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

2022-1027

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, Chief Judge Colm F. Connolly.

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

v.

EUROFINS VIRACOR, INC.,
Defendant-Appellee

2022-1028

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

Decided: July 18, 2022

EDWARD R. REINES, Weil, Gotshal & Manges LLP, Redwood Shores, CA, argued for plaintiffs-appellants. Also represented by DEREK C. WALTER; ANNA DWYER, New York, NY; ZACHARY TRIPP, Washington, DC.

GABRIEL K. BELL, Latham & Watkins LLP, Washington, DC, argued for defendant-appellee Natera, Inc. Also represented by ASHLEY FRY, FAN ZHANG.

WILLIAM M. JAY, Goodwin Procter LLP, Washington, DC, argued for defendant-appellee Eurofins Viracor, Inc. Also represented by JORDAN BOCK, KEVIN JON DEJONG, Boston, MA; DARRYL M. WOO, San Francisco, CA.

Before LOURIE, BRYSON, and HUGHES, *Circuit Judges*.

LOURIE, *Circuit Judge*.

CareDx, Inc. and The Board of Trustees of the Leland Stanford Junior University ("Stanford") (collectively, "CareDx") appeal from a decision of the United States District Court for the District of Delaware holding that U.S. Patents 8,703,652 (the "'652 patent"), 9,845,497 (the "'497 patent"), and 10,329,607 (the "'607 patent") are ineligible for patent under 35 U.S.C. § 101. *See CareDx, Inc. v. Natera, Inc.*, 563 F. Supp. 3d 329 (D. Del. 2021) ("*Decision*"). We affirm.

BACKGROUND

Stanford owns the '652, '497, and '607 patents. All three patents share the same specification and are entitled "Non-Invasive Diagnosis of Graft Rejection in Organ Transplant Patients." These patents discuss diagnosing or predicting organ transplant status by using methods to detect a donor's cell-free DNA ("cfDNA"). When an organ transplant is rejected, the recipient's body, through its natural immune response, destroys the donor cells, thus releasing cfDNA from the donated organ's dying cells into the blood. These increased levels of donor cfDNA—which occur naturally as the organ's condition deteriorates—can be detected and then used to diagnose the likelihood of an organ transplant rejection. Claim 1 of each patent is representative. Claim 1 of the '652 patent reads as follows:

> 1. A method for detecting transplant rejection, graft dysfunction, or organ failure, the method comprising:
>
> > (a) *providing a sample* comprising [cfDNA] from a subject who has received a transplant from a donor;
> >
> > (b) *obtaining a genotype* of donor-specific polymorphisms or a genotype of subject-specific polymorphisms, or obtaining both a genotype of donor-specific polymorphisms and subject-specific polymorphisms, to establish a polymorphism profile for detecting donor [cfDNA], wherein at least one single nucleotide polymorphism (SNP) is homozygous for the subject if the genotype comprises subject-specific polymorphisms comprising SNPs;
> >
> > (c) *multiplex sequencing* of the [cfDNA] in the sample followed by analysis of the sequencing results using the polymorphism

> profile to *detect donor [cfDNA] and subject [cfDNA]*; and
>
> (d) diagnosing, predicting, or monitoring a transplant status or outcome of the subject who has received the transplant by *determining a quantity of the donor [cfDNA]* based on the detection of the donor [cfDNA] and subject [cfDNA] by the multiplexed sequencing, wherein an *increase in the quantity of the donor [cfDNA] over time is indicative of transplant rejection, graft dysfunction or organ failure*, and wherein sensitivity of the method is greater than 56% compared to sensitivity of current surveillance methods for cardiac allograft vasculopathy (CAV).

'652 patent at col. 27 l. 39–col. 28 l. 40 (emphases added).

Claim 1 of the '497 patent is similar, except that it recites high-throughput sequencing or digital polymerase chain reaction ("PCR") instead of multiplex sequencing for "determining" the amount of donor cfDNA.

> 1. A method of detecting donor-specific circulating [cfDNA] in a solid organ transplant recipient, the method comprising:
>
> (a) genotyping a solid organ transplant donor to obtain a single nucleotide polymorphism (SNP) profile of the solid organ transplant donor;
>
> (b) genotyping a solid organ transplant recipient to obtain a SNP profile of the solid organ transplant recipient, wherein the solid organ transplant recipient is selected from the group consisting of: a kidney transplant, a heart transplant, a liver

> transplant, a pancreas transplant, a lung transplant, a skin transplant, and any combination thereof;
>
> (c) obtaining a biological sample from the solid organ transplant recipient after the solid organ transplant recipient has received the solid organ transplant from the solid organ transplant donor, wherein the biological sample is selected from the group consisting of blood, serum and plasma, and wherein the biological sample comprises circulating [cfDNA] from the solid organ transplant; and
>
> (d) determining an amount of donor-specific circulating [cfDNA] from the solid organ transplant in the biological sample by detecting a homozygous or a heterozygous SNP within the donor-specific circulating [cfDNA] from the solid organ transplant in at least one assay, wherein the at least one assay comprises *high-throughput sequencing or digital polymerase chain reaction (dPCR)*, and
>
> wherein the at least one assay detects the donor-specific circulating [cfDNA] from the solid organ transplant when the donor-specific circulating [cfDNA] make up at least 0.03% of the total circulating [cfDNA] in the biological sample.

'497 patent at col. 28 l. 2–col. 29 l. 5 (emphasis added).

Claim 1 of the '607 patent is also similar, except that it recites selective amplification of the cfDNA by PCR before high-throughput sequencing.

1. A method of quantifying kidney transplant-derived circulating [cfDNA] in a human kidney transplant recipient, said method comprising:

(a) providing a plasma sample from said human kidney transplant recipient, wherein said human kidney transplant recipient has received a kidney transplant from a kidney transplant donor, wherein said plasma sample from said human kidney transplant recipient comprises kidney transplant-derived circulating [cfDNA] and human kidney transplant recipient-derived circulating [cfDNA];

(b) extracting circulating [cfDNA] from said plasma sample from said human kidney transplant recipient in order to obtain extracted circulating [cfDNA], wherein said extracted circulating [cfDNA] comprises said kidney transplant-derived circulating [cfDNA] and human kidney transplant recipient-derived circulating [cfDNA];

(c) *performing a selective amplification of target [DNA] sequences*, wherein said selective amplification of said target [DNA] sequences is of said extracted circulating [cfDNA], wherein said selective amplification of said target [DNA] sequences amplifies a plurality of genomic regions comprising at least 1,000 single nucleotide polymorphisms, wherein said at least 1,000 single nucleotide polymorphisms comprise homozygous single nucleotide polymorphisms, heterozygous single nucleotide polymorphisms, or both homozygous single nucleotide polymorphisms and heterozygous single nucleotide polymorphisms, and

wherein said selective amplification of said target deoxyribonucleic acid sequences is by polymerase chain reaction (PCR);

(d) performing a high throughput sequencing reaction, wherein said high throughput sequencing reaction comprises performing a sequencing-by-synthesis reaction on said selectively-amplified target [DNA] sequences from said extracted circulating [cfDNA], wherein said sequencing-by-synthesis reaction has a sequencing error rate of less than 1.5%;

(e) providing sequences from said high throughput sequencing reaction, wherein said provided sequences from said high throughput sequencing reaction comprise said at least 1,000 single nucleotide polymorphisms; and

(f) quantifying an amount of said kidney transplant-derived circulating [cfDNA] in said plasma sample from said human kidney transplant recipient to obtain a quantified amount, wherein said quantifying said amount of said kidney transplant-derived circulating [cfDNA] in said plasma sample from said human kidney transplant recipient comprises using markers distinguishable between said human kidney transplant recipient and said kidney transplant donor, wherein said markers distinguishable between said human kidney transplant recipient and said kidney transplant donor comprises single nucleotide polymorphisms selected from said at least 1,000 single nucleotide polymorphisms identified in said provided sequences from

> said high throughput sequencing reaction, and wherein said quantified amount of said kidney transplant-derived circulating [cfDNA] in said plasma sample from said human kidney transplant recipient comprises at least 0.03% of the total circulating [cfDNA] from said plasma sample from said human kidney transplant recipient.

'607 patent at col. 28 l. 56–col. 30 l. 2 (emphasis added).

In summary, the methods disclosed in the representative claims have four steps for detecting a donor's cfDNA in a transplant recipient:

1. "obtaining" or "providing" a "sample" from the recipient that contains cfDNA;
2. "genotyping" the transplant donor and/or recipient to develop "polymorphism" or "SNP" "profiles";
3. "sequencing" the cfDNA from the sample using "multiplex" or "high-throughput" sequencing; or performing "digital PCR"; and
4. "determining" or "quantifying" the amount of donor cfDNA.

CareDx is the exclusive licensee of the '652, '497, and '607 patents. It sued Natera, Inc. ("Natera"), alleging that Natera's kidney transplant rejection test infringed the '652, '497, and '607 patents. CareDx also sued Eurofins Viracor, Inc. ("Eurofins"), alleging that Eurofins' various organ transplant rejection tests infringed the '652 patent. Natera and Eurofins both moved to dismiss the complaints for failure to state a claim due to lack of patent-eligible subject matter under § 101.

The motions to dismiss were referred to a magistrate judge, who recommended that they be denied. The magistrate judge held that the claims were a "purportedly new, unconventional combination of steps" to detect natural phenomena. *Decision* at 336–37 (quoting J.A. 12). In light

of an amendment in CareDx's complaint against Natera, the district court vacated the magistrate judge's recommendation in Natera's action. The court then adopted the magistrate judge's recommendation in the Eurofins action but modified the reasoning. The court noted that "language in the written description[] of the asserted patent[] suggests that the patented steps are neither new nor unconventional" and that the "specifications raise[d] doubts about the patents' validity." *Id.* at 337 (alterations in original). However, the court was cautious about ruling prematurely, and denied the motion to dismiss so that the parties could conduct limited discovery and develop the record on conventionality.

After expert discovery relating to § 101 had concluded, Natera and Eurofins each moved for summary judgment of ineligibility. The district court denied the motions, concluding that there was a factual dispute as to the conventionality of the techniques for performing the claimed methods. Natera and Eurofins then moved for certification of interlocutory appeals from the court's order denying summary judgment. Following a conference with the parties regarding the motion, the court stated it would reconsider its summary judgment decision in view of case law cited in the certification motion.

Following reconsideration, the district court granted the summary judgment motions of ineligibility. The court first determined that the asserted claims were directed to the detection of natural phenomena, specifically, the presence of donor cfDNA in a transplant recipient and the correlation between donor cfDNA and transplant rejection. The court concluded that, based on the specification's numerous admissions, the claims recited only conventional techniques.

CareDx appealed the district court's grant of Natera's and Eurofins' summary judgment motions. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

We review the district court's grant of summary judgment *de novo* under Third Circuit law. *SRI Int'l, Inc. v. Cisco Sys., Inc.*, 930 F.3d 1295, 1306 (Fed. Cir. 2019). Summary judgment is appropriate when "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). Patent eligibility under § 101 is ultimately a question of law that this court reviews *de novo*. *Berkheimer v. HP Inc.*, 881 F.3d 1360, 1365 (Fed. Cir. 2018).

I

Section 101 provides that "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." 35 U.S.C. § 101. Given the expansive terms of § 101, "Congress plainly contemplated that the patent laws would be given wide scope"; the legislative history likewise indicated that "Congress intended statutory subject matter to 'include anything under the sun that is made by man.'" *Diamond v. Chakrabarty*, 447 U.S. 303, 308–09 (1980) (internal citation omitted).

The Supreme Court has held that § 101 "contains an important implicit exception. '[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) (alteration in original) (quoting *Diamond v. Diehr*, 450 U.S. 175, 185 (1981)). These exceptions exist because monopolizing the basic tools of scientific work "might tend to impede innovation more than it would tend to promote it." *Id.* at 71. However, the Supreme Court has advised that these exceptions must be applied cautiously, as "too broad an interpretation of this exclusionary principle could eviscerate patent law." *Id.*

Laws of nature and natural phenomena are not patentable, but applications and uses of such laws and phenomena may be patentable. A claim to otherwise eligible statutory subject matter does not become ineligible by its use of a law of nature or natural phenomenon. *See Diehr*, 450 U.S. at 187; *Parker v. Flook*, 437 U.S. 584, 590 (1978). On the other hand, adding "conventional steps, specified at a high level of generality," to a law of nature or natural phenomenon does not make a claim to the law or phenomenon patentable. *Mayo*, 566 U.S. at 82.

To distinguish claims to patent-eligible applications of laws of nature and natural phenomena from claims that impermissibly tie up such laws and phenomena, we apply the two-part test set forth by the Supreme Court. First, we examine whether the claims are "directed to" a law of nature or natural phenomenon. *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 573 U.S. 208, 217 (2014). If—and only if—they are, then we proceed to the second inquiry, where we examine whether the limitations of the claim apart from the law of nature or natural phenomenon, considered individually and as an ordered combination, "'transform the nature of the claim' into a patent-eligible application." *Id.* (quoting *Mayo*, 566 U.S. at 78).

II

CareDx argues that, regarding *Alice/Mayo* step one, the patents' claimed advance is not the discovery of a natural correlation between organ rejection and the donor's cfDNA levels in the recipient's blood. Rather, the claimed advance is improved measurement methods spelled out in the claims as superior to the inadequate prior art measurement techniques. CareDx adds that the district court did not properly perform the step one analysis because it concluded that step one is essentially the same as step two and centers on conventionality. It asserts that there is no basis in the law for a one-step application of *Alice/Mayo*.

Regarding *Alice/Mayo* step two, CareDx argues that using digital PCR and next-generation sequencing ("NGS") to identify and measure donor-specific SNPs was an inventive breakthrough and that the patents claim this specific and useful application. CareDx notes that the district court itself acknowledged that there was a factual dispute as to the conventionality of the claimed techniques when it initially denied summary judgment. Lastly, CareDx asks us to reverse the court's decision rather than remand because of what it refers to as a record of irregular proceedings, such as the court backtracking on its denial of summary judgment and improperly making credibility determinations.

Natera responds that CareDx's asserted claims are directed to detecting natural phenomena—the presence of an organ donor's cfDNA in the blood of a transplant recipient and the correlation between elevated levels of that cfDNA and organ transplant rejection. It adds that the claims recite performing this detection using collection and measurement techniques that the specification admits are conventional and further admits can be performed using existing technology without modification. As such, Natera argues, these claims are indistinguishable from other diagnostic method claims that the Supreme Court found ineligible in *Mayo* and that we found ineligible on multiple occasions. Natera's Resp. at 17 (citing *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 915 F.3d 743 (Fed. Cir. 2019); *Genetic Veterinary Scis., Inc. v. LABOKLIN GmbH & Co. KG*, 933 F.3d 1302 (Fed. Cir. 2018); *Roche Molecular Sys., Inc. v. CEPHEID*, 905 F.3d 1363 (Fed. Cir. 2018); *Cleveland Clinic Found. v. True Health Diagnostics LLC*, 859 F.3d 1352 (Fed. Cir. 2017); *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015)).

Natera adds that the district court properly applied *Alice* step one and relied on the express use of the word "detecting" in the claims, and our case law addressing similar "detecting" claims, to conclude that the claims are directed

to a natural phenomenon. Natera further adds that the court recognized that *Alice* step one can overlap with step two.

Lastly, Natera asserts that the procedural background of this case confirms that we should affirm. Natera notes that early in this case, the district court determined that it was premature to resolve the eligibility question without affording the parties an opportunity to develop the record. Subsequently, the court recognized that CareDx's expert testimony and other extrinsic evidence was contrary to, and therefore could not overcome, the admissions in the specification. Natera points out that the court's reconsideration of its summary judgment decision demonstrates that it thoughtfully and thoroughly considered that issue. Eurofins largely echoes Natera's arguments.

We agree with Natera and Eurofins. This is not a case involving a method of preparation or a new measurement technique. *See Illumina, Inc. v. Ariosa Diagnostics, Inc.*, 952 F.3d 1367, *opinion modified by* 967 F.3d 1319, 1327 (Fed. Cir. 2020) (holding that a new and improved "method for preparing" an unnaturally enriched fetal cfDNA fraction from a pregnant woman by separating smaller fetal cfDNA fragments from larger (and likely maternal) fragments was unlike claims merely "directed to starting with a sample that contains" cfDNA and "seeing that the [cfDNA] exists"). CareDx also concedes that it did not invent or discover the relationship between donor cfDNA and the likelihood of organ transplant rejection. *See* Appellant's Br. at 1 ("[S]ince at least 1998, scientists recognized that higher concentrations of donor cfDNA in the organ recipient's bloodstream may be a marker for organ rejection."). Furthermore, as the district court noted, the patents' written description expressly states that the techniques referred to in the claimed steps are, "unless otherwise indicated, conventional techniques of immunology, biochemistry, chemistry, molecular biology, microbiology, cell biology, genomics, and recombinant DNA, which are

well within the skill of art." *Decision* at 335 (citing '652 patent at col. 5 ll. 36–40). Specifically, the written description is replete with characterizations of the claimed techniques in terms that confirm their conventionality.[1] Thus,

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[1] *See, e.g.*, '652 patent at col. 9 ll. 8–14 (stating that "[d]etection, identification and/or quantitation of the donor-specific markers (e.g.[,] polymorphic markers such as SNPs) can be performed using real-time PCR, chips (e.g., SNP chips), high throughput shotgun sequencing of circulating nucleic acids (e.g.[,] [cfDNA]), as well as other methods known in the art"); *id.* at col. 10 ll. 11–12 (stating that, to obtain cfDNA samples, "any technique known in the art may be used, e.g. a syringe or other vacuum suction device"); *id.* at col. 13 ll. 51–53 (stating that step 2 of claimed methods can be performed "using existing genotyping platforms know[n] in the art"); *id.* at col. 15 ll. 6–8 (stating that techniques recited in step 2 of claimed methods "can be accomplished through classic Sanger sequencing methods which are well known in the art"); *id.* at col. 13 ll. 58–61 (stating that "[c]ompanies (such as Applied Biosystems, Inc.) currently offer both standard and custom-designed TaqMan probe sets for SNP genotyping that can in principle target any desired SNP position for a PCR-based assay"); *id.* at col. 20 ll. 31–34 (stating that genotyping recited in claimed methods "may be performed by any suitable method known in the art including those described herein such as sequencing, nucleic acid array or PCR"); *id.* at col. 15 ll. 22–65 (discussing commercial high throughput sequencing products); *id.* at col. 14 ll. 58–67 (citing articles from 2006 and 2007 as supporting the statement that "digital PCR is a much more accurate and reliable method to quantitate nucleic acid species"); *id.* at col. 18 l. 55–col. 19 l. 2 (stating that "[m]ethods for quantifying nucleic acids," including high throughput genotyping, "are known in the art"); *id.* at col. 21 ll. 5–9 (stating that "[t]he presence or absence of one or more nucleic acids from the transplant

CareDx's patents apply conventional measurement techniques to detect a natural phenomenon—the level of donor cfDNA and the likelihood of organ transplant rejection.

The claimed methods are indistinguishable from other diagnostic method claims the Supreme Court found ineligible in *Mayo* and that we found ineligible on multiple occasions. *See Mayo*, 566 U.S. at 82 (applying conventional diagnostic methods to observe a natural correlation is not patent eligible subject matter). Similarly, *Ariosa* involved claims reciting methods for making a diagnosis of certain fetal characteristics based on detecting paternally inherited cell-free fetal DNA ("cffDNA") in the blood of a pregnant female. 788 F.3d at 1376. In *Ariosa*, as here, it was undisputed that the existence of cffDNA in maternal blood was a natural phenomenon. *Id.* And, as here, the recited steps in *Ariosa* included amplifying the cfDNA—in that case cffDNA in the mother's blood—using PCR. *Id.* at 1374. What followed was detecting the paternally inherited cffDNA, again a natural phenomenon. *Id.* at 1373–74. The specification asserted that analyzing cffDNA permitted more efficient determination of genetic defects and that a pregnant woman carrying a fetus with certain genetic defects will have more cffDNA in her blood than will a woman with a normal fetus. *Id.* We held that the claims were directed to a natural phenomenon, identifying the presence of cffDNA, at *Alice/Mayo* step one, and ultimately ineligible. *Id.* at 1376, 1378.

Here, as in *Ariosa*, 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

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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").

correlation between heightened cfDNA levels and transplant health to identify a potential rejection, none of which was inventive. The claims here are equally as ineligible as those in *Ariosa*.

CareDx's step one arguments are unavailing. Its argument that the district court "disregarded the [s]tep [o]ne analysis entirely," Appellant's Br. at 33–34, is contradicted by the record. The court reviewed the claim language (e.g., "detecting" and "quantifying" donor cfDNA in a transplant recipient), along with CareDx's own characterizations, and concluded that the claims recite methods for detecting natural phenomena. *Decision* at 341–42. Based on our precedent, the court noted that claims applying conventional methods "directed to" natural phenomena satisfy *Alice/Mayo* step one.

CareDx also incorrectly characterizes our precedent as limiting the conventionality inquiry to step two. On the contrary, and as the district court recognized, we have repeatedly analyzed conventionality at step one as well. *See Athena*, 915 F.3d at 751 (stating that, at step one "the specification describes the claimed concrete steps for observing the natural law as conventional"); *see also Cleveland Clinic*, 859 F.3d at 1361 (stating that, at step one the claims contained "no meaningful non-routine steps"). Indeed, we have explained 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." *Elec. Power Grp., LLC v. Alstom S.A.*, 830 F.3d 1350, 1353 (Fed. Cir. 2016) (citations omitted). As such, our precedent rejects CareDx's effort to draw a bright line between the two steps.

CareDx argues that the patents' claims are directed not to natural phenomena, but to improved laboratory techniques. CareDx contends 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." Appellant's Br. at 27. In particular, CareDx identifies the use of digital PCR, NGS, and selective amplification to more accurately measure donor SNPs of cfDNA in transplant recipients. However, CareDx does not actually claim any improvements in laboratory techniques—rather, as previously discussed, the actual claims of the patent merely recite the conventional use of existing techniques to detect naturally occurring cfDNA. Furthermore, the specification admits that the laboratory techniques disclosed in the claims require only conventional techniques and off-the-shelf technology. *See supra* note 1.

For these reasons, we affirm the district court's holding that the '652, '497, and '607 patents' asserted claims are directed to natural phenomena under *Alice/Mayo* step one.

Regarding *Alice/Mayo* step two, we also agree with the district court and hold that the asserted claims add nothing inventive because they merely recite standard, well-known techniques in a logical combination to detect natural phenomena. The court thoroughly considered whether any of the claims' additional elements were unconventional and, based on the specification's admissions, properly found that they were not. *See Decision* at 345–46. The specification admits that each step in the purported invention requires only conventional techniques and commercially available technology: (1) collecting the patient's sample using "any technique known in the art," '652 patent at col. 10 l. 11; (2) genotyping the donor and recipient to create SNP profiles using "any suitable method known in the art," *id.* at col. 20 ll. 31–33; (3) sequencing the cfDNA using "well known" techniques and off-the-shelf tools, *id.* at col. 15 ll. 6–8, col. 15 ll. 22–67; and (4) quantifying the donor cfDNA using methods "known in the art," *id.* col. 18 l. 55–col. 19 l. 2. *See supra* note 1. There is no genuine dispute that the claimed techniques add nothing inventive to the natural phenomenon being detected.

We have repeatedly held that applying standard techniques in a standard way to observe natural phenomena does not provide an inventive concept. In *Ariosa*, the specification stated that the preparation and amplification of DNA sequences in plasma, including by PCR were "standard" techniques. 788 F.3d at 1377. In *Athena*, the specification expressly described the recited immunoassay techniques as "standard" or "known per se in the art." 915 F.3d at 753–54. And in *Roche*, the specification stated that the methods for detecting the bacterium used "standard PCR techniques" and failed to disclose "any 'new and useful' improvement to PCR protocols or DNA amplification techniques." 905 F.3d at 1372.

As in each of these cases, CareDx's asserted claims add nothing inventive at step two because they recite detection methods that "simply append[] conventional steps, specified at a high level of generality" to natural phenomena. *Mayo*, 566 U.S. at 82. Each of the methods in the recited steps was already being performed by those in the art. Furthermore, the claimed combination of steps adds nothing inventive. 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. *See* '652 patent at col. 6 l. 57–col. 7 l. 46. Thus, the practice of the asserted method claims does not result in an inventive concept that transforms the natural phenomena into a patentable invention. For these reasons, we affirm the district court's holding with regard to *Alice/Mayo* step two.

Lastly, we note that CareDx's procedural complaints are without merit. First, CareDx asserts that the district court did not "explain[] why it departed from the magistrate judge's reasoning." Appellant's Br. at 54. However, the court explained that it agreed with the magistrate judge insofar as he found it was premature to resolve § 101

on the pleadings. The court then went on to express doubt about the magistrate judge's recommendation on finding eligibility in light of the specification's disclosures suggesting the conventionality of the claimed methods. The court also indicated that it viewed CareDx's claims as akin to ineligible claims in *Athena*. J.A. 60. Moreover, the court's final decision explained why the claims are indeed ineligible.

Second, CareDx points out the irregularity of the district court backtracking on its initial denial of summary judgment and contends that the court erroneously decided issues of fact. However, as Natera and Eurofins argue, the court was entitled to reconsider its summary judgment decision. The court initially denied summary judgment because the warring extrinsic evidence from CareDx, Natera, and Eurofins appeared to create a fact issue. However, the court later found this fact issue non-genuine due to the explicit contradiction between CareDx's extrinsic evidence and the numerous admissions of conventionality in the intrinsic record.

CONCLUSION

We have considered CareDx's remaining arguments but find them unpersuasive. Because the asserted claims in the '652, '497, and '607 patents are directed to a natural law together with conventional steps to detect or quantify the manifestation of that law, they are ineligible under § 101. For the foregoing reasons, we affirm the judgment of the district court.

AFFIRMED