NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

WARNER CHILCOTT COMPANY, LLC, WARNER CHILCOTT (US), LLC,
Plaintiffs-Appellants

v.

TEVA PHARMACEUTICALS USA, INC.,
Defendant-Appellee

RANBAXY, INC., RANBAXY LABORATORIES LIMITED, WATSON LABORATORIES, INC. - FLORIDA,
Defendants

2015-1588

Appeal from the United States District Court for the District of New Jersey in No. 2:11-cv-06936-SRC-CLW, Judge Stanley R. Chesler.

Decided: March 18, 2016

JEFFREY B. ELIKAN, Covington & Burling LLP, Washington, DC, argued for plaintiffs-appellants. Also represented by GEORGE FRANK PAPPAS, KEVIN B. COLLINS, BRADLEY KEITH ERVIN.

ELIZABETH HOLLAND, Goodwin Procter LLP, New York, NY, argued for defendant-appellee. Also represented by ROBERT V. CERWINSKI, LINNEA P. CIPRIANO; CHRISTOPHER T. HOLDING, Boston, MA; WILLIAM M. JAY, Washington, DC; DAVID ZIMMER, San Francisco, CA.

Before LOURIE, DYK, and HUGHES, *Circuit Judges*.

LOURIE, *Circuit Judge*.

Warner Chilcott Company, LLC and Warner Chilcott (US), LLC (collectively, "Warner Chilcott") appeal from the decision of the United States District Court for the District of New Jersey holding claim 16 of U.S. Patent 7,645,459 ("the '459 patent") and claim 20 of U.S. Patent 7,645,460 ("the '460 patent") invalid as obvious. *Warner Chilcott Co., LLC v. Teva Pharm. USA, Inc.*, 89 F. Supp. 3d 641 (D.N.J. 2015) ("*Opinion*"). Because the district court did not err in concluding that the asserted claims are invalid, we *affirm*.

BACKGROUND

Warner Chilcott owns the '459 and '460 patents, which are directed to oral dosage forms comprising risedronate (a bisphosphonate) and disodium ethylenediaminetetraacetic acid (herein referred to as "EDTA"), and methods of treating diseases characterized by abnormal calcium and phosphate metabolism, *e.g.*, osteoporosis. Because risedronate complexes with calcium ions in food, its absorption is significantly diminished when administered in a fed state, *viz.*, taken with or soon after a meal. A chelating agent, such as EDTA, can preferentially bind calcium ions, thus blocking calcium–risedronate complex formation in a fed state and thereby freeing up risedronate for absorption. However, the chelating agent may also bind the calcium ions from the intestinal wall in a fasted state, and thereby increase absorption in a more

undesirable fashion by widening the tight junctions between cells. During prosecution of the patents, the examiner originally rejected the claims as obvious over prior art disclosing the use of EDTA for increasing bisphosphonate absorption. The patentee overcame that rejection by adding the limitation "pharmaceutically effective absorption," which is defined by the specification[1] as:

> an amount of a chelating compound high enough to significantly bind the metal ions and minerals in food but low enough not to significantly alter absorption of the bisphosphonate as compared to absorption in the fasted state. That is, absorption is similar with or without food. Given the high variability of bisphosphonate absorption, fed exposure within about 50% of fasting exposure is expected to be "pharmaceutically effective absorption."

'459 patent, col. 4 ll. 59–66.

Warner Chilcott's commercial embodiment of the '459 and '460 patents is Atelvia®, an oral formulation for treating osteoporosis, comprising 35 mg risedronate and 100 mg EDTA. Teva Pharmaceuticals USA, Inc. ("Teva") filed an Abbreviated New Drug Application ("ANDA") with the U.S. Food and Drug Administration, seeking approval for a generic version of Atelvia®. Warner Chilcott filed suit, asserting infringement of the '459 and '460 patents by the filing of Teva's ANDA. The only claims at issue during trial were claim 16 of the '459 patent and claim 20 of the '460 patent, both of which Teva had stipulated to infringing.

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[1] The '459 and '460 patent specifications are substantially similar, and therefore are referred to jointly.

The asserted dependent claims, with the text of the parent claims incorporated, read as follows:

> 16. An oral dosage form having pharmaceutically effective absorption comprising:
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> (a) [about 35 mg] of risedronate sodium;
>
> (b) [about 100 mg] of disodium EDTA; and
>
> (c) an enteric coating [that is a methacrylic acid copolymer] which provides for release of the risedronate sodium and the disodium EDTA in the lower gastrointestinal tract of a mammal.

'459 patent, col. 38 l. 49 – col. 39 l. 13.

> 20. An oral dosage form having pharmaceutically effective absorption comprising:
>
> (a) [about 35 mg of] risedronate sodium;
>
> (b) [about 100 mg] of disodium EDTA; and
>
> (c) an enteric coating [that is a methacrylic acid copolymer] which provides for immediate release of the risedronate sodium and the disodium EDTA in the small intestine of a mammal.

'460 patent, col. 24 l. 47 – col. 25 l. 20.

The district court held a bench trial and concluded that the asserted claims were invalid as obvious. The court noted that the parties agreed that Brazilian Patent Application BR2001-06601 ("BR '601") contains all of the limitations of the claims except "pharmaceutically effective absorption." *Opinion*, 89 F. Supp. 3d at 646.

First, the district court found that the claimed 35 mg risedronate dose was disclosed as the most commonly prescribed regimen (a 35 mg dose), and by BR '601's teaching of an "effective quantity" of bisphosphonate. *Id.*

at 653–54. The court next found that BR '601 discloses 20–175 mg EDTA, which includes the claimed 100 mg amount. *Id.* at 654–56. Because the compounds "work independently of each other and are not interdependent," as confirmed by the specification's broad disclosure of greatly varying ratios of bisphosphonate to EDTA that all supposedly exhibit pharmaceutically effective absorption, the court found that the claimed 100 mg amount of EDTA was not critical within the range disclosed in the prior art. *Id.* at 655–56. The court therefore found that BR '601 discloses the claimed ingredients and amounts "in the same combination, for substantially the same function." *Id.* at 657.

The district court then analyzed whether BR '601 discloses the "pharmaceutically effective absorption" limitation. The court found that BR '601 teaches using an amount of EDTA sufficient to bind ions in food, albeit an amount inherently low enough not to significantly alter absorption. *Id.* at 657–58. The court credited expert testimony that substantially more than 175 mg of EDTA would be required to increase intestinal permeability even in the fasted state. *Id.* at 658. The court, however, found insufficient evidence to show that any embodiment of BR '601 would necessarily produce similar fed/fasted absorption, and thus found that the reference did not inherently disclose pharmaceutically effective absorption. *Id.* at 658–59. Accordingly, the court found that BR '601 did not anticipate the asserted claims. *Id.* at 659.

Instead, the district court concluded that BR '601 renders the claims obvious. The court found that one of skill would have recognized the food-effect problem with bisphosphonates and the solution of using chelators to block calcium ions. *Id.* at 661. The court characterized that solution as having been "well explored in the literature," and reviewed the references teaching that EDTA increases absorption by reducing calcium–bisphosphonate complex formation, as well as references explicitly noting

that EDTA may also do so by damaging the tight junctions and thereby enhancing permeability. *Id.* at 661–68. The court also found that other references teach using a chelator to solve the food effect and suggest using EDTA for less variable absorption. *Id.* at 661–62. The court noted that another reference disclosed eliminating the food effect for a different drug that also has reduced absorption due to calcium-complexes, by using an amount of EDTA equimolar to the calcium ions expected in the stomach. *Id.* at 662. The court further found that the reference teaches that 250 of mg EDTA does not change absorption in a fasted state and thus provides similar bioavailability irrespective of diet. *Id.*

The district court additionally rejected Warner Chilcott's arguments of teaching away by the prior art, instead finding that the art was either irrelevant or the earlier concerns were addressed by later references like BR '601. *Id.* at 662–68. Instead, the court determined that one of skill in the art would have been motivated to modify or combine BR '601 with other prior art references to achieve the claimed invention, based on the teachings found within the references, with a reasonable expectation of success in achieving similar absorption in fed/fasted states. *Id.* at 675–80.

The district court also considered Warner Chilcott's evidence of objective considerations, but concluded that that evidence did not show nonobviousness. The court found some long-felt need for improving patient compliance, although there existed alternatives such as weekly dosing, but relatedly, no proof of improved compliance as an unexpected result of the claimed invention, *id.* at 668; simultaneous invention by a third party, Takeda, *id.* at 670–71; insufficient evidence of skepticism by skilled artisans, *id.* at 671–72; and no nexus between the claimed invention and Teva's alleged failures or copying, *id.* at 672. The court therefore concluded that the asserted claims would have been obvious in view of the prior art.

Warner Chilcott timely appealed to this court. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

DISCUSSION

Patents are presumed to be valid, and overcoming that presumption requires clear and convincing evidence. 35 U.S.C. § 282; *Microsoft Corp. v. i4i Ltd. P'ship*, 564 U.S. 91, 131 S. Ct. 2238, 2242 (2011). A patent claim is invalid as obvious if an alleged infringer proves that the differences between the claims and the prior art are such that "the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." 35 U.S.C. § 103(a) (2006).[2]

Obviousness is ultimately a conclusion of law premised on underlying findings of fact, including the scope and content of the prior art, the differences between the claimed invention and the prior art, and the evidence of secondary factors, such as long-felt need, industry skepticism, and copying. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 427 (2007); *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966). "The presence or absence of a motivation to combine references in an obviousness determination is [also] a pure question of fact." *Alza Corp. v. Mylan Labs.*, 464 F.3d 1286, 1289 (Fed. Cir. 2006). In addition to common knowledge or teachings in the prior art itself, a "design need or market pressure or other motivation" may provide a suggestion or motivation to combine prior art elements in the manner claimed. *Rolls Royce, PLC v. United Techs. Corp.*, 603 F.3d 1325, 1339 (Fed. Cir. 2010);

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[2] Because the '459 and '460 patents were filed before the effective date of the America Invents Act, the earlier, pre-Act version of § 103(a) applies to this appeal. *See* Leahy–Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284, 293 (2011).

accord KSR, 550 U.S. at 420. Moreover, when there are "a finite number of identified, predictable solutions," one of skill in the art "has good reason to pursue the known options within his or her technical grasp." *KSR*, 550 U.S. at 421.

On appeal from a bench trial, we review a district court's conclusions of law *de novo* and its findings of fact for clear error. *Golden Blount, Inc. v. Robert H. Peterson Co.*, 365 F.3d 1054, 1058 (Fed. Cir. 2004). A factual finding is only clearly erroneous if, despite some supporting evidence, we are left with the definite and firm conviction that a mistake has been made. *United States v. U.S. Gypsum Co.*, 333 U.S. 364, 395 (1948).

Warner Chilcott argues that the district court misinterpreted "pharmaceutically effective absorption" and erroneously equated the invention with overcoming the food effect. Instead, Warner Chilcott insists, the limitation requires *similar* fed and fasted absorption of the drug, not merely absorption of an effective amount in either fed or fasted state. Warner Chilcott further contends that the specific amounts of risedronate and EDTA are critical, as only the claimed formulation has been shown to achieve such absorption. Based on the prior art's warnings against the clinical use of EDTA, Warner Chilcott contends, one of skill in the art would have been dissuaded from using as high as 100 mg of EDTA to increase drug absorption, particularly if that increase was understood to be effectuated at least in part by altering the permeability of the intestinal wall. As a result, Warner Chilcott disputes the district court's finding of a motivation to modify the prior art to achieve the claimed invention. Warner Chilcott lastly faults the district court for discounting the objective evidence of nonobviousness, including evidence of Teva's copying of the claimed formulation, particularly because Teva's expert failed to account for such evidence in his analysis.

Teva responds that the prior art teaches the use of EDTA not only to overcome the food effect but also to achieve similar fed/fasted absorption. Teva points out that the specification teaches that broad ranges of EDTA produce the claimed pharmaceutically effective absorption, and contends that 100 mg is not a critical amount because the compounds work independently and therefore changes to the proportions would not affect drug absorption. Moreover, Teva emphasizes, the claims do not require identical fasted/fed absorption, only similar results with up to ±50% variation. Teva further counters that the prior art teaches increasing bisphosphonate absorption by blocking calcium-complex formation, with an equimolar amount of EDTA to calcium ions at the site of drug release, to achieve a constant rate of absorption. Teva argues that the prior art only inconsistently teaches away from using EDTA, and only from much larger quantities, and that BR '601 addresses the clinical viability concerns with a delayed release formulation. Teva also asserts that the objective evidence presented only further supports the obviousness of providing relatively constant absorption regardless of fasted/fed state.

We agree with Teva that the district court did not err in concluding that the asserted claims would have been obvious to one of skill in the art at the time of the invention. The inventors were not faced with a dearth of prior art: as the district court found, the broad disclosure of BR '601 nearly anticipates, and the only claim limitation it lacks is "pharmaceutically effective absorption." Warner Chilcott gives the pharmaceutically effective absorption limitation the prominence that it must. Although common sense tells us that any pharmaceutical composition entitled to a patent would have to be pharmaceutically effective, as would any such formulation approved by the FDA, the fact is that, without that limitation specifically referring to the fed/fasted absorption defined in the specification, the asserted claims would not have issued from

the original prosecution. Although Warner Chilcott defined the limitation such that it is not equivalent to merely overcoming the food effect, the district court found that pharmaceutically effective absorption would have been a logical and obtainable goal for a drug with bioavailability that is significantly affected by co-administration with food.

We further agree with the district court that Teva proved by clear and convincing evidence that it would have been obvious in view of the prior art to use a chelating agent to bind calcium ions to mitigate the food effect for risedronate and thereby achieve similar fed/fasted absorption. The district court articulated its understanding of the prior art references and the teachings that would have led one of ordinary skill in the art to use EDTA to sufficiently reduce or negate the food effect to obtain the claimed invention. Moreover, in view of the broad disclosures in the specification providing embodiments with varying amounts of EDTA, and nothing in the asserted claims teaching one of skill in the art that or how only the specific 100 mg amount produces pharmaceutically effective absorption, Warner Chilcott failed to show the criticality of the claimed amount. We discern no clear error in the district court's factual findings on the teachings of the prior art or the motivation to modify or combine the art. We therefore find no error in the district court's conclusion that the asserted claims would have been obvious in view of the prior art.

CONCLUSION

We have considered the remaining arguments and conclude that they are unpersuasive. For the foregoing reasons, we conclude that the district court did not err in holding that claim 16 of the '459 patent and claim 20 of the '460 patent are invalid as obvious under 35 U.S.C. § 103, and we therefore affirm the district court's decision.

AFFIRMED