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ANDA Update

Table of Contents

2 First Circuit Maintains Jury Verdict for Defendants in Class Action Pharmaceutical Pay-for-Delay Suit

3 Multiple Actors May Perform Steps in Method Claims for Purposes of Inducement

4 International Non-Proprietary Pharmaceutical Names Have a Plain and Ordinary Meaning

5 Court Rules Deposition Transcripts in Prior Pharmaceutical Litigation Not Relevant to Patent Dispute

5 Prior Art Compound Patent Does Not Inherently Anticipate a Method for Creating a Stable Form of the Compound

6 Without Testing of the Prior Art Defendants Cannot Show a Reasonable Expectation of Success

8 Prior Art Did Not Have the Muscle to Render Testosterone Patents Obvious

PERMANENT INJUNCTIONS

Speculative Evidence of Irreparable Harm Sinks Bayer's Request for Permanent Injunction

Bayer Pharma AG, et al. v. Watson Laboratories, Inc.
(D. Del. December 28, 2016)

Kevin P. Shortsle

Applying the *eBay* factors to Plaintiff Bayer's request for permanent injunction, the US District Court for the District of Delaware denied the request because Bayer failed to establish irreparable harm and that the remedies at law were inadequate. *Bayer Pharma AG, et al. v. Watson Laboratories, Inc.*, Case No. 12-cv-1726, (D. Del. Dec. 28, 2016) (Stark, J.).

After finding Bayer's patent not invalid and infringed by defendant Watson's proposed generic of Natazia®, a combination estrogen/progestin oral contraceptive, the parties agreed to enter an order resetting the US Food and Drug Administration (FDA) approval date of Watson's abbreviated new drug application (ANDA) until after expiration of Bayer's patent, but disputed whether the court should enter a permanent injunction against Watson. The court framed the dispute as whether to limit Watson's activities following its finding of infringement to only those within the "safe harbor" of 35 U.S.C. 271(e)(1) or to allow Watson to conduct all research and pre-commercialization activity that could precede launching its generic product.

In denying Bayer's request, the court first dispensed with the notion that all patentees prevailing in an ANDA case are entitled to a permanent injunction. Instead, the court applied the *eBay* factors, finding Bayer failed to create a record to justify a permanent injunction. While the court found that the balance of hardships and public interest slightly favored Bayer, the court denied the permanent injunction because Bayer did not establish irreparable harm or that the remedies available at law would be inadequate.

In analyzing irreparable harm, the court found Bayer's arguments speculative. First, the court agreed with Watson that Bayer had not provided any data that the filing of Watson's ANDA would lead to lost revenues or that Bayer's changes to its marketing plans for Natazia was due to Watson's ANDA. Instead, the court found the evidence showed Bayer's marketing plans were changed because of the timing of FDA approval of other indications. Second, Bayer argued that Watson would engage in "illegal activity" if an injunction was not granted. The court characterized Bayer's "illegal activity" argument as "entirely unfounded" that Watson would risk criminal sanctions by launching its generic product without FDA approval. The court found the risk of future litigation was slight, and cited *ActiveVideo Networks v. Verizon Comm*. for the proposition that litigation costs cannot support a finding of irreparable harm. 694 F.3d 1312 (Fed. Cir. 2012). Lastly, the court questioned how Bayer could be irreparably harmed when sales of Natazia®'s held a "close-to-inconsequential place" in Bayer's overall portfolio.

The court then rejected Bayer's argument that there was no adequate remedy at law. The court concluded that delaying FDA approval was an adequate remedy, since it was speculative that Watson would launch its product before FDA approval and face significant civil and criminal penalties, and risk its relationship with the FDA over a premature and unlawful launch of a single product.

ANTITRUST

First Circuit Maintains Jury Verdict for Defendants in Class Action Pharmaceutical Pay-for-Delay Suit

In re Nexium (Esomeprazole) Antitrust Litigation
(1st Cir. November 21, 2016)

William Diaz

In the first pharmaceutical pay-for-delay case tried before a jury since the Supreme Court of the United States decision in *FTC v. Actavis, Inc.*, 570 U.S. 756(2013), the US Court of Appeals for the First Circuit maintained the jury's verdict in favor of the defendants that were parties to an allegedly anticompetitive patent settlement. *In re Nexium (Esomeprazole) Antitrust Litigation*, 842 F.3d 34 (1st Cir. 2016) (Lynch, J.).

A pay-for-delay or reverse payment settlement refers to an arrangement whereby a brand name pharmaceutical company that is suing a prospective generic supplier of patent infringement under a Hatch-Waxman Act "Paragraph IV certification," agrees to settle the litigation in a manner that compensates the defendant generic supplier and delays its entry into the market. The Supreme Court in *Actavis* held that these arrangements can violate the antitrust laws when the arrangement's anticompetitive effects outweigh its procompetitive effects.

The class plaintiffs, consisting of wholesale drug distributors, individual customers, third-party payors, union plan sponsors, insurance companies and retail outlets, challenged AstraZeneca's patent settlements with Ranbaxy, Teva and Dr. Reddy under federal and state antitrust laws. The plaintiffs alleged that these settlements were pay-for-delay schemes intended to delay the entry of the generic version of AstraZeneca's heartburn medication, Nexium. Teva and Dr. Reddy settled and dropped out of the lawsuit prior to the jury's verdict.

The plaintiffs brought their lawsuit in the US District Court for the District of Massachusetts and at the end of the trial, the jury found that while the patent settlements were anticompetitive, there was no antitrust injury because AstraZeneca would not have agreed to allow the generic suppliers of Nexium to enter the market earlier than had been agreed to without the unreasonably anticompetitive settlement terms and ruled in favor of AstraZeneca.

The plaintiffs appealed the decision on the grounds that the judge made several errors when it excluded key evidence, granted defendants judgment as a matter of law on the issue of an overarching conspiracy, gave improper jury instructions and granted Defendant's motion for summary judgment that impermissibly cut down the number of causal mechanisms through which the plaintiffs could make their case to the jury. The First Circuit found no reversible error in the lower court's evidentiary rulings, jury instructions or judgment as a matter of law. With the respect to the summary judgment decision, the First Circuit found that "the jury verdict, finding an antitrust violation but not an antitrust injury…renders harmless any error that may have occurred during the summary judgment proceedings[,]" and on that basis held that it need not review the summary judgment for error.

PATENTS//INDUCEMENT/DIVIDED INFRINGEMENT

Multiple Actors May Perform Steps in Method Claims for Purposes of Inducement

Eli Lilly and Co. v. Teva Parental Medicines, Inc.
(Fed. Cir. January 12, 2017)

Mandy H. Kim

Addressing the issue of divided infringement, the US Court of Appeals for the Federal Circuit affirmed the district court's finding of induced infringement even though no single actor performed all steps of the asserted claims in a method patent. *Eli Lilly and Co. v. Teva Parental Medicines, Inc.*, Case No. 15-2067 (Fed. Cir., Jan. 12, 2017) (Prost, C.J.).

The patent at-issue related to methods of administering the chemotherapy drug pemetrexed disodium (pemetrexed) after pretreatment with two common vitamins, folic acid and vitamin B12. Eli Lilly markets pemetrexed under the brand name Alimta®. After the patent issued in 2010, Teva and other drug makers notified Eli Lilly that they had submitted Abbreviated New Drug Applications (ANDAs) seeking approval by the Food and Drug Administration (FDA) to market generic versions of Alimta®, and also filed Paragraph IV certifications declaring the patent invalid, unenforceable and not infringed. Eli Lilly brought suit against Teva and other drug makers, alleging infringement under the Hatch-Waxman Act. The parties agreed that no single actor performed all steps of the asserted claims—rather, the steps are divided between physicians administering vitamin B12 and pemetrexed and patients administering folic acid.

During the litigation in 2013, the defendants conditionally conceded induced infringement under then-current law set forth in the Federal Circuit's *Akamai II* decision. The Supreme Court of the United States, however, reversed *Akamai II* in 2014, holding that liability for inducement cannot be found without direct infringement, and remanded to the Federal Circuit to reconsider the standards for direct infringement. This resulted in the Federal Circuit's *Akamai V* decision in 2015. After applying *Akamai V*, which broadened the circumstances in which others' acts may be attributed to a single actor to support direct-infringement liability in cases of divided infringement, the district court found that defendants still induced infringement. Defendants appealed. Defendants also appealed the district court's finding that the asserted claims were not invalid.

The Federal Circuit affirmed, stating that under *Akamai V*, the performance of method steps is attributable to a single entity in two circumstances: (1) when that entity "directs or controls" others' performance, or (2) when the actors "form a joint enterprise." In the instant case, the question was whether physicians directed or controlled their patients' administration of folic acid. As to that question, the court reiterated the two-prong test set forth in *Akamai V*, where directing or controlling others' performance includes circumstances in which an actor conditions participation in an activity or receipt of a benefit upon others' performance of one or more steps of a patented method, and establishes the manner or timing of that performance. The Court also noted that going forward, "other factual scenarios may arise which warrant attributing others' performance of method steps to a single actor."

Regarding the first prong, the Federal Circuit, after considering the product labeling and expert testimony, agreed with the lower court's finding that physicians condition pemetrexed treatment on folic acid pretreatment. The Court also noted that for purposes of applying the test, "conditioning" was not limited to "legal obligations or technological prerequisites." Regarding the second prong, the Federal Circuit again agreed with the lower court's ruling that, in view of the record evidence, physicians establish the manner and timing of patients' folic acid pretreatment. The Court cautioned, however, that its holding "does not assume that patient action is attributable to a prescribing physician solely because they have a physician-patient relationship" and stated that it "leave[s] to another day what other scenarios also satisfy the 'direction or control' requirement." Turning next to whether Eli Lilly proved the requisite intent to find liability for induced infringement, the Federal Circuit found that the evidence established that the product labeling in issue would inevitably lead some physicians to infringe which was sufficient to establish the requisite intent for inducement.

CLAIM CONSTRUCTION

International Non-proprietary Pharmaceutical Names Have a Plain and Ordinary Meaning

In re Certain Consolidated Roflumilast Cases (D.N.J. October 18, 2016)

Alex M. Grabowski

Construing the claim term "roflumilast," the US District Court for the District of New Jersey rejected both parties' proposed constructions, each of which sought to narrow the term in different ways. *In re Certain Consolidated Roflumilast Cases*, Case No. 15-cv-3375 (D.N.J. Oct. 18, 2016) (Wolfson, J.). Instead, the court found the term was not in need of construction and applied roflumilast's plain and ordinary meaning.

The case related to a family of AstraZeneca patents claiming methods of treating chronic obstructive pulmonary disease with roflumilast, the international non-proprietary name (INN) given to a specific pharmaceutical compound by the World Health Organization.[1] AstraZeneca markets roflumilast under the brand name Daliresp®. Importantly, a large portion of the asserted patents' specifications are dedicated to describing methods of manufacturing highly pure roflumilast. None of the asserted patents claim those methods.

The World Health Organization assigns INNs to pharmaceuticals to provide reliable ways to identify active pharmaceutical ingredients without have to rely on brand names. Nevertheless, the parties in the case disputed the construction of "Roflumilast." Defendants contended that the term roflumilast should be construed as limited to roflumilast that is produced by the synthesis claimed in the patents based on a disclaimer argument.[2] Plaintiffs disagreed with limiting the term in that way, and instead argued that it should be limited to "[the Roflumilast Compound] active pharmaceutical ingredient."

The court analyzed and rejected both proposed constructions. Defendants' construction, it reasoned, unduly narrowed the meaning of Roflumilast because the specification did not meet the high bar for disclaimer. Although much of the specification was devoted to a method of synthesizing roflumilast, none of the asserted patents actually claimed that method. Additionally, the court noted that there is a strong presumption against requiring claimed product be manufactured by a certain process unless they are explicitly claimed that way. The court found that presumption particularly compelling in this instance because certain claims in the patent family did specifically require manufacture by that process. Therefore, the court declined to read a product by process limitation into the claim.

Similarly, the court rejected Plaintiffs' construction on the basis that there was no justification for reading "active pharmaceutical ingredient" into the definition of Roflumilast. While the World Health Organization assigns INNs to pharmaceutical ingredients, the term refers to the compound alone, divorced from its use. Moreover, some of the claims in the patent used the transitional phrase "[a] composition comprising" while others used, "[a] pharmaceutical composition comprising." The court held that reading "active pharmaceutical ingredient" into the construction of roflumilast would eliminate that difference.

After rejecting both parties' constructions, the court noted that during claim construction "[t]he judge's task is not to decide which of the adversaries is correct. Instead, the judge must independently…declare the meaning of the claims." Following this principle, the court ultimately construed roflumilast using its plain and ordinary meaning of the Roflumilast Compound.

[1] The compound's chemical name is N-(3,5-dichloropyrid-4-yl)-3-cyclopropylmethoxy-4-difluoromethoxybenzamide ("the Roflumilast Compound").

[2] Defendants' proposed construction was "[the Roflumilast Compound] synthesized using a molar ratio of the anion of 4-amino-3, 5-dichloropyridine to the activated derivative of 3-cyclopropylmethodx-4-difluoromethoxybenzoic acid of at least 1.5 and at most 3."

DISCOVERY

Court Rules Deposition Transcripts in Prior Pharmaceutical Litigation Not Relevant to Patent Dispute

Depomed, Inc. v. Purdue Pharma L.P.
(D.N.J. October 14, 2016)

Shon Lo

Depomed sued Purdue in 2013, alleging that Purdue's OxyContin® product infringes three patents directed to extending the duration of drug release within the stomach and polymer mixtures for gastric retentive tablets. *Depomed, Inc. v. Purdue Pharma L.P.,* Case No. 13-cv-517 (D.N.J. Oct. 14, 2016) (Cooper, J.). A fourth patent was later added. Claims relating to this fourth patent and another of the patents-in-suit were dismissed with prejudice by agreement of the parties. In January 2014, Purdue filed petitions for *inter partes* review (IPR) on all asserted claims from the remaining two patents-in-suit. The US Patent and Trade Office (PTO) instituted IPR on all but two of the asserted claims. The US District Court for the District of New Jersey granted Purdue's request to stay the litigation pending the outcome of the IPR. (Dkt. 89). The PTO affirmed patentability of all challenged claims, and the US Court of Appeals for the Federal Circuit affirmed. *See Purdue Pharma L.P. v. Depomed, Inc.,* Case no. 2015-2029, -2030, -2032 (Fed. Cir. Mar. 24, 2016). The stay in the district court litigation was lifted that same month by consent of the parties.

In the course of discovery, Depomed sought production of deposition and trial transcripts from the 23 different prior litigations or proceedings involving OxyContin. Depomed argued that "there was a very high probability" that Purdue's witnesses had testified on issues relevant to the present litigation, such as how OxyContin is released over time, and the extent to which Purdue made use of the controlled release delivery system. Depomed also pointed to its own production of transcripts from other litigations involving the patents-in-suit. The magistrate judge found that the information requested was not relevant because the patents asserted by Depomed were not litigated in the prior cases involving Purdue and declined to order production by Purdue. (Dkt. 176). Depomed appealed the magistrate judge's decision to the district court judge.

On appeal, Depomed argued that the magistrate judge's decision was clearly erroneous because it had adequately explained why the prior testimony of the same Purdue witnesses who would be deposed for the instant case would likely contain relevant information. Depomed also argued that fairness required production of the transcripts for potential impeachment purposes. Judge Mary Cooper was not persuaded that the magistrate judge's decision was clearly erroneous or contrary to law, specifically noting that the patents-in-suit were not at issue in the prior litigations. Therefore, just because some of the same Purdue witnesses testified in the prior litigations did not necessarily mean there is a "very high probability" that their testimony related to the key infringement issues and the value of the invention at issue in this litigation.

ANTICIPATION/OBVIOUSNESS

Prior Art Compound Patent Does Not Inherently Anticipate a Method for Creating a Stable Form of the Compound

Merck Sharp & Dohme Corp. v. Hospira Inc.
(D. Del. October 7, 2016)

Zachary D. Miller

After reviewing a manufacturing patent related to the antibiotic, ertapenem, the US District Court for the District of Delaware determined that the prior art did not inherently anticipate the patent. *Merck Sharp & Dohme Corp. v. Hospira Inc.,* Case No. 14-cv-915, (D. Del. Oct. 7, 2016) (Andrews, J.)

In May 2014, Hospira filed an abbreviated new drug application (ANDA) seeking approval to market a generic version of Merck's Invanz® product—the antibiotic ertapenem. Merck sued Hospira for infringement of two patents—US Patent Nos. 5,952,323 (the '323 patent) and 6,486,150 (the '150 patent). Each patent claims different methods relevant to the production of a stable form of ertapenem. Ertapenem was first claimed in US Patent No. 5,478,820 (the '820 patent), which issued in 1995—but was unable to be commercially marketed because it is highly unstable. Merck created a stable form of ertapenem by forming a carbamate adduct by reacting ertapenem with a carbon dioxide source at a specific pH range of 6.0 to 9.0. The '323 patent describes and claims the carbamate adduct form of

ertapenem. The '150 patent claims a process for making a formula with a generic chemical compound that encompasses the carbamate adduct of ertapenem.

During a bench trial, the court heard testimony regarding Hospira's generic product, the two patents-at-issue, and the prior art and determined (1) that Hospira's generic product infringed both patents; (2) that the '323 patent was not anticipated or obvious in view of the prior art—namely the '820 patent; and (3) that the '150 patent was obvious in view of the disclosure in the '323 patent.

The '323 Patent. During the bench trial, Hospira conceded that its product would infringe the claims of the '323 patent. However, Hospira argued that the '323 patent was anticipated, obvious and invalid for lack of written description. First, Hospira's expert testified that the '820 patent inherently anticipated the '323 patent—that is, if a person of ordinary skill in the art simply followed the steps of the '820 patent, the carbamate adduct of ertapenem would be formed. The court disagreed. Instead, the court found that the '820 patent did not disclose the pH range between 6.0 and 9.0 necessary to form the adduct. While Hospira's expert testified that that pH "is where you would want to be if you are going to be formulating the drug," the court instead sided with Merck's expert, who identified at least three different processes that were consistent with the '820 patent and would not form the adduct. Since the teachings of the '820 patent could be practiced in a way that would not result in the formation of the adduct, the '820 patent did not inherently anticipate the '323 patent.

Hospira also argued that the '323 patent was obvious in view of the '820 patent and other prior art that addressed compounds related to ertapenem (but not ertapenem itself). The other prior art disclosed carbamate adduct forms of compounds similar to ertapenem and also disclosed that other similar compounds were stable at a pH range between 6.0 and 9.0. However, the court found that there were important differences between the structure of the similar compounds and ertapenem, such that the prior art did not teach a person of ordinary skill in the art to combine ertapenem and a carbon dioxide source at the necessary pH, nor that the formation of a carbamate adduct of ertapenem would stabilize the compound. In addition, the court found that the commercial success of Merck's Invanz product, as well as Hospira's decision to copy the process and formulation of Invanz were secondary considerations of non-obviousness. Therefore, the court found that the '323 patent was not obvious.

Finally, Hospira argued that since '323 patent was invalid for lack of written description because the claims did not contain any restriction on the pH used to create the carbamate adduct, and the specification of the '323 patent disclosed that the carbamate adduct could only be created at a pH range of 6.0 to 9.0. However, the court dismissed this argument, as Merck was not required to include a pH limitation in the claims.

The '150 Patent. The court next analyzed infringement and invalidity of the '150 patent. With respect to infringement, the only question was whether the generic product met the '150 patent requirement of a "high rate conversion" from ertapenem to the carbamate adduct. The court determined that anything that produced a stable ertapenem mixture—and found that Hospira's product infringed.

Hospira then argued that the '150 patent was obvious in view of the teachings of the '323 patent. While the '323 patent did not describe the specific steps—in order—as claimed in the '150 patent, it did describe all of the conditions necessary to produce the carbamate adduct (*e.g.*, a pH between 6.0 and 9.0 and a low temperature during the reaction). The court found that the only way to meet the conditions described in the '323 patent for the production of the carbamate adduct was to use a procedure that included the same steps as claimed in the '150 patent. Thus, the '150 patent was held invalid as obvious.

ANTICIPATION/OBVIOUSNESS

Without Testing of the Prior Art Defendants Cannot Show a Reasonable Expectation of Success

Endo Pharmaceuticals Inc. v. Amneal Pharmaceuticals, LLC (D. Del. October 7, 2016)

Jeffrey R. Gargano

Plaintiffs, Endo Pharmaceuticals Inc. (Endo) and Mallinckrodt LLC (Mallinckrodt) brought patent infringement actions against Amneal Pharmaceuticals (Amneal) and Teva Pharmaceuticals

(Teva) for separately filing abbreviated new drug applications (ANDA) seeking to engage in the marketing of generic versions of Endo's Opana® ER (oxymorphone HCl) product. *Endo Pharmaceuticals Inc. v. Amneal Pharmaceuticals, LLC* Case No. 14-cv-1382, (D. Del., Oct. 7, 2016) (Andrews, J.). Plaintiffs alleged that the defendants' ANDAs infringed US Patent No. 8,871,779 ("the '779 patent), which covers oxymorphone HCl having low levels of oxymorphone ABUK, an undesired impurity. After the defendants conceded infringement, the court conducted a bench trial on the defendants' claims of obviousness, and Teva's defense of implied license. The US District Court for the District of Delaware held that the defendants failed to make a *prima facie* showing that the '779 patent would have been obvious to a person of ordinary skill in the art, and that based on the parties' past conduct, no implied license existed between Teva and Mallinckrodt.

Oxymorphone HCl was first patented in 1955 and prior to 2002, manufacturers regularly sold oxymorphone HCl with the impurity oxymorphone ABUK in the range of hundreds of parts per million (ppm). In 2004, the US Food and Drug Administration (FDA) mandated that opioid manufacturers lower the levels of ABUK in opioid pharmaceuticals to less than 10 ppm. In 2005, Mallinckrodt succeeded in reaching the low ABUK levels mandated by the FDA for oxymorphone HCl. Mallinckrodt applied for and received the '779 patent, which claims a hydrochloride salt of oxymorphone comprising less than 0.001 percent of oxymorphone ABUK (low-ABUK oxymorphone). Mallinckrodt exclusively licensed the '779 patent to Endo which used the low-ABUK oxymorphone in its Opana ER crush-resistant formulation product.

Defendants' obviousness defense centered on two prior art references: (1) Weiss, a paper published in 1957 that generally describes hydrogenating oxymorphone ABUK into oxymorphone HCl; and (2) Chapman, a 2005 patent application, which defendants contend disclose "real-life experiments" that corroborate the expectation of success one would expect from Weiss. Weiss did not provide all the reaction conditions required to reproduce the described reaction. In addition, Weiss did not provide any information about the level of oxymorphone ABUK or other impurities remaining after hydrogenation. Between the publication date of Weiss in 1957 and the invention date of 2005, no other prior art reference mentioned oxymorphone ABUK. Chapman did not disclose oxymorphone at all. Instead, Chapman described a process for hydrogenating oxycodone ABUK into oxycodone.

Defendants' expert opined that a hydrogenation action, like the one described in Weiss, carried out to its completion, *i.e.*, equilibrium, would eventually result in a low concentration of the initial reactant —in this case oxymorphone ABUK. In other words, if a person of ordinary skill in the art ran a hydrogenation reaction for a sufficient amount of time, one would ultimately end up with low-ABUK oxymorphone. Defendants' expert referred to this all as "basic chemistry." On the other hand, Plaintiffs argued that it was extremely challenging to remove impurities like ABUK to levels below 10 ppm, and in fact, there were very few methods available to even measure such low levels of impurities.

The court rejected Defendants' basic chemistry theory because there was no indication and no experimental evidence that the hydrogenation procedure described in Weiss could result in ABUK levels below 10 ppm. In addition, there was evidence that oxymorphone had numerous impurities, including oxymorphone diol, which converted to oxymorphone ABUK under certain conditions. This was critical because at every stage of the hydrogenation process, the court found that oxymorphone diol may regenerate oxymorphone ABUK, even if the ABUK had been previously reduced to low levels. The court also noted that because Defendants' expert did not attempt the hydrogenation process described in Weiss, his basic chemistry theory did not account for the complexities involved in reducing ABUK levels below 10 ppm.

As for Defendants' argument that Chapman corroborates the hydrogenation procedure described in Weiss, the court noted that Chapman describes the hydrogenation of oxycodone, rather than oxymorphone. The evidence also suggested that oxycodone and oxymorphone react in different ways. In fact, Chapman found that a single hydrogenation reaction was not sufficient to reach the desired lower ABUK levels in oxycodone.

Accordingly, the court found: (1) neither Weiss, nor Chapman, disclose low-ABUK oxymorphone; and (2) Defendants have not proven that the combination of Weiss and Chapman would enable a person of ordinary skill in the art to make low-ABUK oxymorphone with a reasonable expectation of success.

Teva also contended that it had an implied license under the '779 patent as a result of two low-ABUK oxymorphone API purchase orders and a letter of authorization (LOA) for low-ABUK oxymorphone API from Mallinckrodt. The court rejected this defense for several reasons. First, the court found that a LOA is a regulatory document where a drug master file (DMF) holder (here Mallinckrodt) grants an ANDA applicant permission to incorporate their active pharmaceutical ingredient (API) into the ANDA. It does not create any binding commercial obligations. Thus, although Mallinckrodt was the only API supplier listed in the Teva ANDA, Mallinckrodt was under no obligation to actually supply low-ABUK oxymorphone API to Teva. Second, the court found that the terms and conditions of the purchase orders did not extend beyond the manufacture of goods covered by the purchase orders, *i.e.,* the low-ABUK oxymorphone API actually purchased by Teva. Thus, the indemnification to hold Teva harmless from any claim for patent infringement did extend to Teva's commercial sale of final products embodying the '779 patent through the use of low-ABUK oxymorphone API not covered by the purchase orders. In other words, the purchases of low-ABUK oxymorphone API did not create an implied license to use that API in a generic version of Endo's Opana ER crush-resistant formulation product.

OBVIOUSNESS

Prior Art Did Not Have the Muscle to Render Testosterone Patents Obvious

Endo Pharms. Inc. and Strakan Int'l S.A.R.L. v. Actavis Labs. UT, Inc. (Fed. Cir. October 14, 2016)

Krista Vink Venegas

In this non-precedential decision, the US Court of Appeals for the Federal Circuit affirmed the finding by the US District Court for the Eastern District of Texas that Strakan's asserted patents were valid in spite of Actavis' prior art challenge. *Endo Pharms. Inc. and Strakan Int'l S.A.R.L. v. Actavis Labs. UT, Inc.*, Case No. 2016-1146 (Fed. Cir. Oct. 14, 2016)(Taranto, C.J.).

Strakan is the owner of two patents (US Pat. Nos. 6,579,865 and 6,319,913) for testosterone compositions and methods of using the same, which expire in November of 2018. Endo is the exclusive licensee, and in 2010, Endo received approval from the US Food and Drug Administration (FDA) to market Fortesta®, a hormone replacement therapy for men having conditions associated with a deficiency or absence of endogenous testosterone. In 2013, Watson filed an abbreviated new drug application (ANDA) seeking to market a generic version of the testosterone gel product, and Watson later transferred its interest in the ANDA to Actavis.

The limited issue addressed in this decision was whether Actavis proved by clear and convincing evidence that each asserted patent claim was invalid for obviousness in view of prior art teachings related to the transdermal delivery of steroids. The court noted that "Actavis made an 'all-or-nothing, across-the-board obviousness argument,'" such that "Actavis' "approach properly considers differences between prior art and *any* of the [ten] asserted claims."

Each asserted claim requires a specified amount of testosterone (or a derivative) in a three-part penetration enhancing formulation (including oleic acid with various amounts of glycol and an alcohol). The court found that for each prior art reference "there is a gap between its teaching and at least one of the asserted claims." The court's opinion provided examples of how prior art references appeared to lack disclosure of the three-part penetration enhancer in combination with testosterone, and the court stated that expert testimony did not support a conclusion otherwise. The court also noted that one prior art reference did disclose all components of the claimed formulations, but also included an additional ingredient, methyl laurate. As such, this reference did not comply with the requirement of the asserted '865 patent claims which limited the claimed composition to those "consisting essentially of" testosterone and the three-part penetration enhancer with a gelling agent. The court did not comment on the applicability of this reference to the asserted claims of the '913 patent which claimed compositions "comprising" the same components.

Further, the court agreed with Endo and Strakan that a skilled artisan would not have bridged the gaps between the prior art and the claimed inventions. The court found the "only relevant problem identified in the record was balancing delivery effectiveness with acceptable irritation for testosterone." While the court found the route of administration and the use of

penetration enhancers obvious, the court found the claimed combinations (including the amounts of testosterone and penetration enhancers) were not. The court found obviousness was not established due to the "tremendous numbers of penetration enhancers" available and lack of a reasonable expectation of success (or "ready predictability" as the district court stated) for an acceptable effectiveness/irritation profile. The court found it unnecessary to consider teaching away or secondary indicia of non-obviousness in view of the lack of motivation to pursue the claimed combinations.

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