United States Court of Appeals for the Federal Circuit

ATHENA DIAGNOSTICS, INC., OXFORD UNIVERSITY INNOVATION LTD., MAX-PLANCK-GESELLSCHAFT ZUR FORDERUNG DER WISSENSCHAFTEN E.V.,
Plaintiffs-Appellants

v.

MAYO COLLABORATIVE SERVICES, LLC, DBA MAYO MEDICAL LABORATORIES, MAYO CLINIC,
Defendants-Appellees

2017-2508

Appeal from the United States District Court for the District of Massachusetts in No. 1:15-cv-40075-IT, Judge Indira Talwani.

Decided: February 6, 2019

ADAM GAHTAN, Fenwick & West LLP, New York, NY, argued for plaintiffs-appellants. Also represented by ERIC M. MAJCHRZAK, VANESSA PARK-THOMPSON; ANDREW JOSEPH KABAT, EMMETT J. MCMAHON, Robins Kaplan LLP, Minneapolis, MN; DIMITRIOS T. DRIVAS, White & Case LLP, New York, NY.

JONATHAN ELLIOT SINGER, Fish & Richardson, PC, San

Diego, CA, argued for defendants-appellees. Also represented by JOHN CAMERON ADKISSON, ELIZABETH M. FLANAGAN, PHILLIP GOTER, DEANNA JEAN REICHEL, Minneapolis, MN.

AARON BARKOFF, McAndrews, Held & Malloy, Ltd., Chicago, IL, for amicus curiae The Chartered Institute of Patent Attorneys.

KEVIN EDWARD NOONAN, McDonnell, Boehnen, Hulbert & Berghoff, LLP, Chicago, IL, for amicus curiae Five Life Sciences Patent Practitioners. Also represented by JOHN DOMINIC CRAVERO, AARON VINCENT GIN, MICHAEL S. GREENFIELD, ANDREA KAY ORTH.

MELISSA A. BRAND, Biotechnology Innovation Organization, Washington, DC, for amicus curiae Biotechnology Innovation Organization. Also represented by HANSJORG SAUER; BRIAN PAUL BARRETT, Eli Lilly and Company, Indianapolis, IN.

MATTHEW JAMES DOWD, Dowd Scheffel PLLC, Washington, DC, for amici curiae Dan L. Burk, Richard A. Epstein, Christopher Michael Holman, Gus Hurwitz, Adam Mossoff, Kristen J. Osenga, Michael Risch, Mark F. Schultz, Ted M. Sichelman, Brenda M. Simon.

KATHLEEN M. SULLIVAN, Quinn Emanuel Urquhart & Sullivan, LLP, New York, NY, for amicus curiae ARUP Laboratories, Inc. Also represented by BRIAN C. CANNON, Redwood Shores, CA.

Before NEWMAN, LOURIE, and STOLL, *Circuit Judges*.

Opinion for the court filed by *Circuit Judge* LOURIE.

Dissenting opinion filed by *Circuit Judge* NEWMAN.

LOURIE, *Circuit Judge*.

Athena Diagnostics, Inc., Oxford University Innovation Ltd., and the Max-Planck-Gesellschaft zur Forderung der Wissenschaften E.V. (collectively, "Athena") appeal from the order of the United States District Court for the District of Massachusetts holding that claims 6–9 of U.S. Patent 7,267,820 (the "'820 patent") are invalid under 35 U.S.C. § 101 and dismissing Athena's complaint under Rule 12(b)(6). *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 275 F. Supp. 3d 306 (D. Mass. 2017) ("*Decision*"). Because the district court correctly concluded that the claims at issue are directed to a natural law and lack an inventive concept, we affirm.

I. BACKGROUND

Athena Diagnostics is the exclusive licensee of the '820 patent, covering methods for diagnosing neurological disorders by detecting antibodies to a protein called muscle-specific tyrosine kinase ("MuSK"). '820 patent Abstract. Athena also markets a test called FMUSK that functions by evaluating those antibodies. After Mayo Collaborative Services, LLC ("Mayo") developed two competing tests that allegedly practice each step of one or more claims of the '820 patent, Athena accused Mayo of infringing its patent. Mayo moved to dismiss under Rule 12(b)(6), arguing that the asserted claims of the '820 patent were invalid under 35 U.S.C. § 101. The district court granted Mayo's motion, concluding that the claims were invalid under § 101 for claiming ineligible subject matter. This appeal solely concerns whether claims 6–9 are patent eligible under § 101.

A.

Myasthenia gravis ("MG") is a neurological disorder where patients experience muscle weakness and symptoms including drooping eyelids, double vision, and slurred speech. '820 patent col. 1 ll. 13–23. It was previously discovered that MG is an autoimmune disease caused by a

patient generating antibodies against her own acetylcholine receptors. *Id.* col. 1 ll. 24–26. Antibodies which recognize a person's own proteins as foreign antigens are known as autoantibodies. *Id.* col. 1 ll. 42–45.

About 80% of patients with MG produce acetylcholine receptor autoantibodies. *Id.* col. 1 ll. 34–36. The other 20% do not, but they do experience the same MG symptoms. *Id.* col. 1 ll. 36–38. The named inventors of the '820 patent discovered that many of the 20% of MG patients without acetylcholine receptor autoantibodies instead generate autoantibodies to a membrane protein called MuSK. *Id.* col. 1 ll. 54–61. Prior to their discovery, no disease had been associated with MuSK. *Id.* col. 2 ll. 35–37.

Having discovered the association between MuSK autoantibodies and MG, the inventors of the '820 patent disclosed and claimed methods of diagnosing neurological disorders such as MG by detecting autoantibodies that bind to a MuSK epitope.[1] *Id.* col. 2 ll. 61–65. Claim 1, not at issue in this appeal, is the only independent claim and reads as follows:

> 1. A method for diagnosing neurotransmission or developmental disorders related to [MuSK] in a mammal comprising the step of detecting in a bodily fluid of said mammal autoantibodies to an epitope of [MuSK].

Id. col. 12 ll. 31–35. Claim 7 is at issue and depends from claim 1. It recites:

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[1] An epitope, also known as an antigenic determinant, is a segment of a protein recognized by an antibody. *See* Bruce Alberts, *Molecular Biology of the Cell* 449–50 (6th ed. 2015). The specification of the '820 patent disclosed that autoantibodies in MG patients recognize a MuSK epitope located on the protein's extracellular amino-terminal domain. '820 patent col. 1 ll. 54–57.

> 7. A method according to claim 1, comprising
>
> contacting MuSK or an epitope or antigenic determinant thereof having a suitable label thereon, with said bodily fluid,
>
> immunoprecipitating any antibody/MuSK complex or antibody/MuSK epitope or antigenic determinant complex from said bodily fluid and
>
> monitoring for said label on any of said antibody/MuSK complex or antibody/MuSK epitope or antigen determinant complex,
>
> wherein the presence of said label is indicative of said mammal is suffering from said neurotransmission or developmental disorder related to [MuSK].

Id. col. 12 l. 62–col. 13 l. 5 (spacing added). Claim 8 depends from claim 7 and recites that the label is a radioactive label. *Id.* col. 13 ll. 6–7. Claim 9 depends from claim 8 and further recites that the radioactive label is 125I, a radioactive isotope of iodine. *Id.* col. 13 ll. 8–9. We focus on claim 9, the most specific one at issue, which requires: (1) contacting MuSK or an epitope thereof having a 125I label, with bodily fluid; (2) immunoprecipitating any antibody/MuSK complex; and (3) monitoring for the label on the complex, wherein the presence of the label indicates the presence of a MuSK-related disorder.

The specification of the '820 patent further explains what the steps of iodination and immunoprecipitation entail. First, MuSK is iodinated using radioactive 125I. *Id.* col. 10 ll. 50–52. Then iodinated MuSK is separated from any free 125I by gel filtration. *Id.* col. 10 ll. 55–56. Next, the 125I-labeled MuSK is added to a small volume of the patient's bodily fluid and left overnight. *Id.* col. 10 ll. 56–58. If MuSK autoantibodies are present in the patient's bodily fluid, they will bind to the 125I-labeled MuSK. Any 125I-labeled MuSK in the sample is then immunoprecipitated by adding a secondary antibody that binds to any

MuSK autoantibodies present. *Id.* col. 10 ll. 58–60. The resulting precipitate is finally centrifuged, washed, and counted for radioactivity, which may be indicative of MG. *Id.* col. 10 ll. 60–61.

It is undisputed that iodination and immunoprecipitation were known techniques at the time of the invention. The '820 patent specification states that "[t]he actual steps of detecting autoantibodies in a sample of bodily fluids may be performed in accordance with immunological assay techniques known per se in the art," such as radioimmunoassays. *Id.* col. 3 ll. 33–37. With respect to the relevant individual steps in the radioimmunoassay, the specification also discloses that "[i]odination and immunoprecipitation are standard techniques in the art." *Id.* col. 4 ll. 10–11.

Claim 6 is additionally at issue in this appeal and depends from claim 3. While claim 6 also involves detecting MuSK autoantibodies by contacting a patient's bodily fluid with MuSK or an epitope thereof, the labelling occurs somewhat differently than in claims 7–9. Instead of labeling MuSK with a radioisotope, claim 3 recites that the secondary antibody is "tagged or labeled with a reporter molecule." *Id.* col. 12 ll. 47–49. Claim 6 additionally requires that "the intensity of the signal from the [secondary] antibody is indicative of the relative amount of the anti-MuSK autoantibody in the bodily fluid when compared to a positive and negative control reading." *Id.* col. 12 ll. 57–61. This claimed technique exemplifies the ELISA method,[2] which, like radioimmunoassays, the '820 patent specification lists as an example of "immunological assay techniques known per se in the art." *Id.* col. 3 ll. 33–36.

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[2] ELISA stands for enzyme-linked immunosorbent assay. The technical details of this assay are not relevant to this appeal.

B.

The district court concentrated its analysis on claims 7–9. Athena did not present any arguments specific to claim 6. Applying the test for subject matter eligibility established by the Supreme Court in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66 (2012) and *Alice Corp. v. CLS Bank International*, 573 U.S. 208 (2014), the court first concluded that the claims were directed to a law of nature, *Decision*, 275 F. Supp. 3d at 312. According to the court, the claims focused on the interaction of 125I-labeled MuSK with MuSK autoantibodies in bodily fluid, an interaction which occurs naturally. *Id.* at 310. The district court also determined that the claims lacked an inventive concept, as the recited steps involved only standard techniques in the art. *Id.* at 312–13.

The district court thus dismissed Athena's complaint for failure to state a claim. Athena appealed. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

II. DISCUSSION

We review the district court's dismissal for failure to state a claim under regional circuit law. *BASCOM Glob. Internet Servs., Inc. v. AT&T Mobility LLC*, 827 F.3d 1341, 1347 (Fed. Cir. 2016). The First Circuit reviews such dismissals *de novo*, accepts all well-pleaded facts alleged in the complaint to be true, and draws all reasonable inferences in favor of the non-movant. *In re Loestrin 24 Fe Antitrust Litig.*, 814 F.3d 538, 549 (1st Cir. 2016). Patent eligibility under § 101 is a question of law based on underlying facts, *see Aatrix Software, Inc. v. Green Shades Software, Inc.*, 882 F.3d 1121, 1125 (Fed. Cir. 2018); *Berkheimer v. HP Inc.*, 881 F.3d 1360, 1364–65 (Fed. Cir. 2018), that may be resolved on a Rule 12(b)(6) motion when the undisputed facts require a holding of ineligibility, *SAP Am., Inc. v. Investpic, LLC*, 898 F.3d 1161, 1166 (Fed. Cir. 2018).

Section 101 provides that "[w]hoever 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"; some of 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).

Under the law as set forth by the Supreme Court, § 101, while broad, "contains an important implicit exception. '[L]aws of nature, natural phenomena, and abstract ideas' are not patentable." *Mayo*, 566 U.S. at 70 (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 are not patentable, but applications of such laws may be patentable. A claim to otherwise statutory subject matter does not become ineligible by its use of a law of nature. *See Diehr*, 450 U.S. at 187; *Parker v. Flook*, 437 U.S. 584, 590 (1978). But, on the other hand, adding "conventional steps, specified at a high level of generality," to a law of nature does not make a claim to the law of nature patentable. *Mayo*, 566 U.S. at 82.

To distinguish claims to patent-eligible applications of laws of nature from claims that impermissibly tie up such laws, 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. *Alice*, 573 U.S. at 217. If they are, then

we proceed to the second inquiry, where we ask whether the limitations of the claim apart from the law of nature, 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). To so transform the claim, the additional limitations must "ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself." *Mayo*, 566 U.S. at 73.

We first address claims 7–9 and then turn to claim 6.

A.

Athena argues that claims 7–9 are not directed to a natural law at step one because they recite innovative, specific, and concrete steps that do not preempt a natural law. Rather, Athena contends that the claims are directed to a new laboratory technique that makes use of man-made molecules.

Mayo responds that the claims are directed to a natural law: the correlation between naturally-occurring MuSK autoantibodies and MuSK-related neurological diseases like MG. According to Mayo, the remaining steps apart from the natural law are concededly standard immunoassay techniques that still leave the claim directed to a natural law. Indeed, Mayo argues that the specificity and concreteness of the claimed steps are irrelevant to whether a claim is directed to a natural law. And, as in *Mayo*, Mayo contends that it makes no difference to eligibility that the claimed diagnostic method uses man-made materials.

We ultimately agree with Mayo that, under *Mayo*, the claims are directed to a natural law. As an initial matter, we must identify what the relevant natural law is. Here, it is the correlation between the presence of naturally-occurring MuSK autoantibodies in bodily fluid and MuSK-

related neurological diseases like MG.[3] This correlation exists in nature apart from any human action. There can thus be no dispute that it is an ineligible natural law.

However, as Athena correctly observes, not every claim that involves a natural law is directed to a natural law. "[A]ll inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas." *Mayo*, 566 U.S. at 71. The Supreme Court's two-step test thus "plainly contemplates that the first step of the inquiry is a meaningful one, i.e., that a substantial class of claims are *not* directed to a patent-ineligible concept." *Enfish, LLC v. Microsoft Corp.*, 822 F.3d 1327, 1335 (Fed. Cir. 2016).

The step one "directed to" inquiry focuses on the claim as a whole. *E.g.*, *Elec. Power Grp., LLC v. Alstom S.A.*, 830 F.3d 1350, 1353 (Fed. Cir. 2016). To determine whether a claim is directed to an ineligible concept, we have frequently considered whether the claimed advance improves upon a technological process or merely an ineligible concept, based on both the written description and the claims. *See Cleveland Clinic Found. v. True Health Diagnostics LLC*, 859 F.3d 1352, 1361 (Fed. Cir. 2017); *Rapid Litig. Mgmt. Ltd. v. CellzDirect, Inc.*, 827 F.3d 1042, 1047–49 (Fed. Cir. 2016); *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1376 (Fed. Cir. 2015); *see also McRO, Inc. v.*

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[3] We note that the district court held that the "focus of the claims" was the binding of MuSK to MuSK antibodies in bodily fluid. *Decision*, 275 F. Supp. 3d at 310. Our cases have not described a claim to the binding of two molecules during a sequence of chemical manipulations (here, after MuSK labeling and before immunoprecipitation) as a claim to a natural law, even if such binding occurs according to natural laws. We need not resolve that issue here, as we agree with Mayo's identification of the natural law.

Bandai Namco Games Am. Inc., 837 F.3d 1299, 1314–15 (Fed. Cir. 2016); *Elec. Power Grp.*, 830 F.3d at 1354.

For example, in *CellzDirect* we considered claims that covered a method for producing a preparation of a type of liver cell (called hepatocytes) that involved multiple freeze-thaw cycles. 827 F.3d at 1046, 1048. Although the inventors discovered the cells' ability to survive multiple freeze-thaw cycles, a discovery that the district court understood to be a natural law, we concluded that the claims were not directed to that natural law. *Id.* at 1048–50. This was because the claims as a whole recited "a new and improved way of preserving hepatocyte cells for later use," "not simply an observation or detection of the ability of hepatocytes to survive multiple freeze-thaw cycles." *Id.* at 1048. The claimed advance harnessed a natural law to produce a technological improvement that was patent eligible. *See id.* at 1048–49; *see also, e.g.*, *Enfish*, 822 F.3d at 1335–39 (holding improvement in computer-related technology not directed to abstract idea).

In contrast, in *Cleveland Clinic* we reiterated that claims that merely recite observing naturally occurring biological correlations "with no meaningful non-routine steps in between" are directed to a natural law. 859 F.3d at 1361; *see Ariosa*, 788 F.3d at 1376. There, the specification indicated that the claimed inventors discovered a natural correlation between a molecule called MPO and cardiovascular disease. *Cleveland Clinic*, 859 F.3d at 1360–61. The claims at issue recited detecting MPO or other MPO-related products in a patient sample and then predicting a patient's risk of having or developing cardiovascular disease. *Id.* at 1361. As the claims only covered the correlation between MPO and cardiovascular disease, an ineligible discovery, together with "well-known techniques to execute the claimed method," we held that the claims were directed to a natural law. *Id.*

The claims at issue here involve both the discovery of a natural law and certain concrete steps to observe its operation. Claim 9, the most specific claim at issue, recites the following method to detect MuSK autoantibodies: (1) mixing MuSK or an epitope thereof having a 125I label with bodily fluid; (2) immunoprecipitating any resulting antibody/MuSK complex; and (3) monitoring for the label on the complex. '820 patent col. 12 l. 62–col. 13 l. 9. The claim then concludes in the wherein clause with a statement of the natural law, *i.e.*, the discovery that MuSK autoantibodies naturally present in a patient sample, detected with the 125I label bound to the MuSK/antibody complex, indicate that the patient is suffering from a MuSK-related neurological disorder. *Id.* col. 13 ll. 2–5.

As in *Cleveland Clinic* and *Ariosa*, we conclude that claims 7–9 are directed to a natural law because the claimed advance was only in the discovery of a natural law, and that the additional recited steps only apply conventional techniques to detect that natural law. The specification of the '820 patent highlights the discovery of the natural law, explaining that "[t]he present inventors surprisingly found that many of the 20% of MG patients [who] do not exhibit any autoantibodies to [the acetylcholine receptor], instead have . . . antibodies directed against the extracellular [amino]-terminal domains of MuSK." *Id.* col. 1 ll. 54–57. Further, the specification describes the claimed concrete steps for observing the natural law as conventional. It teaches that "[t]he actual steps of detecting autoantibodies in a sample of bodily fluids may be performed in accordance with immunological assay techniques known per se in the art," including radioimmunoassays and ELISA. *Id.* col. 3 ll. 33–37. Likewise, the specification identifies "[i]odination and immunoprecipitation" as "standard techniques in the art." *Id.* col. 4 ll. 10–12. The '820 patent thus describes the claimed invention principally as a discovery of a natural law, not as an improvement in the underlying immunoassay technology.

Consistent with the specification, the claims are directed to that law.

Athena argues that the claims at issue, like the claims in *CellzDirect*, are directed to an innovative laboratory technique, not a law of nature. However, Athena does not point to any innovation other than its discovery of the natural law. *CellzDirect* did not suggest that appending standard techniques to detect a natural law rendered claims not directed to a natural law; rather, we expressly distinguished the eligible claims in that case from ineligible claims that "amounted to nothing more than observing or identifying the ineligible concept itself." 827 F.3d at 1048. In that case, we concluded that the "end result" of the claims at issue was "not simply an observation or detection" of a natural law. *Id.* We cannot so conclude here, since the claims before us only involve detecting a natural law "with no meaningful non-routine steps." *Cleveland Clinic*, 859 F.3d at 1361.

Athena also points to the specificity of the claimed concrete steps, contending that they preempt no natural law and therefore the claims cannot be directed to a natural law. Although we agree that claim 9 leaves open to the public other ways of interrogating the correlation between MuSK autoantibodies and MuSK-related disorders without practicing the claim's concrete steps, that does not disturb our conclusion at step one. Preemption is sufficient to render a claim ineligible under § 101, but it is not necessary. *Flook*, 409 U.S. at 71–72 (holding claim involving mathematical formula invalid under § 101 that did not preempt a mathematical formula); *Ariosa*, 788 F.3d at 1379; *In re BRCA1- & BRCA2-Based Hereditary Cancer Test Patent Litig.*, 774 F.3d 755, 764 n.4 (Fed. Cir. 2014). The claims here are directed to a natural law because they recite only the natural law together with standard techniques for observing it. That the routine steps are set forth with some specificity is not enough to change that conclusion.

Finally, Athena argues that the claims at issue differ from prior diagnostic claims we have held ineligible under § 101 because they require labeling MuSK with a man-made substance. We disagree. As Mayo argues, the use of a man-made molecule is not decisive if it amounts to only a routine step in a conventional method for observing a natural law. For example, *Mayo* involved claims requiring administering a man-made molecule (a drug "providing" 6-thioguanine) to a patient. 566 U.S. at 74–75. Some of the claims in *Ariosa* likewise required amplification through the polymerase chain reaction, which makes use of man-made reagents, *see* U.S. Patent 6,258,540 col. 5 ll. 6–26, or using a specific probe that binds to DNA, 788 F.3d at 1374. And the claims in *BRCA1* also involved hybridizing a synthetic DNA probe to a DNA strand. *BRCA1*, 774 F.3d at 763–64. Nonetheless, in each of these cases either the Supreme Court or this court held the claims directed to a natural law and invalid under § 101. *Mayo*, 566 U.S. at 92; *Ariosa*, 788 F.3d at 1380; *BRCA1*, 774 F.3d at 765. We thus reaffirm that use of a man-made molecule in a method claim employing standard techniques to detect or observe a natural law may still leave the claim directed to a natural law.

We consider it important at this point to note the difference between the claims before us here, which recite a natural law and conventional means for detecting it, and applications of natural laws, which are patent-eligible. *See Vanda Pharm. Inc. v. West-Ward Pharm. Int'l Ltd.*, 887 F.3d 1117, 1133–36 (Fed. Cir. 2018) (holding that method of treatment by administering drug at certain dosage ranges based on a patient's genotype was not directed to a natural law). Claiming a natural cause of an ailment and well-known means of observing it is not eligible for patent because such a claim in effect only encompasses the natural law itself. But claiming a new treatment for an ailment, albeit using a natural law, is not claiming the natural law.

As we conclude that claims 7–9 are directed to a natural law, we turn to the second step of the *Mayo/Alice* test.[4]

B.

At step two, "we consider the elements of each claim both individually and 'as an ordered combination' to determine whether the additional elements 'transform the nature of the claim' into a patent-eligible application." *Alice*,

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[4] The dissent states much that one can agree with from the standpoint of policy, and history, including that "the public interest is poorly served by adding disincentive to the development of new diagnostic methods." Dissent at 12. We would add further that, in our view, providing patent protection to novel and non-obvious diagnostic methods would promote the progress of science and useful arts. But, whether or not we as individual judges might agree or not that these claims only recite a natural law, *cf. Berkheimer v. HP Inc.*, 890 F.3d 1369, 1374 (Fed. Cir. 2018) (Lourie, J., concurring in the denial of rehearing en banc) (discussing traditional laws of nature such as "Ohm's Law, Boyle's Law, [and] the equivalence of matter and energy"), the Supreme Court has effectively told us in *Mayo* that correlations between the presence of a biological material and a disease are laws of nature, *see* 566 U.S. at 77, and "[p]urely 'conventional or obvious' '[pre]-solution activity' is normally not sufficient to transform an unpatentable law of nature into a patent-eligible application of such a law," *id.* at 79 (second alteration in original) (quoting *Flook*, 437 U.S. at 590). We have since confirmed that applying somewhat specific yet conventional techniques (such as the polymerase chain reaction) to detect a newly discovered natural law does not confer eligibility under § 101. *Ariosa*, 788 F.3d at 1377; *see also Cleveland Clinic*, 859 F.3d at 1356, 1362 (addressing other conventional techniques such as flow cytometry). Our precedent leaves no room for a different outcome here.

573 U.S. at 217 (quoting *Mayo*, 566 U.S. at 78, 79). "Purely 'conventional or obvious' '[pre]-solution activity' is normally not sufficient to transform an unpatentable law of nature into a patent-eligible application of such a law." *Mayo*, 566 U.S. at 79 (second alteration in original) (quoting *Flook*, 437 U.S. at 590). The transformative "inventive concept" supplied by the claim elements not drawn to ineligible subject matter must be "sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself." *Alice*, 573 U.S. at 217–18 (quoting *Mayo*, 566 U.S. at 73).

1.

Athena argues that the claims provide an inventive concept: an innovative sequence of steps involving man-made molecules. Prior to its discovery, Athena contends that there was no disclosed method to detect MuSK autoantibodies. In addition, Athena argues that the existence of factual disputes precluded dismissal under Rule 12(b)(6).

Mayo responds that the claims lack an inventive concept because the specification describes the steps for detecting MuSK autoantibodies as standard techniques in the art. Furthermore, Mayo argues that no factual issues precluded the district court's dismissal under Rule 12(b)(6).

We agree with Mayo that the steps of the claims not drawn to ineligible subject matter, whether viewed individually or as an ordered combination, only require standard techniques to be applied in a standard way. As previously discussed, the specification of the '820 patent plainly states that "[t]he actual steps of detecting autoantibodies in a sample of bodily fluids may be performed in accordance with immunological assay techniques known per se in the art," such as radioimmunoassays. '820 patent col. 3 ll. 33–37. Iodination and immunoprecipitation are likewise described as standard techniques. *Id.* col. 4 ll. 9–12. Because the specification defines the individual immunoprecipitation and iodination steps and the overall

radioimmunoassay as conventional techniques, the claims fail to provide an inventive concept. *Cleveland Clinic*, 859 F.3d at 1362; *Ariosa*, 788 F.3d at 1378.

Our decisions in *CellzDirect* and *BASCOM* are consistent with the principle that applying standard techniques in a standard way to observe a natural law does not provide an inventive concept. In *CellzDirect*, we considered a combination of claimed steps involving two freeze/thaw cycles. 827 F.3d at 1051. We held that this combination of steps was not conventional because the prior art methods only disclosed using one freeze/thaw cycle and, in fact, taught away from using multiple freeze/thaw cycles. *Id.* Similarly, in *BASCOM* we held that the ordered combination of claim limitations was not routine and conventional because they placed a filtering tool at a specific location that improved on prior art technology. 827 F.3d at 1350. The inventive concept was "found in the non-conventional and non-generic arrangement of known, conventional pieces." *Id.* In contrast, claims 7–9 of the '820 patent employ a conventional technique for detecting autoantibodies, a radioimmunoassay, which the specification acknowledges was "known per se in the art." '820 patent col. 3 ll. 33–37. The individual constituent steps of that technique, iodination and immunoprecipitation, are similarly described as standard. *Id.* col. 4 ll. 9–12. Thus, unlike the claimed limitations at issue in *CellzDirect* and *BASCOM*, the recited steps here were conventional both as an ordered combination and individually.

Athena also argues that the claimed steps were unconventional because they had not been applied to detect MuSK autoantibodies prior to Athena's discovery of the correlation between MuSK autoantibodies and MG. Even accepting that fact, we cannot hold that performing standard techniques in a standard way to observe a newly discovered natural law provides an inventive concept. This is because "[t]he inventive concept necessary at step two . . . cannot be furnished by the unpatentable law of nature

. . . itself." *Genetic Techs. Ltd. v. Merial L.L.C.*, 818 F.3d 1369, 1376 (Fed. Cir. 2016); *see Mayo*, 566 U.S. at 73 (considering whether the "claimed processes (apart from the natural laws themselves)" were routine and conventional). Rather, to supply an inventive concept the sequence of claimed steps must do more than adapt a conventional assay to a newly discovered natural law; it must represent an inventive application beyond the discovery of the natural law itself. Because claims 7–9 fail to recite such an application, they do not provide an inventive concept.

Similar to its step one argument, Athena further argues that the claims recite an inventive concept because they use a man-made molecule, *i.e.*, labeled MuSK. Athena analogizes its methods involving labeled MuSK to the composition claims involving cDNA held eligible in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 594–95 (2013). However, the method claims at issue here are unlike the claims held eligible in *Myriad*, which recited a new composition of matter that was not a natural product. *Id.* For the same reasons that we have concluded that attaching a label to MuSK did not make the claims directed to an eligible concept at step one, we conclude that appending labeling techniques to a natural law does not provide an inventive concept where, as here, the specification describes 125I labeling as a standard practice in a well-known assay.

2.

Athena also argues that the district court needed to conduct fact-finding before resolving the § 101 issue. But, unlike in *Aatrix*, 882 F.3d at 1128, Athena directs us to no factual allegations in its complaint—amended three times—that the radioimmunoassay technique recited in claims 7–9 is anything other than standard and "known per se in the art." '820 patent, col. 3 ll. 33–37. Instead, Athena relies on an expert declaration submitted with its opposition to Mayo's motion to dismiss, asserting that iodination

and immunoprecipitation were not routine as applied to the claimed invention. In dismissing Athena's complaint under Rule 12(b)(6), the district court did not consider the declaration. Athena argues that was error. We disagree.

In the First Circuit, under Rule 12(b)(6) a district court may generally "consider only facts and documents that are part of or incorporated into the complaint; if matters outside the pleadings are considered, the motion must be decided under the more stringent standards applicable to a Rule 56 motion for summary judgment." *Trans-Spec Truck Serv., Inc. v. Caterpillar Inc.*, 524 F.3d 315, 321 (1st Cir. 2008). Certain documents, like the '820 patent here, are also considered to "merge[] into the pleadings" where the "complaint's factual allegations are expressly linked to" and dependent upon a document, the authenticity of which is undisputed. *Id.* (quoting *Beddall v. State St. Bank & Trust Co.*, 137 F.3d 12, 16–17 (1st Cir. 1998)).

District courts in the First Circuit have discretion whether to convert a motion to dismiss into a motion for summary judgment. *Id.* (citing Fed. R. Civ. P. 12(d)). "[I]f the district court chooses . . . to ignore supplementary materials submitted with the motion papers and determine the motion under the Rule 12(b)(6) standard, no conversion occurs and the supplementary materials do not become part of the record for purposes of the Rule 12(b)(6) motion." *Id.*

We conclude that the district court did not abuse its discretion in declining to consider Athena's expert declaration and convert the motion into one for summary judgment. The declaration does not "merge into the pleadings," as the complaint does not reference it or otherwise depend on it. Nor is the declaration an official public record, another type of document a court may consider with the pleadings. *See Watterson v. Page*, 987 F.2d 1, 3–4 (1st Cir. 1993).

Athena does not expressly argue that the district court abused its discretion, but does contend, primarily citing non-binding authority, that the plaintiff may freely allege facts without support in responding to a motion to dismiss as long as those facts are consistent with the complaint, *see Early v. Bankers Life & Casualty Co.*, 959 F.2d 75, 79 (7th Cir. 1992), and that its expert declaration alleged such consistent facts that create a dispute of material fact.

Even assuming this general principle applies in the First Circuit—an assumption that Athena meagerly supports—the district court did not need to consider the allegations in the expert declaration because they were not consistent with the complaint read in light of the '820 patent. These technical allegations include: (1) that detecting MuSK autoantibodies required the "creative step" of breaking up MuSK into smaller fragments, J.A. 623, 625; (2) that identifying a specific site on MuSK to label would not have been routine because many factors contribute to whether a binding site for a label is adequate, J.A. 626–28; and (3) that immunoprecipitation is generally uncertain and not routine, J.A. 630. None of these details are recited in the claims of the '820 patent: no claim requires breaking MuSK into fragments as opposed to using the entire MuSK protein; no claim is limited to a particular MuSK binding site; and no claim recites any detail with respect to immunoprecipitation. Those omissions are consistent with the specification's description of iodination, immunoprecipitation, and the overall radioimmunoassay as standard techniques. Because Athena's expert declaration made allegations inconsistent with the '820 patent, the district court was not obliged to accept them as true. For these reasons, the district court did not err in dismissing Athena's complaint under Rule 12(b)(6).

C.

Claim 6 recites a method for detecting MuSK autoantibodies different from claims 7–9. While claims 7–9 recite

a radioimmunoassay, claim 6 recites an ELISA method. Like radioimmunoassays, the specification describes ELISA as an "immunological assay technique[] known per se in the art." '820 patent col. 3 ll. 32–36. The main technical difference pertinent to this appeal between an ELISA and a radioimmunoassay is that in an ELISA, the secondary antibody rather than the antigen is labeled.

Athena argues that since the district court did not specifically analyze claim 6, which involves a different technology, and implicitly treated claims 7–9 as representative, we should remand at least with respect to claim 6. Mayo responds that the district court properly grouped claim 6 with claims 7–9 because Athena grouped them together, and that Athena waived any separate arguments regarding claim 6 by not specifically addressing that claim in its briefing.

During the district court proceedings, Athena represented that it would not assert claims 1–5 and 10–12, and Mayo then moved to dismiss Athena's complaint, specifically addressing claims 6–9. In its response, Athena did not make any particularized arguments regarding claim 6, and, in an earlier response, indicated that the same arguments pertaining to claims 7–9 were also applicable to claim 6. *See* J.A. 180 ("While the claim does not require radioactive MuSK or complexes, many other arguments relating to claims 7-9 apply to claim 6."). The district court did not address claim 6 in its order beyond listing it among the other claims. *Decision*, 275 F. Supp. 3d at 309–10.

Given this history, we agree with Mayo that Athena waived its arguments specific to claim 6 by not making them before the district court. We apply regional circuit law to the issue of waiver, as it is not unique to patent law. *Riverwood Int'l Corp. v. R.A. Jones & Co.*, 324 F.3d 1346, 1352 (Fed. Cir. 2003) (citing *Midwest Indus., Inc. v. Karavan Trailers, Inc.*, 175 F.3d 1356, 1359 (Fed. Cir. 1999) (en banc in relevant part)). In the First Circuit, an argument

may be deemed waived that was not presented to the district court. *Butler v. Deutsche Bank Tr. Co. Ams.*, 748 F.3d 28, 36 (1st Cir. 2014). Although Athena recognized that claim 6 was at issue, it concededly did not present any specific arguments concerning the eligibility of claim 6. Appellant's Br. 15. It was not incumbent on the district court to address arguments that Athena did not make. We thus find no error in the district court considering claims 7–9 as representative of claim 6. Even if we had reached the issue, we would hold claim 6 ineligible. The specification describes ELISA as an "immunological assay technique[] known per se in the art." '820 patent col. 3 ll. 32–36. Claim 6 merely recites the application of this standard technique to observe a natural law. This does not provide an inventive concept under step two.

CONCLUSION

We have considered Athena's remaining arguments but find them unpersuasive. Because claims 6–9 of the '820 patent recite only a natural law together with conventional steps to detect that law, they are ineligible under § 101. For the foregoing reasons, we affirm the judgment of the district court.

AFFIRMED

United States Court of Appeals for the Federal Circuit

ATHENA DIAGNOSTICS, INC., OXFORD UNIVERSITY INNOVATION LTD., MAX-PLANCK-GESELLSCHAFT ZUR FORDERUNG DER WISSENSCHAFTEN E.V.,
Plaintiffs-Appellants

v.

MAYO COLLABORATIVE SERVICES, LLC, DBA MAYO MEDICAL LABORATORIES, MAYO CLINIC,
Defendants-Appellees

2017-2508

Appeal from the United States District Court for the District of Massachusetts in No. 1:15-cv-40075-IT, Judge Indira Talwani.

NEWMAN, *Circuit Judge,* dissenting.

Until discovery of the diagnostic method described in U.S. Patent No. 7,267,820 ("the '820 patent"), some 20% of patients suffering from the neurological disorder *Myasthenia Gravis* were not capable of being diagnosed. My colleagues rule that this new diagnostic method is not patent-eligible, although new and unobvious. However, "[t]his new and improved technique, for producing a tangible and useful result, falls squarely outside those categories of inventions that are 'directed to' patent-ineligible concepts." *Rapid Litig. Mgmt. Ltd. v. CellzDirect, Inc.*, 827 F.3d 1042,

1050 (Fed. Cir. 2016). The court again departs from the cautious restraints in the Supreme Court's *Mayo/Alice* application of laws of nature and abstract ideas.

This court's decisions on the patent-ineligibility of diagnostic methods are not consistent, and my colleagues today enlarge the inconsistencies and exacerbate the judge-made disincentives to development of new diagnostic methods, with no public benefit. I respectfully dissent.

The claims are for a multi-step method of diagnosis, not a law of nature

The '820 inventors did not patent their scientific discovery of MuSK autoantibodies. Rather, they applied this discovery to create a new method of diagnosis, for a previously undiagnosable neurological condition. The district court summarized this new diagnostic method as follows:

> For the 20% of Myasthenia Gravis patients who do not have the AChR [acetylcholine receptor] autoantibodies, the '820 patent inventors discovered that they had IgG [immunoglobulin G] antibodies that attack the N-terminal domains of muscle specific tyrosine kinase ("MuSK"), a receptor that is located on the surface of neuromuscular junctions. . . . [A] radioactive label is attached to MuSK (or a fragment thereof) and is then introduced to a sample of bodily fluid. . . . [T]he MuSK autoantibodies, if present, attach to the labeled fragment . . . [and] is immunoprecipitated, the presence of the radioactive label on any antibody indicates that the person is suffering from Myasthenia Gravis.

Dist. Ct. Order, at 307–08[1] (citing '820 patent, col. 1, ll. 55–61). The claims recite the method, including preparation of the new radioactive entities and their chemical reactions to detect autoantibodies to the protein muscle-specific tyrosine kinase (MuSK). At issue are patent claims 7–9, shown with claim 1 (not in suit) from which they depend:

> 1. A method for diagnosing neurotransmission or developmental disorders related to muscle specific tyrosine kinase (MuSK) in a mammal comprising the step of detecting in a bodily fluid of said mammal autoantibodies to an epitope of muscle specific tyrosine kinase (MuSK).
>
> 7. A method according to claim 1, comprising
>
> contacting MuSK or an epitope or antigenic determinant thereof having a suitable label thereon, with said bodily fluid,
>
> immunoprecipitating any antibody/MuSK complex or antibody/MuSK epitope or antigenic determinant complex from said bodily fluid and
>
> monitoring for said label on any of said antibody/MuSK complex or antibody/MuSK epitope or antigen determinant complex,
>
> wherein the presence of said label is indicative of said mammal is suffering from said neurotransmission or developmental disorder related to muscle specific tyrosine kinase (MuSK).
>
> 8. A method according to claim 7 wherein said label is a radioactive label.

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[1] *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 275 F. Supp. 3d 306 (D. Mass. 2017) ("Dist. Ct. Order").

> 9. A method according to claim 8 wherein said label is 125I [iodine isotope 125].

The reaction between the antibody and the MuSK protein was not previously known, nor was it known to form a labeled MuSK or its epitope, nor to form the antibody/MuSK complex, immunoprecipitate the complex, and monitor for radioactivity, thereby diagnosing these previously undiagnosable neurotransmission disorders.

Claims 7–9 require specific steps by which the diagnostic method is performed. The panel majority ignores these steps, and instead holds that "claims 7–9 are directed to a natural law because the claimed advance was only in the discovery of a natural law, and that the additional recited steps only apply conventional techniques to detect that natural law." Maj. Op. at 12. This analysis of patent-eligibility is incorrect, for the claim is for a multi-step method of diagnosing neurotransmission disorders related to muscle specific tyrosine kinase, by detecting autoantibodies using a series of chemical and biological steps as set forth in the claims. Eligibility is determined for the claim considered as a whole, including all its elements and limitations. Claim limitations cannot be discarded when determining eligibility under Section 101, as explained in *Diamond v. Diehr*, 450 U.S. 175 (1981):

> In determining the eligibility of respondents' claimed process for patent protection under § 101, their claims must be considered as a whole. It is inappropriate to dissect the claims into old and new elements and then to ignore the presence of the old elements in the analysis.

Id. at 188; *see Parker v. Flook*, 437 U.S. 584, 594 (1978) ("[A] patent claim must be considered as a whole."); *see also Aro Mfg. Co. v. Convertible Top Replacement Co.*, 365 U.S. 336, 344 (1961) ("[I]f anything is settled in the patent law, it is that the combination patent covers only the totality of the elements in the claim and that no element, separately

viewed, is within the grant."); *Mercoid Corp. v. Minneapolis-Honeywell Regulator Co.*, 320 U.S. 680, 684 (1944) ("[A] patent on a combination is a patent on the assembled or functioning whole, not on the separate parts.").

The requirement that a claim is considered as a whole was not changed by the *Mayo/Alice* protocol of searching for an inventive concept within a claim that is directed to a law of nature or an abstract idea. It is incorrect to excise from the claims any steps that are performed by conventional procedures. This is misconstruction of claims, and misapplication of Section 101. As reiterated in *Bilski v. Kappos*, 561 U.S. 593 (2010):

> Section 101 is a dynamic provision designed to encompass new and unforeseen inventions. A categorical rule denying patent protection for inventions in areas not contemplated by Congress . . . would frustrate the purposes of the patent law.

Id. at 605 (internal citations and quotation marks omitted).

Applied to the '820 patent, the claimed method is a new method of diagnosing *Myasthenia Gravis*. After eliminating the "conventional" procedures, my colleagues rule that this new method is a "law of nature." However, these inventors are not claiming the scientific fact of a newly described autoantibody; they are claiming a new multi-step diagnostic method. This is not a law of nature, but a man-made reaction sequence employing new components in a new combination to perform a new diagnostic procedure.

Section 101 describes patent-eligible subject matter in broad and general terms

Section 101 does not exclude new methods of diagnosis of human ailments.

35 U.S.C. § 101 Inventions Patentable

> 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.

Section 101 recites the subject matter of patent law, as distinguished from copyright law, which is also authorized by Article I, Section 8. This framework is "cast in broad terms," as the Court observed in *Diamond v. Chakrabarty*, 447 U.S. 303 (1980):

> The subject-matter provisions of the patent law have been cast in broad terms to fulfill the constitutional and statutory goal of promoting "the Progress of Science and the useful Arts" with all that means for the social and economic benefits envisioned by Jefferson. Broad general language is not necessarily ambiguous when congressional objectives require broad terms.

Id. at 315.

The Court has often discussed the exceptions to patent eligibility, stating that: "Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work." *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972). "Thus, a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that $E=mc^2$; nor could Newton have patented the law of gravity. Such discoveries are 'manifestations of . . . nature, free to all men and reserved exclusively to none'." *Chakrabarty*, 447 U.S. at 309 (quoting *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948)). In *Funk Brothers* the Court explained:

> The qualities of these bacteria, like the heat of the sun, electricity, or the qualities of metals, are part of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men

> and reserved exclusively to none. He who discovers a hitherto unknown phenomenon of nature has no claim to a monopoly of it which the law recognizes. If there is to be invention from such a discovery, it must come from the application of the law of nature to a new and useful end.

Id. at 130.

The Court early drew the distinction between scientific knowledge and its technological application. An oft-cited example is the case of *O'Reilly v. Morse*, 56 U.S. 62 (15 How.) (1854), where the Court declined patent-eligibility of Morse's claim 8 to "electro-magnetism, however developed for marking or printing intelligible characters, signs, or letters, at any distances," *id.* at 112–13, but sustained Morse's claims to "us[ing] [] the motive power of magnetism . . . as means of operating or giving motion to machinery, which may be used to imprint signals . . . for the purpose of telegraphic communication at any distances." *Id.* at 85; *see id.* at 112. The Court criticized the breadth of Morse's claim 8, and stated:

> In fine he claims an exclusive right to use a manner and process which he has not described and indeed had not invented, and therefore could not describe when he obtained his patent.

Id. at 113; *see* Adam Mossoff, *O'Reilly v. Morse*, George Mason Law & Econ. Research Paper No. 14-22 (Aug. 18, 2014), *available at* http://ssrn.com/abstract=2448363. In *Mackay Radio & Telegraph Co. v. Radio Corp. of America*, 306 U.S. 86 (1939), the Court explained that: "While a scientific truth, or the mathematical expression of it, is not patentable invention, a novel and useful structure created with the aid of knowledge of scientific truth may be." *Id.* at 94. These principles are the foundation of the truism that natural phenomena and abstract ideas are not patent-eligible.

As science and its applications advanced, particularly in the new fields of digital electronics and biotechnology, the jurisprudence kept pace. In *Chakrabarty* the Court considered a man-made bacterium, and held that eligibility under Section 101 applies to "anything under the sun that is made by man." 447 U.S. at 309.

The most recent Court updates are *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66 (2012) (biotechnology), and *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 573 U.S. 208 (2014) (digital electronics). The Court reviewed Section 101 eligibility in these new fields, building on the vast body of jurisprudence since the first patent was analyzed by Thomas Jefferson as Secretary of State in 1790. *See generally* Ten Law Professors Br.;[2] Five Life Sciences Patent Practitioners Br.[3] These *amici curiae* explain the policy concern for preemption of scientific principles, and apply this concern to the case at bar, advising that the scientific information of the new autoantibody and its protein reactivity is available to all, and that the '820 patent claims 7–9 "did not preempt any 'law of nature' upon which the claimed diagnostic method relied." Five Life Sciences Patent Practitioners Br. at 1.

In *Alice*, the Court summarized the procedural framework for eligibility for patenting:

> First, we determine whether the claims at issue are directed to one of those patent-ineligible concepts. 132 S. Ct., at 1296–1297. If so, we then ask, "[w]hat else is there in the claims before us?" 132

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[2] *Amici Curiae* Ten Law Professors, ECF No. 54 (Nov. 13, 2017) ("Ten Law Professors Br.").

[3] *Amici Curiae* Five Life Sciences Patent Practitioners, ECF No. 52 (Nov. 13, 2017) ("Five Life Sciences Patent Practitioners Br.").

> S. Ct., at 1297. To answer that question, we consider the elements of each claim both individually and "as an ordered combination" to determine whether the additional elements "transform the nature of the claim" into a patent-eligible application. 132 S. Ct., at 1298, 1297.

Alice, 573 U.S. at 217 (quoting *Mayo)*.

This analysis comports with precedent, and the Court reiterated its caution that "too broad an interpretation of this exclusionary principle could eviscerate patent law. For all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas." *Mayo*, 566 U.S. at 71; *see Alice*, 573 U.S. at 217 ("At the same time, we tread carefully in construing this exclusionary principle lest it swallow all of patent law."). We have echoed this concern, stating in *Rapid Litigation Management*, 827 F.3d at 1050, "[a]t step one, therefore, it is not enough to merely identify a patent-ineligible concept underlying the claim; we must determine whether that patent-ineligible concept is what the claim is 'directed to,'" (quoting *Alice*, 573 U.S. at 217).

The panel majority departs from this guidance, for the claimed diagnostic method as a whole satisfies step one. The majority does not distinguish between the question of whether the claimed method as a whole is eligible, and the question of whether the separate steps use conventional procedures. Instead, my colleagues hold that since the separate procedures are conventional, it is irrelevant that the method as a whole is a new method. The majority misconstrues the claims, in holding that claims 7–9 are directed to the "concept" of "the correlation between the presence of naturally-occurring MuSK autoantibodies in bodily fluid and MuSK-related neurological diseases like MG." Maj. Op. at 9–10. The claimed method determines whether this correlation is present, for diagnostic purposes, but the concept itself is not claimed.

It is incorrect to separate the claim steps into whether a step is performed by conventional techniques, and then to remove those steps from the claims and their "conjunction with all of the other steps" for the purpose of Section 101 analysis. *Diehr*, 450 U.S. at 187. All of the claim steps must be considered in the claimed combination. "It is inappropriate to dissect the claims into old and new elements and then to ignore the presence of the old elements in the analysis." *Id.* at 188. The Court explained that a new process may be a combination of known steps:

> This is particularly true in a process claim because a new combination of steps in a process may be patentable even though all the constituents of the combination were well known and in common use before the combination was made.

Id. The Court stated that:

> The "novelty" of any element or steps in a process, or even of the process itself, is of no relevance in determining whether the subject matter of a claim falls within the § 101 categories of possibly patentable subject matter.

Id. at 188–89. The Court again recognized this principle in *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398 (2007), stating that:

> [I]nventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.

Id. at 418–19. This court applied this principle in *McRO, Inc. v. Bandai Namco Games America Inc.*, 837 F.3d 1299, 1313 (Fed. Cir. 2016) (internal quotation marks omitted) and cautioned that "courts must be careful to avoid oversimplifying the claims by looking at them generally and failing to account for the specific requirements of the claims"—a caution disregarded today.

The panel majority contravenes the requirements of precedent, now holding that all of the steps of claims 7–9—that is, radioactive labelling, complexing, precipitating, and monitoring—are removed from consideration in the Section 101 analysis because they use conventional procedures; the majority holds that "[t]he '820 patent thus describes the claimed invention principally as a discovery of a natural law, not as an improvement in the underlying immunoassay technology." Maj. Op. at 12. However, that is not the claimed invention. In *Mayo*, 566 U.S. at 71, the Court cautioned that "too broad an interpretation of this exclusionary principle could eviscerate patent law. For all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas."

Applying the *Mayo/Alice* protocol of two-step claim analysis, claims 7–9 of the '820 patent are patent-eligible under Step 1, for this method of diagnosing *Myasthenia Gravis* is not a law of nature, but a man-made chemical-biomedical procedure. Claims 7–9 recite a combination of technologic steps, all of which are limitations to the claims and cannot be disregarded whether for patentability or patent-eligibility or infringement. The court today violates this rule, in holding that because "the . . . individual steps . . . [of] '[i]odination and immunoprecipitation are standard techniques in the art,'" Maj. Op. at 6, these steps do not count under Section 101. *Id.* at 12–13.

Section 101 does not turn on whether any claim steps are "standard techniques." The appropriate analysis of the role of conventional process steps in claims to a new method is under Sections 102 and 103, not Section 101.

The amici curiae raise strong concerns for the consequences for biomedical diagnostics

This court's decisions have not been consistent. Today's decision is not consistent with, for example, *Rapid Litigation Management*, 827 F.3d at 1048, where the court

held that although the general type of cell was known, and the manipulation of these specific cells was conducted in a conventional manner, the overall method was eligible under Section 101.

Amici curiae point out that the public interest is poorly served by adding disincentive to the development of new diagnostic methods. This is a severe criticism; and when presented by the entire industry, and stressed by thoughtful scholars, it warrants judicial attention.

The Biotechnology Innovation Organization[4] pleads for consistency in judge-made law, citing the

> unabated uncertainty about the patent-eligibility of many biotechnological inventions, with diagnostic and prognostic methods being particularly affected. The unstable state of patent-eligibility jurisprudence affects modern biotechnologies ranging from biomarker-assisted methods of drug treatment to companion diagnostic tests, fermentation products, industrial enzyme technology, and marker-assisted methods of plant breeding.

BIO Br. at 1. International concerns are presented by The Chartered Institute of Patent Attorneys,[5] an organization of the United Kingdom, stating that this decision conflicts with the eligibility of diagnostic methods under the Patent Cooperation Treaty and the European Patent Convention, and is inconsistent with the obligations of the United States under Article 27 and Note 5 of the Agreement on Trade-Related Aspects of Intellectual Property Rights

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[4] *Amicus Curiae* Biotechnology Innovation Organization, ECF No. 53 (Nov. 13, 2017) ("BIO Br.").

[5] *Amicus Curiae* The Chartered Institute of Patent Attorneys, ECF No. 51 (Nov. 13, 2017) ("CIPA Br.").

(TRIPS) administered by the World Trade Organization. CIPA Br. at 2.

Amici curiae Five Life Sciences Patent Practitioners point out that "The Supreme Court has recognized that patent ineligibility determinations (by courts or the Patent Office) have the potential to inhibit innovation," Five Life Sciences Patent Practitioners Br. at 6 (citing *Bilski v. Kappos*, 561 U.S. 593, 605 (2010)). They state concerns of the inventing/investing communities with respect to the future of diagnostics, because "[medical] diagnostic methods . . . are so tightly bound to underlying natural laws and phenomen[a], they are especially susceptible to undue expansion of the eligibility standards implemented to protect the judicial exceptions as they have been explicated by the Supreme Court." *Id.* at 6–7.

Amici curiae Ten Law Professors direct us to the cost to develop and commercialize a new diagnostic, reported as $50-100 million, *see* Ten Law Professors Br. at 18–19 (citing Diaceutics Group, *Mystery Solved! What is the Cost to Develop and Launch a Diagnostic?* (2013)*, available at* https://www.diaceutics.com/?expert-insight=mystery-solved-what-is-the-cost-to-develop-and-launch-a-diagnostic).

Undoubtedly there are a variety of interests in diagnostic procedures, and we take note that *amicus curiae* ARUP Laboratories[6] states that diagnostic tests should not be patentable at all. *See generally* ARUP Br. However, for procedures that require extensive development and federal approval, unpredictability of patent support is a

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[6] *Amicus Curiae* ARUP Laboratories, ECF No. 76 (Feb. 6, 2018) ("ARUP Br.").

disincentive to development of new diagnostic methods.[7] The loser is the afflicted public, for diagnostic methods that are not developed benefit no one.[8]

The judicial obligation is to provide stable, consistent application of statute and precedent, to implement the legislative purpose. With all respect to my colleagues on this panel, they misapply precedent and misinterpret the statute, adding discrepancies and disincentives to this important area of biomedicine. Claims 7–9 meet the Section 101 eligibility rules, for the claims are to a new and useful method.

Applying the statute correctly, diagnostic claims should be evaluated for novelty and unobviousness, specificity and enablement. A method that meets these statutory criteria is within the system of patents, whether the diagnosed event occurs in the human body or in an

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[7] This court has invalidated patents on new diagnostic methods in *Roche Molecular Sys., Inc. v. CEPHEID*, 905 F.3d 1363, 1374 (Fed. Cir. 2018); *Cleveland Clinic Found. v. True Health Diagnostics LLC*, 859 F.3d 1352, 1363 (Fed. Cir. 2017); *Genetic Techs. Ltd. v. Merial L.L.C.*, 818 F.3d 1369, 1380 (Fed. Cir. 2016); *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1378 (Fed. Cir. 2015); *In re BRCA1- & BRCA2-Based Hereditary Cancer Test Patent Litig.*, 774 F.3d 755, 765 (Fed. Cir. 2014).

[8] It is estimated that 66% of all medical treatment decisions are based on the results of *in vitro* diagnostic testing. Ulrich-Peter Rohr, et al., *The Value of In Vitro Diagnostic Testing in Medical Practice: A Status Report*, 11 PLoS One 1, 2, 11, 13 (2016), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4778800/pdf/pone.0149856.pdf. *See* Ten Law Professors Br. at 18.

extraneous device. From my colleagues' contrary conclusion, I respectfully dissent.