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Applicability of §101 Challenges in ANDA Pharmaceutical Litigation

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Any patent practitioner knows that §101 challenges are filed as a matter of course in patent infringement cases involving software and business methods. On the other hand, challenges under §101 are rarely used in cases. In fact, of the 490 ANDA cases filed since the Supreme Court's decision in *Alice Corp. Pty. v. CLS Bank Int'l* 134 S.Ct. 2347 (2014), only six appear to address §101 (*Alice*) challenges. By utilizing §101 motions less than 2 percent of the time, generics are not fully availing themselves of the Supreme Court's decisions in *Alice*, *Mayo*, and *Myriad*. As an example, and without providing an exhaustive list, generic pharmaceutical companies should, at a minimum, consider filing §101 motions in cases involving method of treatment, pK profiles, or polymorph patents.

Section 101: Interpretation and Applications

35 U.S.C. §101 provides that a patent may be granted to "[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof[.]"

Since the decision in *Bilski v. Kappos*, 561 U.S. 593 (2010), a plethora of cases have dissected the various terms and phrases of §101. *Alice*, a decision whereby the Supreme Court invalidated patents for mitigating settlement risk in financial transactions, set the definitive two-prong test for analyzing challenges under §101. The first prong inquires whether the claims at issue are directed at "a patent-ineligible concept." If yes, the court moves to the second prong and searches for an "inventive concept" to determine whether the additional claim elements "transform the nature of the claim." Id. at 2355.

Prior to *Alice*, the Supreme Court examined the patent eligibility of biotechnology inventions in *Mayo v. Prometheus Lab.*, 566 U.S. 66 (2012) and *Ass'n for Molecular Pathology v. Myriad Genetics*, 569 U.S. 576 (2013). In *Mayo*, the court applied an analysis, later adopted by *Alice*, to find that claims for a method of administering a drug, measuring drug metabolites, and adjusting the dosage were not directed to patent-eligible subject matter because it involved a routine and obvious activity. The court emphasized that the patent merely claimed the "entirely natural" process of how well drug compounds are metabolized by the human body. 566 U.S. at 77. The court held: "If a law of nature is not patentable, then neither is a process reciting a law of nature, unless that process has additional features [that are] more than a drafting effort designed to monopolize the law of nature itself." Id.

Likewise, in *Myriad*, the court relied on §101 to invalidate Myriad's patent for an isolated segment of two genes and primers used in diagnostics. By identifying the possible mutation of those genes, Myriad developed medical tests to detect and assess the patient's risk of breast cancer. The court found DNA to be inherently a product of nature and held that Myriad's patent claims did not meet the §101 standard because it simply recited pre-existing genes without "creat[ing] or alter[ing]" the genetic information. 569 U.S. at 577.

The holdings that the *Myriad* and *Mayo* claims were not eligible for patent protection because they failed to "add something to the natural laws themselves," *Mayo*, 566 U.S. at 87, in combination with the standard articulated in *Alice*, opens the door for generics to challenge previously accepted patent claims. Generics now have more ammunition with which to challenge claims directed to, inter alia, methods of treatment, PK profiles, and polymorphs.

Method of Treatment Claims

In *Mallinckrodt Hosp. Prod. IP Ltd. v. Praxair Distribution*, No. CV 15-170-GMS, 2017 WL 3867649 (D. Del. Sept. 5, 2017), Judge Gregory Sleet in Delaware construed a claim for a method of treating patients with inhaled nitric oxide (iNO) that "reduces the risk that inhalation of nitric oxide gas will induce an increase in pulmonary capillary wedge pressure (PCWP) leading to pulmonary edema in neonatal patients with hypoxic respiratory failure." Id. at *16. Relying upon *Mayo*, the court determined that the claimed invention "is really a patient populations' natural physiological response to [the amount of] inhaled nitric oxide treatment and remains a recitation of natural laws rather than an innovation." Id. at *17. The court held the invention failed the second prong as lacking in innovation, citing "the application step of the claimed method simply tells the relevant audience about the natural phenomenon and directs the audience to take that phenomenon into account when treating patients." Id. at *18. *Mallinkrodt* is currently on appeal at the Federal Circuit.

Likewise, Judge Peter Sheridan in *Boehringer Ingelheim Pharm. v. HEC Pharm Co.*, No. 15CV5982PGSTJB, 2016 WL 7177704 (D.N.J. Dec. 8, 2016) found method of treatment claims to be invalid. The claim at issue was:

> A method of treating and/or preventing metabolic diseases in a patient for whom metformin therapy is inappropriate due to at least one contraindication against metformin comprising orally administering to the patient a DPP-IV inhibitor wherein the contraindication is selected from the group consisting of: renal

> disease, renal impairment or renal dysfunction, unstable or acute congestive heart failure, acute or chronic metabolic acidosis, and hereditary galactose intolerance.

Id. at *7-8.

The court found this claim to be similar to *Mayo*, stating that "the improvement of having the DPP-IV inhibitors excreted via the liver, instead of the kidney, is performed at the anatomical level of the human body, where a series of reactions in the human body process the DPP-IV inhibitor under the natural biological process." Id. at *9. Turning to the second prong, the court found that merely reciting an improvement of not requiring dose adjustment over conventional DPP-IV inhibitors with renal impairment was insufficient to transform the abstract idea to patent-eligible subject matter. The court reasoned that DPP-IV inhibitors are mainly excreted via the liver, not the kidney, and therefore do not affect renal issues. Id. Thus, reciting well-understood, routine, conventional activity was insufficient to make these claims patent-eligible subject matter, and the court granted the motion to dismiss. Id. at 11.

In contrast, Judge Sleet in *Vanda Pharmaceuticals v. Roxane Laboratories*, 203 F. Supp. 3d 412 (D. Del Aug. 25, 2016) found claims directed to, inter alia, a method of administering iloperidone to patients suffering from schizoaffective disorder valid. The court found that the Vanda's '610 patent "depend[ed] upon laws of nature" and focused on the second prong analyzing "whether the claims incorporate some additional step sufficient to transform the claims." The court determined that Vanda had transformed the claim by "conducting [genotyping] tests to determine the appropriate dose of iloperidone to reduce [related risks] … [and] Roxane had not proven by clear and convincing evidence that the precise test and the discovered results were routine or conventional. The court found the claims of Vanda's '610 patent valid as sufficiently limiting the patent's applicability to a "specific patient population based upon their genetic composition." Id. at 429-30.

Further, the U.S. Patent and Trademark Office (PTO) Patent and Trial Appeal Board (PTAB) has recently invalidated method of treatment claims relying upon §101 *Alice* two-prong analysis and 2014 Interim Guidance on Patent Subject Matter Eligibility. For example, in *Ex Parte John Chamberlain, Halina Fitz-Clarence, & Mark Thomas*, APPEAL 2014-009849, 2017 WL 244123, (Jan. 18, 2017), the PTAB invalidated a method of treatment for identification and treatment of an individual with bone disorders. The PTAB labeled the identification of genotypes expressions of laws of nature and non-patentable subject matter and sought for "inventive concept." The PTAB invalidated the claims because "administering bisphosphonate to the individual having bone disorders is a well understood and routine treatment step for such patients." Id. at 4. The PTAB rulings demonstrate a road map for generic companies in raising §101 challenges in district courts.

As these decisions demonstrate, courts and the PTO are finding method of treatment claims lacking under the first prong of *Alice* and focusing on the second prong to determine validity. This focus will allow generics different avenues to challenge method of treatment claims under §101.

Potential Additional §101 Claims: pK Profiles, Polymorphs, and More

While our focus thus far has been on §101 challenges to method of treatment claims, generics may find success in raising §101 challenges to claims directed to the pharmacokinetic (pK) profiles of known drug compounds and polymorphs of known drug compounds.

Brand companies are increasingly filing patent claims merely directed to the pK profiles of known drug products for life cycle management. The courts have not directly addressed §101 challenges to pK profiles, but generics should consider challenging these types of claims. In fact, Judge Sheridan in *Boehringer Ingelheim Pharm. v. HEC Pharm Co.*, supra, provides a road map to attacking these types of claims by focusing on the mere recitation of routine activity of known drug products.

Challenges to claims to polymorphs may also be fruitful. Polymorphism is the ability of a solid material to exist in two or more forms or crystalline structures of the same chemical compound—in essence, same compound, different lattice structure. There are two common methods (powder X-ray diffraction and infrared reflection absorption spectroscopy) to identify and differentiate each polymorphic form (its "fingerprint"). Therefore, filing a new patent *after* a patent for the original compound application could lead to invalidity under §101 as discovering a polymorph is merely discovering a natural concept that existed in nature at the time the original compound was discovered. Under the second prong, there is no inventive concept. All that was "discovered" is something that existed in nature at the time the original compound was discovered, and identifying its "fingerprint" should not allow the issuance of additional patents on known compounds.

Adding to the ANDA Litigant's Arsenal: A Look Into the Future

The recent judicial interpretations of §101 provide ample opportunity for ANDA litigants to challenge whether certain types of patents are truly patent-eligible or merely recitations of natural laws. Generic companies should consider adding §101 to their arsenal of challenges, especially for claims directed to a method of treatment, PK profiles, and polymorphs. Section 101 challenges may very well prove fruitful for other types of claims, though—and creative ANDA litigators are sure to test this in the coming years.

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