2017-2508

United States Court of Appeals for the Federal Circuit

ATHENA DIAGNOSTICS, INC., OXFORD UNIVERSITY INNOVATION LTD., MAX PLANCK GESELLSCHAFT ZUR FÖRDERUNG DER WISSENSCHAFTEN e.V.,

Plaintiffs-Appellants,

– v. –

MAYO COLLABORATIVE SERVICES, LLC, d/b/a Mayo Medical Laboratories, MAYO CLINIC,

Defendants-Appellees.

On Appeal from the United States District Court for the District of Massachusetts in Case No. 1:14-cv-40075-IT (Honorable Indira Talwani, Judge)

BRIEF OF THE BIOTECHNOLOGY INNOVATION ORGANIZATION (BIO), PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA (PHRMA), CROPLIFE INTERNATIONAL (CLI), AND WISCONSIN ALUMNI RESEARCH FOUNDATION (WARF) AS *AMICI CURIAE* IN SUPPORT OF APPELLANTS' PETITION FOR REHEARING *EN BANC*

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APRIL 22, 2019

CERTIFICATE OF INTEREST

Counsel for *Amici Curiae* certifies the following:

1. The full name of every party or *amicus curiae* represented is:

   Biotechnology Innovation Organization (BIO); Pharmaceutical Research and Manufacturers of America (PhRMA), CropLife International (CLI), and Wisconsin Alumni Research Foundation (WARF).

2. The name of the real parties in interest represented by us is:

   None.

3. All parent corporations and any publicly held companies that own 10 percent of the stock of the party or *amicus curiae* represented by us are:

   None.

4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court (and who have not or will not enter an appearance in this case) are:

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   Hans Sauer
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   Brian P. Barrett
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5. The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal. *See* Fed. Cir. R. 47. 4(a)(5) and 47.5(b):

None.

Dated: April 22, 2019

/s/ *Melissa A. Brand*

Melissa A. Brand

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STATEMENT OF INTEREST OF AMICI CURIAE

The Biotechnology Innovation Organization (BIO) is the principal trade association representing the biotechnology industry domestically and abroad. BIO has more than 1,000 members, which span the for-profit and non-profit sectors and range from small start-up companies and biotechnology centers to research universities and Fortune 500 companies. Approximately 90% of BIO's corporate members have annual revenues of under $25 million.

CropLife International (CLI) is a global federation representing the plant science industry as well as a network of regional and national associations in ninety-one countries. CLI's member companies are committed to sustainable agriculture through innovative research and development in the areas of crop protection, pest control, and seed and plant technologies that increase crop yields and enhance human and animal nutrition and food security, and decrease reliance on pesticides, herbicides, irrigation, and nutrients, thus benefitting the environment, farmers, and the public.

The Pharmaceutical Research and Manufacturers of America (PhRMA) represents the country's leading innovative biopharmaceutical research companies, which are devoted to discovering and developing medicines that enable patients to live longer, healthier, and more productive lives. Since 2000, PhRMA member

companies have invested more than $600 billion in the search for new treatments and cures, including an estimated $71.4 billion in 2017 alone.

The Wisconsin Alumni Research Foundation (WARF) is one of the oldest university patenting and licensing operations in the world. Incorporated as a nonprofit foundation in 1925, WARF has a founding purpose "to promote, encourage, and aid scientific investigation and research at and within the University of Wisconsin-Madison." In pursuit of that mission WARF has built an investment portfolio valued at $2.8 billion as of 2018, which over ninety-three years has funded more than $2.6 billion in research grants to UW-Madison when adjusted for inflation. WARF also serves as the designated technology transfer office for UW-Madison, and in that capacity has acquired more than 3,000 patents, including 1,900 active patents and an additional 400 invention disclosures and 55 revenue-generating licenses each year.

Amici's members are concerned that more than seven years after the Supreme Court decided *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66 (2012), there continues to be 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. As inventors, developers, and investors in such technologies, *amici's* members have a strong interest in clear and predictable rules of patent-eligibility.

Amici submit this brief in the hope that it will assist the court in the orderly development of law in this important area. *Amici* have no direct stake in the result of this appeal and take no position on the ultimate validity of the patent at issue. No counsel for a party authored this brief in whole or in part, and no such counsel or party, nor any person other than *amici* or their counsel, made a monetary contribution intended to fund the preparation or submission of this brief. This brief reflects the consensus view of *amici's* members, but not necessarily the view of any individual member.

Pursuant to F.R.A.P. 29 and Fed. Cir. R. 35, *amici* submit this brief along with an accompanying motion for leave to file.

ARGUMENT

The application of *Mayo* to biotechnology patent cases has caused great uncertainty to the industry, and divergence in this court's post-*Mayo* jurisprudence has called into doubt innumerable biotech patents. While cohesive guidance is developing regarding patent-eligibility for certain technological sectors, no such trends are emerging for diagnostic technology. Inconsistent guidance in this critical area of the law leaves the industry questioning whether any diagnostic method will

survive an eligibility challenge and whether other biotechnological methods involving naturally-occurring substances are similarly at risk. *Amici* respectfully submit that this case presents an opportunity for the full court to intervene and provide necessary direction to the industry.

A. This Case is a Proper Vehicle for the Court to Clarify *Mayo*.

This case presents an opportunity for the court to elucidate the contours of *Mayo*, particularly as applied to diagnostic technologies. The Supreme Court never said that diagnostic claims are per se patent-ineligible. Yet since *Mayo*, this court has repeatedly held diagnostic claims ineligible. *See, e.g.*, *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015); *Cleveland Clinic Foundation v. True Health Diagnostics LLC*, 859 F.3d 1352 (Fed. Cir. 2017); *Roche Molecule Sys., Inc. v. CEPHEID*, 905 F.3d 1363 (Fed. Cir. 2018). While many of the principles annunciated in *Mayo* form the basis for modern patent-eligibility determinations (hence the "*Mayo/Alice* test"), *amici* respectfully submit that this court can and should provide clear guidance as to how to apply the Court's eligibility framework in *Mayo* to diagnostic claims. It is unclear how to read these decisions while considering the patent claims at issue and determine with any reasonable predictability whether an important diagnostic patent will meet or fail current patent-eligibility standards.

The proper application of the Court's *Mayo* framework would find Athena's claims patent-eligible. The inventors created new reagents, which they use to detect a naturally occurring antibody to diagnose a subset of patients that had never been identified before. Prior to Athena's inventions, no one had used these man-made molecules to diagnose this particular subset of patients.[1] The *Mayo* Court cited *Diamond v. Diehr*, 450 U.S. 175, 187 (1981) for the proposition that "a process is not unpatentable simply because it contains a law of nature or a mathematical algorithm." 566 U.S. at 71 (citations and quotations omitted). It further explained that "an application of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection." *Id.* (citing *Diehr*, 450 U.S. at 187). Athena's method may contain a naturally occurring element, but it goes well beyond merely claiming a law of nature and as such, should be found patent-eligible under the *Mayo* framework.

There are meaningful differences between the claims at issue and those in *Mayo* that went unacknowledged in the panel opinion. For example, Athena's claims require the use of a MuSK protein (or epitope or antigenic determinant thereof) having a label thereon to form an antigen-antibody complex to diagnose MG. Prior

[1] Prior to Athena's inventions, about 20% of individuals with Myasthenia Gravis (MG) could not be diagnosed using prior technology because prior tests looked for a different type of antibody. *Athena Diagnostics, Inc. v. Mayo Collab. Servs.*, 915 F.3d 743, 746 (Fed. Cir. 2019).

art MG diagnostic techniques did not use these complexes but instead sought to identify an entirely different type of antibody produced by only about 80% of MG patients. Accordingly, Athena's claims recite new and improved methods for diagnosing MG, they permit an entire patient population to be diagnosed using a particular assay where this was not previously possible, and they claim the use of new, particularized man-made molecules to accomplish these feats.

The claims in *Mayo* had none of these features: they did not involve any new diagnostic technology nor the creation and use of any new molecules. The thiopurine drug metabolites tested for in the *Mayo* claims were already known and understood to be associated with the likelihood that a particular dosage could cause harm or be ineffective. *Mayo*, 566 U.S. at 73-74. The *Mayo* claims did not specify any new laboratory test to be performed, but rather the patent stated that "methods for determining metabolite levels were well known in the art" and scientists "routinely measured" such metabolites in investigating "the relationships between metabolite levels and efficacy and toxicity of thiopurine compounds." *Id.* at 79.

Thus, while the Court found the *Mayo* claim limitations to reflect "well-understood, routine, conventional activity, previously engaged in by those in the field," *id.* at 82, this is not the case with Athena's claims. Like many life sciences patents, Athena's claims are built upon what the court considered to be a natural law, i.e., naturally-occurring MuSK antibodies and MuSK related disorders. The

additional limitations, however, reflect novel additional features "that provide practical assurance that the process is more than a drafting effort designed to monopolize the law of nature itself." *See id.* at 77. The Court has signaled that claims with less conventional features and those that confine their reach to applications of natural laws may be patent-eligible. For this reason, the Court in *Mayo* indicated that "a typical patent on a new drug or a new way of using an existing drug" is likely patent-eligible. *Id.* at 87. Moreover, in *Myriad* the Court stressed that its decision did not implicate "patents on new applications of knowledge about the BRCA1 and BRCA2 genes." *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 596 (2013). To the contrary, the Court assumed that effective patent protection would remain available for new and useful inventions applying such knowledge, including for the development of diagnostic tests.[2]

Outside the diagnostics space, this court has applied the Supreme Court's direction and at the same time distinguished the facts of *Mayo* to uphold method of treatment claims. In these cases, claim limitations requiring specific, new treatment steps supported findings of patent-eligibility even where the claims were considered to embody laws of nature. *See Vanda Pharm. Inc. v. West-Ward Pharm. Int'l Ltd.*,

[2] *Myriad* quotes approvingly from the panel decision where Judge Bryson had "aptly noted that, '[a]s the first party with knowledge of the [BRCA1 and BRCA2] sequences, Myriad was in an excellent position to claim applications of that knowledge." *Id.* (citations omitted).

887 F.3d 1117, 1135 (Fed. Cir. 2018); *Endo Pharm. Inc. v. Teva Pharm. USA, Inc.*, 2019 WL 1387988, at *5 (Fed. Cir. 2019)*; Natural Alts. Int'l Inc .v Creative Compounds, LLC*, 918 F.3d 1338, 1344 (Fed. Cir. 2019). For example, the *Vanda* court explained that while the claims reflect the inventors' recognition of the natural relationship between the drug, genetic variation, and side effects, the inventors "claimed an application of that relationship." 887 F.3d at 1135. To support that conclusion, the court pointed to the claims' requirement that "a treating doctor administer [the drug in particular doses] depending on the result of a genotyping assay." *Id*.

The Athena patent claims are more analogous to those upheld in the *Vanda* trilogy than those held ineligible in *Mayo*. Like *Vanda*, the Athena claims require performance of an entirely new method involving concrete chemical and biological steps. In contrast, the *Mayo* Court identified the only contribution of the claimed method to be the precise correlation between metabolite levels and potential harm or efficacy. *Mayo*, 566 U.S. at 74.

Accordingly, this case is an excellent vehicle for the court to address looming questions about the application of *Mayo* to diagnostic technology. As explained by Judge Newman in dissent, the panel decision "departs from the cautious restraints in the Supreme Court's *Mayo/Alice* application of laws of nature and abstract ideas" and reflects that "[t]his court's decisions on the patent-ineligibility of diagnostic

methods are not consistent." *Athena*, 915 F.3d at 757. Direction concerning the types of diagnostics claims that will reliably and predictably survive post-*Mayo* is critically needed by practitioners, the public, and the USPTO. Biotechnology is often identified as one of the technological areas most dependent upon effective and predictable patent protection, in the absence of which investors may choose to invest in other, arguably less socially beneficial technologies. *See In re Bilski*, 545 F.3d 943, 1014 (Fed. Cir. 2008) (J. Rader, dissenting).

B. This Court's Section 101 Jurisprudence is Not Being Applied Equally to Biotech Patents.

The panel decision reflects a troubling divergence in this court's section 101 jurisprudence between software and biotech inventions. In software cases, the step 1 analysis often focuses on whether the claim offers a technical improvement over prior art solutions or improves the operation of previously-used methods. Yet the *Athena* panel and courts in biotechnology cases more generally appear to simplify the step 1 analysis by analogizing subject claims to those in *Mayo* and *Myriad*, without considering the technological contribution of each claim.

For example, in *McRo, Inc. v. Bandai Namco Games America Inc.*, this court held the claims at issue patent-eligible because they were directed to "a specific asserted improvement" in computer animation. 837 F.3d 1299, 1314 (Fed. Cir. 2016). The court emphasized that there was no evidence that the claims simply automate a process previously used by those in this technological area. *Id*. In *Enfish,*

LLC v. Microsoft Corp., the claims were held patent-eligible because they were "directed to an improvement in the function of a computer." 822 F.3d 1327, 1337-38 (Fed. Cir. 2016). This specific improvement to a particular technology-type analysis has assisted this court in holding other software claims patent-eligible. *See, e.g.*, *DDR Holdings, LLC v. Hotels.com, L.P.*, 773 F.3d 1245 (Fed. Cir. 2014) (holding claims directed to a solution that overcomes a problem arising in computer networks patent-eligible); *Trading Techs. Int'l, Inc. v. CGW, Inc.*, 675 F. App'x 1001 (Fed. Cir. Jan. 18, 2017) (recognizing that "specific technologic modifications to solve a problem or improve the functioning of a known system generally produce patent-eligible subject matter").

In life sciences cases, courts are not taking the same approach. Such decisions often fail to analyze how a claim provides a technological improvement to the way a diagnostic or laboratory technique was performed prior to the claimed invention. The *Athena* panel failed to assess whether the asserted claims recited a technological improvement over prior methods of diagnosing MG. Before the inventions of the patent-in-suit, no one had used the man-made molecule (^{125}I-MuSK) to form a radiolabeled antibody-antigen complex, nor had they used such a complex to diagnose the 20% of the patient population that could not be identified using prior art diagnostic techniques. It is indisputable that these methods improved the way these patients could be diagnosed, yet this fact was given no weight. There is by now

a widespread concern in the industry that a new diagnostic method might only be patentable if one also invents a new laboratory reagent or analytical apparatus. Yet, if software inventors can patent new processes that use conventional computers, why is it effectively impossible to patent diagnostic inventions that use conventional laboratory processes?

Guidance from this court to clarify that patent eligibility considerations in the software area may translate into the biotech area would be helpful.

C. Without Intervention by the En Banc Court, Significant Doubt Will Be Cast Over the Eligibility of Biotech Claims Incorporating Naturally Occurring Substances.

If the panel decision is left to stand, it will be unclear how to draft a claim to a diagnostic method that will predictably withstand a patent-eligibility challenge. In addition, *amici* ask this court to consider the implications of the panel decision on the patentability of method claims utilizing naturally occurring substances other than in the diagnostic method and method of treatment spaces. Inventive preparations based on naturally-occurring substances and methods of using such preparations are of great importance in biotechnology. Examples include the use of crop protection products, plant breeding, fermentation methods, and processes involving industrial enzymes. Without serious consideration and intervention by the entire court, investment in the U.S. diagnostic industry may disappear, and the harm could spread to other biotech sectors.

CONCLUSION

For these reasons, *amici* respectfully request that the court grant rehearing *en banc* to address these issues.

Respectfully submitted,

April 22, 2019

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APPENDIX A – FULL LIST OF REPRESENTATIVES FOR *AMICI CURIAE*

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United States Court of Appeals
for the Federal Circuit

Athena Diagnostics, Inc. v. Mayo Collaborative Services, 2017-2508

CERTIFICATE OF SERVICE

I, Robyn Cocho, being duly sworn according to law and being over the age of 18, upon my oath depose and say that:

Counsel Press was retained by BIOTECHNOLOGY INNOVATION ORGANIZATION, Attorneys for Amici Curiae to print this document. I am an employee of Counsel Press.

On **April 22, 2019,** counsel has authorized me to electronically file the foregoing **Brief of The Biotechnology Innovation Organization (BIO), Pharmaceutical Research and Manufacturers of America (PhRMA), Croplife International (CLI), and Wisconsin Alumni Research Foundation (WARF) as Amici Curiae in Support of Appellants' Petition for Rehearing *En Banc*** with the Clerk of Court using the CM/ECF System, which will serve via e-mail notice of such filing to all counsel registered as CM/ECF users, including any of the following:

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Any counsel appearing at the time of filing will also be served via CM/ECF email notice.

In addition, the required copies have been sent to the court today via Federal Express.

April 22, 2019

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CERTIFICATE OF COMPLIANCE WITH TYPE-VOLUME LIMITATION, TYPEFACE REQUIREMENTS AND TYPE STYLE REQUIREMENTS

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Respectfully submitted,

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