipient's

blood and its correlation to transplant rejection. Op. 12-17. As the panel held, these claims are just like the diagnostic claims found ineligible in *Mayo* and numerous other cases. Op. 15-16. CareDx's step one arguments lack merit for four reasons.

First, CareDx argues that the panel "fail[ed] to consider" that the patents' "claimed advance is new, different, and better ways to measure a natural correlation." Pet. 3. But, as it did in its briefing to the panel, CareDx is simply trying to rewrite its claims as improved "measurement" methods. Pet. 1-4, 12-14, 16-17. In so doing, CareDx does not focus on the words of the claims—"detecting" and "quantifying."

The panel expressly considered and correctly rejected CareDx's attempt to rewrite its claims. Op. 13, 16-17. As the panel explained, "CareDx does not actually claim any improvements in laboratory techniques—rather, … the actual claims of the patent merely recite the conventional use of existing techniques to detect naturally occurring cfDNA." Op. 17. Indeed, "the written description is replete with characterizations of the claimed techniques in terms that confirm their conventionality." Op. 14 & n.1.[1] Merely "appending standard techniques to detect"

[1] There is no dispute that CareDx "does not actually claim any improvements in laboratory techniques." Op. 17. CareDx conceded at the district court that the patents do not claim improvements to the recited detection techniques. *See* Appx252 (Tr. 54:17-55:1) (CareDx's counsel agreeing that the claims are "not an invention of a new sequencing method"); Appx255 (Tr. 69:3-7) ([Court]: "Does the patent claim a technology that increased quantitative accuracy? [CareDx's counsel]: Over what

natural phenomena does not constitute "an innovative laboratory technique" or render claims patent eligible. *Athena Diagnostics, Inc. v. Mayo Collaborative Servs. LLC*, 915 F.3d 743, 751-52 (Fed. Cir. 2019).

Thus, "[t]he claimed methods are indistinguishable from other diagnostic method claims the Supreme Court found ineligible in *Mayo* and that [this Court] found ineligible on multiple occasions," such as in *Ariosa*. Op. 15; *see, e.g.*, *Ariosa*, 788 F.3d at 1377 (ineligible claims recited detecting cell-free fetal DNA by amplifying using "ordinary PCR or more sophisticated developments thereof" (citation omitted)); *Genetic Veterinary Scis., Inc. v. LABOKLIN GmbH & Co. KG*, 933 F.3d 1302, 1315-19 (Fed. Cir. 2019) (ineligible claims recited genotyping to detect specific mutation using selective amplification and "real-time PCR"); *Roche Molecular Sys., Inc. v. CEPHEID*, 905 F.3d 1363, 1371 (Fed. Cir. 2018) (ineligible claims recited detecting bacterium by PCR amplification); Op. 18.

CareDx attempts to distinguish this precedent by arguing that the "inventors here did not purport to discover the natural phenomenon." Pet. 17. This argument fails because acknowledging that a natural phenomenon is well-known does not make the phenomenon patentable. *See Mayo*, 566 U.S. at 78-79. The analysis under *Alice/Mayo* step one is whether the claims as a whole are "directed to" a natural

---

everyone else could do at the time? No."); Appx301 (Tr. 252:24-253:3) (CareDx's expert admitting that "[t]here's no specific technique for how th[e] determination of the quantity [of donor derived DNA] needs to be done in the patent claims").

phenomenon or natural law—*not* whether that ineligible principle was previously known. *See Parker v. Flook*, 437 U.S. 584, 591 (1978) ("[T]he novelty of the [ineligible principle] is not a determining factor at all."); *O'Reilly v. Morse*, 56 U.S. (15 How.) 62, 129 (1853) (holding ineligible claim directed to the natural law of electro-magnetism, which patentee did not discover). Thus, the fact that the patentee did not discover the natural phenomena does not change the focus of the claims. Op. 13. Where, as here, the claims recite using conventional techniques to detect natural phenomena (whether newly discovered or not), they are directed to the natural phenomena at step one. *See Ariosa*, 788 F.3d at 1376.

CosmoKey Solutions GmbH & Co. KG v. Duo Security LLC, 15 F.4th 1091 (Fed. Cir. 2021) (cited at Pet. 12-13), is not to the contrary. There, the district court misinterpreted a single passage in the specification as admitting conventionality of the claimed computer invention when in fact that passage was describing the state of the prior art. *Id.* at 1098. Moreover, the specification in that case disclosed a "technical solution" to a problem in prior-art networks and computers, and "nothing in the specification" showed that the majority of the claimed method steps were conventional. *Id*. In contrast, as the panel explained, the specification here "is *replete* with characterizations of the claimed techniques in terms that confirm their conventionality." Op. 14 & n.1 (emphasis added).

Second, CareDx contends that the panel's step one holding improperly relied on "a 'conventionality' analysis that duplicates step two." Pet. 3. CareDx misreads this Court's precedent. As the panel recognized, this Court has "repeatedly analyzed conventionality at step one as well." Op. 16; *see Athena*, 915 F.3d at 751 (step one: "the specification describes the claimed concrete steps for observing the natural law as conventional"); *Cleveland Clinic Found. v. True Health Diagnostics LLC*, 859 F.3d 1352, 1361 (Fed. Cir. 2017) (step one: claims contained "no meaningful non-routine steps"); *Chamberlain Grp., Inc. v. Techtronic Indus. Co.*, 935 F.3d 1341, 1347 (Fed. Cir. 2019) (step one: claim "directed to" ineligible concept because it was implemented by a "conventional form of communication"). The panel reiterated the principle that "the two stages are plainly related: not only do many of our opinions make clear that the two stages involve overlapping scrutiny of the content of the claims, but … there can be close questions about when the inquiry should proceed from the first stage to the second." Op. 16 (alteration in original) (quoting *Elec. Power Grp., LLC v. Alstom S.A.*, 830 F.3d 1350, 1353 (Fed. Cir. 2016)); *see Amdocs (Israel) Ltd. v. Openet Telecom, Inc.*, 841 F.3d 1288, 1294 (Fed. Cir. 2016) (recognizing "considerable overlap" between the steps). Per this precedent, the panel correctly rejected CareDx's "effort to draw a bright line between the two steps." Op. 16.

Third, CareDx asserts that the claims are eligible because they employ "human-made" methods that differ from prior art "human-made" methods. Pet. v, 1-3, 11-13. But reciting "human-made" methods does not render the claims eligible. Indeed, *Ariosa* and numerous other decisions involved claims that employed "human-made" methods, including PCR, amplification, and genotyping, that departed from prior "human-made" methods, but this Court nonetheless held that they were directed to natural phenomena and not any improvement to the techniques themselves. *See, e.g.*, *Ariosa*, 788 F.3d at 1374-76; *Genetic Veterinary Scis.*, 933 F.3d at 1315, 1318; *Roche Molecular Sys.*, 905 F.3d at 1371; *supra* at 5. Here, the panel correctly concluded (consistent with the patents and CareDx's own expert) that the "claims boil down to collecting a bodily sample, analyzing the cfDNA using conventional techniques, including PCR, identifying naturally occurring DNA from the donor organ, and then using the natural correlation between heightened cfDNA levels and transplant health to identify a potential rejection, none of which was inventive." Op. 15-16; *see* Appx80-81 & n.4 (citing Appx280-282 (169:19-170:5, 174:10-23, 175:25-176:10, 176:22-177:8) (CareDx's expert)).

Fourth, CareDx contends that because the claims do not "preempt usage of the natural phenomenon, or even measuring of the phenomenon." Pet. 12; *see also* ECF No. 65-2 at 4 (*Amicus Curiae*: "The claimed invention does not preempt all uses of the underlying natural phenomenon."). But the law is clear that while

"preemption may signal patent ineligible subject matter, the absence of complete preemption does not demonstrate patent eligibility." *Ariosa*, 788 F.3d at 1379. Where, as here, "a patent's claims are deemed only to disclose patent ineligible subject matter under the *Mayo* framework, … preemption concerns are fully addressed and made moot." *Id.*; *see Flook*, 437 U.S. at 586-88 (complete preemption not required); *Athena*, 915 F.3d at 752 (claims ineligible even though "routine steps [we]re set forth with some specificity"); *Roche Molecular Sys.*, 905 F.3d at 1374 ("[T]he method claims … cannot gain subject matter eligibility solely because they are limited to specific signature nucleotides."); *Cleveland Clinic*, 859 F.3d at 1363 (rejecting patentee's argument narrow preemptive scope rendered claims eligible).

* * *

The panel correctly determined at step one that CareDx's claims are directed to "detecting" the natural phenomena of cfDNA in a transplant recipient's blood and its correlation to transplant rejection. Beyond this, the claims recite only "standard techniques for observing" these natural phenomena. *See Athena*, 915 F.3d at 752. Thus, the claim language in view of the specification confirms that the focus of the claims is detecting the natural phenomena.

II. THE PANEL CORRECTLY HELD THAT THE CLAIMS ADD NOTHING INVENTIVE TO THE NATURAL PHENOMENA

At *Alice/Mayo* step two, the panel correctly held that the asserted claims "add nothing inventive because they merely recite standard, well-known techniques in a

logical combination to detect natural phenomena." Op. 17 (citing admissions in specification). CareDx argues that the panel's opinion "wrongly excludes human-made improvements when they employ existing tools." Pet. 3. In particular, CareDx contends that the patents explain the "shortcomings" of conventional techniques and "how the claimed methods are new, different, and better than those conventional methods." *Id.* at 3-4. Like its step one arguments, CareDx's step two arguments fail under this Court's precedent. None of them warrant en banc review.

First, CareDx contends that the claims are eligible because they "apply existing tools to a different context to arrive at a new solution to a problem that had eluded determined prior artists." Pet. 14. But even the alleged novelty of applying admittedly conventional techniques in a particular context—detecting donor cfDNA—does not render those techniques eligible. "Eligibility and novelty are separate inquiries." *Two-Way Media Ltd. v. Comcast Cable Commc'ns, LLC*, 874 F.3d 1329, 1340 (Fed. Cir. 2017); *see Flook*, 437 U.S. at 591 (assuming mathematical formula was "novel" yet nonetheless holding claims ineligible).[2] Applying those same standard techniques from the prior art to detect donor cfDNA does not give rise to patent-eligible subject matter, even if the combination is new.

[2] For these reasons, the arguments of the *Amicus Curiae* do not warrant en banc review. *See* ECF No. 65-2 at 2 (claims that "use a novel and nonobvious combination of techniques that yield a novel and nonobvious result" should be patent eligible).

For example, in *Ariosa*, the patent "combined and utilized man-made tools of biotechnology in a new way that revolutionized prenatal care"—indeed, "before the … patent, *no one* was using the plasma or serum of pregnant mothers to amplify and detect paternally-inherited cffDNA." 788 F.3d at 1379 (citations omitted). But this Court nonetheless held the claims were ineligible because they were directed to detecting a natural phenomenon and added nothing inventive. *Id.* And in *Athena*, this Court similarly held ineligible purportedly new techniques, rejecting the patentee's argument that "the claimed steps were unconventional because they had not been applied to detect" certain natural phenomena prior to patentee's discovery. 915 F.3d at 754; *see also Cleveland Clinic*, 859 F.3d at 1355 (claims ineligible even though patentee "purportedly discovered how to 'see' [a particular enzyme] in blood and correlate" to risk); *Genetic Techs. Ltd. v. Merial L.L.C.*, 818 F.3d 1369, 1373 (Fed. Cir. 2016) (claims ineligible despite "various advantages over prior art"); *Content Extraction & Transmission LLC v. Wells Fargo Bank, Nat'l Ass'n*, 776 F.3d 1343, 1348 (Fed. Cir. 2014) (limiting the ineligible concept "to a particular technological environment" is insufficient to render claims eligible). Likewise, here, applying admittedly known laboratory techniques to detect natural phenomena in a particular context does not confer eligibility.

Second, CareDx contends that the combination of techniques in the claims was unconventional and "groundbreaking," even if each individual technique was

preexisting. Pet. 17. But as the panel observed, the "specification confirms that the claimed combination of steps—collecting a sample, genotyping, sequencing, and quantifying—was a straightforward, logical, and conventional method for detecting cfDNA previously used in other contexts, including cancer diagnostics and prenatal testing." Op. 18 (citing Appx120-121 ('652 patent 6:57-7:46)). Nothing in the specification suggests that the recited combination of steps was inventive in any way. Thus, as in *Mayo* and the other diagnostic method cases discussed, the claimed combination of steps "when viewed as a whole, add nothing significant beyond the sum of their parts taken separately." *Mayo*, 566 U.S. at 79-80.[3]

Third, CareDx points to the district court's initial decision denying summary judgment of patent ineligibility in an effort to undermine the panel's holding. In particular, CareDx states that the "district court denied summary judgment on the inventiveness of the claimed combination of steps, thus confirming that the improved method could not be dismissed as merely 'conventional' overall." Pet. 15 (emphasis omitted). But what really happened was that the district court initially

[3] As Natera's expert Dr. Quackenbush observed, the specification does not describe any special protocols or modifications of standard protocols for performing the recited steps differently than how they were previously performed. Appx269 (Tr. 122:5-123:10) (Quackenbush). And when asked by the district court, CareDx's counsel failed to explain *how* the order of steps was unconventional, even noting that "primarily, most persuasively, it's the application of [the order of recited steps] to the context of cell-free DNA" that renders the claims eligible. Appx252 (Tr. 56:15-24).

denied summary judgment because *both* sides submitted extrinsic evidence on the issue of conventionality. Op. 19; *see* Appx64; Appx67. The district court denied summary judgment because the warring extrinsic evidence initially appeared to create a fact issue that the court later found to be "non-genuine due to the explicit contradiction between CareDx's extrinsic evidence and the numerous admissions of conventionality in the intrinsic record." Op. 19; *see* Appx64; Appx67; Appx105-106; Op. 13-14 & n.1, 17; *see also, e.g.*, *Athena*, 915 F.3d at 756 ("Because Athena's expert declaration made allegations inconsistent with the '820 patent, the district court was not obliged to accept them as true."). The panel correctly affirmed the district court's decision.

* * *

The panel correctly determined that the asserted claims add nothing inventive at step two because they merely recite standard, well-known techniques in a logical, standard combination to detect natural phenomena. Applying standard techniques from the prior art in a particular context—i.e., to detect donor cfDNA—does not give rise to patent-eligible subject matter. Nothing about the panel's decision warrants rehearing.

CONCLUSION

The Court should deny CareDx's rehearing petition.

Dated: November 14, 2022

Respectfully submitted,

/s/ Gabriel K. Bell

Gabriel K. Bell
Ashley M. Fry
LATHAM & WATKINS LLP
555 Eleventh Street, NW, Suite 1000
Washington, DC 20004
(202) 637-2200

Counsel for Appellee Natera, Inc.

CERTIFICATE OF COMPLIANCE

Pursuant to Federal Rule of Appellate Procedure 32(g)(1) and Federal Circuit Rule 35, I hereby certify that the foregoing response complies with the type-volume limitations in Federal Rule of Appellate Procedure 35(b)(2), (e) and Federal Circuit Rule 35(e)(2) because it contains 3,034 words, excluding the parts of the response exempted by Federal Rule of Appellate Procedure 32(f) and Federal Circuit Rule 32(b).

I further certify that this response complies with the typeface requirements of Federal Rule of Appellate Procedure 32(a)(5), (6) because this brief was prepared using Microsoft Word 365 in 14-point Times New Roman font.

/s/ Gabriel K. Bell
Gabriel K. Bell