CLAIMS DIRECTED TO DIAGNOSTIC CORRELATION AND METHOD OF TREATMENT ARE PATENT ELIGIBLE SUBJECT MATTER

A recent decision from the Federal Circuit, *Endo Pharmaceuticals Inc., v. Teva Pharmaceuticals USA, Inc.*, Appeal Nos 2017-1240, 2017-1455, 2017-1887 (Fed. Cir. March 28, 2019) held that claiming a new treatment for an ailment using a natural law can be patent eligible under 35 U.S.C. §101. Section 101 of the Patent Act states 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." However, §101 contains implicit exceptions: laws of nature, natural phenomena and abstract ideas. The panel of judges of Wallach, Clevenger and Stoll held unanimously that the claims at issue were not directed to a natural law and were patent eligible under §101.

In *Endo*, the plaintiff sued the defendants for patent infringement of U.S Patent No. 8,808,737. Claim 1, which is representative of the claims of the '737 patent, reads as follows:

1. A method of treating pain in a renally impaired patient comprising the steps of:

    a. Providing a solid oral controlled release dosage from comprising:
        i. about 5 mg to about 80 mg of oxymorphone or a pharmaceutically acceptable salt thereof as the sole active ingredient; and
        ii. a controlled release matrix;
    b. measuring a creatinine clearance rate of the patient and determining it to be
        (a) less than about 30 ml/min.
        (b) about 30 mL/min to about 50 mL/min
        (c) about 51 mL/min to about 80 mL/min or
        (d) above about 80 mL/min; and
    c. orally administering to said patient, in dependence on which creatinine clearance rate is found, a lower dosage of the dosage form to provide pain relief:

        whererin after said administration to said patient, the average AUC of oxymorphone over a 12-hour period is less than about 21 ng-hr/mL.

The '737 patent relates to the discovery that patients with moderately or severely impaired kidney function in need of pain relief need less oxymorphone (a potent opiod analgesic drug) "than usual" to achieve a certain level of pain management. In other words, "the treatment method allows patients with renal impairment to ingest less oxymorphone while still treating their pain." Technically, "the inventor found that there was a statistically significant correlation between plasma AUC" (area under the curve- that is underneath the concentration versus time curve, which measures the total amount of drug observed in a patient's bloodstream over time after administration of the drug) "for oxymorphone and a patient's degree of renal impairment, as indicated by their creatinine clearance rate." (Creatinine is a waste byproduct which the kidney filters and excretes in urine. The clearance rate of creatinine measures how effective the kidneys are in removing creatinine and thus measures how well the kidneys are functioning.)

Endo sued the defendant for patent infringement in the district court in Delaware; the defendants moved to dismiss the patent infringement claims, alleging that the claims were invalid under §101. The district agreed and held that the claims are "directed to 'the connection between the severity of renal impairment and the bioavailability of oxymorphone' or in other words, the reaction of the human body of a renally impaired individual to oxymorphone, which is unquestionably a natural law."

The Federal Circuit reversed the district court's decision. Applying Step I of the subject eligibility test under §101 in accordance with the holdings in *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66 (2012) and *Alice Corp. Pty. v. CLS Bank Int'l*, 573 U.S. 208 (2014), the Court determined "whether the claims at issue are directed to one of those patent - ineligible concepts." The Court noted that the Supreme Court established a two-step framework to determine subject matter eligibility under §101; however, the *Endo* Court noted that if the claims are not directed to a patent ineligible concept in step one, it need not address step two of the inquiry. Step one required the Court to determine whether the claims are directed to one of the patent ineligible concepts. The *Endo* Court held that the claims are not directed to a patent - ineligible concept. According to the *Endo* Court, "the claims are directed to a patent eligible method of using oxymorphone or pharmaceutically salt thereof to treat pain in a renally impaired patient." For example, according to the *Endo* Court, claim 1 requires specific steps, such as (a) providing a pharmaceutical of 5-80 mg of oral controlled-release oxymorphone or one of its pharmaceutically acceptable salts; (b) testing the patient for a disease state of reduced kidney function based on creatinine clearance rate and then (c) administering the pharmaceutical, which was a lower dose of oxymorphone) based on the creatinine clearance rate to achieve AUC of oxymorphone over a 12-hour period of less than 21 ng-hr/mL. The *Endo* Court further reasoned that the abstract, patent title and summary of the invention describe the invention as a method of treating pain in patients having renal impairment. It indicated that the specification describes the invention as a method for treating renal-impaired pain patients with less oxymorphone while still treating the pain. The *Endo* Court further reasoned that the specification explains that the method "avoids possible issues in dosing", while allowing for treatment with "the lowest possible dose" for patients suffering from renal impairment.

The *Endo* Court referred to a recent case, *Vanda Pharmaceuticals Inc. v. West-Ward Pharmaceuticals International Ltd.*, 887 F3d 1117 (Fed. Cir. 2018), in which it held similar claims patent eligible. In *Vanda*, the claims related to a method of treating schizophrenia patients with a drug (iloperidone) where the administered dose is adjusted based on whether or not the patient is a poor metabolizer." As the Court explained:

> The claims at issue here are legally indistinguishable from the representative claim in *Vanda.* The *Vanda* patent claims recite the steps of carrying out a dosage regimen based on the results of genetic testing... Here the claims similarly recite the steps of carrying out a dosage regimen, though the steps are based on the results of kidney function testing. Additionally, the claims in both cases require specific treatment steps...Like the claims in *Vanda*, the claims here "are directed to a specific method of treatment for specific patients using a specific compound at specific doses to achieve a specific outcome." *See Vanda*, 887 F3d at 1136.

Further the Court distinguished the claims from those in *Mayo*.

> Although the representative claim in *Mayo* recited administering a thiopurine drug to a patient, the claim as a whole was not directed to the application of a drug to treat a particular disease... Furthermore, the administering step in *Mayo* is distinguishable from the administering step in the '737 patent because the administering step in *Mayo* is the first step in the method that simply describes giving the drug to a patient with a certain disorder. By contrast, the administering step in the '737 patent is the step that describes giving a specific dose of the drug based on the results of kidney function testing... In *Vanda*, the inventors recognized the relationship between iloperidone dosage and the patient's CYP2D6 poor metabolizer genotype, but that was not what they claimed. Similarly, the inventor here recognized the relationship between oxymorphone and patients with renal impairment, but that is not what he claimed. Rather, he claimed an application of that relationship--specifically a method of treatment including specific steps to adjust or lower the oxymorphone dose for patients with renal impairment. The claims are thus directed to more than just reciting the natural relationship.

Unlike in *Mayo*, the *Endo* Court reasoned where the metabolic level in blood indicated a need to increase dosage without prescribing a particular dosage, the *Endo* Court reasoned that the claims in the '537 patent "…recite the steps of carrying out a dosage regimen based on the results of kidney function testing. The claims require doctors to "orally administer to said patient, in dependence on which creatinine clearance rate is found, a lower dosage of the dosage form to provide pain relief" in such a way that after period is less than about 21 ng-hr/mL... These are specific treatment steps. The claims prescribe a specific dosage regimen through the wherein clause, under which the physician administers oxymorphone to achieve a specific range of AUC of oxymorphone based on the patient's creatinine clearance rate."

The *Endo* Court emphasized that the claims in the '737 patent were directed to a treatment method, not a detection method. According to the *Endo* Court, the claims do not start and end with a naturally occurring phenomenon. The *Endo* Court held that the claims in the '737 patent do more for they recite a specific method of treatment based on the recognition "that patients with severe renal impairment have a mean oxymorphone AUC, on average, 1.7 times greater than healthy subjects."

Further, the *Endo* Court distinguished the outcome from that in *Athena Diagnostics, Inc, v. Mayo Collaborative Servs.*, 915 F.3d 743 (Fed. Cir. 2019). In this case, "the court held that the claim recited a natural law and conventional means for detecting it." The *Athena Diagnostics* Court concluded that the claim at issue were "claiming a natural cause of an ailment and well -known means of observing it; as such the claim is not eligible for a patent because such a claim encompasses the natural law itself." In contrast, in *Endo,* the claims were directed to a new treatment for an ailment using a natural law or phenomenon. As such, the claims in Endo are patent eligible.

As footnote, the *Vanda* case referred to in *Endo* is currently appealed to the US Supreme Court where the accused infringer is arguing that the holding therein improperly stands for the proposition that all claims directed to methods of treatment are now patent-eligible, thereby eviscerating the holding in *Mayo.*

The *Endo* decision contrasts the different outcome with respect to patent eligibility of a claim directed to a diagnostic method relative to a method of treatment claim. Claims directed to diagnosing a disease or condition in general using conventional methods and discovering a correlation of the risk of contracting a disease or condition with the presence of a particular natural biological marker above or below a threshold concentration have been held to be ineligible for patent protection because such a claim in effect encompasses the natural law itself. However, a claim directed to a new treatment for treating a disease with a specific dosage regimen based on the correlation of the presence of a natural marker above or below a threshold concentration and the patients risk factor of contracting a disease or condition has been held by the *Endo* Court to be subject matter eligible for protection under §101 for it is using the natural law or phenomenon. Thus, a strategy for converting such a diagnostic claim which is not patent eligible to a claim which is patent eligible under§101 is to rewrite the diagnostic claim as a novel method of treatment claim that recites a dosage regimen or other added steps to take as a result of that correlation for treating the disease or condition.