



Client Alert

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Federal Court Ruling Addresses Patent Issue: When is a Combination Drug Obvious?

Therapies using combinations of two or more drugs have become more common in recent years. Often these combinations are produced from already known and FDA approved products. Not only do the combination drugs provide a health benefit, it is also desired that they produce a patent benefit as well. While patent protection may have already run out for the individual ingredients, the new combination product may be able to get its own patent protection. In fact, it is this "combo" protection that can help offset the development costs for researching and moving the combination product through the regulatory process. In Ortho-McNeil Pharmaceutical Inc. v. Teva Pharmaceuticals Industries Ltd. Slip Opinion 2008-1549, -1550 (Fed. Cir. 2009) the Federal Circuit looked at the patentability of a well known combination formulation, and in so doing provided some direction as to the value of patents and applications on combination drug products.

Ortho-McNeil patented a combination drug containing Tramadol and Acetaminophen (US patent No 5,336,691, the "691 patent") which was sold as Ultracet®. After filing lawsuits against several generic drug companies, the generics alleged the '691 patent was invalid for anticipation and obviousness. During the litigation, Ortho-McNeil entered reexamination on the '691 patent to overcome prior art involving Tramadol and p-acetamino-phenol (Acetaminophen). After narrowing all but one of their claims, the new claims were allowed and issued in reissue patent RE 39,221 (the "221 patent").

Upon grant of the '221 patent, Ortho sued Teva Pharmaceuticals, KALI Laboratories and Caraco Pharmaceutical Laboratories for infringement. The district court issued a summary judgment invalidating all of the claims in the '221 patent as obvious. On Appeal, the Federal Circuit vacated the district court's summary judgment of invalidity for all claims but claim 6 (the one claim that was not amended in the reexam).

Looking at the different reasoning used by the Federal Circuit in maintaining claim 6 as invalid, and overturning the finding of obviousness of the remanded claims sheds light on the patentability of combination claims in general. Claims 43-48, 51, 54, 67, 69, 72, 74 (the "remanded claims") covered a combination "consisting of" Tramadol and Acetaminophen in a ratio of 1:5 to 1:19. The art disclosed a combination product having four active pharmaceutical ingredients (APIs), including Tramadol and Acetaminophen. Ortho-McNeil submitted evidence that drugs and their interactions with other drugs are unpredictable and that there would not be an expectation that the combination of just Tramadol and Acetaminophen in the absence of the other two APIs

would work at the ratios claimed, based on the prior art. Therefore, the results of Ortho-McNeil's combination would be unexpected. This was persuasive to the Federal Circuit which vacated the holding of invalidity on summary judgment and remanded for trial on the merits of the evidence submitted.

On the other hand, the court distinguished Claim 6, which was drawn to a composition "comprising" Tramadol and Acetaminophen in "about a 1:5 ratio". The court reasoned the term "comprising" gives a broad, open meaning to the composition. Therefore, the only difference between the prior composition with four APIs and the claimed composition of Ortho-McNeil with two APIs was the specific ratio of the APIs in the formulation. The court concluded this limitation in claim 6 that the ratio was about a 1:5 ratio, did not provide a sufficient limitation to make it nonobvious over the prior art which taught a 1:10 ratio. The court relied on well established law that a minor difference in ranges is not enough to overcome a prima facie case of obviousness. Ortho at 9 (citing, Haynes Int'l, Inc. v. Jessop Steel Co, 8 F.3d 1573, 1577 n.3 (Fed. Cir. 1993). "[W]hen the difference between the claimed invention and the prior art is the range or value of a particular variable, then a prima facie rejection is properly established when the difference in range or value is minor.")

Ortho provides a number of take home lessons for combination drug innovators. First, absent clear unexpected results or a significant teaching away from a particular formulation, the ratios of the APIs in the formulation alone, as a matter of law, may be insufficient to rebut a prima facie case of obviousness over art disclosing a composition having the same APIs but at different ratios. Second, if a combination of drugs is different than any prior art combination of drugs, evidence of unpredictability in combining different drugs and unexpected results can overcome a prima facie case of obviousness. Ortho found this to be true even when the art combined the same APIs claimed in the their combination, but did so along with other APIs.

Lastly, the importance of the link between claim scope, patentability, and ultimate value cannot be overstated. Patenting combination drugs requires well thought out claims that are broad enough to cover your product and likely infringers, yet narrow enough to properly exclude art which may be out there. The positive result for the patentee in Ortho, largely turned on a one word change in the claims: "comprising" to "consisting". The evidence of non-obviousness arose from the results of "just" Tramadol and Acetaminophen in the combination, nothing more. Ortho-McNeil significantly narrowed its claim, such that the claim would not prevent use of a combination of Tramadol, Acetaminophen and just one more API, but because of this narrowing, these claims were not obvious as a matter of law.

While generally it is believed that broad claims are more powerful than narrow claims, in the arena of pharmaceuticals where barriers to entry for different or new products are substantial, a narrow claim along with the data exclusivity granted to innovators in the regulatory process can be just as powerful as, and more valuable than, the broad claim. Just ask Ortho-McNeil, who is surely thankful for having a narrow claim, covering a competitor's infringing product, that survived an invalidity challenge when their broad claim did not.

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