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# PTAB HIGHLIGHTS

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## PTAB Denies Lupin's IPR in Win for Pozen – Claimed Tablet That Provided Coordinated Drug Release Not Suggested by Prior Art, Which Had a Preferred Formulation That Provided the Reverse Release

By Robert H. Resis

March 9, 2016 — The Patent Trial and Appeal Board recently denied institution of a Lupin *inter partes* review against a Pozen patent covering VIMOVO® (naproxen/esomeprazole magnesium delayed-release tablets, commercially sold by Horizon Pharma plc).

[IPR2015-01774 – Lupin Ltd. et al. v. Pozen Inc. \(Paper 15\)](#)

A key takeaway from this case is that a patent challenger should avoid relying on a prior art reference having a preferred formulation that provides the reverse result from the result provided by the claimed invention, even if seemingly valid arguments could be made that it would have been obvious to modify the prior art's preferred formulation to provide the claimed invention.

Lupin's petition asserted five obviousness grounds against claims of Pozen's U.S. 8,852,636 (the '636 patent), entitled "Pharmaceutical Compositions for the Coordinated Delivery of NSAIDs [non-steroidal anti-inflammatory drugs]." Pozen's Preliminary Response (Paper 14) contended that all of Lupin's asserted grounds failed. While not stating so in its denial to institute, the PTAB largely agreed with Pozen. The PTAB found that Lupin failed to establish a reasonable likelihood that it would prevail in showing the challenged claims unpatentable under 35 U.S.C. § 103(a).

The '636 patent discloses a drug composition that provides for the coordinated release of an acid inhibitor and a NSAID, such that there is a reduced likelihood of causing unwanted gastrointestinal side effects, when administered as a treatment for pain. More specifically, the '636 patent discloses a drug composition wherein the acid inhibitor is released first, and the release of the NSAID is delayed until after the pH in the patient's gastrointestinal tract (GI) has risen — i.e., such that a polymeric barrier coating surrounding an inner core comprising the NSAID does not dissolve unless the surrounding medium is at a pH of at least 3.5. Representative claim 1 of the '636 patent is directed to a unit dosage form as a tablet where the acid inhibitor is esomeprazole, and the NSAID is naproxen. Claim 1 recites that esomeprazole is in one or more layers outside a core comprising naproxen, wherein the one or more layers A) do not include a naproxen; B) are not surrounded by an enteric coating; and C) upon ingestion of said tablet by a patient, release said esomeprazole into said patient's stomach.

Lupin's asserted Ground 1 was based on a prior patent to Chen (U.S. 6,544,556) in view of an article of Chandramouli et al., and Ground 2 was passed on the Chen '556 patent in view of a prior patent to Gimet (U.S. 5,698,225). Lupin contended that Chen discloses an oral solid dosage form, e.g., a tablet, comprising a therapeutically effective amount of an NSAID and a proton pump inhibitor (PPI) in an amount effective to inhibit or prevent gastrointestinal side effects normally associated with the NSAID. Lupin also contended that Chen expressly discloses that the NSAID may be naproxen and the PPI may be omeprazole or omeprazole's *S*-enantiomer, esomeprazole, both of which were known in the art for reducing the risk of gastroduodenal injury associated with NSAID use.

Lupin acknowledged that Chen "discloses a preferred formulation that would release the NSAID in the stomach [i.e., first] and omeprazole in the small intestine [i.e., second]," but argued that Chen "is not limited to such formulations," and discloses generally "formulations with pH-dependent and pH-independent coatings to permit the coordinated release of one drug before the other." Lupin relied on its expert's testimony that it would have been obvious for one of ordinary skill in the art "to develop a . . . tablet with esomeprazole released before naproxen," specifically, "a core with naproxen surrounded by a pH-dependent enteric coating and non-enteric coated esomeprazole."

Additionally, in support of the assertion that one of ordinary skill in the art "would have known at least a portion of non-enteric coated, unbuffered esomeprazole would be bioavailable upon oral administration," Lupin and its expert cited a prior art study by Pilbrant, which according to Lupin, "compar[es] the bioavailability of non-enteric coated omeprazole when administered with and without a buffer and teaches a substantial portion of the uncoated omeprazole is bioavailable." Lupin further contended that in prior litigation, the Federal Circuit "has acknowledged that Pilbrant teaches non-enteric solid dosage forms of PPIs as a 'viable alternative to enteric coating.'"

The PTAB was not persuaded. First, the PTAB found that Lupin relied on selective portions of Chen, without adequate consideration of the surrounding context. Further, the PTAB found that

Lupin did not point to where Chen discloses or suggests doing the reverse, i.e., enterically coating a NSAID so that it is released further down the GI tract (where the pH is higher), and releasing “unprotected” PPI at any pH, such as in the stomach (where the pH is lower). As to Pilbrant, the PTAB found that reference teaches preparing buffered suspensions of non-enteric coated omeprazole, but teaches away from preparing non-enteric coated tablets of the drug. The PTAB found that Lupin did not explain sufficiently why an ordinary artisan would have had a reasonable expectation of success in making a tablet comprising esomeprazole with no coating or a non-enteric coating, that releases the PPI regardless of the pH, i.e., in the stomach, as required by the claims of the '636 patent.

The PTAB was also not persuaded that Lupin had established a reasonable likelihood of prevailing on its other obviousness grounds not based on Chen. Thus, Pozen was able to stop an IPR attempted by Lupin before it was instituted. Restricted by IPR rules against submitting its own expert declaration in its preliminary response to Lupin’s petition, and restricted against new evidence in general, Pozen nevertheless was able to present an effective argument from the petition-cited references themselves. Effective use of available evidence by the patent owner that demonstrates non-obviousness, e.g., showing that it would not have been obvious to modify the prior art’s preferred formulation to provide the opposite result, is another key takeaway. The petitioner anticipating such a take-down effort and preparing a petition that will survive it is another.

*The Leahy-Smith America Invents Act established new patent post-issuance proceedings, including the inter partes review, post grant review and transitional program for covered business method patents, that offer a less costly, streamlined alternative to district court litigation. With the U.S. Patent and Trademark Office’s Patent Trial and Appeal Board conducting a large and increasing number of these proceedings, and with the law developing rapidly, Banner & Witcoff will offer weekly summaries of the board’s significant decisions and subsequent appeals at the U.S. Court of Appeals for the Federal Circuit.*



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