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"DOES IT SMELL LIKE *MAYO*?": THE FEDERAL CIRCUIT'S OVERSIMPLIFICATION OF THE *MAYO* FRAMEWORK IN METHOD OF TREATMENT/DIAGNOSIS CASES

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"Does it smell like *Mayo*?": The Federal Circuit's Oversimplification of the *Mayo* Framework in Method of Treatment/Diagnosis Cases

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I. Introduction

Under 35 U.S.C. § 101, only a "new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof" is patent eligible.[1] Long-recognized judicial exceptions to § 101 bar patenting laws of nature, natural phenomena, and abstract ideas.[2] Since the U.S. Supreme Court's decisions in *Mayo* and *Alice* developed the exceptions,[3] courts, commentators, and patent practitioners have been seeking clarification on the contours of patent eligibility under 35 U.S.C. § 101.

In 2019, the U.S. Congress was poised to hand those constituencies exactly that, with Senators Thom Tillis and Chris Coons introducing a draft bill that would largely abrogate the judicial exceptions to patent eligibility.[4] But subsequent hearings made clear that key stakeholders did not agree on the proposed changes, leading Senator Tillis to conclude that "absent stakeholder consensus I don't see a path forward for producing a bill—much less steering it to passage—in this Congress."[5]

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[1] 35 U.S.C. § 101 (2018).

[2] Alice Corp. v. CLS Bank Int'l, 573 U.S. 208, 216 (2014).

[3] *See id.*, Mayo Collaborative Servs. v. Prometheus Labs., Inc., 566 U.S. 66 (2012).

[4] *Sens. Tillis and Coons and Reps. Collins, Johnson, and Stivers Release Draft Bill Text to Reform Section 101 of the Patent Act,* THOM TILLIS: PRESS RELEASE (May 22, 2019), https://www.tillis.senate.gov/2019/5/sens-tillis-and-coons-and-reps-collins-johnson-and-stivers-release-draft-bill-text-to-reform-section-101-of-the-patent-act.

[5] *Exclusive Q&A with Sen. Thom Tillis*, INTELLECTUAL PROP. OWNERS ASS'N, https://ipo.org/index.php/exclusive-qa-with-sen-thom-tillis/ (last visited Mar. 5, 2020). Senator Tillis's comments followed extensive hearings in which stakeholders expressed diametrically conflicting concerns. For criticism of the proposed changes, *see, e.g.*, *The State of Patent Eligibility in America: Part I Before the Subcomm. on Intellectual Prop. of the S. Comm. on the Judiciary*, 116th Cong. (2019) (testimony by Charles Duan, Director, Technology and Innovation Policy, R Street Institute) ("The draft legislation is contrary to scientific norms, medical ethics, and human rights. Patents on scientific discoveries draw scientists away from contributing to the public store of knowledge. Patents on diagnostic test results force medical professionals to choose between infringing patents and giving their patients potentially lifesaving information. And patents on human genes distort notions of bodily integrity and rights of self-determination.").

Also in 2019, the U.S. Patent and Trademark Office (USTPO) significantly revised its examining procedures for patent eligibility by incorporating the U.S. Court of Appeals for the Federal Circuit's post-*Mayo* case law on § 101.[6] While the revisions potentially help patent applicants and examiners, the Federal Circuit has previously expressed resistance to the USPTO's interpretation of judicial exceptions to § 101,[7] making it unlikely that the guidance will affect litigated issues of patent eligibility.

Meanwhile, the Supreme Court has not shown interest in clarifying its patent eligibility case law: In January 2020, the Court declined to hear several cases on patent eligibility.[8] The move establishes the Federal Circuit as the best situated institutional player to address the inconsistencies of the Supreme Court's § 101 jurisprudence. Yet, the Federal Circuit's efforts to clarify the post-*Mayo* line of cases in the biotechnology field have been ineffective at best, and incompatible with Supreme Court precedent at worst. In the chaos, one clear line has emerged: method of treatment claims are patent eligible, while method of diagnosis claims are not.

In applying the *Mayo* framework to diagnostic technologies, the Federal Circuit has taken *Mayo* too literally. Rather than refining *Mayo*'s broad principles, the Federal Circuit's test is basically: "Does it smell like *Mayo*?"[9] This Comment argues that this approach is inconsistent with the *Mayo* Court's articulation of the law of nature exception to § 101. Diagnostic technologies should not be per se patent ineligible, even under *Mayo*'s broad framework. In applying *Mayo* to diagnostic technologies in particular, the Federal Circuit must find patent eligibility by interpreting claims as a whole where the patentee has discovered a novel way of measuring a biomarker.

Part I provides a brief overview of *Mayo* and the disparate approach the Federal Circuit has taken towards treatment and diagnostic inventions. Part II criticizes the approach for relying too much on—and misinterpreting—*Mayo*'s strange factual backdrop and ill-conceived dicta. This approach can also be attributed to another error: importing the search for improvements from Step 2 to Step 1 of the *Mayo* framework, much to the detriment of diagnostic methods. Part II also advances a better approach that the Federal Circuit could undertake: Specifically, it

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[6] 2019 Revised Patent Subject Matter Eligibility Guidance, 84 Fed. Reg. 50 (Jan. 7, 2019), https://www.govinfo.gov/content/pkg/FR-2019-01-07/pdf/2018-28282.pdf.

[7] For example, in *Cleveland Clinic II*, Judge Lourie wrote: "[W]e are not bound by [the USPTO's] guidance . . . especially regarding the issue of patent eligibility and the efforts of the courts to determine the distinction between claims directed to natural laws and those directed to patent-eligible applications of those laws, we are mindful of the need for consistent application of our case law." Cleveland Clinic Found. v. True Health Diagnostics LLC (*Cleveland Clinic II*), 760 F. App'x 1013, 1020 (Fed Cir. 2019).

[8] Susan Decker, *Supreme Court Declines to Consider Medical Diagnostic Patents*, BLOOMBERG TECH. (Jan. 13, 2020, 6:45 AM), https://www.bloomberg.com/news/articles/2020-01-13/supreme-court-declines-to-consider-medical-diagnostic-patents. *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 915 F.3d 743 (Fed. Cir. 2019) and *Vanda Pharm. Inc. v. West-Ward Pharm. Int'l Ltd.*, 887 F.3d 1117 (Fed. Cir. 2018), both discussed *infra* Part II.B., were included among the cases the Supreme Court declined to review.

[9] Laura Pedraza-Fariña et al., *13th Annual Northwestern Journal of Technology and Intellectual Property Symposium Panel Discussion: Medical Technology*, 16 NW. J. TECH. & INTELL. PROP. 1 (2018).

emphasizes the need to consider claims as a whole to ensure that diagnostic methods that include non-routine steps as claim limitations are patent eligible.

II. Part I: Background

A. The Familiar *Mayo* Framework

In *Mayo*, the Supreme Court developed a two-step framework for determining the patent eligibility of claims under 35 U.S.C. § 101 in light of previously established judicial exceptions: laws of nature, natural phenomena, and abstract ideas.[10] Step 1 asks if the claim at issue is "directed to" one of the judicial exceptions.[11] If it is, Step 2 looks to 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."[12]

The claim at issue in *Mayo* recited a method for optimizing dosage of thiopurine drugs by: (1) administering the drug to a patient, (2) determining the resulting metabolite level, and (3) a wherein step describing the metabolite threshold above or below which doctors would need to increase or decrease the drug dosage.[13] Critically, the claim did not require a doctor to increase or decrease dosage as a result of the test.[14] Before the patentee's invention of the method, scientists had generally understood the correlation between the metabolite and the drug's efficacy.[15]

The Supreme Court found that the administering, determining, and wherein steps—considered alone or as an ordered combination—added nothing of significance to the natural correlation.[16] In an attempt likely aimed at assuaging life sciences stakeholders, the Court added: "Unlike, say, a typical patent on a new drug or a new way of using an existing drug, the patent claims do not confine their reach to particular applications of those laws."[17] This purported reassurance has ironically caused more confusion than clarity for the Federal Circuit.

B. The Federal Circuit's Method of Treatment/Diagnosis Distinction

Post-*Mayo*, the Federal Circuit has tried to narrow the number of claims that would be classified as unpatentable as a result of the § 101 judicial exceptions.[18] This is especially true for method of treatment claims. As Judge Moore succinctly explained: "[C]laims that are directed to

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[10] Mayo Collaborative Servs. v. Prometheus Labs., Inc., 566 U.S. 66, 76 (2012). The test was later formalized in *Alice*. Alice Corp. v. CLS Bank Int'l, 573 U.S. 208, 217 (2014).
[11] *Alice Corp.*, 573 U.S. at 217. I refer to this step as "Step 1" throughout this Comment.
[12] *Id.* I refer to this step as "Step 2" throughout this Comment.
[13] *Mayo*, 566 U.S. at 76.
[14] *Id.* at 75–76.
[15] *Id.* at 73–74.
[16] *Id.* at 87.
[17] *Id.*
[18] *See infra* Part II.B.

particular methods of treatment are patent eligible."[19] Even method of treatment claims where the dose is determined by reference to underlying natural law—the relationship between disease and a patient's creatinine clearance rate in *Endo*[20] or a patient's genotype in *Vanda*[21]—have been deemed not directed to a natural law.

Vanda illustrates this approach. The claims at issue in *Vanda* recited a method of treatment for schizophrenia, requiring "(1) determining the patient's CYP2D6 metabolizer genotype by (a) obtaining a biological sample and (b) performing a genotyping assay; and (2) administering specific dose ranges of iloperidone depending on the patient's CYP2D6 genotype."[22] In finding these claims directed to "a novel method of treating disease" under Step 1 of the *Mayo* framework, Judge Lourie distinguished *Mayo* on the ground that the *Vanda* claims required a doctor to administer the drug after the dosing determination was made.[23] Moreover, the claims were confined to specific dosing ranges unlike the claims at issue in *Mayo*.[24]

In *Endo* the Federal Circuit took a similarly narrow approach to the Step 1 inquiry of the Mayo framework. The claims covered "(a) providing a pharmaceutical [oxymorphone] . . . (b) testing the patient for a [kidney] disease . . . and then (c) administering the pharmaceutical . . . based on the creatine clearance rate."[25] The claims were found not directed to the natural correlation between the disease and oxymorphone sensitivity, but rather "the application of a drug to treat a particular disease."[26] Unlike in *Mayo*, the administering step was performed after identifying the specific dosage.[27]

Unlike method of treatment claims, diagnostic claims have not fared well at the Federal Circuit post-*Mayo*. Recognizing *Mayo*'s broad sweep, in *Ariosa* the Federal Circuit found methods for detecting paternally inherited cffDNA in pregnant women patent-ineligible.[28] The Federal Circuit found the claims directed to a natural phenomenon, namely, the existence of cffDNA in maternal blood.[29] In concluding its analysis under *Mayo* Step 1, the Federal Circuit gestured

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[19] Nat. Alts. Int'l, Inc. v. Creative Compounds, LLC, 918 F.3d 1338, 1344 (Fed. Cir. 2019); *see also* Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC, 915 F.3d 743, 753 (Fed. Cir. 2019) (noting under its Step 1 analysis that "claiming a new treatment for an ailment, albeit using a natural law, is not claiming the natural law").
[20] Endo Pharm. Inc. v. Teva Pharm. USA, Inc., 919 F.3d 1347, 1348–49 (Fed. Cir. 2019).
[21] Vanda Pharm. Inc. v. West-Ward Pharm. Int'l Ltd., 887 F.3d 1117, 1134–36 (Fed. Cir. 2018).
[22] *Id.* at 1134.
[23] *Id.* at 1135.
[24] *Id.* This was insignificant for Judge Prost: "[R]eciting specific metes and bounds in the claims did not prevent the Supreme Court from concluding those claims set forth a natural law in *Mayo*." *Id.* at 1141 (Prost, J., dissenting).
[25] *Endo*, 919 F.3d at 1353.
[26] *Id.* at 1354.
[27] *Id.*
[28] Ariosa Diagnostics, Inc. v. Sequenom, Inc., 788 F.3d 1371, 1373–74 (Fed. Cir. 2015).
[29] *Id.* at 1376. Applying *Mayo* Step 2, the Federal Circuit held that the amplification of cffDNA and subsequent detection steps were well-understood, routine, and conventional. *Id.* at 1376–78. For instance, independent Claim 25 recited:

towards a new test for this part of the inquiry: whether the method begins and ends with a natural phenomenon.[30]

The Federal Circuit applied this new approach in *Cleveland Clinic I*, finding diagnostic claims that relied on the correlation between cardiovascular disease and the heightened presence or activity of the enzyme myeloperoxidase (MPO) patent-ineligible.[31] The claims recited characterizing the level of MPO in a patient presenting with chest pain and comparing it to a control population to determine disease risk.[32] Under *Mayo* Step 1, the Federal Circuit concluded that the claims were directed to a natural law because "just like in *Ariosa*, the method starts and ends with naturally occurring phenomena with no meaningful non-routine steps in between."[33] In *Cleveland Clinic II*, the Court reached the same conclusion on claims reciting a more specific detection step, namely, the use of anti-MPO antibodies.[34]

Athena, like *Cleveland Clinic II*, provides another illustrative example. In *Athena*, the Federal Circuit found a method of diagnosing neurological diseases by detecting MuSK antibodies patent-ineligible.[35] Claim 7, at issue on appeal, recited:

> 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 resulting complex], wherein the presence of said label is indicative of [neurological disease related to MuSK].[36]

The claims were found directed to the correlation between MuSK antibodies in bodily fluid and MuSK-related disease because the specification "highlight[ed] the discovery of the natural law," and described the immunoprecipitation and radiolabeling steps as "standard techniques in the art."[37] Thus, under Step 1 of the *Mayo* framework, the "patent describe[d] the claimed invention

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> A method for performing a prenatal diagnosis on a maternal blood sample, which method comprises obtaining a non-cellular fraction of the blood sample amplifying a paternally inherited nucleic acid from the non-cellular fraction and performing nucleic acid analysis on the amplified nucleic acid to detect paternally inherited fetal nucleic acid.

Id. at 1374.

At Step 2, the panel concluded that because the amplification and preparation steps were routine steps specified at a high level of generality, the steps "amount[ed] to a general instruction to doctors to apply routine, conventional techniques when seeking to detect cffDNA." *Id.* at 1376–77.

[30] *See id.* at 1376.

[31] Cleveland Clinic Found. v. True Health Diagnostics LLC (*Cleveland Clinic I*), 859 F.3d 1352, 1361 (Fed. Cir. 2017).

[32] *Id.* at 1356–57.

[33] *Id.* at 1361. The Court then held that the claims were not sufficiently transformative under Step 2. *Id.* at 1362.

[34] Cleveland Clinic Found. v. True Health Diagnostics LLC (*Cleveland Clinic II*), 760 F. App'x 1013, 1018–19 (Fed. Cir. 2019).

[35] Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC, 915 F.3d 743, 746 (Fed. Cir. 2019).

[36] *Id.* at 747.

[37] *Id.* at 750–51.

principally as a discovery of a natural law."[38] The Federal Circuit declined to hear the case *en banc* in July 2019.[39]

Praxair involved the patenting of a discovery very similar to the one at issue in *Athena*. Though inhaled nitric oxide (iNO) had been used to treat neonatal hypoxic respiratory failure since the 1990s, a 2004 study demonstrated that infants with a particular congenital heart defect—left ventricular dysfunction (LVD)—were at increased risk for developing pulmonary edema if treated with iNO.[40] Claim 1 of the patent at issue covered a method of treating patients who were candidates for iNO treatment that reduces the risk of pulmonary edema development, comprising:

> (a) identifying . . . candidates for 20 ppm [iNO] treatment;
> (b) determining that a first patient of the plurality does not have [LVD];
> (c) determining that a second patient of the plurality has [LVD], so is at particular risk of . . . [developing] pulmonary edema upon treatment with [iNO];
> (d) administering 20 ppm [iNO] treatment to the first patient; and
> (e) excluding the second patient from treatment with [iNO], based on the determination that the second patient has [LVD], so is at particular risk of . . . [developing] pulmonary edema upon treatment with [iNO].[41]

Highlighting just how fine the distinction between diagnostic and treatment claims may be, the *Praxair* Court—over judge Newman's dissent[42]—found the claim ineligible under § 101.[43] The majority found the claim directed to a natural phenomenon under Step 1 of the *Mayo* framework because the exclusion step amounted to nothing more than "an instruction not to act."[44] The majority reasoned that unlike *Vanda*, the claims did not recite an improved treatment for the subset of patients that did not respond to standard methods of treatment, and thus were not patent-eligible.

This brief review of select decisions is not an exhaustive overview of life sciences case law at the Federal Circuit post-*Mayo*. But the sample highlights the disparate approaches of Federal Circuit panels towards the patent eligibility of method of treatment and method of diagnosis claims.

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[38] *Id.*
[39] Athena Diagnostics, Inc. v. Mayo Collaborative Servs., 927 F.3d 1333 (Fed. Cir. 2019). The Federal Circuit denied *en banc* review 7-5, with the judges writing eight opinions featuring multiple pleas to Congress and the Supreme Court to clarify the boundaries of § 101. *Id.*
[40] INO Therapeutics LLC v. Praxair Distribution Inc., 782 F. App'x 1001, 1002–03 (Fed. Cir. 2019).
[41] *Id.* at 1003.
[42] Judge Newman criticized the majority for failing to follow the clear line of Federal Circuit authority finding method of treatment claims patent eligible. Judge Newman persuasively characterized the claims as "recit[ing] a multi-step method of *administering* [iNO] so that patients with [LVD] are at reduced risk of adverse events." *Id.* at 1016 (Newman, J., dissenting) (emphasis added).
[43] *Id.* at 1006–07.
[44] *Id.*

III. Part II: The Federal Circuit's Approach is Inconsistent with Supreme Court Precedent

A. The Federal Circuit's Step 1 Approach Misunderstands *Mayo*

Determining when a claim is directed to a judicial exception remains the most difficult part of the *Mayo* framework. To make that determination, the Federal Circuit has relied in part on the peculiar facts of *Mayo*. In *Vanda* for example, the *Mayo* Step 1 analysis focused on the differences between the *Vanda* and *Mayo* claims.[45] Reflecting the Federal Circuit's general approach to *Mayo*, Judge Lourie characterized the *Mayo* claims as directed to a "diagnostic method," rather than a "novel method of treating disease" like the *Vanda* claims.[46] But this conclusion is an oversimplification of the *Mayo* claims—claims that were not exactly a paragon of clarity.

Unlike method of treatment claims, the *Mayo* claims did not require a doctor to actually treat a patient by increasing or decreasing the drug's dose.[47] But unlike method of diagnosis claims, the end result of the claim is not the detection of a disease or condition, but rather the optimal drug dosage for treatment purposes.[48] Of course, one could just as easily characterize this claim as diagnosing the need to increase or decrease the drug's dosage, but therein lies the problem: There is no principled way to settle on the appropriate level of abstraction. Thus, relying on the facts of *Mayo* to determine whether a claim is directed to a natural phenomenon under *Mayo* Step 1 is equally unprincipled.

To be fair, the *Mayo* Court's reassurance about the patent eligibility of new ways of using existing drugs provides some support to Judge Lourie's position. But this statement does not support the conclusion that all method of treatment claims are exempt from *Mayo* Step 2, as its broader context indicates:

> We need not, and do not, now decide whether were the steps at issue here less conventional, these features of the claims would prove sufficient to invalidate them. For here, as we have said, the steps add nothing of significance to the natural laws themselves. *Unlike, say, a typical patent on a new drug or a new way of using an existing drug, the patent claims do not confine their reach to particular applications of those laws*.[49]

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[45] Vanda Pharm. Inc. v. West-Ward Pharm. Int'l Ltd., 887 F.3d 1117, 1134–36 (Fed. Cir. 2018).
[46] *Id.* at 1135.
[47] Mayo Collaborative Servs. v. Prometheus Labs, Inc., 566 U.S. 66, 74–75 (2012) ("[W]herein the level of [6-TG] less than about 230 pmol per $8x10^8$ red blood cells indicates a need to *increase* the amount of said drug subsequently administered . . . and wherein the level of [6-TG] greater than about 400 pmol per $8x10^8$ red blood cells indicates a need to *decrease* the amount of said drug subsequently administered . . . .") (emphasis added).
[48] Indeed, the preamble for the '623 patent recited "[a] method of optimizing therapeutic efficacy *for treatment* of an immune-mediated gastrointestinal disorder." *Id.* at 74 (emphasis added).
[49] *Mayo*, 566 U.S. at 86–87 (emphasis added). For examples of how this turn of phrase has served inconsistent ends, compare *Vanda*, 887 F.3d at 1135 ("Thus, the '610 patent claims are 'a new way of using an existing drug' that is safer for patients because it reduces the risk of QTc prolongation.") with *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*,

At most, the emphasized language indicates that a new way of using an existing drug typically contains an inventive concept sufficient to overcome *Mayo* Step 2. Read with the preceding sentence, it implies that these inventions are still a confined application of a natural law. In other words, those types of patent claims are directed to a natural law under *Mayo* Step 1, but with sufficient additional steps to survive *Mayo* Step 2. Following this logic, the method of treatment claim in *Vanda*—a new way of using an existing drug[50]—would similarly be directed to a natural law or phenomenon under *Mayo* Step 1, contrary to Judge Lourie's ultimate conclusion.

But reading patents for a new drug or a new way of using an existing drug with this level of abstraction for Step 1 is in tension with the Supreme Court's warning that broadly interpreting the judicial exceptions would "eviscerate patent law."[51] The *Mayo* dicta then seems nothing more than an attempt to emphasize this. This language does not support the conclusion that method of treatment claims are broadly not directed to a judicial exception.

B. The Federal Circuit's Step 1 Approach Blurs the Line Between Step 1 and Step 2

The other error in the Federal Circuit's life sciences case law is the premature search for improvements in *Mayo* Step 1.[52] As indicated in *Alice*, whether a claim recites improvements on existing technology is certainly part of the § 101 inquiry.[53] But *Alice* discussed improvements to computer functioning under Step 2, not Step 1.[54]

The Federal Circuit blurred the lines on this point in *CellzDirect*, where a panel upheld the eligibility of a method of preserving hepatocytes, a type of liver cell frequently used in research.[55] Although based on the underlying discovery of the hepatocytes' natural ability to withstand multiple freeze-thaw cycles, the Federal Circuit found the method claim was directed to "new and useful laboratory technique for preserving hepatocytes."[56] This standard is easy to manipulate. Indeed, the Federal Circuit found the *Ariosa* claims were directed to a patent-ineligible concept despite the fact that the detection method could fairly be characterized as a new and useful laboratory technique for detecting chromosomal abnormalities.[57]

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809 F.3d 1282, 1293 (Fed. Cir. 2015) (Newman, J., dissenting from the denial of *en banc* review)) ("In *Mayo*, both the medicinal product and its metabolites were previously known, leaving sparse room for innovative advance in using this information as a diagnostic dosage tool. Nonetheless, the Court recognized the principle that patent eligibility is not disabled when science is put to practical use, stating that 'a new way of using an existing drug' is patent-eligible under Section 101.").

[50] *See Vanda*, 887 F.3d at 1121 (noting that the FDA approved iloperidone for schizophrenia treatment in 2009).

[51] *Mayo*, 566 U.S. at 71.

[52] *See* Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC, 915 F.3d 743, 750 (Fed. Cir. 2019) (citing other Federal Circuit life science cases, including *Cleveland Clinic, Cellzdirect*, and *Ariosa*).

[53] Alice Corp. v. CLS Bank Int'l, 573 U.S. 208, 226 (2014). The text of §101 itself clearly provides some support for this approach since it mentions "new and useful improvement[s]." *See* 35 U.S.C. § 101 (2018).

[54] *Alice*, 573 U.S. at 226.

[55] *See* Rapid Litig. Mgmt. v. CellzDirect, Inc., 827 F.3d 1042, 1045 (Fed. Cir. 2016).

[56] *Id.* at 1048.

[57] *See* Ariosa Diagnostics, Inc. v. Sequenom, Inc., 788 F.3d 1371, 1381 (Fed. Cir. 2015) (Linn, J., concurring).

The search for improvements in Step 1 of the *Mayo* framework is also problematic because the directed-to inquiry is not tethered to the prior art like the conventional-steps inquiry of Step 2. Under Step 2, evaluating whether additional steps are sufficiently inventive requires knowledge of the prior art.[58] Indeed, the *CellzDirect* panel found that the claims passed Step 2 because the prior art taught away from two freeze cycles.[59] By contrast, nothing in *Mayo* suggests that the prior art has any bearing on whether a claim is directed to a natural law under Step 1.

Take *Athena,* for example. The inventors discovered that twenty percent of patients with Myasthenia Gravis (MG) produced MuSK antibodies instead of acetylcholine receptor antibodies.[60] The patentee claimed a method for diagnosing MG using radiolabeled MuSK fragments and epitopes for detection of MuSK antibodies indicative of MG.[61] Following the logic of *CellzDirect*, the claims are arguably directed to an improved laboratory technique for diagnosing MG using radiolabeled MuSK because the end result is a more effective way to diagnose the disease in the twenty percent of patients who produce MuSK.[62]

The majority dismissed this argument, flatly noting that the only innovation claimed was the natural law discovery, to which the patentee appended standard immunoprecipitation and radiolabeling steps.[63] The use of MuSK antigens or fragments was itself a "first of any type for detecting MuSK autoantibodies, or for diagnosing MG through such detection."[64] That numerous aspects of the patentee's claimed invention were improvements over the prior art did not matter for the majority's Step 1 analysis. As evident in *Athena*, the *CellzDirect* approach hardly seems to provide a consistent limiting principle.

C. How the Federal Circuit Should Refine *Mayo*

While *Mayo* is not a model of clarity, patent practitioners and district courts would be best served by the Federal Circuit's consistent applications of *Mayo*'s framework. This can be achieved by emphasizing the need to evaluate claims as a whole.

In *Diehr*, the Supreme Court made clear that "[i]t is inappropriate to dissect the claims into old and new elements and then to ignore the presence of the old elements in the analysis."[65] There is certainly some tension between *Diehr* and *Mayo*. The search for an inventive concept in Step 2 of the *Mayo* framework seems incompatible with the *Diehr* Court's reminder that "[t]he

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[58] *See* Berkheimer v. HP Inc., 881 F.3d 1360, 1368–70 (Fed. Cir. 2018).
[59] *CellzDirect*, 827 F.3d at 1051 ("Repeating a step that the art taught should be performed only once can hardly be considered routine or conventional.").
[60] Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC, 915 F.3d 743, 747 (Fed. Cir. 2019).
[61] *Id.* at 747–48.
[62] Indeed, the *Athena* patent's specification noted that "the identification of this new subclass or subtype of MG patients will allow for *more accurate and speedy diagnosis* of individuals by medical practitioners." U.S. Patent No. 7,267,820 (issued Sept. 11, 2007) (emphasis added).
[63] *Athena*, 915 F.3d at 751–52.
[64] Brief for Plaintiffs-Appellants at 18, *Athena*, 915 F.3d 743 (No. 17-2508).
[65] Diamond v. Diehr, 450 U.S. 175, 188 (1981).

'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."[66] But the requirement that claims are to be read as a whole survived *Mayo*. The Court in *Mayo* considered the administering, determining, and wherein steps "as an ordered combination," and found these steps insufficiently inventive because doctors had been performing all of these steps together long before the patentee's discovery.[67]

Despite the Supreme Court's exhortations to avoid disassembling claims, Judge Lourie did exactly that in *Athena*, finding that the claim recited nothing more than a law of nature with immunoprecipitation and radiolabeling steps that were standard techniques in the art.[68] In contrast, Judge Newman's dissent followed *Diehr* and explained that when considering the claim limitations as a whole in the Step 1 analysis, the patentee's claims were directed to "a man-made chemical-biomedical procedure"[69]—an analytical assay.

Praxair provides an illustrative example of failing to consider claims as a whole with respect to Step 1. The majority singled out the exclusion step as the basis for patent ineligibility: "Properly understood, [the exclusion] step is simply an instruction not to act. In effect, the claim is directed to detecting the presence of LVD in a patient and then doing nothing but leaving the natural processes taking place in the body alone for the group of LVD patients."[70] This reasoning ignores the fact that even with the exclusion step, doctors would still administer iNO to those patients without LVD. The majority effectively rewrote the patentee's claim, entirely omitting the treatment of non-LVD patients. To put it another way, the majority took a claim that says "treat every candidate with iNO, except those that have LVD," and revised it to "don't treat candidates with iNO if they have LVD," engaging in the claim disassembling that the Supreme Court cautioned against in *Mayo*.[71]

While Judge Newman's approach offers merit, applying the principle that claims are to be interpreted as a whole makes more sense in Step 2 of the *Mayo* framework because the inventiveness of the additional steps can more reliably be ascertained by comparison to the prior art. Even assuming the *Athena* claims were directed to the natural law, the additional elements

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[66] *Id.* at 188–89.

[67] Mayo Collaborative Servs. v. Prometheus Labs., Inc., 566 U.S. 66, 77–79 (2012). Moreover, consistency with the other requirements of patentability such as §§ 102, 103 also requires reading patent claims "as a whole." *See* Brief of Amici Curiae Ten Law Professors at 23, Athena, 915 F.3d 743 (No. 17-2508) (arguing that canons of statutory construction require adopting a "claim as a whole" requirement for § 101 because § 102 requires "one-to-one symmetry between a claim *as a whole* and a single pre-existing example of the invention in the prior art" and § 103 expressly notes that "the differences between the claimed invention and the prior art are such that the claimed invention *as a whole* would have been obvious before the effective filing date.").

[68] *Athena*, 915 F.3d at 752.

[69] *Id.* at 762 (Newman, J., dissenting).

[70] INO Therapeutics LLC v. Praxair Distribution Inc., 782 F. App'x 1001, 1006 (Fed. Cir. 2019).

[71] The Court, summarizing it's subject-matter eligibility jurisprudence, recognized "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.

under Step 2 would have been found sufficiently inventive if interpreted as a whole. While immunoprecipitation and iodination may have been standard lab techniques,[72] this level of generality fails to take the precise limitations of the *Athena* claims into account. Instead, those steps were part of the application of a novel man-made substance: the use of labeled MuSK and MuSK epitopes for detecting MuSK antibodies indicative of MG. As *Athena* emphasized in its *en banc* petition, in contrast to *Mayo* where doctors routinely performed the additional steps claimed, "no one had ever attempted to detect MuSK [auto]antibodies for *any* reason."[73] As such, the labelling, complexing, precipitating, and monitoring steps can hardly be categorized as "well-understood, routine and conventional"[74] when the claim is interpreted as a whole. Where, as in *Athena*, a diagnostic claim recites non-routine steps as concrete limitations in addition to a law of nature, the claim should be patent-eligible even under *Mayo*'s broad test.

IV. Conclusion

With both Congress and the Supreme Court unlikely to address § 101 anytime soon, the Federal Circuit is best positioned to provide much-needed clarity to the subject-matter eligibility landscape. If the Federal Circuit is concerned that diagnostic patents add little value beyond the natural discovery or hamper follow-on innovation, broad interpretations of the *Mayo*/*Alice* framework are not the appropriate tool for addressing these concerns. The Federal Circuit need not wait for Congress or the Supreme Court to act: Refining *Mayo* by emphasizing the need to interpret claims as a whole is one possible way forward.

[72] *Athena*, 915 F.3d at 748.
[73] Warren Woessner, *Athena's Petition for Rehearing En Banc – Not All Diagnostic Claims are Equal Under s. 101*, NAT'L L. REV. (Apr. 15, 2019) (emphasis added) (quoting Athena's *en banc* petition), https://www.natlawreview.com/article/athena-s-petition-rehearing-en-banc-not-all-diagnostic-claims-are-equal-under-s-101.
[74] Berkheimer v. HP Inc., 881 F.3d 1360, 1368 (Fed. Cir. 2018).