

Summary of Subject Matter Eligibility: Biotech/Pharma Inventions

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It has nearly been ten years since the Supreme Court's landmark *Mayo v. Prometheus* (132 S.Ct. 1289 (2012)) decision, in which the Court established a two-prong test for determining patentable subject matter under 35 U.S.C. § 101. And, yet, the law regarding patent eligibility for biotech/pharma inventions remains unsettled. In part, this is due to the paucity of appellate court decisions confirming the eligibility of claims under 35 U.S.C. §101. As highlighted in the court's opinion in denying *en banc* rehearing of *Athena v. Mayo*¹, intervention from either the Supreme Court or Congress will likely be required to provide clarity on the matter. However, based on the Court's reluctance in taking up such cases² and Senator Tillis' recent comments³, significant modification to the existing legal framework for determining patentable subject matter under 35 U.S.C. § 101 is unlikely to take place any time soon.

Under *Mayo's* two-prong test, the first step asks whether a claim is directed to a judicially recognized exception, *i.e.*, natural product, natural phenomenon, or abstract idea. If the answer is no, the claimed subject matter is patent eligible. If the answer is yes, however, the claim is further examined in step two to determine whether the additional elements recited in the claim, considered both individually and as an ordered combination, "transform the nature of the claim" into a patent eligible application by reciting an "inventive concept" that is "sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself" (*i.e.*, not well-understood, routine, conventional activity). *Mayo* at 1294. For step two of the analysis, the judicially recognized exception is treated as if it was part of the prior art base.

To facilitate examination and to help fill the void left by the Supreme Court and Congress, the USPTO has released Interim Guidance documents with example claims (*see, e.g.*, Eligibility Examples) that it considers eligible under current case law⁴. A revised Guidance was published on January 7, 2019 ("January Guidance")⁵, with further updates (*e.g.*, Examples 43-36) and clarification provided more recently on October 17, 2019⁶. The January Guidance differs from the earlier Guidance in several ways. First, the January Guidance provides that all "abstract ideas" should fall into one of three categories⁷: (1) mathematical concepts (*e.g.*, mathematical relationships, mathematical formulas or equations, mathematical calculations), (2) certain methods of organizing human activities (*e.g.*, fundamental economic principles or practices, commercial or legal interactions, managing personal behavior or relationship or interactions between people), and (3) mental processes (*e.g.*, concepts performed in the human mind)⁸. Next, the January Guidance breaks step one of the above-described two-prong test into two sub-steps⁹: (i) whether the claim recites a judicial exception; and (ii) if the claim recites a judicial exception, whether the judicial exception is integrated into a practical application. In assessing this latter sub-step, the January Guidance expressly provides that "whether the additional elements represent well-understood, routine, conventional activity" should be excluded¹⁰. Such analysis should be reserved for step two of the two-prong test, which is only conducted if step one of the test is satisfied. Accordingly, claims reciting a judicial exception may be directed to patentable subject matter even where the additional elements that integrate the judicial exception into a practical application are well-understood, routine, and/or conventional.

To help understand when additional elements recited in a claim integrates a judicial exception into a practical application, the January Guidance provides several non-limiting examples: (i) "additional element reflects an improvement in the functioning of a computer, or an improvement to other technology or technical field" (*e.g.*, *Rapid Litigation Management Ltd. v. CellzDirect, Inc.*, 827 F.3d 1042 (Fed. Cir. 2016)); (ii) "additional element that applies or uses a judicial exception to effect a particular treatment or prophylaxis for a disease or medical condition" (*e.g.*, *Vanda Pharmaceuticals Inc. v. West-Ward Pharmaceuticals International Limited*, 887 F.3d 1117 (Fed. Cir. 2018)); (iii) "additional element implements a judicial exception with, or uses a judicial exception in conjunction with, a particular machine or manufacture that is integral to the claim" (*e.g.*, claim directed to a delivery device comprising a natural product (*e.g.*, denveric acid); *see* Example 44 in Appendix 1 of October 2019 Patent Eligibility Guidance Update); (iv) "additional element effects a transformation or reduction of a particular article to a different state or thing"; and (v) "additional element applies or uses the judicial exception in some other meaningful way beyond generally linking the use of the judicial exception to a particular technological environment, such that the claim as a whole is more than a drafting effort designed to monopolize the exception." Non-

limiting examples of additional elements that do not integrate a judicial exception into a practical application include: (i) “additional element merely recites the words ‘apply it’ (or an equivalent) with the judicial exception, or merely includes instructions to implement an abstract idea on a computer, or merely uses a computer as a tool to perform an abstract idea; (ii) additional element adds insignificant extra-solution activity to the judicial exception; and (iii) additional element does not more than generally link the use of a judicial exception to a particular technological environment or field of use.”

In biotech/pharma, claims can often recite a naturally occurring product or a variant thereof. Drafting these claims so that they are not “directed to a judicially recognized exception” under step one offers the safest path to patent eligibility as it altogether avoids the step two analyses. One way to achieve this goal is by ensuring that the composition recited in the claim is “markedly different” from its naturally occurring counterpart. In cases where the composition used is a product of nature, method/process claims using that composition in a non-natural way can offer a path to eligibility without the step two analyses.

In 2013, the Supreme Court held that a man-made isolated polynucleotide comprising the BRCA1 gene sequence constitutes a product of nature exception because it is not “markedly different” from the naturally occurring BRCA1 gene. *Ass’n for Molecular Pathology v. Myriad*, 133 S.Ct. 2107, 2111 (2013). The Court found, however, that a cDNA encoding BRCA1 is a patent eligible composition because it is markedly different from the naturally-occurring polynucleotides. *Id.* Similarly, the Federal Circuit in *Natural Alternatives International, Inc. v. Creative Compounds, LLC*, 918 F.3d 1338, 1348 (Fed. Cir. 2019), concluded that a claim directed to a human dietary supplement comprising a beta-alanine (a natural product) “in a unit dosage of between about 0.4 grams to 16 grams” is patent eligible, where the “claimed dosage forms can be used to increase athletic performance in a way that naturally occurring beta-alanine cannot.” The court also noted that a claim directed to a composition comprising a beta-alanine in combination with glycine (also natural product) can be patentable where “the claimed combination of glycine and beta-alanine could have synergistic effects allowing for outcomes that the individual components could not have.” *Id.* The court reasoned that the claims at issue “incorporate natural products, but they have different characteristics and can be used in a manner that beta-alanine as it appears in nature cannot.” *Id.*

Moreover, the Eligibility Examples mentioned previously further provide useful insight into USPTO’s view on what would be considered a “marked difference” for the purpose of eligibility. They include structural differences (*e.g.*, difference in molecular structure, crystal forms, amino acid sequence, and genetic composition) as well as functional ones (*e.g.*, increased stability, increased solubility, or new activity/function). When drafting the claims, however, care must be taken to ensure that the recited composition does not encompass a product of nature in addition to the otherwise patent eligible “markedly different” embodiments. *See, e.g., In re Roslin Institute*, 750 F.3d 1333, 1338 (Fed. Cir. 2014) (holding that claims directed to a “live-born clone of a pre-existing, non-embryonic, donor mammal” were ineligible because any differences between the clones and their donor mammals were unclaimed).

Cellzdirect, a recent Federal Circuit decision emphatically confirms that claims directed to a “method of producing a desired preparation of multi-cryopreserved hepatocytes” are patent eligible, even if the process uses a product of nature and even if the transformation is governed by the laws of nature. *Rapid Litigation Management v. Cellzdirect*, 827 F.3d 1042 (Fed. Cir. 2016) (“This type of constructive process, carried out by an artisan to achieve ‘a new and useful end,’ is precisely the type of claim that is eligible for patenting.”). The Court further found that the claims were not “directed to” a patent-ineligible concept, and therefore need not be analyzed under step two of the *Mayo/Alice* framework.

The patent eligibility of method of treatment claims was affirmed in *Vanda Pharmaceuticals* in which the Federal Circuit held that claims directed to a method of treating schizophrenia was patent eligible. 887 F.3d 1117 at 1134. The Court reasoned that the claims were not directed to a law of nature (*i.e.*, relationship between iloperidone, CYP2D6 metabolism, and QTc prolongation) and instead “directed to a specific method of treatment for specific patients using a specific compound at specific doses to achieve a specific outcome.” *Id.* at 1136.

However, when drafting method of treatment claims that incorporate a judicial exception, it is important that the treatment aspect is the focus of the claims. In *INO Therapeutics LLC v. Praxair Distribution Inc.*, 782 Fed.Appx. 1001, 1005 (Fed. Cir. 2019) (not precedential), the Federal Circuit held that claims directed to a “method of treating patients who are candidate for inhaled nitric oxide treatment” were “directed to [a] natural phenomenon” and not patent eligible. The Court noted that, unlike the claims at issue in *Vanda*, when analyzed as a whole, the claim is not directed to “a new way of actually treating the underlying condition of hypoxic respiratory failure,” but instead the focus is directed to “screening for a

particular adverse condition that, once identified, requires iNO treatment be withheld.” *Id.* at 1007.

Thus, cases such as *Cellzdirect*, *Vanda*, and *Endo* confirm the USPTO’s position expressed in the Eligibility Examples that process claims, including method of treatment claims, are generally patent eligible unless the true focus of the claims are to claim a judicially recognized exception itself, such as was the case in *INO Therapeutics*.

Patents directed to diagnostic assays were the hardest hit by the post-*Mayo* changes in § 101 jurisprudence. All appellate decisions involving a claim directed to a diagnostic assay found it to be directed to a judicially recognized exception and not eligible after step two analysis. See, e.g., *Myriad Genetics; In re BRCA1- and BRCA2-Based Hereditary Cancer Test Patent Litigation*, 774 F.3d 755 (Fed. Cir. 2014); *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015) (*en banc petition denied*) (*cert. denied*); *Genetic Tech. Ltd. v. Merial LLC*, 818 F.3d 1369 (Fed. Cir. 2016); *Cleveland Clinic Foundation v. True Health Diagnostics LLC*, 859 F.3d 1352 (Fed. Cir. 2017); *Roche Molecular Systems, Inc. v. CEPHEID*, 905 F.3d 1363 (Fed. Cir. 2018); *Genetic Veterinary Sciences, Inc. v. Laboklin GmbH & Co. KG*, 933 F.3d 1302 (Fed. Cir. 2019); *Cleveland Clinic Foundation v. True Health Diagnostics LLC*, 760 Fed.Appx. 1013 (Fed. Cir. 2019); *Athena Diagnostics, Inc. v. Mayo Collaborative Services, LLC*, 915 F.3d 743 (Fed. Cir. 2019). In each of these cases, the claims were drawn broadly to capture all diagnostic uses of the underlying natural phenomena regardless of the reagents employed or the starting samples used. And, in each of these cases, the courts found the claims not eligible because once the newly discovered natural phenomenon is removed from the claims, the remaining elements merely recite routine, conventional, and well-understood steps that cannot provide the inventive concept needed to transform the methods into patent eligible subject matter.

Recently the Federal Circuit in *Illumina, Inc. v. Ariosa Diagnostics, Inc.*, No. 2019-1419 (Fed. Cir. Mar. 17, 2020) provided a potential option to avoid patent eligibility issues. The Federal Circuit reversed the district court’s grant of summary judgment, holding that the claims of U.S. Patent Nos. 8,580,751 and 9,738,931 were directed to patent-eligible subject matter and were not invalid under 35 U.S.C. § 101. The representative claim of the ’931 patent is provided below:

1. A method, comprising:

- ◇ (a) extracting DNA comprising maternal and fetal DNA fragments from a substantially cell-free sample of blood plasma or blood serum of a pregnant human female;
- ◇ (b) producing a fraction of the DNA extracted in (a) by:
 - » (i) size discrimination of extracellular circulatory fetal and maternal DNA fragments, and
 - » (ii) selectively removing the DNA fragments greater than approximately 300 base pairs, wherein the DNA fraction after (b) comprises extracellular circulatory fetal and maternal DNA fragments of approximately 300 base pairs and less and a plurality of genetic loci of the extracellular circulatory fetal and maternal DNA fragments; and
- ◇ (c) analyzing DNA fragments in the fraction of DNA produced in (b).

Reversing the district court’s grant of summary judgement that the claims lack patent eligibility, the Federal Circuit remanded the case for further proceedings. The Court noted that “[t]his is not a diagnostic case. And it is not a method of treatment case. It is a method of preparation case.” Applying step one of the *Alice/Mayo* test, the majority of the Court held that the claims were directed to a patent-eligible method that “exploit[s] that discovery in a method for preparation of a mixture enriched in fetal DNA.”

This decision is coherent with the USPTO’s Eligibility Examples: to be considered eligible, a diagnostic claim may need to recite the use of an assay or reagent that was not well known and in common use. If all elements of the claim were well known and in common use, it may need to recite a new, inventive combination of these elements.

While the above cases and the USPTO’s patent eligibility Guidance documents provide some guidance, there is still much uncertainty that need to be resolved. For instance, while the USPTO’s guidance provides many helpful examples, in *Cleveland Clinic Foundation v. True Health Diagnostics LLC*, the court explicitly noted that it was “not bound by its guidance.” 760 Fed. Appx. 1013, 1020 (Fed. Cir. 2019). Therefore, it remains to be seen whether the Courts agree with the USPTO’s more recent eligibility analysis put forth in the January Guidance. Thus, IP practitioners developing a patent portfolio for biotech/pharma inventions must continue to carefully monitor the new developments in § 101 case law, or until Congress finally decides to step in and help resolve the issue.

¹*Athena Diagnostics, Inc. v. Mayo Collaborative Services, LLC*, 927 F.3d 1333, 1336 (Judge Lourie, concurring in declining en banc rehearing) (“Accordingly, as long as the Court’s precedent stands, the only possible solution [to patent eligibility of diagnostic claims] lies in the pens of claim drafters or legislators. We are neither.”)

²See *Athena Diagnostics*, 927 F.3d (Fed. Cir. 2019), *cert. denied*, No. 19-430, 2020 WL 129579; *Vanda Pharmaceuticals Inc. v. West-Ward Pharmaceuticals International Limited*, 887 F.3d 1117 (Fed. Cir. 2018), *cert. denied*, No. 18-817 2020 WL 129534.

³Michael Borella, *The Zombie Apocalypse of Patent Eligibility Reform and a Possible Escape Route*, http://www.patentdocs.org/patent_legislation/ (last visited Feb. 10, 2020) (“Tilis stated ‘[g]iven the reasonable concerns that have been expressed about the draft as well as the practical realities of the difficulty of passing legislation, absent stakeholder consensus I don’t see a path forward for producing a bill—much less steering it to passage—in this Congress.’”)

⁴<https://www.uspto.gov/patent/laws-and-regulations/examination-policy/subject-matter-eligibility>

⁵The 2019 Revised Patent Subject Matter Eligibility Guidance, 84 Fed. Reg. 50 (January 7, 2019).

⁶October 2019 Patent Eligibility Guidance Update, *available at* <https://www.uspto.gov/patent/laws-and-regulations/examination-policy/subject-matter-eligibility>

⁷84 Fed. Reg. 52 (January 7, 2019)

⁸The January Guidance provides six additional examples relating to abstract ideas (Examples 37-42).

⁹*Id.* at 53

¹⁰*Id.* at 55