United States Court of Appeals for the Federal Circuit

THE CLEVELAND CLINIC FOUNDATION, CLEVELAND HEARTLAB, INC.,
Plaintiffs-Appellants

v.

TRUE HEALTH DIAGNOSTICS LLC,
Defendant-Appellee

2016-1766

Appeal from the United States District Court for the Northern District of Ohio in No. 1:15-cv-02331-PAG, Judge Patricia A. Gaughan.

Decided: June 16, 2017

LAWRENCE D. ROSENBERG, Jones Day, Washington, DC, argued for plaintiffs-appellants. Also represented by SUSAN M. GERBER, Cleveland, OH.

ADAM LOUIS MARCHUK, Perkins Coie LLP, Chicago, IL, argued for defendant-appellee. Also represented by MICHAEL ROBERT OSTERHOFF, MARK T. SMITH, CAROLINE AYRES TEICHNER; DAN L. BAGATELL, Hanover, NH.

Before LOURIE, REYNA, and WALLACH, *Circuit Judges*.

REYNA, *Circuit Judge*.

The Cleveland Clinic Foundation and Cleveland Heartlab, Inc. accused True Health Diagnostics LLC of infringement of three patents that claim methods for testing for myeloperoxidase in a bodily sample and a fourth patent that claims a method for treating a patient that has cardiovascular disease. The United States District Court for the Northern District of Ohio found that the asserted claims of the three testing patents are not directed to patent-eligible subject matter and that Cleveland Clinic failed to state a claim of contributory or induced infringement of the fourth patent. For the reasons explained below, we affirm.

BACKGROUND

In 2003, researchers at the Cleveland Clinic Foundation developed methods for detecting the risk of cardiovascular disease in a patient. When an artery is damaged or inflamed, the body releases the enzyme myeloperoxidase, or MPO, in response. MPO is an early symptom of cardiovascular disease, and it can thus serve as an indicator of a patient's risk of cardiovascular disease.

The prior art taught that MPO could be detected in an atherosclerotic plaque or lesion that required a surgically invasive method. Another prior art method *indirectly* detected for MPO in blood. Yet another known method could detect MPO in blood but yielded results that were not predictive of cardiovascular disease. The inventors here purportedly discovered how to "see" MPO in blood and correlate that to the risk of cardiovascular disease.

The patents disclose methods for detecting MPO and correlating the results to cardiovascular risk.[1] The pa-

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[1] The testing patents are U.S. Patent No. 7,223,552, U.S. Patent No. 7,459,286, and U.S. Patent No. 8,349,581.

tents disclose that "[m]yeloperoxidase activity may be determined by any of a variety of standard methods known in the art." *E.g.*, J.A. 39 at col. 8 ll. 32–33. These methods include colorimetric-based assay, flow cytometry, and enzyme-linked immunosorbent assay ("ELISA"). Additionally, the patents disclose MPO detection kits modified from commercially available kits "by including, for example, different cut-offs, different sensitivities at particular cut-offs, as well as instructions or other printed material for characterizing risk based upon the outcome of the assay." *E.g.*, J.A. 38 at col. 6 ll. 21–24.

In addition to ways to "see" MPO, the inventors developed a way to correlate MPO with risk of developing cardiovascular disease. To do this, the inventors compiled MPO data from a population to create a "predetermined" or "control" value. Then, using statistical methods, the inventors analyzed the data based on whether the person was "apparently healthy" or had some cardiovascular disease. *E.g.*, J.A. 45 at col. 20 ll. 32–43. Diagnosers could then use this data to determine whether a patient presents a risk of cardiovascular disease:

> If the level of the present risk predictor in the test subject's bodily sample is greater than the predetermined value or range of predetermined values, the test subject is at greater risk of developing or having [cardiovascular disease] than individuals with levels comparable to or below the predetermined value or predetermined range of values.

J.A. 46 at col. 21 ll. 37–42.

The fourth patent, which relates to a method for treating a patient, is U.S. Patent No. 9,170,260. The '552 patent and '260 patent share a specification, as do the '286 patent and '581 patent.

The '552 patent claims methods for characterizing a test subject's risk for cardiovascular disease by determining levels of MPO in a bodily sample and comparing that with the MPO levels in persons not having cardiovascular disease. The dependent claims limit the way MPO is detected and how the MPO values in the control subjects are evaluated. The district court analyzed claims 11, 14, and 15, which provide:

> 11. A method of assessing a test subject's risk of having atherosclerotic cardiovascular disease, comprising
>
> comparing levels of myeloperoxidase in a bodily sample from the test subject with levels of myeloperoxidase in comparable bodily samples from control subjects diagnosed as not having the disease, said bodily sample being blood, serum, plasma, blood leukocytes selected from the group consisting of neutrophils, monocytes, sub-populations of neutrophils, and sub-populations of monocytes, or any combination thereo[f];
>
> wherein the levels of myeloperoxidase in the bodily from the test subject relative to the levels of [m]yeloperoxidase in the comparable bodily samples from control subjects is indicative of the extent of the test subject's risk of having atherosclerotic cardiovascular disease.

J.A. 50 at col. 30 ll. 48–62.

> 14. A method of assessing a test subject's risk of developing a complication of atherosclerotic cardiovascular disease comprising:
>
> determining levels of myeloperoxidase (MPO) activity, myeloperoxidase (MPO) mass, or both in a bodily sample of the test subject, said bodily sample being blood, serum, plasma, blood leukocytes

> selected from the group consisting of neutrophils and monocytes, or any combination thereof;
>
> wherein elevated levels of MPO activity or MPO mass or both in the test subject's bodily sample as compared to levels of MPO activity, MPO mass, or both, respectively in comparable bodily samples obtained from control subjects diagnosed as not having the disease indicates that the test subject is at risk of developing a complication of atherosclerotic cardiovascular disease.

J.A. 51 at col. 31 ll. 8–23.

> 15. The method of claim 14, wherein the test subject's risk of developing a complication of atherosclerotic cardiovascular disease is determined by comparing levels of my[elo]peroxidase mass in the test subject's bodily sample to levels of myeloperoxidase mass in comparable samples obtained from the control subjects.

J.A. 51 at col. 31 ll. 24–29.

The '286 patent and '581 patent further claim ways of detecting MPO. The dependent claims of the '286 patent limit MPO detection by flow cytometry and further require detection of another compound, troponin. Other dependent claims of the '286 patent and '581 patent require detection of MPO byproducts. The district court analyzed claims 21 and 22 of the '286 patent and claim 5 of the '581 patent, which provide:

> 21. A method of assessing the risk of requiring medical intervention in a patient who is presenting with chest pain, comprising
>
> characterizing the levels of myeloperoxidase activity, myeloperoxidase mass, or both, respectively in the bodily sample from the human patient, where-

> in said bodily sample is blood or a blood derivative,
>
> wherein a patient whose levels of myeloperoxidase activity, myeloperoxidase mass, or both is characterized as being elevated in comparison to levels of myeloperoxidase activity, myeloperoxidase mass or both in a comparable bodily samples obtained from individuals in a control population is at risk of requiring medical intervention to prevent the occurrence of an adverse cardiac event within the next six months.

J.A. 71 at col. 23 l. 45–col. 24 l. 10.

> 22. A method of determining whether a patient who presents with chest pain is at risk of requiring medical intervention to prevent an adverse cardiac event within the next six months comprising:
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> comparing the level of a risk predictor in a bodily sample from the subject with a value that is based on the level of said risk predictor in comparable samples from a control population, wherein said risk predictor is myeloperoxidase activity, myeloperoxidase mass, a myeloperoxidase-generated oxidation product, or any combination thereof, and wherein said bodily sample is blood, serum, plasma, or urine,
>
> wherein a subject whose bodily sample contains elevated levels of said risk predictor as compared to the control value is at risk of requiring medical intervention to prevent an adverse cardiac event within 6 months of presenting with chest pain, and
>
> wherein the difference between the level of the risk predictor in the patient's bodily sample and the level of the risk predictor in a comparable bod-

> ily sample from the control population establishes the extent of the risk to the subject of requiring medical intervention to prevent an adverse cardiac event within the next six months.

J.A. 71 at col. 24 ll. 11–33.

> 5. A method of determining whether a patient who presents with chest pain is at risk of requiring medical intervention to prevent an adverse cardiac event within the next six months comprising:
>
> determining the level of risk predictor in a bodily sample from the subject, wherein said risk predictor is myeloperoxidase activity, myeloperoxidase mass, a myeloperoxidase (MPO)-generated oxidation product or any combination thereof,
>
> wherein said bodily sample is blood, serum, plasma or urine,
>
> wherein said myeloperoxidase-generated oxidation product is nitrotyrosine or a myeloperoxidase-generated lipid peroxidation product selected from [list of products] or any combination thereof, and
>
> comparing the level of said risk predictor in the bodily sample of the patient to the level of said risk predictor in comparable samples obtained from a control population,
>
> wherein a subject whose bodily sample contains elevated levels of said risk predictor as compared to the control value is at risk of requiring medical intervention to prevent an adverse cardiac event within 6 months of presenting with chest pain.

J.A. 86 at col. 20 ll. 12–50.

The '260 patent builds on these patents and requires administration of a lipid lowering drug to a patient at risk

of cardiovascular disease. Claim 1 of the '260 patent recites:

> 1. A method for administering a lipid lowering agent to a human patient based on elevated levels of myeloperoxidase (MPO) mass and/or activity comprising:
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> (a) performing an enzyme linked immunosorbent assay (ELISA) comprising contacting a serum or plasma sample with an anti-MPO antibody and a peroxidase activity assay to determine MPO activity in the serum or plasma sample;
>
> (b) selecting a patient who has elevated levels of MPO mass and/or activity compared to levels of MPO mass and/or activity in apparently healthy control subjects; and
>
> (c) administering a lipid lowering agent to the selected human patient.

J.A. 117 at col. 30 ll. 10–23.

True Health is a diagnostic laboratory. It purchased the assets of Health Diagnostics Lab, which had contracted with the Cleveland Clinic to perform MPO testing. Rather than continue the relationship with Cleveland Clinic, True Health opted to perform its own MPO testing. In November 2015, Cleveland Clinic sued True Health, asserting infringement of the testing patents. Cleveland Clinic moved for a temporary restraining order and preliminary injunction, which the district court denied. *Cleveland Clinic Found. v. True Health Diagnostics, LLC*, No. 1:15 CV 2331, 2015 WL 7430082, at *6 (N.D. Ohio Nov. 18, 2015).

After the district court denied the motion for temporary restraining order and preliminary injunction, Cleveland Clinic amended its complaint to add allegations of infringement of the '260 patent. True Health moved to

dismiss the amended complaint, arguing that the testing patents were directed to patent-ineligible subject matter and that Cleveland Clinic failed to state a claim for indirect infringement of the '260 patent.

The district court granted True Health's motion. *Cleveland Clinic Found. v. True Health Diagnostics, LLC*, No. 1:15 CV 2331, 2016 WL 705244, at *9 (N.D. Ohio Feb. 23, 2016). The district court found all the claims of the testing patents patent ineligible under 35 U.S.C. § 101 (2012). *Id.* at *5–7. The district court also dismissed the contributory and induced infringement claims of the '260 patent, and denied leave to amend the complaint. *Id.* at *7–9.

Procedurally, the district court found that it was proper to consider § 101 at the motion to dismiss stage. Although Cleveland Clinic argued that the district court should first conduct formal claim construction on some identified terms, the district court reasoned that "plaintiff offer[ed] no proposed construction for these terms." *Id.* at *3. And though Cleveland Clinic objected to treating any claims as representative of others, the district court found it appropriate to consider the above asserted claims representative because "plaintiff fail[ed] to point out any claim that is not represented by the aforementioned claims." *Id.*

The district court next found the testing patents patent ineligible under the two-step framework for analyzing patent subject matter eligibility under § 101 articulated in *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2355 (2014). *See Cleveland Clinic*, 2016 WL 705244, at *7. The district court found that the testing patents' claims were directed to a law of nature under *Alice* step one because the claims were directed to "the correlation between MPO in the blood and the risk of [cardiovascular disease]." *Id.* at *6. Under *Alice* step two, the district court found there was no saving inventive

concept. First, the patents employ well-known methods to detect MPO. *Id.* Second, comparing MPO levels with a control value could be a bare mental process. *Id.* Finally, even looking at the claims as a whole, the steps in combination "simply instruct a user to apply a natural law, *i.e.*, that an increase in MPO mass or MPO activity in a blood sample correlates to an increase in [cardiovascular disease] risk." *Id.*

Regarding infringement of the '260 patent, the district court found that True Health's testing service was not a "material or apparatus" that could form the basis for contributory infringement. *Id.* at *7–8 (citing *In re Bill of Lading Transmission & Processing Sys. Patent Litig.*, 681 F.3d 1323, 1337 (Fed. Cir. 2012) ("Contributory infringement occurs if a party sells or offers to sell, a material or apparatus for use in practicing a patented process, and that 'material or apparatus' is material to practicing the invention, has no substantial non-infringing uses, and is known by the party to be especially made or especially adapted for use in an infringement of such patent.") (internal quotation marks and citation omitted)).

Regarding induced infringement, the district court found that Cleveland Clinic did not allege facts sufficient to show the specific intent to induce a third party to infringe. The district court reasoned that, "in generic terms, the third-party direct infringer must administer a lipid lowering agent based on elevated levels of MPO in order to infringe the '260 patent." *Id.* at *9. Hence, the "plaintiff must sufficiently allege that defendant specifically intends to induce doctors to administer a lipid lowering agent based on elevated levels of MPO. The complaint is completely devoid of any factual allegations supporting this theory." *Id.*

In response to the motion to dismiss, Cleveland Clinic sought leave to amend its complaint in the event the claim was dismissed. *Id.* The district court denied Cleve-

land Clinic's request. *Id.* (citing *PR Diamonds, Inc. v. Chandler*, 364 F.3d 671, 699 (6th Cir. 2004)).

Cleveland Clinic timely appealed. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

We first address whether the testing patents are patent ineligible under § 101 and conclude that they are. We next address whether the district court properly dismissed the '260 patent infringement claims and conclude that it did.

1. § 101 Subject Mater Eligibility

A. Standard of Review

For procedural questions not unique to patent law, we review a grant of a motion to dismiss according to the law of the regional circuit, which in this case is the Sixth Circuit. *See, e.g.*, *Univ. of Utah v. Max-Planck-Gesellschaft zur Forderung der Wissenschaften E.V.*, 734 F.3d 1315, 1319 (Fed. Cir. 2013). The Sixth Circuit reviews de novo dismissals for failure to state a claim. *Bovee v. Coopers & Lybrand C.P.A.*, 272 F.3d 356, 360 (6th Cir. 2001). We also review de novo whether a claim is patent-ineligible under the judicially created exceptions to § 101. *McRO, Inc. v. Bandai Namco Games Am. Inc.*, 837 F.3d 1299, 1311 (Fed. Cir. 2016).

B. Procedural Challenges

As a preliminary matter, we address Cleveland Clinic's procedural challenges to the district court's patentable subject matter eligibility analysis. Cleveland Clinic argues that the district court erred by analyzing only certain claims from each of the testing patents as representative. Cleveland Clinic also argues that the district court should have undertaken claim construction and developed the factual and expert record before analyzing

whether the claims were eligible under § 101. We do not find these arguments persuasive.

As to Cleveland Clinic's first procedural challenge, we find no error in the district court addressing claims 11, 14, and 15 of the '552 patent, claims 21 and 22 of the '286 patent, and claim 5 of the '581 patent as representative. Although Cleveland Clinic argues that the unexamined dependent claims provide sufficient inventive concepts over the representative claims, our examination reveals the opposite. For example, Cleveland Clinic argues that the district court failed to take into consideration claims that require specific analytical techniques, claims that limit the predetermined comparison values to a single value or representative value or ranges, or claims that measure the presence of specific MPO-generated oxidation products. Each limitation Cleveland Clinic raises, however, merely recites known methods of detecting MPO or MPO derivatives and applies the correlation between these biomarkers and cardiovascular health. Where, as here, the claims "are substantially similar and linked to the same" law of nature, analyzing representative claims is proper. *Content Extraction & Transmission LLC v. Wells Fargo Bank, N.A.*, 776 F.3d 1343, 1348 (Fed. Cir. 2014).

As to Cleveland Clinic's second procedural challenge, we have repeatedly affirmed § 101 rejections at the motion to dismiss stage, before claim construction or significant discovery has commenced. *See, e.g.*, *Genetic Techs. Ltd. v. Merial L.L.C.*, 818 F.3d 1369, 1373–74 (Fed. Cir. 2016) ("We have repeatedly recognized that in many cases it is possible and proper to determine patent eligibility under 35 U.S.C. § 101 on a Rule 12(b)(6) motion."); *OIP Techs, Inc. v. Amazon.com, Inc.*, 788 F.3d 1359, 1362 (Fed. Cir. 2015) (similar); *Content Extraction*, 776 F.3d at 1349 (similar); *buySAFE, Inc. v. Google, Inc.*, 765 F.3d 1350, 1355 (Fed. Cir. 2014) (similar). In any event, Cleveland Clinic provided no proposed construction of any terms or

proposed expert testimony that would change the § 101 analysis. Accordingly, it was appropriate for the district court to determine that the testing patents were ineligible under § 101 at the motion to dismiss stage.

C. *Alice* Step One

Section 101 of the Patent Act defines patent eligible subject matter:

> 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. The Supreme Court has long held that there are certain exceptions to this provision: laws of nature, natural phenomena, and abstract ideas. *Alice*, 134 S. Ct. at 2354 (collecting cases).

To determine whether a claim is invalid under § 101, we employ the two-step *Alice* framework. In step one, we ask whether the claims are directed to ineligible subject matter, such as a law of nature. *Alice*, 134 S. Ct. at 2355; *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66, 75–77 (2012), *McRO*, 837 F.3d at 1311–12; *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1375 (Fed. Cir. 2015). While method claims are generally eligible subject matter, method claims that are directed only to natural phenomena are directed to ineligible subject matter. *Ariosa*, 788 F.3d at 1376. If the claims are directed to eligible subject matter, the inquiry ends. *Thales Visionix Inc. v. United States*, 850 F.3d 1343, 1349 (Fed. Cir. 2017).

The claims of the testing patents are directed to multistep methods for observing the law of nature that MPO correlates to cardiovascular disease. *E.g.*, J.A. 50 at col. 30 ll. 47–52; J.A. 71 at col. 24 ll. 11–18; J.A. 86 at col. 20 ll. 12–44. Moreover, the testing patents' specifica-

tions similarly instruct that the inventions are "based on the discovery that patients with cardiovascular disease have significantly greater levels of leukocyte and [MPO]," J.A. 36 at col. 2 ll. 33–36; *see* J.A. 67 at col. 16 ll. 56–67 (describing the study's results as to MPO levels), 68 at col. 17 ll. 30–39 (same), and they do not purport to alter MPO levels in any way, *see Genetic Technologies*, 818 F.3d at 1376 (evaluating the asserted patents' specification in support of its conclusion that the claims were focused on a patent-ineligible law of nature because, inter alia, they "involved[d] no creation or alteration of DNA sequences"). Cleveland Clinic's invention thus involves "seeing" MPO already present in a bodily sample and correlating that to cardiovascular disease. Because the testing patents are based on "the relation [between cardiovascular disease and heightened MPO levels that] exists in principle apart from human action," they are directed to a patent-ineligible law of nature. *Mayo*, 566 U.S. at 77.

This case is similar to our decision in *Ariosa*. In *Ariosa*, the ineligible claims were directed to a method of detecting paternally inherited cell-free fetal DNA, which is naturally occurring in maternal blood. 788 F.3d at 1376. The inventors there did not create or alter any of the genetic information encoded in that DNA. *Id.* Likewise, here, the testing patents purport to detect MPO and other MPO-related products, which are naturally occurring in bodily samples. The method then employs the natural relationship between those MPO values and predetermined or control values to predict a patient's risk of developing or having cardiovascular disease. Thus, just like *Ariosa*, the method starts and ends with naturally occurring phenomena with no meaningful non-routine steps in between—the presence of MPO in a bodily sample is correlated to its relationship to cardiovascular disease. The claims are therefore directed to a natural law. *Id.*

Cleveland Clinic argues that its invention is similar to the patent-eligible invention described in *Rapid Litigation*

Management Ltd. v. CellzDirect, Inc., 827 F.3d 1042 (Fed. Cir. 2016). In *CellzDirect*, the inventors developed cryopreservation techniques to preserve liver cells for later use. *Id.* at 1045. We held that the claims were not directed to a natural law because they were "simply not directed to the ability of [liver cells] to survive multiple freeze-thaw cycles. Rather, the claims of the [asserted patent were] directed to a new and useful laboratory technique for preserving [liver cells]." *Id.* at 1048. Unlike *CellzDirect*, the asserted claims of the testing patents are directed to the natural existence of MPO in a bodily sample and its correlation to cardiovascular risk rather than to "a new and useful laboratory technique" for detecting this relationship. Indeed, Cleveland Clinic has not created a new laboratory technique; rather, it uses well-known techniques to execute the claimed method. The specifications of the testing patents confirm that known testing methods could be used to detect MPO, and that there were commercially available testing kits for MPO detection. *E.g.*, J.A. 39 at col. 8 ll. 32–33; J.A. 38 at col. 6 ll. 21–24.

Because the claims of the testing patents are directed to a natural law, we turn to the second step of the *Alice* framework.

D. *Alice* Step Two

In *Alice* step two, we examine the elements of the claims to determine whether they contain an inventive concept sufficient to transform the claimed naturally occurring phenomena into a patent-eligible application. *Mayo*, 566 U.S. at 71–72; *McRO*, 837 F.3d at 1312 (quoting *Alice*, 134 S. Ct. at 2355). We must consider the elements of the claims both individually and as an ordered combination to determine whether additional elements transform the nature of the claims into a patent-eligible concept. *Ariosa*, 788 F.3d at 1375 (citations omitted). "To save a patent at step two, an inventive

concept must be evident in the claims." *RecogniCorp, LLC v. Nintendo Co.*, 855 F.3d 1322, 1327 (Fed. Cir. 2017).

We conclude that the practice of the method claims does not result in an inventive concept that transforms the natural phenomena of MPO being associated with cardiovascular risk into a patentable invention. *Mayo* and *Ariosa* make clear that transforming claims that are directed to a law of nature requires more than simply stating the law of nature while adding the words "apply it." *Mayo*, 566 U.S. at 72; *Ariosa*, 788 F.3d at 1377.

In *Ariosa*, the challenged claims involved a method that was a general instruction to doctors to apply routine, conventional techniques when seeking to detect paternally inherited cell-free fetal DNA in the blood serum of a pregnant woman. *Ariosa*, 788 F.3d at 1377. The same is true here. The '552 patent and '581 patent contain a "determining" step that requires analyzing MPO levels. Cleveland Clinic does not purport to have invented colorimetric-based assay, flow cytometry, or ELISA, or any of the claimed methods to "see" MPO and its derivatives in bodily samples. Rather, the claims here instruct that MPO levels be detected or determined using any of these known techniques. The claims of the testing patents also contain a "comparing" step where MPO levels are compared to statistically derived control or predetermined values. Here too, Cleveland Clinic does not purport to derive new statistical methods to arrive at the predetermined or control levels of MPO that would indicate a patient's risk of cardiovascular disease. Known statistical models can be employed, as described, for example, in the specification of the '552 patent:

> Predetermined values of MPO activity or MPO mass, such as for example, mean levels, median levels, or "cut-off" levels, are established by assaying a large sample of individuals in the general

> population or the select population and using a statistical model such as the predictive value method for selecting a positivity criterion or receiver operator characteristic curve that defines optimum specificity (highest true negative rate) and sensitivity (highest true positive rate) as described in Knapp, R.G., and Miller, M.C. (1992) . . . .

J.A. 46 at col. 21 ll. 12–20.

The claims, whether considered limitation-by-limitation or as a whole, do not sufficiently transform the natural existence of MPO in a bodily sample and its correlation to cardiovascular risk into a patentable invention. The process steps here merely tell those "interested in the subject about the correlations that the researchers discovered." *Mayo*, 566 U.S. at 78.

Cleveland Clinic's invention here is distinct from the *CellzDirect* invention when examining *Alice* step two. In *CellzDirect*, the inventors took the discovery that certain liver cells will survive multiple freeze-thaw cycles and applied that to improve existing methods for preserving liver cells. *CellzDirect*, 827 F.3d at 1051. Here, the testing patents here do not extend their discovery that MPO correlates to cardiovascular risk to a patentable method. They require only conventional MPO detection methods and compare those values to predetermined or control values derived from conventional statistical methods.[2]

Cleveland Clinic argues that its invention is narrowly preemptive and thus should be patent eligible. However, "[w]here a patent's claims are deemed only to disclose

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[2] The '260 patent, which claims a method of treating a patient that is determined to have a risk of cardiovascular disease, is not challenged under § 101.

patent ineligible subject matter under the *Mayo* framework, as they are in this case, preemption concerns are fully addressed and made moot." *Ariosa*, 788 F.3d at 1379. Likewise, while Cleveland Clinic argues that its discovery of the relationship between MPO and cardiovascular health was groundbreaking, "even such valuable contributions can fall short of statutory patentable subject matter, as it does here." *Id.* at 1380.

Accordingly, we affirm the district court's determination that the testing patents are directed to patent-ineligible subject matter.

2. '260 Patent Infringement

The '260 patent is a method-of-treatment patent whose claims require "administering a lipid lowering agent to the selected human patient." J.A. 117 at col. 30 ll. 22–24. Cleveland Clinic does not allege that True Health directly infringes this patent, rather, it alleges that True Health indirectly infringes via contributory and induced infringement. As discussed below, we find that the district court properly dismissed Cleveland Clinic's claims.

A. Standard of Review

In the Sixth Circuit, courts employ two standards of review for denials of motions to amend complaints: (1) abuse of discretion, the general standard when a court denies a motion for leave to amend; or (2) de novo, the standard when a court denies leave to amend because the amended pleading would not withstand a motion to dismiss. *Pulte Homes, Inc. v. Laborers' Int'l Union of N. Am.*, 648 F.3d 295, 304–05 (6th Cir. 2011) (citations omitted). Here, like in *Pulte*, Cleveland Clinic did not file a motion for leave to amend, but rather "buried its request . . . in its brief opposing the motion to dismiss" and the district court "did not explain why it withheld leave to

amend. The lesser standard, abuse of discretion, therefore applies." *Id.* at 305.

B. The District Court Properly Dismissed Cleveland Clinic's Contributory Infringement Claims

Contributory infringement occurs if a party sells, or offers to sell, a material or apparatus for use in practicing a patented process, and that "material or apparatus" is material to practicing the invention, it has no substantial non-infringing uses, and it is known by the party "to be especially made or especially adapted for use in an infringement of such patent." 35 U.S.C. § 271(c); *Bill of Lading*, 681 F.3d at 1337. A party that provides a service, but no "material or apparatus," cannot be liable for contributory infringement. *PharmaStem Therapeutics, Inc. v. ViaCell, Inc.*, 491 F.3d 1342, 1357 (Fed. Cir. 2007) ("Under the plain language of the statute, a person who provides a service that assists another in committing patent infringement may be subject to liability under § 271(b) for active inducement of infringement, but not under § 271(c) for contributory infringement.").

True Health provides MPO testing services. The only "material or apparatus" that Cleveland Clinic claims True Health sells are lab reports documenting the results of True Health's testing services. We agree with the district court that the "lab reports attached to the complaint reflect the manner in which defendant reports the results of the service it provides." *Cleveland Clinic*, 2016 WL 705244, at *8. They are not a "material or apparatus." Accordingly, it was not an abuse of discretion for the district court to dismiss Cleveland Clinic's contributory infringement claims and deny leave to amend.

C. The District Court Properly Dismissed Cleveland Clinic's Induced Infringement Claims

"Whoever actively induces infringement of a patent shall be liable as an infringer." 35 U.S.C. § 271(b). "How-

ever, knowledge of the acts alleged to constitute infringement is not enough." *DSU Med. Corp. v. JMS Co.*, 471 F.3d 1293, 1305 (Fed. Cir. 2006) (en banc) (citations omitted). The mere knowledge of possible infringement by others does not amount to inducement; specific intent and action to induce infringement must be proven. *Id.*

It is undisputed that True Health does not sell or prescribe lipid lowering drugs to patients. Cleveland Clinic argues that True Health's lab reports are sufficient to create the reasonable inference that a doctor who ordered such a report would rely on the results and would administer a lipid lowering agent where the results indicated the patient had a cardiovascular disease risk. Cleveland Clinic alleges no facts that suggest any connection between True Health and doctors that may prescribe lipid lowering drugs. Cleveland Clinic thus falls short of showing "specific intent and action" on behalf of True Health to induce infringement of the '260 patent. It was not an abuse of discretion for the district court to dismiss Cleveland Clinic's induced infringement claims and deny leave to amend.

CONCLUSION

We have considered Cleveland Clinic's other arguments and do not find them persuasive. We thus affirm the district court's grant of True Health's motion to dismiss.

AFFIRMED