IP Alert: Is a New Crystal Polymorph Useful and Non-Obvious Over a Prior Art Form of the Same Chemical Formula?

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By Sarah A. Kagan

Four Abbreviated New Drug Application (ANDA) litigants presented their competing theories of utility, obviousness, and inducement to infringe patents related to the opioid tapentadol

hydrochloride in oral arguments to a panel of the U.S. Court of Appeals for the Federal Circuit on September 4, 2018. Grunenthal GMBH, Depomed, Inc., v. Alkem Laboratories Limited, West-Ward Pharmaceuticals International Limited, Actavis Elizabeth LLC, Case Nos. 2017-1153, 2017-2048, 2017-2049, 2017-2050. The parties appealed and cross-appealed parts of a decision from a bench trial in the U.S. District Court for the District of New Jersey, in which the court found all three patents not invalid and not unenforceable, two of the three patents infringed by all three defendants, one patent infringed by inducement by one party only, and no contributory infringement.

The number of parties, number of issues, and number of patents made for a wide-ranging but somewhat disjointed hearing, during which the three defendants focused on different legal issues. ANDA-filer West-Ward focused on the alleged lack of utility of U.S. Patent 7,994,364 (the ’364 patent), directed to a polymorphic form of the opioid. ANDA-filer Alkem focused on the alleged obviousness of the ’364 patent. ANDA-filer Actavis focused on actions it took to avoid inducing infringement. A scorecard would have been helpful to follow the hearing, as presiding Judge Reyna intimated in his introduction.

Obviousness

Judge Taranto was intrigued by the obviousness issue framed by Alkem: can a routine method applied to a known substance produce a non-obvious product, particularly where no evidence of secondary considerations is presented? Alkem urged that it could not. Judge Taranto said that Alkem’s position may be “crossing a doctrinal bridge.” He also said that it “feels newish,” even “potentially dangerous.”

Judge Chen probed Alkem on whether the process of finding polymorphic forms was actually cookie-cutter or trial-and-error: was there “an answer book?” he asked. Alkem admitted that the cited reference only guided the first step of the process of identifying polymorphic forms. When licensee Depomed began its argument, Judge Taranto immediately asked it to address the obviousness issue. Licensee Depomed highlighted the uncertainties, foremost among them whether a polymorphic form would even exist for the substance that was known in the art. If such a form existed, it was not known whether it would be bioactive or stable. The cited reference that taught how to screen for polymorphs was not an answer book, licensee Depomed answered Judge Chen’s question to Alkem, and in any event the claims were directed to a new chemical entity with a new structure, not to the screening process for polymorphs. Depomed reminded the panel that Section 103 of the patent statute specifically states that how the invention was made is immaterial: “Patentability shall not be negatived by the manner in which the invention was made.” Although Alkem’s legal theory on obviousness seemed to generate the most interest among the panel, the facts (the prior art teachings) did not seem to support its theory.

During Alkem's rebuttal time, Judge Taranto asked Alkem what case holds that a reasonable expectation of success can exist when the result is unknown. Alkem pointed to In re Kubin,[1] a case in which a nucleic acid encoding a protein was found obvious over prior art disclosing the protein, a monoclonal antibody specific for the protein, and instructions for isolating the particular claimed nucleic acid. Judge Taranto distinguished that case because the existence of the nucleic acid was predictable, but the existence of the polymorph in the current case was not. Another distinction not noted in the oral arguments was a specific teaching in the prior art of Kubin of how to obtain the particular gene. Thus the prior art in Kubin had more elements and more specificity than the prior art in the current appealed case.

Utility

West-Ward seemed to advance a multi-pronged challenge to the utility of the claimed polymorph, form A of tapentadol hydrochloride. First, it characterized claimed form A as an improvement over prior art form B. It advanced the theory that the statutory language of 35 U.S.C. § 101 requires that the improvement itself must be new and useful, which requires a new use for the improvement different from that of the base invention. The utility of the prior art form B, West-Ward urged, could not be used as the utility that supports patentability for recited form A. The statute reads (emphasis added):

> Whoever invents or discovers a 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.

In its second prong, West-Ward urged that the utilities found by the district court for the claimed polymorph (same pharmaceutical activity as the prior art polymorph and increased stability) were legally erroneous. Because the claimed form A converts to prior art form B, and the two forms have the same pharmaceutical activity, the so-called increased stability is illusory. West-Ward asked what benefit over form B does form A provide? Seeming to dismiss West-Ward's assertion, both Judges Taranto and Chen noted that the law does not require an improvement over the prior art. West-Ward's novel statutory construction of Section 101 pushed the boundaries of existing law, and the panel did not seem to be persuaded.

In its brief, West-Ward asserted a third prong: failure to comply with 35 U.S.C. § 101 because the patent did not disclose data showing efficacy of form A or increased stability of form A. In its rebuttal time, West-Ward mentioned that to show stability one needs dissolution testing. It asserted that patent owner Grunenthal had the results of dissolution testing, but had not disclosed them, seeming to echo its position that data must be disclosed in a patent application to support an asserted utility.

Inducement to Infringe

The FDA-approved label for the branded tapentadol hydrochloride (Nucynta®) lists two indications: (1) severe chronic pain, and (2) polyneuropathic pain. Each of the ANDA filers deleted indication (2) from its proposed label. The issue of inducement arises in this case because the two indications are not separate and distinct. Rather, indication (2) is a subset of indication (1). The ANDA-filers asserted that they do not specifically induce infringement because their labels only mention the generic indication (1). NDA-holder Depomed urged that because the population of patients with polyneuropathic pain is a large proportion of the population with severe chronic pain, prescribers invariably will be induced to infringe simply by following indication (1). Depomed also urged that the ANDA-filers would contributorily infringe because the non-infringing use for severe chronic pain that is not polyneuropathic pain would be rare. The unusual genus/species relationship of the clinical indications recited in the patent claim and recited on the ANDA-filers' drug labels could perhaps lead the Federal Circuit to reconsider the district court's findings of no inducement to infringe and/or no contributory infringement.

ANDA-filer Actavis urged that its deletion of indication (2) constituted a carve-out that shows that it had no intention to encourage the practice of prescribing for indication (2). Judge Chen asked if prescribing doctors would know about the carve-out. Actavis said they would see it. Judge Chen asked if prescribing doctors would know that the branded version of the drug had two indications. His question implied that if they knew, they would be alerted to the absence of indication (1) in the ANDA-filers' labels.

Depomed responded to Actavis' position by reminding the court that a label with only indication (1) still includes treatment of polyneuropathic pain. Depomed said that the district court found that 95 percent of uses would be for polyneuropathic pain. Depomed asserted that the court legally erred in permitting a small amount of non-infringing use to negate the inducement to infringe.

We look forward to seeing which, if any, of the interesting issues advanced by the parties has sufficient traction to cause the Federal Circuit to change the disposition reached by the district court.

Click here to listen to oral arguments in Grunenthal GMBH, Depomed, Inc., v. Alkem Laboratories Limited, West-Ward Pharmaceuticals International Limited, Actavis Elizabeth LLC.

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[1] 561 F.3d 1351 (Fed. Cir. 2009)

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