# United States Court of Appeals for the Federal Circuit

03-1300

KNOLL PHARMACEUTICAL COMPANY, INC. and
THE JOHN AND LOIS ARNOLD FAMILY LIMITED LIABILITY PARTNERSHIP,

Plaintiffs-Appellants,

v.

TEVA PHARMACEUTICALS USA, INC.,

Defendant-Appellee.

James R. Ferguson, Mayer, Brown, Rowe & Maw LLP, of Chicago, Illinois, argued for plaintiffs-appellants. With him on the brief was Michele L. Odorizzi.

Kenneth A. Cohen, Goodwin Procter LLP, of Boston, Massachusetts, argued for defendant-appellee. With him on the brief were Carl M. DeFranco, Jr. and Greer N. Shaw.

Appealed from: United States District Court for the Northern District of Illinois

Judge John W. Darrah

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DECIDED: May 19, 2004

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Before NEWMAN, Circuit Judge, ARCHER, Senior Circuit Judge, and PROST, Circuit Judge.

PER CURIAM.

In this patent litigation between Knoll Pharmaceutical Company, Inc. and The John and Lois Arnold Family Limited Liability Partnership (collectively "Knoll") and Teva Pharmaceuticals USA, Inc. ("Teva"), Knoll appeals the summary judgment of invalidity of United States Patent No. 4,587,252 ("the '252 patent"), entered by the United States District Court for the Northern District of Illinois.[1] The judgment is reversed. We remand for further proceedings.

BACKGROUND

[1] Knoll Pharm. Co. v. Teva Pharms. USA, Inc., No. 01-C1646, 2002 WL 31050138 (N.D. Ill. Sep. 13, 2002).

The '252 patent is directed to methods and compositions for treating pain by administering a combination of hydrocodone and ibuprofen in specified amounts. The claims are as follows:

> 1. A process for treating pain in a mammal which comprises administering to the mammal an amount of a pharmaceutical composition effective to provide an analgesic effect, said pharmaceutical composition comprising hydrocodone or a pharmaceutically acceptable acid addition salt thereof and ibuprofen or a pharmaceutically acceptable acid addition salt thereof, the ratio of hydrocodone to ibuprofen being within the range that the administration of a therapeutic amount of said composition to a mammal will provide a greater analgesic effect than the effect obtainable by use of either hydrocodone or a pharmaceutically acceptable acid addition salt thereof or ibuprofen or a pharmaceutically acceptable acid addition salt thereof alone.
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> 2. A pharmaceutical composition which comprises hydrocodone or a pharmaceutically acceptable acid addition salt thereof and ibuprofen or a pharmaceutically acceptable acid addition salt thereof in amounts that are sufficient to provide an analgesic effect, the ratio of hydrocodone to ibuprofen being within the range that the administration of a therapeutic amount of said composition to a mammal will provide a greater analgesic effect than the effect obtainable by use of either hydrocodone or a pharmaceutically acceptable acid addition salt thereof or ibuprofen or a pharmaceutically acceptable acid addition salt thereof alone.
>
> 3. A process for treating pain in a mammal which comprises administering to the mammal one part by weight of hydrocodone or a pharmaceutically acceptable acid addition salt thereof and about 20 to 80 parts by weight of ibuprofen or a pharmaceutically acceptable salt thereof.
>
> 4. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and an analgesically effective amount of:
>
> (a) one part by weight of an analgesic agent selected from the group consisting of hydrocodone and pharmaceutically acceptable acid addition salts thereof, and
>
> (b) about 20 to 80 parts by weight of ibuprofen or a pharmaceutically acceptable salt thereof.
>
> 5. A process for treating pain in a mammal which comprises administering to the mammal a dosage unit comprising about 5 to 10 mg. of hydrocodone or a pharmaceutically acceptable acid addition salt thereof

and about 200 to 400 mg. of ibuprofen or a pharmaceutically acceptable salt thereof.

6. A pharmaceutical composition in unit dosage form comprising a pharmaceutically acceptable carrier and (a) about 5 to 10 mg. of an analgesic agent selected from the group consisting of hydrocodone and pharmaceutically acceptable acid addition salts thereof, and

(b) about 200 to 400 mg. of ibuprofen or a pharmaceutically acceptable salt thereof.

In 1997 Knoll received approval from the Food and Drug Administration to market Vicoprofen®, a pharmaceutical composition in tablet form containing 7.5 mg of hydrocodone bitartrate and 200 mg of ibuprofen, for pain relief. In 2000 Teva filed an Abbreviated New Drug Application ("ANDA"), in accordance with the Hatch-Waxman Act, seeking authorization to market tablets containing 7.5 mg of hydrocodone bitartrate and 200 mg of ibuprofen, and asserting under 21 U.S.C. §355(j)(2)(A)(vii)(IV) that the '252 patent is invalid, unenforceable, and/or not infringed. On the basis of Teva's ANDA, Knoll brought suit under 35 U.S.C. §271(e)(2) for infringement of the '252 patent. On Teva's motion for summary judgment, the district court ruled that the patent is invalid on the ground of obviousness.

## DISCUSSION

We review grants of summary judgment de novo. Conroy v. Reebok Int'l Ltd., 14 F.3d 1570, 1575 (Fed. Cir. 1994). In a patent case, as in any other, summary judgment may be granted when there are no disputed issues of material fact, Chore-Time Equip., Inc. v. Cumberland Corp., 713 F.2d 774, 778-79 (Fed. Cir. 1983), or when the non-movant cannot prevail on the evidence submitted when viewed in a light most favorable to it. See Caterpillar Inc. v. Deere & Co., 224 F.3d 1374, 1379 (Fed. Cir. 2000) ("When ruling on a motion for summary judgment, all of the nonmovant's evidence is to be

credited, and all justifiable inferences are to be drawn in the nonmovant's favor.") The grant of summary judgment of invalidity for obviousness must be done on a claim by claim basis. Dayco Prods., Inc. v. Total Containment, Inc., 329 F.3d 1358, 1371 (Fed. Cir. 2003). The accused infringer must prove by clear and convincing evidence that each claim that is challenged cannot reasonably be held to be non-obvious. Monarch Knitting Machinery Corp. v. Sulzer Morat GmbH, 139 F.3d 877, 881 (Fed. Cir. 1998).

The district court held that the subject matter of all the claims was obvious in view of the prior art, and granted summary judgment of invalidity. The court stated:

> The prior art expressly teaches one of ordinary skill in the art to combine an opioid with an NSAID. Furthermore, based on the prior art, a person of ordinary skill in the art of pain management would have had a reasonable expectation of success in combining hydrocodone, a narcotic analgesic, with ibuprofen, an NSAID.

Knoll, 2002 WL 31050138, at *13.

Although the prior art appears to suggest combining an opioid, such as hydrocodone, with various NSAIDs, such as ibuprofen, we conclude, based on the evidence adduced by Knoll, that a genuine factual dispute exists as to the obviousness of the asserted claims which makes summary judgment based on the present record evidence improper. There appears to be no record of evidence of prior art teaching or suggesting the enhanced biomedical effect of the combination of hydrocodone and ibuprofen. The district court refused to consider evidence Knoll presented to show unexpected results using the combination of hydrocodone and ibuprofen, for the reason that the "unexpected benefits or results were discovered after the '252 patent had been issued." Knoll, 2002 WL 31050138, at *14. Contrary to the district court's perception, the specification expressly acknowledges that the efficacy of the combination is "surprising," in that it provides an analgesic effect greater than that obtained by

increasing the dose of either constituent administered alone. '252 patent, col. 1, lines 26-29. In the experimental models in the specification, the analgesia provided by the combination was said to be greater "than that obtained by using either analgesic alone even if the dose is increased." Id. at col. 2, lines 3-5, 13-17.

To further demonstrate the unexpected activity of the claimed combination, Knoll submitted additional data directed to similar showings of efficacy. Three of the later studies submitted to the district court concerned the synergistic interaction of hydrocodone and ibuprofen when administered together for pain relief. The fourth study reported enhanced muscle repair after exercise following administration of the combination of hydrocodone and ibuprofen, an aspect not unrelated to pain relief. Evidence developed after the patent grant is not excluded from consideration, for understanding of the full range of an invention is not always achieved at the time of filing the patent application. It is not improper to obtain additional support consistent with the patented invention, to respond to litigation attacks on validity. There is no requirement that an invention's properties and advantages were fully known before the patent application was filed, or that the patent application contains all of the work done in studying the invention, in order for that work to be introduced into evidence in response to litigation attack. Nor is it improper to conduct additional experiments and provide later-obtained data in support of patent validity.

Knoll also argues that the district court erred in refusing to consider evidence of the failure of others to develop an opioid-NSAID combination, including abandonment of certain FDA registration applications. The so-called "objective" criteria must always be considered, Graham v. John Deere Co., 383 U.S. 1, 17-18 (1966), and given whatever weight is warranted by the evidence presented. See Pro-Mold & Tool Co. v. Great

Lakes Plastics, Inc., 75 F.3d 1568, 1572 (Fed. Cir. 1996) (considering failure of others to find a solution to the problem); Transmatic, Inc. v. Gulton Indus., Inc., 53 F.3d 1270, 1275 (Fed. Cir. 1995) (considering failure of others to make the invention). The proffered objective evidence was the failure of two pharmaceutical companies to obtain FDA approval for codeine-naproxen sodium and codeine-ibuprofen combinations. The district court did not ignore this evidence, but pointed to several other opioid-NSAID compositions available on the market, and concluded that Knoll's evidence was insufficient for a finding of failure by others. The district court erred by failing to view the evidence in an appropriate light, namely, in a light most favorable to Knoll. At a minimum, the conflicting evidence reinforces the patentee's argument that the activity observed for the patented combination is not routinely present for all opioid-NSAID combinations.

The evidence adduced did not establish undisputed facts to support the summary judgment of invalidity. That judgment is reversed and remanded for further proceedings in regard to validity and infringement.

REVERSED AND REMANDED