No. 22-1066

IN THE
# Supreme Court of the United States

CAREDX INC., ET AL.

*Petitioners,*

v.

NATERA, INC., ET AL.,

*Respondents.*

On Petition for a Writ of Certiorari to the
United States Court of Appeals for the Federal Circuit

## BRIEF FOR RESPONDENT EUROFINS VIRACOR, LLC IN OPPOSITION


DARRYL M. WOO
GOODWIN PROCTER LLP
Three Embarcadero Ctr.
San Francisco, CA 94111

KEVIN J. DEJONG
JORDAN BOCK
GOODWIN PROCTER LLP
100 Northern Ave.
Boston, MA 02210

WILLIAM M. JAY
*Counsel of Record*
GOODWIN PROCTER LLP
1900 N St., N.W.
Washington, DC 20036
*wjay@goodwinlaw.com*
(202) 346-4000

*Counsel for Respondent Eurofins Viracor, LLC*


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## QUESTION PRESENTED

This Court has long recognized that "[l]aws of nature, natural phenomena, and abstract ideas are not patentable." *Mayo Collaborative Servs. v. Prometheus Lab'ys, Inc.*, 566 U.S. 66, 70 (2012) (citation omitted). Because these categories involve "the basic tools of scientific and technological work," "monopolization of those tools through the grant of a patent might tend to impede innovation more than it would promote it." *Id.* at 71.

The question presented is:

Whether the courts below correctly concluded that merely applying a conventional measurement technique to observe a previously discovered natural phenomenon is not eligible for patent protection.

## PARTIES TO THE PROCEEDING

Respondent Eurofins Viracor, Inc. has changed its name to Eurofins Viracor, LLC. The caption of the petition otherwise correctly lists the parties to the proceeding.

## RULE 29.6 STATEMENT

Eurofins Clinical Testing US Holdings, Inc. and Eurofins Scientific SE are parent corporations of Eurofins Viracor, LLC. There is no other company that owns 10% or more of Eurofins Viracor's stock.

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## INTRODUCTION

Section 101 of the Patent Act precludes patenting a natural phenomenon—a prohibition that is now more than a century old. Patent owners regularly petition this Court to reinterpret that statutory provision in their favor, and this Court regularly denies those petitions, including twice since this petition was filed. And this case would be a poor vehicle to reconsider the interpretation of Section 101 in any event, because petitioners ("CareDx") so clearly are attempting to do what this Court's decisions forbid—claim ownership of subject matter that is ineligible for patenting.

Just since June 2022, this Court has denied at least four petitions seeking a new interpretation of Section 101. Three were brought by patent owners seeking to loosen the limits Section 101 imposes. *See Interactive Wearables, LLC v. Polar Electro Oy*, No. 21-1281 (cert. denied May 15, 2023); *Tropp v. Travel Sentry, Inc.*, No. 22-22 (cert. denied May 15, 2023); *Am. Axle & Mfg., Inc. v. Neapco Holdings LLC*, No. 20-891 (cert. denied June 30, 2022). The fourth was brought by a defendant contending that Section 101's limits are not tight enough. *Avery Dennison Corp. v. ADASA Inc.*, No. 22-822 (cert. denied May 30, 2023). The Court declined each of these invitations.

Nothing about this case's subject matter calls for a different result. The Court unanimously concluded more than a decade ago that medical-diagnostic patents may not claim ownership of the inferences to be drawn from observations of the human body—that is just another attempt to patent a law of nature. *Mayo Collaborative Servs. v. Prometheus Lab'ys, Inc.*, 566 U.S. 66 (2012). Since *Mayo*, this Court has repeatedly

denied petitions asking it to change its application of Section 101 to medical-diagnostic patents. *E.g.*, *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, No. 19-430 (cert. denied Jan. 13, 2020); *Hikma Pharms. USA Inc. v. Vanda Pharms. Inc.*, No. 18-817 (cert. denied Jan. 13, 2020); *Cleveland Clinic Found. v. True Health Diagnostics LLC*, No. 17-997 (cert. denied June 11, 2018); *Sequenom, Inc. v. Ariosa Diagnostics, Inc.*, No. 15-1182 (cert. denied June 27, 2016).

If anything, the arguments against granting certiorari to revisit this issue have grown only stronger. Not only have the Patent Office, patent owners, and patent challengers relied on this Court's decisions going back to *Mayo* and beyond, Congress is actively considering whether to amend the statute. Whereas this Court is bound by the existing statute, Congress is free to rewrite it.

Not only is now not the right time to revisit Section 101, this is not the right petition. CareDx's claim to patentability is highly unusual among Section 101 cases: CareDx claims its patent is eligible for protection because of discoveries it did not make. As CareDx acknowledges—indeed, emphasizes—the core of U.S. Patent No. 8,703,652 ("the '652 patent") involves a long-known natural phenomenon: After an organ transplant, an increase in the amount of the organ donor's DNA found floating in the recipient's blood is correlated with organ rejection. That is exactly the type of natural law that *Mayo* holds is not patent-eligible. Yet the '652 patent (the only one asserted against Eurofins Viracor) claims the application of conventional measurement techniques to observe that correlation. CareDx argues that its claims are eligible for patent protection despite *Mayo* because it applied

a known measurement technique (which it did not invent) to a known natural phenomenon (which it did not discover). CareDx calls this an improved measurement technique, but it is nothing of the sort. Borrowing a conventional pair of binoculars is not an improved *measurement technique*, even if the borrower uses them to observe a new natural phenomenon.

"For there to be a patent eligible application of a natural law, there must be a 'discover[y].'" *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 927 F.3d 1333, 1341 (Fed. Cir. 2019) (Dyk, J., concurring in the denial of rehearing en banc). Here, there is no discovery—just the patentees' selection of a known technique to observe a known correlation. CareDx argues that this process alone is patentable, but its approach would eviscerate Section 101. In *every* diagnostic case, the patentee is necessarily the first to apply a particular measurement technique to detect the underlying phenomenon. Thus, patentees who had actually discovered the natural phenomenon at play (unlike the patentees here) could avoid Section 101 merely by claiming the application of a measurement technique to observe it. And patentees who (like the patentees here) did not discover *anything* could nevertheless lay claim to a natural phenomenon merely by patenting it in combination with a known measurement technique that they likewise did not discover. Not surprisingly, the Federal Circuit unanimously rejected CareDx's arguments in a straightforward opinion. And unlike in previous Section 101 cases, the court of appeals then denied rehearing en banc with no noted dissents.

There may be hard cases under Section 101, but this is not one of them. The Court should deny the petition.

## STATEMENT

### A. The '652 patent is directed to observing the natural correlation between organ rejection or failure and an increase in the quantity of donor cell-free DNA.

#### 1. The presence of cell-free DNA in bodily fluids is used as a diagnostic tool in a variety of medical contexts.

DNA (deoxyribonucleic acid) is made up of repeating sets of nucleotides (chemical bases) arranged in a sequence. *See Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 581-582 (2013). Differences among individuals' DNA sequences are known as polymorphisms, where a single nucleotide polymorphism refers to a single variation between nucleotides on a particular stretch of DNA. C.A.J.A. 123 (11:24-35).[1] Over the last several decades, scientists have developed a variety of methods to "genotype" and "sequence" DNA to identify the particular individual from which it came. *See* C.A.J.A. 121-122 (8:50-9:3); C.A.J.A. 1274-1275 (Decl. ¶ 71). Genotyping refers generally to identifying an individual's genetic makeup, while sequencing is the specific process of determining the order of nucleotide bases in a stretch of

[1] Citations with a (column:line) parenthetical are to the '652 patent, which appears in the appendix and the addendum to the opening brief below. It is also available at https://image-ppubs.uspto.gov/dirsearch-public/print/downloadPdf/8703652. The parenthetical accompanying each citation indicates the specific column and line being cited.

DNA. C.A.J.A. 1258-1259 (Decl. ¶ 43); C.A.J.A. 1281 (Decl. ¶ 84).

Multiplex sequencing, also called "high-throughput" or "Next Generation" sequencing,[2] involves sequencing multiple stretches of DNA in parallel, allowing scientists to more quickly analyze large volumes of genetic material. C.A.J.A. 1290 (Decl. ¶ 100). Multiplex sequencing is itself an umbrella term that covers several different techniques for simultaneously sequencing DNA. *See* C.A.J.A. 1290-1292 (Decl. ¶¶ 101-102) (discussing "sequencing-by-synthesis" and "shotgun sequencing," both forms of multiplex sequencing). The '652 patent specification acknowledges that multiplex sequencing dates back to at least the year 2000, C.A.J.A. 125 (16:9-13), ten years before the '652 patent's priority date, C.A.J.A. 109.

While most DNA is found inside cells, scientists discovered as early as 1948 that "cell-free DNA" (cfDNA) circulates in blood and other bodily fluids after being released by dead or dying cells. C.A.J.A. 120-121 (6:57-67, 7:40-46); C.A.J.A. 1261-1262 (Decl. ¶¶ 47-48). The presence and quantity of cfDNA is a well-recognized diagnostic tool in a range of medical contexts. In cancer patients, for example, tumor cells die and release cfDNA into the patient's blood. C.A.J.A. 1265-1266 (Decl. ¶¶ 54-55 ). Because tumor-derived cfDNA bears unique "hallmark signs of the disease," scientists can monitor the level of tumor-derived cfDNA to assist with "cancer detection and treatment." C.A.J.A. 121 (7:1-2, 7:18-19). The same

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[2] Like CareDx, Eurofins uses these terms interchangeably. *See* Pet.5-6; *see also* C.A.J.A. 303 (258:20-24).

is true for patients with bacterial infections: bacterial cells die and release bacterial cfDNA into the patient's blood, providing clinicians with a diagnostic tool for monitoring the infection. C.A.J.A. 1266 (Decl. ¶ 56).

The presence of cfDNA can also be used to detect fetal abnormalities. In 1996, scientists discovered that cell-free fetal DNA can be found in maternal plasma during pregnancy. C.A.J.A. 1264 (Decl. ¶ 52); *see also Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1373 (Fed. Cir. 2015) (discussing the discovery and subsequent uses of cell-free fetal DNA in maternal plasma). This fetal cfDNA reflects the child's (rather than the mother's) genotype, allowing doctors to test for certain genetic markers and detect certain disorders before birth. C.A.J.A. 1264-1265 (Decl. ¶¶ 52-53); *see also* C.A.J.A. 121 (7:19-27); *Ariosa*, 788 F.3d at 1373. For instance, the quantity of fetal cfDNA in maternal plasma can be an indicator for certain genetic abnormalities. *Ariosa*, 788 F.3d at 1373; C.A.J.A. 121 (7:23-25).

At issue here is the comparable role of cfDNA from an organ transplant. When a patient receives a donor organ, cells from that organ naturally die, releasing cfDNA into the transplant recipient's blood. Pet.App.3a; *see also* C.A.J.A. 1263-1264 (Decl. ¶¶ 50-51). Because the donated organ has the donor's DNA, the cfDNA released from the donated organ will differ from the recipient's. C.A.J.A. 121 (7:37-46); C.A.J.A. 1262-1264 (Decl. ¶¶ 49-51). If a transplanted organ is failing or being rejected by the recipient, cells in the organ die at a faster rate than other cells in the body, thereby releasing more foreign cfDNA into the patient's bodily fluids than would be expected from a healthy transplant. Pet.App.3a; C.A.J.A. 1263-1264

(Decl. ¶ 51). As a result, elevated quantities of donor cfDNA naturally correlate with organ rejection or failure. Scientists recognized that correlation as early as 1998, more than a decade before the filing of the '652 patent. *See* C.A.J.A. 121 (7:48-8:21); C.A.J.A. 1491-1492.

**2. The '652 patent recites well-known diagnostic methods to detect DNA from an organ donor in the bodily fluids of a transplant recipient.**

The '652 patent uses this natural phenomenon to claim a method for detecting organ rejection or failure. The patentees proposed using multiplex sequencing and other techniques well-known in the art to identify the level of donor cfDNA in the blood of a transplant recipient and identify any increase.

Representative claim 1 of the '652 patent comprises four steps, each described at a high level of generality. Pet.App.3a-4a, 8a-9a. They are: (a) providing a sample containing cfDNA from a transplant recipient; (b) creating a polymorphism profile using DNA polymorphisms specific to the donor, the recipient, or both; (c) multiplex sequencing the cfDNA in the sample and analyzing the results using the polymorphism profile to detect donor and recipient cfDNA; and (d) determining the quantity of donor cfDNA to monitor the transplant outcome, where an increase in the quantity of donor cfDNA over time indicates organ rejection. Pet.App.3a-4a; C.A.J.A. 131 (27:39-28:40). As the specification explains, each step is performed using one of any number of conventional techniques known in the art.

For step (a), "providing a sample," the specification states that "any technique known in the art may be used" to obtain a sample, including, for example, "a syringe or other vacuum suction device." C.A.J.A. 122 (10:11-12). The same is true for step (b), "obtaining a genotype": The specification acknowledges that "[g]enotyping of the transplant donor and/or the transplant recipient may be performed by any suitable method known in the art," C.A.J.A. 127 (20:31-34), and proposes "using existing genotyping platforms known in the art," C.A.J.A. 124 (13:52-53). Likewise, for step (c), "multiplex sequencing," the specification cites multiple commercially available options and notes that multiplex sequencing systems "include those disclosed" in articles from 2000, 2001, and 2003. C.A.J.A. 125 (15:22-16:13). The specification also identifies "high-throughput shotgun sequencing of circulating nucleic acids (e.g. cell-free DNA)" among the recited "methods known in the art." C.A.J.A. 122 (9:11-13).

Finally, for step (d), "monitoring … [the] quantity of donor [cfDNA]," the specification explains that detecting "donor-specific markers" can be accomplished through a series of "methods known in the art," C.A.J.A. 122 (9:8-14), and further that "[t]he presence or absence of one or more nucleic acids from the transplant donor in the transplant recipient may be determined by any suitable method known in the art," C.A.J.A. 128 (21:5-8). Step (d) also includes functional language to the effect that the "sensitivity of the method is greater than 56% compared to sensitivity of current surveillance methods"—reflecting the sensitivity of commercially available methods. C.A.J.A. 131 (27:67-28:40); *see also* C.A.J.A. 129 (23:34-36) ("In

some embodiments, the methods described herein have at least 56% sensitivity.").

Each of these steps is recited in the claims at a high level of generality, and neither the claim language nor anything else in the intrinsic record narrows the method to anything more precise. In addition, the specification broadly notes that the invention "employs, unless otherwise indicated, conventional techniques of immunology, biochemistry, chemistry, molecular biology, microbiology, cell biology, genomics and recombinant DNA, which are within the skill of the art." C.A.J.A. 120 (5:36-48).

### B. Both the district court and the Federal Circuit held that the patent claims ineligible subject matter.

1. Petitioner CareDx Inc. and respondents Eurofins Viracor, LLC ("Eurofins") and Natera, Inc. are competitors in the field of medical diagnostics. All have products on the market designed to monitor and assess the probability of organ failure following a kidney transplant. CareDx Inc. licenses the '652 patent from Stanford. In 2019, CareDx sued Eurofins and, separately, Natera for allegedly infringing the '652 patent. C.A.J.A. 352; C.A.J.A. 363. CareDx later asserted two additional patents[3] against Natera, but not Eurofins. C.A.J.A. 374; *see also* Pet.App.9a.

2. From the outset, Eurofins has asserted that the '652 patent is directed to patent-ineligible subject matter—detecting the natural correlation between increased donor cfDNA and transplant rejection. Under this Court's longstanding construction of 35 U.S.C.

[3] U.S. Patent No. 9,845,497 and U.S. Patent No. 10,329,607.

§ 101, "'[l]aws of nature, natural phenomena, and abstract ideas' are not patentable." *Mayo*, 566 U.S. at 70 (quoting *Diamond v. Diehr*, 450 U.S. 175, 185 (1981), and citing cases going back to 1853).

Eurofins first moved to dismiss on Section 101 grounds, but the district court determined that the issue was better decided on an early motion for summary judgment. The district court initially referred the motion to dismiss to a magistrate judge, Pet.App.70a n.1, who recommended that the court deny it, Pet.App.70a-81a. The district court adopted the magistrate judge's proposed disposition of the motion to dismiss, but not his reasoning or conclusion that the claims were directed to eligible subject matter. Pet.App.67a. Rather, the court thought that deciding the Section 101 merits would be "premature." Pet.App.67a. The court highlighted that the specification "raise[d] doubts" as to the patent's validity: "language in the written description[] … suggest[ed] that the patented steps are neither new nor unconventional." Pet.App.67a. Given the "doubts about the patent's validity," the court decided to "entertain … early dispositive motion practice" on the question of subject-matter eligibility. Pet.App.67a-68a.

3. The district court granted summary judgment to Eurofins and Natera, holding the patents ineligible under Section 101. C.A.J.A. 74.[4] The court concluded

[4] The district court initially denied summary judgment, briefly stating that CareDx's expert declaration and a handful of articles created a dispute of fact on whether multiplex sequencing had become routine. Pet.App.63a-65a. But the court decided to revisit this ruling after Eurofins and Natera sought certification of an interlocutory appeal and explained that a patentee cannot use

that the claims were directed to the detection of natural phenomena—*i.e.*, "donor-specific cfDNA and the correlation donor-specific cfDNA has with organ rejection." Pet.App.46a. The court further determined that it was clear from the patentees' own admissions, recited in the patent, that "the claimed detection methods are conventional." *Id.* As the court explained, "where the specification admits the additional claim elements are well understood, routine and conventional, it will be difficult, if not impossible, for a patentee to show a genuine dispute" with respect to subject-matter eligibility. C.A.J.A. 229 (14:22-15:1) (quoting *Aatrix Software, Inc. v. Green Shades Software, Inc.*, 890 F.3d 1354, 1356 (Fed. Cir. 2018) (Moore, J., concurring in denial of rehearing en banc)). Thus, the court concluded, the intrinsic evidence established that the '652 patent claimed ineligible subject matter and did not add any "inventive concept" that could make it patent-eligible. Pet.App.45a-56a.

4. The Federal Circuit affirmed in a straightforward, unanimous opinion. As the panel explained, contrary to CareDx's persistent descriptions, its claims do not involve "a method of preparation or a new measurement technique." Pet.App.14a. Indeed, "CareDx does not actually claim any improvements in laboratory techniques," and "the actual claims of the patent merely recite the conventional use of existing techniques to detect naturally occurring cfDNA." Pet.App.18a. Nor, for that matter, does CareDx claim that it "invent[ed] or discover[ed] the relationship between donor cfDNA and the likelihood of organ

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a litigation expert to contradict admissions made in the patent itself—admissions that here proved highly relevant to the Section 101 analysis. Pet.App.39a.

transplant rejection," a correlation that was unearthed by other scientists "at least" as early as 1998. Pet.App.14a. In short, the patents "apply conventional measurement techniques to detect a natural phenomenon—the level of donor cfDNA and the likelihood of organ transplant rejection." Pet.App.16a.

In so holding, the Federal Circuit rejected CareDx's argument that the district court improperly conflated the two steps of the patent-eligibility analysis—namely, whether (1) "the claims at issue are directed to one of th[e] patent-ineligible concepts" (natural laws, natural phenomena, or abstract ideas), and (2) if so, whether the otherwise ineligible claims contain "an inventive concept sufficient to transform the claimed abstract idea into a patent-eligible application," thus saving the patent from ineligibility. *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 573 U.S. 208, 217-222 (2014) (internal quotation marks omitted); *see also Mayo*, 566 U.S. at 76-80. Rather, the Court explained, the district court concluded at step one that the claims' focus on "detecting" and "quantifying" cfDNA revealed that the claims were "directed to" natural phenomena." Pet.App.17a. And at step two, the Federal Circuit agreed with the district court that the asserted claims "merely recite standard, well-known techniques in a logical combination." Pet.App.18a. While both steps involved considerations of conventionality, that was a natural consequence of CareDx's argument at step one. Pet.App.18a. To evaluate CareDx's argument that the patents' claims were directed to improved laboratory techniques, the court had to consider whether the patents in fact claimed any such improved laboratory techniques, rather than "the conventional use of existing techniques." Pet.App.18a.

5. CareDx filed a combined petition for panel rehearing and rehearing en banc. The Federal Circuit denied the petition with no noted dissents. Pet.App.82a-84a.

## REASONS FOR DENYING THE PETITION

The Federal Circuit's unanimous opinion broke no new ground and made no new law. To the contrary, the decision below is entirely consistent with this Court's precedents and with fundamental principles of patent eligibility. There is no reason for the Court to take this straightforward case after repeatedly declining Section 101 cases—cases that had drawn considerably more amicus support and attracted considerably more controversy. Indeed, this case would not be a suitable vehicle even if the Court were actively seeking a Section 101 case to review.

First, this case follows ineluctably from the Court's prior precedents interpreting Section 101. As the Federal Circuit explained, the claimed methods here are "indistinguishable" from the diagnostic claims at issue in *Mayo*. Pet.App.16a. Step for step, the claims in the '652 patent mirror the claims in *Mayo*. While CareDx avoids raising this possibility, this Court could reach a different decision only by overruling or dramatically reshaping *Mayo*. CareDx has not raised the type of extraordinary justification necessary to overrule prior statutory-interpretation precedent—nor is there any reason for the Court to reinterpret the current statute just when Congress is actively considering a bill to rewrite it. Congress is the proper audience for CareDx's request to revise the categories of eligible subject matter.

Second, this case does not present the question CareDx says is presented. CareDx asks the Court to consider "whether a new and useful method for measuring a natural phenomenon, that improves upon prior methods for measuring that very same phenomenon, is eligible for patent protection under Section 101." Pet.i. But the '652 patent does not involve a new and improved laboratory method. Rather, the patentees applied *concededly conventional* laboratory techniques to observe a *known* natural phenomenon. And there is no need for the Court to consider whether using a known technique to observe a known natural phenomenon is eligible for patent protection.

While CareDx argues that the patentees were the first to apply a known technique to a particular context, that is true in *every* comparable diagnostic case: even where the patentee also discovered the underlying correlation, the patentee is necessarily the first to apply a particular measurement technique to detect the correlation. CareDx's approach would extend patent eligibility to *every* natural phenomenon. Not surprisingly, this issue has neither divided the Federal Circuit nor led to the purported concerns that CareDx identifies.

## I. This Court's decision in *Mayo* directly controls this case.

1. As the Federal Circuit recognized, this case is *Mayo*: "The claimed methods are indistinguishable from other diagnostic method claims the Supreme Court found ineligible in *Mayo*." Pet.App.16a (citing *Mayo*, 566 U.S. at 82). Both here and in *Mayo*, the asserted claims direct doctors to use conventional techniques to determine the level of a particular substance in the patient's blood. From there, they can

draw a conclusion in light of a previously discovered law of nature: in *Mayo*, the correlation between metabolite levels and drug toxicity; here, the even simpler correlation between increasing donor cfDNA levels over time and organ rejection.

The patent at issue in *Mayo* claimed a method for "optimizing therapeutic efficacy" of a drug by linking the amount administered to the concentration of certain metabolites in the patient's blood. 566 U.S. at 73-75. That drug was tricky to dose: it was difficult for doctors to assess "whether for a particular patient a given dose is too high, risking harmful side effects, or too low, and so likely ineffective." *Id.* at 73. Scientists had previously discovered that after a patient takes the drug, metabolites form in the patient's blood. *Id.* The patentees ascertained the concentrations of metabolites that correlated with drug concentrations that were too high or too low. *Id.* at 74. The patent directed doctors to harness those correlations by "determining" the level of metabolites in a patient's blood stream, "wherein" metabolites above a certain level "indicate[]" that drug levels are too high (and that doctors should thus decrease the amount of the drug), while metabolites below a certain level "indicate[]" that drug levels are too low (and that doctors should thus increase the amount of the drug). *Id.* at 74-75. The "upshot" is that these steps "simply tell doctors to gather data from which they may draw an inference in light of the correlations." *Id.* at 79.

So too here: In broad strokes, the patents at issue direct doctors to measure the level of donor cfDNA in a patient's bloodstream to draw an inference about the health of the donor organ. Claim 1 of the '652 patent recites using standard laboratory techniques to

"detect" the amount of donor cfDNA in a sample, "wherein" an increase—any increase—in the amount of donor cfDNA over time indicates organ rejection or failure. C.A.J.A. 131 (27:39-28:40). Just as directing doctors to use conventional "methods for determining metabolite levels" was "not sufficient to transform an unpatentable law of nature into a patent-eligible application of such a law," 566 U.S. at 79, neither is directing doctors to use conventional methods to detect cfDNA levels. Thus, this claim is not patent-eligible under *Mayo*.

2. CareDx makes no real effort to argue otherwise. CareDx does not explain how claim 1 is different from the claims in *Mayo* or why the Federal Circuit was wrong to deem them "indistinguishable." Pet.App.16a.

Instead, CareDx points to an 1880 case, *Tilghman v. Proctor*, 102 U.S. 707. That case primarily concerned other aspects of patent law, such as anticipation and infringement. But even treating it as a subject-matter eligibility case (and even if it were appropriate to skip over the next century and a half of precedent), the contrast between *Tilghman* and this case shows why the Federal Circuit got it right here. In *Tilghman*, the patentee had invented a particular process for "decomposing fats into glycerine and fat acids," *i.e.*, "mixing them with water, and subjecting the mixture to a high degree of heat under a pressure sufficient to prevent the conversion of the water into steam." *Id.* at 717, 729. He was "the original discoverer of this process." *Id.* at 713. CareDx emphasizes (at 23) that Tilghman had not discovered the underlying "chemical fact"—"that the elements of neutral fat require to be severally united with an atomic

equivalent of water in order to separate from each other and become free." *Id.* at 729. But Tilghman did invent a specific way of "bringing about the desired chemical union between the fatty elements and water"—involving heat and pressure. *Id.* That is quite unlike CareDx's claim regarding observing a known natural phenomenon using conventional technology.

Thus, unlike *Tilghman*, "[t]his is not a case involving a method of preparation or a new measurement technique." Pet.App.14a. The Court explained in *Tilghman* that the patentee had invented a new process for preparing matter. 102 U.S. at 730. Here, however, CareDx "does not actually claim any improvements in laboratory techniques." Pet.App.18a. Instead, the only limitation in the '652 patent beyond the "mere[] recit[ation]" of "the conventional use of existing techniques" is the natural correlation itself. *Id.*[5] Had CareDx invented a novel type of sequencing, it might have obtained a patent on that process. Having failed to do so, it was left with just the unpatentable principle.

3. The Court can uphold the '652 patent only by overruling *Mayo*. But "*stare decisis* is a foundation stone of the rule of law," and "this Court has always held that 'any departure' from the doctrine 'demands special justification.'" *Michigan v. Bay Mills Indian Cmty.*, 572 U.S. 782, 798 (2014). That is all the more true for statutory decisions: "[U]nlike in a constitutional case, critics of [the] ruling can take their objections across the street, and Congress can correct any mistake it sees." *Kimble v. Marvel Entm't, LLC*, 576

[5] The amicus brief (which does not mention the '652 patent) simply misunderstands this aspect of what CareDx claims.

U.S. 446, 456 (2015). And here in particular, "Congress legislates actively with respect to patents, considering concerns of just the kind" CareDx identifies in its petition. *Id.* at 465. These principles apply "even when a decision has announced a 'judicially created doctrine' designed to implement a federal statute." *Id.* at 456 (citation omitted). These decisions, too, "effectively become part of the statutory scheme, subject (just like the rest) to congressional change." *Id.* "Absent special justification, they are balls tossed into Congress's court, for acceptance or not as that branch elects." *Id.*

There is no such "special justification" here. To start, the petition scrupulously avoids *Mayo*: it does not ask the Court to overrule the decision, and therefore does not identify any reason to take this drastic step. To the contrary, all signs suggest the Court should decline to overhaul (or even tinker with) its Section 101 jurisprudence, as Congress is poised to make significant changes to Section 101. On June 22, 2023, Senators Thom Tillis and Chris Coons (the chair and ranking member of the subcommittee with jurisdiction over intellectual property) introduced the Patent Eligibility Restoration Act of 2023, which would revise the scope of patent eligibility under Section 101. The bill would replace this Court's articulation of the exceptions to patent-eligible subject matter with delineated categories, including, as relevant here, "a mental process performed solely in the human mind" or "occur[ing] in nature wholly independent of, and prior to, any human activity"; an "unmodified human gene, as that gene exists in the human body"; and an "unmodified natural material, as that material exists in nature." Patent Eligibility Restoration Act of 2023, S. 2140, 118th Cong. § 3 (2023).

Given this action in Congress, former Judge Michel—who filed an amicus brief supporting CareDx's petition—views legislative change to Section 101 as "imminent[]." As he explained recently, Congress is the correct venue to modify Section 101, and changes are likely "to happen quite soon."[6] Even Judge Michel's amicus brief confirms that Congress is the proper arena for change. According to the brief, Section 101 "has sharply split the Executive and Judicial Branches on patentable subject matter." Michel Amicus Br. 2; *see also id.*, at 3 (referring to "the inter-branch split between the Federal Circuit and the Solicitor General"). Even if that premise were correct, it would merely underscore that the dispute is one properly resolved by the Legislative Branch. Congress, unlike the Court, is able to facilitate a public debate about the proper scope of patent eligibility, with assistance from hearings, public commentary, and industry feedback. *See Athena*, 927 F.3d at 1337 (Hughes, J., concurring in the denial of rehearing en banc) (noting Congress's "distinctive role in making the factual and policy determinations relevant to setting the proper balance of innovation incentives under patent law").

At bottom, whether a patent is eligible for protection under the proposed statute presents an entirely different question from whether it is eligible for protection under the Court's governing caselaw. There is no reason for the Court to revise the governing

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[6] Eileen McDermott, *Michel Puts Hope in "Imminent" Patent Bills Following SCOTUS Eligibility Denials*, IPWatchdog (May 16, 2023), https://ipwatchdog.com/2023/05/16/michel-puts-hope-imminent-patent-bills-following-scotus-eligibility-denials/id=160910/.

caselaw when the entire scheme is potentially on the precipice of a dramatic overhaul. Rather, by "adhering to [its] precedent[s]," and leaving this matter for imminent Congressional action, the Court "promote[s] the rule-of-law values to which courts must attend while leaving matters of public policy to Congress." *Kimble*, 576 U.S. at 465.

## II. This case is a poor vehicle for revisiting Section 101.

CareDx asserts that the "Court needs to take another Section 101 case." Pet.10. The Court itself evidently disagrees. At the end of last Term, the Court denied the petitions in *Tropp* and *Interactive Wearables* that feature so prominently in CareDx's petition, as well as the petition in *Avery Dennison*. *See supra*, p. 1. The year before, the Court denied the petition in *American Axle & Manufacturing, Inc. v. Neapco Holdings LLC*, No. 20-891 (cert. denied June 30, 2022). Nothing has changed in the intervening months to suggest that the Court should now take up Section 101. To the contrary, the only relevant event—the renewed effort to amend Section 101—weighs strongly *against* this Court's review of Section 101. *See supra*, pp. 18-20.

Nor is there a pressing need for the Court to grant a petition involving medical diagnostics. Pet.10-11. As the sole amicus brief notes, the Federal Circuit has upheld some such patents. Michel Amicus Br. 21. That does not reflect a "split"—it simply means that some claims are properly directed to the patentable innovation rather than to a natural phenomenon or its observation. Thus, this Court has repeatedly denied petitions in the medical and life sciences fields, including as recently as 2020. *E.g.*, *Athena Diagnostics, Inc.*

*v. Mayo Collaborative Servs., LLC*, No. 19-430 (cert. denied Jan. 13, 2020); *Hikma Pharms. USA Inc. v. Vanda Pharms. Inc.*, No. 18-817 (cert. denied Jan. 13, 2020); *Cleveland Clinic Found. v. True Health Diagnostics, LLC*, No. 17-997 (cert. denied June 11, 2018); *Sequenom, Inc. v. Ariosa Diagnostics, Inc.*, No. 15-1182 (cert. denied June 27, 2016).

Moreover, as CareDx recognizes, the Solicitor General recommended that the Court grant certiorari in both *Tropp* and *Interactive Wearables*—neither of which involved medical diagnostics. The Solicitor General suggested that, while "this Court's Section 101 precedents have attracted particular attention in certain fields, such as medical diagnostics," the purported concerns with Section 101 "extend to 'all fields.'" U.S. Br. 22, *Tropp v. Travel Sentry, Inc.*, No. 22-22 (Apr. 5, 2023) (quoting *Yu v. Apple Inc.*, 1 F.4th 1040, 1049 (Fed. Cir. 2021) (Newman, J., dissenting)). Indeed, the Solicitor General proposed that the Court's review would be aided by selecting a case (such as *Tropp* or *Interactive Wearables*) with "comparatively less complex inventions" than those typically at play in the medical-diagnostics sphere. *Id.* The same was true in *American Axle*: the Solicitor General recommended granting a petition in a non-medical case involving the mechanical arts, again rebuffing suggestions that the application of Section 101 to medical-diagnostic patents is especially worthy of review. U.S. Br. 20, *Am. Axle & Mfg., Inc. v. Neapco Holdings*, No. 20-891 (May 24, 2022).

This would not be a suitable case to clarify how Section 101 applies to medical diagnostics in any event. CareDx asks the Court to address whether an "improved method for measuring a previously known

natural phenomenon" is patent-eligible, suggesting that the patentees here invented that improved method. Pet.12. They did not. Rather, they took a known technique (which they did not invent) and applied it to a known natural phenomenon (which they did not discover); there is no "improved method" for the Court to consider. Indeed, the patent does not identify a particular measurement method with any meaningful degree of detail, but rather claims the application of any conventional sequencing techniques to the organ transplant context. As the Federal Circuit recognized (with no dissent from any judge, on or off the panel), this is an easy case: There is nothing to the patent other than the observation of a natural correlation, and thus nothing unresolved for this Court to address.

### A. The question CareDx seeks to present is not actually presented here.

CareDx asks the Court to grant the petition to address the treatment of "new" diagnostic methods. But "[t]his is not a case involving … a new" diagnostic method. Pet.App.14a. Rather, as the Federal Circuit explained, CareDx "did not invent or discover the relationship between donor cfDNA and the likelihood of organ transplant rejection." *Id.* Nor did it discover the methods used to measure that relationship; "the written description is replete with characterizations of the claimed techniques in terms that confirm their conventionality." Pet.App.15a. Rather, "CareDx's patents apply conventional measurement techniques to detect a natural phenomenon—the level of donor cfDNA and the likelihood of organ transplant rejection"—that was already well established. Pet.App.15a-16a. As a result, this case does not

provide the Court with an opportunity to tackle the question CareDx presents: "whether a *new* and useful method for measuring a natural phenomenon" is eligible for protection under Section 101. Pet.i (emphasis added).

1. CareDx's petition rests on its assertion that the patent claims an "improved measurement method[]" for detecting donor cfDNA in the recipient's blood. Pet.App.12a. While actively "disclaim[ing]" any other potential innovations, CareDx maintains that the "only claimed advance" of the patents "is to improve upon" the prior methods for measuring donor cfDNA "by devising a new and better test for measuring that very same correlation." Pet.22. That is, at best, a sleight of hand. The patentees here did not "devis[e]" anything. Rather, as the Federal Circuit recognized, the measurement methods listed in the claims involve "only conventional techniques and off-the-shelf technology" for high-throughput sequencing; the patentees did nothing to improve on those methods. Pet.App.18a. By "improve[d]" process, CareDx means only that the patentees were the first to patent the selection of certain conventional techniques for measuring a particular natural correlation (a correlation they likewise did not discover, *see infra*, pp. 26-27, and admit they cannot patent). CareDx cannot refashion this exercise into an inventive process worthy of this Court's review.

To start, CareDx's current description of the invention is entirely at odds with the '652 patent itself. The '652 patent is notable for the degree to which they emphasize the conventionality of the measurement techniques. As the Federal Circuit described, "the written description is replete with characterizations of the

claimed techniques in terms that confirm their conventionality." Pet.App.15a. The court then proceeded to catalogue those references, identifying ten separate places in the specification where the patentees stressed that the claimed detection could be carried out using conventional techniques. Pet.App.15a-16a n.1. The specification explains, for example, that the required genotyping "may be performed by any suitable method known in the art including those described herein such as sequencing, nucleic acid array or PCR," and likewise that "[t]he presence or absence of one or more nucleic acids from the transplant donor in the transplant recipient may be determined by any suitable method known in the art including those described herein such as sequencing, nucleic acid arrays or PCR." *Id.* Thus, the patent, unlike the petition, is entirely clear about the nature of the purported invention: application of a known technique to a known phenomenon.

CareDx suggests that the patents claim an "improved" measurement technique because high-throughput sequencing provides a more effective method for detecting donor cfDNA than the available alternatives. Pet.12. In other words, the patentees did nothing to improve any of the available methods for genetic sequencing, but rather selected a different technique from the menu of options. No matter how CareDx describes it, this selection does nothing to change whether the patent claims patent-eligible subject matter. If, as CareDx seems to acknowledge, the prior techniques for detecting organ failure were ineligible for patent protection, then there is nothing further to consider with a different technique.

While CareDx repeatedly harps on the difficulties scientists had in quantifying cfDNA prior to 2009, these patents do little more than direct doctors to use a broad class of then-existing tools for genetic sequencing. As a result, this case does not present the question of how the analysis might evolve if, as CareDx seems to contemplate, a patentee were the first to apply a particular measurement technique in a novel context—in other words, if there were something inventive about the recognition that a technique could be used in a particular context. Rather, the '652 patent discloses applying several existing genetic-sequencing techniques to an entirely expected context: sequencing a type of DNA. Again, there is nothing "new" or "improved" for the Court to consider.

2. Even were the Court inclined to consider the eligibility of applying a known technique to a known phenomenon, the petition does not present that question either. The '652 patent does not claim a particular measurement technique with any meaningful degree of detail, and is thus little different from a patent that merely discloses the observation of a particular phenomenon (rather than, as CareDx suggests, a particular approach for doing so).

The '652 patent claims its measurement step at the highest level of generality: "multiplex sequencing" of the sample, followed by "analysis of the sequencing results" to observe the natural phenomenon and look for any increase over time. C.A.J.A. 131 (27:41-28:40). That is all. The patent does not claim any specific type or method of multiplex sequencing, nor does it provide any particular instructions for using multiplex sequencing in this context. Rather, the written description provides only high-level directives to use

conventional, commercially available means. C.A.J.A. 122 (9:8-14); C.A.J.A. 125 (15:22-16:41); C.A.J.A. 128 (21:5-8). Consider, also, the two other patents that CareDx asserted only against Natera, which replace multiplex sequencing with high-throughput sequencing or digital polymerase chain reactions (PCR), while similarly failing to provide any particular instructions for use in this context. Pet.App.3a-8a. So in full, CareDx is claiming the detection of cfDNA using either multiplex sequencing *or* high-throughput sequencing *or* digital PCR—the suite of conventional methods for genetic sequencing. *See* Pet.App.15a n.1. In short, the '652 patent does nothing materially more than "simply state the law of nature while adding the words 'apply it,'" *Mayo*, 566 U.S. at 72.

3. This case is in fact even further detached from the question presented and the issues typically presented in a Section 101 dispute. As CareDx repeatedly acknowledges (indeed, emphasizes), the patentees did not discover the natural phenomenon at issue here (*i.e.*, the correlation between the proportion of cell-free donor DNA and organ rejection). Rather, "the patents *disclaim* discovery of that natural phenomenon." Pet.8. CareDx attempts to turn this to its advantage, suggesting that, if the patentees did not discover the natural phenomenon, then the '652 patent *must be* directed to something other than the phenomenon—and that something else *must be* eligible for patent protection.

In that sense, this case is fundamentally different from the recent medical-diagnostic petitions the Court has considered (and, even then, ultimately denied). In those cases, the patentees actually discovered the phenomenon at the heart of the case. In *Ariosa*, for

example, the patent owners had themselves "discovered cell-free fetal DNA ('cffDNA') in maternal plasma and serum," "implemented a method for detecting" cffDNA "to determine fetal characteristics," and then obtained a patent claiming "methods of using cffDNA." 788 F.3d at 1373. The same was true in *Athena Diagnostics, Inc. v. Mayo Collaborative Services, LLC*, 915 F.3d 743 (Fed. Cir. 2019), in which the patentees "discovered the association between MuSK autoantibodies and" the neurological disorder myasthenia gravis. *Id.* at 747. "Prior to their discovery, no disease had been associated with MuSK." *Id.* And "[h]aving discovered the association between MuSK autoantibodies and MG, the inventors … disclosed and claimed methods of diagnosing neurological disorders" using this association. *Id.*; *see also Cleveland Clinic Found. v. True Health Diagnostics LLC*, 859 F.3d 1352, 1363 (Fed. Cir. 2017) (discussing Cleveland Clinic's "discovery of the relationship between [the enzyme] MPO and cardiovascular health").

CareDx's approach also makes little sense: if the discoverer of an unknown natural phenomenon cannot get a patent for applying conventional measurement techniques to observe it, someone who *did not discover* the phenomenon should not get a patent for applying conventional measurement techniques to observe that *known* natural phenomenon. Moreover, this theory works only if there is in fact something else for the patent to claim. If not, the patentee is simply left with a patent claiming a natural phenomenon that the patentee did not discover. That is precisely the case here.

### B. CareDx does not claim an "improvement" to an existing method, and CareDx's newfound emphasis on that term provides no reason to grant certiorari.

Section 101 extends patent protection to "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof." 35 U.S.C. § 101. CareDx argues that this Court should grant the petition to consider the "application of Section 101 to an 'improvement' upon a preexisting useful process." Pet.21. Contrary to CareDx's suggestion, this case would not provide the Court "an opportunity to focus on the text of that clause," nor does CareDx provide any reason this would be a useful exercise.

1. As discussed at length above, this case does not involve an "improvement" because CareDx has not "improve[d]" any existing method. *See supra*, pp. 23-25; *see also* Pet.App.18a (recognizing that "CareDx does not actually claim any improvements in laboratory techniques"). Had the patentees in fact invented an improvement to a process (*e.g.*, an improvement on high-throughput sequencing), they could have instead claimed that in their patents.

In an effort to wedge itself into the statute, CareDx characterizes as an "improvement" its selection of conventional sequencing methods for the purpose of detecting donor cfDNA. *E.g.*, Pet.21-22. That is not an improvement of any existing "process," as the statutory text ("any new and useful process …, or any new and useful improvement thereof") requires. Even taking a charitable view of CareDx's argument, the *selection of a process* for achieving a designated end is not itself an improvement on a process.

2. Regardless, CareDx does not provide any reason why it would be beneficial for this Court to consider patent eligibility in the context of the "improvement" prong of the statute, as opposed to a "new" "machine," "method," or "composition of matter." This Court has always treated "natural phenomena" as an "important implicit exception" to Section 101. *Mayo*, 566 U.S. at 70. Thus, the question whether the claims are "formally addressed to patent-eligible subject matter," by reciting a "machine" or a "method," has never been the end of the inquiry. *Alice*, 573 U.S. at 224. Eligibility turns on substance, not "the draftsman's art." *Id.* (quoting *Parker v. Flook*, 437 U.S. 584, 593 (1978)). Indeed, CareDx does not dispute that a patent can be directed to ineligible subject matter even if it formally recites a "method" or a "machine." There is no apparent reason why the statutory term "improvement" would receive a different construction, and CareDx provides none. Nor did CareDx provide one to the Federal Circuit, as it never argued below—not even in its rehearing petition—that this case should come out differently because it involves an "improvement" to a method rather than a "new" method. That argument is new on certiorari—and its premise is incorrect, as shown above.

### C. This case does not implicate CareDx's policy concerns regarding medical-diagnostic patents.

CareDx argues that the Federal Circuit's approach to Section 101 is dampening investment in medical diagnostics. Notably, no amicus has appeared to validate that concern—in sharp contrast with the robust amicus participation in previous Section 101 cases. But even if policy concerns like these were properly

addressed to this Court rather than Congress, the outcome of this case plainly serves as no disincentive to invest in diagnostic inventions. Again, the patentees here did not invent *anything*: They did not discover the natural correlation between donor cfDNA and organ failure, nor did they discover the claimed diagnostic techniques. There was no discovery to dampen. *Compare Mayo*, 566 U.S. at 91 (discussing the patentee's argument "that a principle of law denying patent coverage" in that case would "interfere significantly with … research leading to the discovery of laws of nature"). Had the patentees here actually discovered or improved a process for measuring donor cfDNA, they might have obtained a patent on the process instead.

More broadly, this argument has played out time and again in every aspect of patent law. As this Court has explained, while patent exclusivity might provide "monetary incentives that lead to creation, invention, and discovery," granting exclusivity *over natural phenomena* would "impede the flow of information that might permit, indeed spur, invention." *Mayo*, 566 U.S. at 92. And "patent law's general rules must govern inventive activity in many different fields of human endeavor, with the result that the practical effects of rules that reflect a general effort to balance these considerations may differ from one field to another." *Id.* ("Patent protection is, after all, a two-edged sword."). Ultimately, whether diagnostic methods should be entitled to increased patent protection is a "policy" matter appropriate for Congress. *Id.* ("recogniz[ing] the role of Congress in crafting more finely tailored rules where necessary").

Here in particular, CareDx's proposed approach implicates the precise concerns animating Section 101: the "monopolization" of "the basic tools of scientific and technological work." *Mayo*, 566 U.S. at 71. The breadth of the patents (which together cover *all* modern sequencing methods, *see supra*, p. 26) would have a dramatic preemptive effect. This case thus embodies the "substantial risk … that granting overbroad patents could reward a mere concept"—the use of sequencing to detect donor cfDNA—"rather than the work subsequently done by the actual inventor"—here, quite little. *Athena*, 927 F.3d at 1340 (Dyk, J., concurring in the denial of rehearing en banc). While CareDx's claims may not include every single method of detecting cfDNA, this Court has never suggested that a patentee can save a patent directed to measuring a natural phenomenon merely because there may be some *other* way to measure the natural phenomenon. *See, e.g.*, *Parker*, 437 U.S. at 589-90 (invalidating a patent even though it did not "wholly preempt the mathematical formula").[7]

Against this backdrop, granting CareDx patent protection for applying an accepted sequencing technique to do precisely what that technique is intended to do (sequence DNA) would dramatically alter this Court's Section 101 jurisprudence. To start, *every* diagnostic patent involves the application of a measurement technique to a natural correlation; otherwise, discovery of the natural correlation would be of little

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[7] While elevating total preemption to an absolute requirement for patent eligibility, CareDx also repeatedly asserts that the prior methods for detecting an increase in donor cfDNA had significant flaws. Pet.4-5 (describing the "detection of organ rejection [as] difficult and impractical").

use. Under CareDx's approach, the discoverer of the natural correlation could avoid Section 101's strictures merely be claiming the measurement of the correlation, rather than the correlation itself. *See Parker*, 437 U.S. at 590 (noting that "[a] competent draftsman could attach some form of post-solution activity to almost any mathematical formula"). Even beyond that, if an inventor could claim patent protection by being the first to apply a known technique to a new context, *every* natural phenomenon would be patent-eligible in pieces—one for each conventional technique used to observe it. Thus, under CareDx's approach, a patentee could bypass Section 101 entirely merely by using a known measurement technique to detect a natural correlation (even if the patentee had nothing to do with the discovery of the natural correlation). This approach is flatly inconsistent with this Court's precedents and general principles of patent eligibility, and there is no basis for this Court entertain it.

### D. The Federal Circuit properly applied considerations of conventionality and lack of novelty.

CareDx finally contends that the Federal Circuit misapplied the two steps of the *Mayo* inquiry— by not confining "conventionality" to the second step, and further by conflating Section 101's subject-matter restriction with other requirements for patent validity (novelty, 35 U.S.C. § 102, nonobviousness, 35 U.S.C. § 103, and enablement, 35 U.S.C. § 112). Neither argument is persuasive.

1. CareDx first suggests that conventionality should play no role at step one, on the theory "that it is only at 'step two'" that courts can consider whether

the patentee has provided an inventive concept beyond the natural phenomenon. Pet.25. CareDx does not identify anything in this Court's caselaw imposing that rule or otherwise suggesting that conventionality plays no part in determining whether an invention is "drawn to" ineligible subject matter at step one. Pet.25. Nor does CareDx give any reason why this disagreement with one aspect of the Federal Circuit's opinion would warrant certiorari.

CareDx's theory of the case also made conventionality unavoidable at step one. In the typical Section 101 case, the patentee discovered the natural phenomenon at the heart of the case. *See supra*, pp. 26-27. But not here—leading to the question of what CareDx did in fact claim to invent. The Federal Circuit could not answer that question without considering the nature of the claimed measurement techniques, including whether CareDx had invented a new technique or merely adopted a preexisting one. As the Federal Circuit explained, CareDx "contend[ed] that the 'claimed advance' is 'an improved, human-devised method for measuring increases in donor cfDNA in a recipient's body to identify organ rejection.'" Pet.App.18a. "In particular, CareDx identifie[d] the use of digital PCR, [next-generation sequencing], and selective amplification to more accurately measure donor SNPs of cfDNA in transplant recipients." *Id.* CareDx thus asked the Federal Circuit to assess whether these techniques were in fact an "advance," or were instead conventional. Having directly teed up this issue for the court below, CareDx cannot now complain that the Court engaged with its argument.

2. CareDx next argues that, while the Federal Circuit was correct to consider conventionality at step two, the court's conventionality analysis improperly strayed into issues of obviousness and novelty. Pet.26-30.[8] Not so. Following this Court's caselaw, the Federal Circuit properly considered whether the steps of the patent, "when viewed as a whole," were "sufficient to transform unpatentable natural correlations into patentable applications of those regularities." *Mayo*, 566 U.S. at 80. Having done so, the court concluded that "the claimed combination of steps … was a straightforward, logical, and conventional method for detecting cfDNA previously used in other contexts, including cancer diagnostics and prenatal testing." Pet.App.20a. Thus, contrary to CareDx's suggestion, the Federal Circuit properly determined that there was no "result heretofore unknown in the art." Pet.28 (quoting *Diamond*, 450 U.S. at 193 n.15); *see also* Pet.App.20a ("affirm[ing] the district court's holding with regard to *Alice/Mayo* step two" because "the practice of the asserted method claims does not result in an inventive concept that transforms the natural phenomena into a patentable invention").

While CareDx accuses the courts below of blurring, in particular, obviousness and patent-eligibility, it is in fact CareDx that conflates the two. CareDx argues that the Federal Circuit erred by failing to recognize that the claimed process was "brand new." Pet.27.

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[8] While CareDx "strongly disagree[s] with the Federal Circuit's understanding of the specification's language," Pet.28, it does not suggest (nor could it) that a factual dispute over the conventionality of high-throughput sequencing in 2009 is worthy of this Court's review.

Whether scientists had previously tried a particular combination of steps is an issue of novelty; it does not answer the question whether the invention is directed to patent-ineligible subject matter. The patents could be novel in a literal sense (as CareDx argues here) and yet directed to patent-ineligible subject matter. By contrast, CareDx's approach "would make the 'law of nature' exception to § 101 patentability a dead letter," *Mayo*, 566 U.S. at 89, by shifting all of *Alice/Mayo* step two, *see supra*, p. 12, to other statutory sections.

## CONCLUSION

The petition for a writ of certiorari should be denied.

Respectfully submitted.

DARRYL M. WOO
GOODWIN PROCTER LLP
Three Embarcadero Ctr.
San Francisco, CA 94111

KEVIN J. DEJONG
JORDAN BOCK
GOODWIN PROCTER LLP
100 Northern Ave.
Boston, MA 02210

WILLIAM M. JAY
*Counsel of Record*
GOODWIN PROCTER LLP
1900 N St., N.W.
Washington, DC 20036
*wjay@goodwinlaw.com*
(202) 346-4000

*Counsel for Respondent Eurofins Viracor, LLC*

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