NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

PURDUE PHARMA PRODUCTS L.P.,
AND NAPP PHARMACEUTICAL GROUP LTD.,
Plaintiffs-Appellants,

AND

ORTHO-MCNEIL, INC.,
Plaintiff,

v.

PAR PHARMACEUTICAL, INC.
AND PAR PHARMACEUTICAL COMPANIES, INC.,
Defendants-Cross Appellants.

2009-1553, -1592

Appeals from the United States District Court for the District of Delaware in consolidated Case No. 1:07-CV-00255, Circuit Judge Kent A. Jordan (sitting by designation).

Decided: June 3, 2010

ROBERT J. GOLDMAN, Ropes & Gray LLP, of East Palo Alto, California, argued for plaintiffs-appellants. With him on the brief were SASHA G. RAO; PABLO D. HENDLER and SONA DE, of New York, New York.

DANIEL G. BROWN, Wilson Sonsini Goodrich & Rosati, of New York, New York, argued for defendants-cross appellants. With him on the brief were RON E. SHULMAN, of Palo Alto, California; JENNIFER KOH, of San Diego, California; and NICOLE W. STAFFORD, of Austin, Texas.

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

LOURIE, *Circuit Judge*.

Purdue Pharma Products L.P. and Napp Pharmaceutical Group Ltd. (collectively, "Purdue") appeal from a decision of the United States District Court for the District of Delaware holding U.S. Patents 6,254,887 ("the '887 patent") and 7,074,430 ("the '430 patent") invalid for obviousness. Par Pharmaceutical, Inc. and Par Pharmaceutical Companies, Inc. (collectively, "Par") cross-appeal from the district court's decision finding the '887 and '430 patents not unenforceable due to inequitable conduct. We affirm.

BACKGROUND

Purdue owns the '887 and '430 patents, which claim controlled-release tramadol formations suitable for once-daily oral dosing. Tramadol is an opioid analgesic used to treat moderate to moderately severe pain, including pain from arthritis. Certain claims further limit the tramadol formulation to certain dissolution rates and W_{50} values[1] between ten and thirty-three hours. Ortho-McNeil, Inc. sells once-daily tramadol (branded as Ultram® ER) under a license from Purdue. Par filed an abbreviated new drug application ("ANDA") seeking FDA approval to market generic Ultram® ER, and Purdue filed suit alleging infringement of claims 3, 13, 27, and 29 of the '887 patent and 5, 7, and 11 of the '430 patent. Par counterclaimed that the asserted patents were invalid under 35 U.S.C. § 112 for lack of enablement and written description, invalid under § 103 for obviousness, and unenforceable due to inequitable conduct.

After a five-day bench trial, the district court held that Par's proposed generic tramadol product literally infringed the asserted patents, that the asserted patents were not unenforceable, but that the asserted claims were invalid for obviousness. *Purdue Pharma Prods. L.P. v. Par Pharm., Inc.*, 642 F. Supp. 2d 329 (D. Del. 2009). With regard to invalidity, the district court held that the asserted claims would have been obvious in light of (1) U.S. Patent 5,580,578 ("Oshlack"), which describes formulations of opioid analgesics, including tramadol, for once-daily dosing and (2) what was known in the art about tramadol and once-daily formulations. The court reasoned that the Oshlack patent taught the use of tramadol as one of fourteen different opioid analgesics to be used

[1] The W_{50} value equals the width of an administered drug's plasma profile (plasma concentration over time) at half the drug's maximum plasma concentration.

and that any differences in incorporating tramadol as the active ingredient in a once-a-day formulation would have involved only routine experimentation. *Id.* at 369-73. The court then rejected Purdue's claims of secondary considerations, finding evidence of copying not compelling in the ANDA context where bioequivalency is a prerequisite to FDA approval, and that Purdue's evidence of commercial success was "underwhelming." *Id.* at 373-74.

With regard to unenforceability, the district court found that Par had failed to prove intent to deceive by clear and convincing evidence. Specifically, while finding that the applicants had withheld material experimental data and had submitted a materially misleading declaration ("the Malkowska declaration"), the district court found plausible the inference that the applicants were merely overly aggressive in trying to put a positive spin on the experimental results without intending to deceive the United States Patent and Trademark Office ("PTO"). In reaching that conclusion, the district court relied, *inter alia*, on the credibility of Ms. Malkowska's testimony and the applicants' later disclosure of the more pertinent Napp repeat experiments generated for a foreign litigation. *Id.* at 375-79.

Both Purdue and Par appealed. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

DISCUSSION

Purdue appeals from the district court's decision holding claims 3, 13, 27, and 29 of the '887 patent and 5, 7, and 11 of the '430 patent invalid as obvious. Par cross-appeals from the decision that the asserted patents are not unenforceable due to inequitable conduct. Par also cross-appeals from the district court's finding of infringement in light of the court's claim construction, but, as that

argument merely asserts another ground for affirmance of non-liability, it is not appropriate for cross-appeal, *Voda v. Cordis Corp.*, 536 F.3d 1311, 1324 n.4 (Fed. Cir. 2008), nor is it persuasive. We consider each appeal in turn.

Obviousness

While the ultimate question of obviousness under 35 U.S.C. § 103 is a question of law, reviewed *de novo*, it is based on several underlying factual determinations, which we review after a bench trial for clear error. *Golden Blount, Inc. v. Robert H. Peterson Co.*, 365 F.3d 1054, 1058 (Fed. Cir. 2004). The relevant factual determinations include 1) the scope and content of the prior art, 2) the level of ordinary skill in the art, 3) the differences between the claimed invention and the prior art, and 4) evidence of secondary factors. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966).

Purdue challenges the district court's finding of obviousness on multiple grounds.[2] First, Purdue argues that the district court erred in finding that it would have been obvious in light of Oshlack to select tramadol as an active ingredient for use in a once-daily formulation. Rather, according to Purdue, the prior art teaches away from

[2] Purdue also argues that the district court made two factual errors, erroneously finding that (1) two patents, including Oshlack, were not before the PTO and (2) the use of tramadol disclosed in those patents did not represent work "by another" under § 102(e). Because the outcome is the same regardless whether Oshlack was before the PTO, we need not address this argument. As for Purdue's § 102(e) argument, Purdue raises it for the first time on appeal, and thus it has been waived. *See Sage Prods., Inc. v. Devon Indus., Inc.*, 126 F.3d 1420, 1426 (Fed. Cir. 1997). Even if it had not been waived, Purdue presented no evidence that the disclosures in the two cited patents were the invention of the inventors of the presently contested patents.

selecting tramadol, reporting it as unpredictable and poorly understood, and the development of a one-a-day formulation for tramadol involved time-intensive design (*i.e.*, invention) not routine experimentation. Purdue next argues that the district court erred in finding that the claimed twenty-four hour therapeutic effect and W_{50} values were obvious since, at the time, there were no oral opioid formulations effective for greater than twelve hours and the W_{50} values, which were not disclosed in the prior art, do not emerge from routine experimentation. Finally, Purdue argues that the court gave insufficient weight to its secondary considerations of nonobviousness, including Par's copying of the invention and Ultram® ER's commercial success.

Par responds that the district court correctly found that one skilled in the art would have been motivated to make the claimed tramadol formulation in light of Oshlack's listing of tramadol for use in a once-daily formulation and the prior art's reports of its favorable characteristics. According to Par, Purdue presented no evidence of unexpected results over the Oshlack patent's controlled-release formulations and failed to rebut evidence that only routine experimentation was required to make the claimed formulation. Par also contends that the claimed twenty-four hour therapeutic effect and the claimed W_{50} values (the latter argument raised for the first time on appeal) were obvious as the Oshlack patent disclosed a formulation with a twenty-four hour effective blood concentration that would necessarily have a W_{50} value within the claimed range of ten to thirty-three hours. Finally, Par argues that the district court rightly rejected Purdue's secondary considerations, correctly finding that evidence of copying is not compelling in the Hatch-Waxman context and that the evidence of commercial success was "underwhelming."

We agree with Par and affirm the district court's decision finding the '887 and '430 patents would have been obvious in view of Oshlack. Purdue's asserted claims require (1) a tramadol formulation, (2) a controlled-release coating, and (3) a dosing that is suitable for administration every twenty-four hours or that provides a therapeutic effect for about twenty-four hours. Some claims further recite very broad *in vitro* dissolution ranges, some claims recite an *in vivo* W_{50} value of between ten to thirty-three hours, and some claims recite a controlled-release coating consisting of a water-insoluble wax, a water-insoluble polymer, a water-insoluble cellulose, a mixture of the foregoing, or the water-insoluble cellulose polyvinylpyrrolidone. In comparison, Oshlack discloses a controlled-release tramadol formulation with a similarly broad, although truncated, dissolution profile that provides effective blood levels for about twenty-four hours. '578 patent col.43 l.48–col.44 l.36 claims 43, 44, 47. It also discloses at least one opioid analgesic formulation with a W_{50} value of approximately twelve hours. *Id.* col.37 ll.28-31 Fig 8. And it discloses controlled-release coatings comprising polymethacrylate, a water-insoluble polymer, and polyvinylpyrrolidone.

Purdue's main argument is that a person of skill in the art would not have selected tramadol out of the myriad other possible active ingredients for use in a once-daily formulation. But Oshlack makes that very selection; it lists tramadol as one of fourteen different opioid analgesics to use in a controlled-release formulation that provide effective blood levels for twenty-four hours. As such, Oshlack itself renders the selection of tramadol obvious regardless whether or not the patent lists tramadol as a preferred embodiment. *See Perricone v. Medicis Pharm. Corp.* 432 F.3d 1368, 1376 (Fed. Cir. 2005) ("This court rejects the notion that one of [14 listed] ingredients cannot anticipate because it appears without

special emphasis in a longer list."); *see also Merck & Co. v. Biocraft Labs., Inc.*, 874 F.2d 804, 807 (Fed. Cir. 1989) (holding that the prior art's disclosure of a multitude of combinations failed to render any particular formulation less obvious).

Purdue's alternative formulation of its argument, that the selection of a once-daily dose with twenty-four hour effect for tramadol was not obvious, similarly fails. Again, Oshlack expressly teaches once-daily formulations, *see, e.g.*, Oshlack col.12 ll.17-18; col.33 ll.33-34; col.34 ll.4-7, with dissolution rates designed to provide effective blood levels for about twenty-four hours, *compare id.* col.12 ll.12-18, *with id.* col.43 l.48–col.44 l.9 claim 43. And it claims such formulations for use with tramadol. *Id.* col.44 ll.29-36 claim 47. To the extent that Purdue is arguing that the Oshlack patent fails to enable a once-daily tramadol formulation, this argument also fails. For purposes of § 103, a prior art reference need not itself be enabled but is prior art for all that it discloses. *Symbol Techs., Inc. v. Opticon, Inc.*, 935 F.2d 1569, 1578 (Fed. Cir. 1991). Oshlack discloses a once-daily formulation of tramadol, and the district court found that in light of the knowledge in the art about once-daily formulations and about tramadol, persons of skill in the art would have been able to achieve a once-daily tramadol formulation with the claimed properties through routine experimentation. *Purdue Pharma*, 642 F. Supp. 2d at 373. We see no clear error in that finding.

Although argued on appeal, Purdue does not appear to have distinguished the Oshlack patent on the basis of the claimed W_{50} values before the district court, waiving the argument. *See Sage Prods., Inc. v. Devon Indus., Inc.*, 126 F.3d 1420, 1426 (Fed. Cir. 1997). Yet, we note that Oshlack does in fact disclose a once-daily formulation with a W_{50} value within the broad range of ten to thirty-

three hours claimed in claim 13 of the '887 patent and claim 11 of the '430 patent. Specifically, Figure 8 graphs the plasma concentration of the opioid analgesic morphine from Example 20 over time, revealing a W_{50} value of approximately twelve hours. Thus, Oshlack itself provides a motivation to prepare a once-a-day tramadol formulation with a W_{50} value within the claimed range whether or not such a W_{50} value is, as the district court found, necessarily a characteristic of a one-a-day tramadol formulation. *Purdue Pharma*, 642 F. Supp. 2d at 373.

Finally, we also reject Purdue's argument that the district court placed insufficient weight on its secondary considerations of nonobviousness. Such considerations here do not rebut Par's clear case of obviousness. *See Agrizap, Inc. v. Woodstream Corp.*, 520 F.3d 1337, 1344 (Fed. Cir. 2008). Moreover, we do not find compelling Purdue's evidence of copying in the ANDA context where a showing of bioequivalency is required for FDA approval. Nor do we find compelling Purdue's sales figures without any evidence giving context to such figures. Accordingly, we affirm the district court's final judgment holding the asserted claims of the '887 and '430 patents invalid as obvious.

Inequitable Conduct

This court reviews the district court's inequitable conduct determination under a two-tier standard; we review the underlying factual determinations for clear error but the ultimate decision on inequitable conduct for an abuse of discretion. *Star Scientific, Inc. v. R.J. Reynolds Tobacco Co.*, 537 F.3d 1357, 1365 (Fed. Cir. 2008). A conclusion of inequitable conduct requires an accused infringer to show that the applicant (1) made an affirmative misrepresentation of material fact, failed to disclose material

information, or submitted false material information, and (2) did so with intent to deceive the PTO. *Id.* Both materiality and intent to deceive must be proven by clear and convincing evidence, after which the court must balance the equities to determine whether the conduct was egregious enough to warrant holding the entire patent unenforceable. *Id.*

Par argues that the district court erred in not finding intent to deceive because Purdue offered no credible explanation for withholding material experimental data and submitting a materially misleading declaration by Ms. Malkowska that reported other, more favorable, data to the PTO. In fact, according to Par, the district court's characterization of the Malkowska declaration as an overly aggressive attempt to put a positive spin on the data is effectively a finding of deceptive intent under this court's case law, citing *Cargill, Inc. v. Canbra Foods, Ltd.*, 476 F.3d 1359 (Fed. Cir. 2007) and *Paragon Podiatry Laboratory, Inc. v. KLM Laboratories, Inc.*, 984 F.2d 1182 (Fed. Cir. 1993). Par also asserts that the district court incorrectly relied on irrelevant evidence of good faith, including Ms. Malkowska's failure to recall why the data were not submitted; the potential that the formulators did not recognize the data's import to patentability when the evidence showed that they did; and the applicants' later submission of similar data, the Napp repeat experiments.

Purdue responds that the district court correctly found no intent to deceive based on the credibility of Purdue's witnesses in light of the entire record, including that the Malkowska declaration was prepared to rebut, not a rejection of obviousness by the PTO, but inherent anticipation in an EPO proceeding, and that the applicants timely disclosed more pertinent experimental results, the Napp repeat experiments, generated for a foreign litigation. Furthermore, according to Purdue, no

evidence of good faith was required since Par did not meet its burden of showing intent to deceive, which cannot be inferred from materiality alone. Regardless, Purdue argues, the record supports a credible excuse: The omitted data did not reproduce conditions from the prior art and revealed dissolution rates outside those claimed in the asserted patents.

We agree with Purdue and affirm the district court's decision of no inequitable conduct. Even assuming that the applicants withheld material data and submitted a materially misleading declaration, as the district court found, *Purdue Pharma*, 642 F. Supp. 2d at 378, we find no clear error in the district court's finding that Par failed to present clear and convincing evidence of intent to deceive, *id.* at 379. Specifically, the fact that the applicants later submitted to the PTO the Napp repeat experiments strongly suggests that the applicants did not act with deceptive intent when they omitted similar data from the Malkowska declaration or when they submitted the Malkowska declaration with its omitted data to the PTO. *Cf. Cargill*, 476 F.3d at 1366 (finding intent to deceive when applicants repeatedly omitted highly relevant test data). In fact, the Napp repeat experiments were even more pertinent than the withheld data as they revealed dissolution rates that fell directly within—rather than near—the claimed rates. Therefore, another reasonable inference is that the applicants believed (rightly or wrongly) that the withheld data were irrelevant, either because the experimental conditions did not replicate those of the prior art or because they did not replicate those in an earlier Malkowska declaration.

Any inference of deceptive intent in the preparation of the declaration itself is further undermined by the fact that the applicants prepared the Malkowska declaration, not to respond directly to a rejection by the PTO, but for

an EPO proceeding regarding a related patent. *Cf. Ferring B.V. v. Barr Labs., Inc.*, 437 F.3d 1181, 1193 (Fed. Cir. 2006); *Paragon Podiatry*, 984 F.2d at 1191. That further diminishes the reasonableness of inferring that any omission or misleading statement in the preparation of the declaration was made with the specific intent of deceiving the PTO. *See Star Scientific*, 537 F.3d at 1366. Because intent to deceive is not the single most reasonable inference that can be drawn from the evidence, *id.*, we affirm the district court's determination of no inequitable conduct.

We have considered the parties remaining arguments, including Par's alternative ground for affirming the district court's invalidity decision, and do not find them persuasive. Accordingly, we affirm.

AFFIRMED