United States Court of Appeals for the Federal Circuit

PAR PHARMACEUTICAL, INC., PAR STERILE PRODUCTS, LLC, ENDO PAR INNOVATION COMPANY, LLC,
Plaintiffs-Appellants

v.

EAGLE PHARMACEUTICALS, INC.,
Defendant-Appellee

2021-2342

Appeal from the United States District Court for the District of Delaware in No. 1:18-cv-00823-CFC-JLH, Chief Judge Colm F. Connolly.

Decided: August 18, 2022

MARTIN JAY BLACK, Dechert LLP, Philadelphia, PA, argued for plaintiffs-appellants. Also represented by SHARON K. GAGLIARDI, BRIAN GOLDBERG, LUKE M. REILLY, ROBERT RHOAD, DANIEL ROBERTS; JONATHAN LOEB, Mountain View, CA.

JOHN C. O'QUINN, Kirkland & Ellis LLP, Washington, DC, argued for defendant-appellee. Also represented by WILLIAM H. BURGESS; BRYAN SCOTT HALES, Chicago, IL; BENJAMIN ADAM LASKY, JEANNA WACKER, New York, NY.

Before MOORE, *Chief Judge*, PROST and HUGHES, *Circuit Judges*.

MOORE, *Chief Judge*.

Par Pharmaceutical, Inc., Par Sterile Products, LLC, and Endo Par Innovation Company, LLC (collectively, Par) appeal a District of Delaware decision finding that Eagle Pharmaceuticals, Inc.'s abbreviated new drug application (ANDA) does not infringe any claim of U.S. Patent Nos. 9,744,209 and 9,750,785 under 35 U.S.C. § 271(e)(2). Par also appeals the district court's denial of declaratory judgment that Eagle's planned sale of a product produced in accordance with its ANDA would infringe under 35 U.S.C. § 271(a) and (b). For the following reasons, we affirm.

BACKGROUND

Par manufactures and sells Vasostrict®, a vasopressin injection product used to treat patients with critically low blood pressure. The FDA approved the Vasostrict® new drug application in April 2014, and Par began selling Vasostrict® in November 2014. *Par Pharm., Inc. v. Eagle Pharms. Inc.*, No. 18-0823, 2021 WL 3886418, at *2, ¶2 (D. Del. Aug. 31, 2021) (*Decision*). Following FDA approval, Vasostrict® was added to the Orange Book, which identified the '785 and '209 patents, each of which is owned by Par, as encompassing Vasostrict®. *Id.* The '785 patent is directed to vasopressin compositions, while the '209 patent is directed to methods of increasing blood pressure using those compositions. The claims of both patents require the vasopressin composition to have a rounded pH between 3.7–3.9, i.e., a pH between 3.65–3.94 before rounding. *See* '785 patent, claim 1; '209 patent, claim 1; *Decision*, at *3, ¶ 8.

In 2018, Eagle filed an ANDA to manufacture and sell a generic version of Vasostrict® before the '209 and '785

patents expired. *Decision*, at *4, ¶ 9. Eagle's ANDA specified the acceptable pH range of Eagle's proposed product during different stages of manufacture and the product's shelf life. *Id.* at ¶ 12. In particular, Eagle represented in its release specification, which defines the properties of the product when it is released for distribution, that the pH range would be between 3.4–3.6, i.e., 3.35–3.64 before rounding. *Id.*; J.A. 2927. Likewise, in its stability specification, which defines the product's properties during its shelf life, Eagle represented the pH would stay between 3.4–3.6 (after rounding). *Decision*, at *4, ¶ 9; J.A. 2926–27, 2955.

Eagle's ANDA also contained a certification under 35 U.S.C. § 355(j)(2)(A)(vii)(IV) that the '785 and '209 patents are invalid or will not be infringed by Eagle's proposed product. *Decision*, at *4, ¶ 11. In response, Par sued Eagle in the District of Delaware for infringement of the '209 and '785 patents under 35 U.S.C. § 271(e)(2). In addition, Par sought a declaratory judgment that Eagle's product would infringe under 35 U.S.C. § 271(a) and (b). Before the district court, Eagle stipulated that its proposed product would meet all asserted claim limitations except the claimed pH range of 3.7–3.9. *Decision*, at *9.

While conceding that the nominal pH range of Eagle's proposed product does not overlap with the pH range claimed in the '209 and '785 patents, Par argued that two "undisputed facts compel a finding of infringement." *Decision*, at *9. First, it contended "real-world" evidence shows the pH of Eagle's product drifts up over time. *Id.* Second, it observed that Eagle had sought authority to release products into the marketplace with a pH of 3.64, just 0.01 beneath the infringing range. *Id.* According to Par, these facts taken together compelled a finding that Eagle's proposed product would more likely than not infringe since a product released at a pH of 3.64 would inevitably drift into Par's claimed range. *Id.*

The district court disagreed. After a three-day bench trial, it found these facts "neither undisputed nor correct." *Id.* Specifically, it found the minor fluctuations in pH value identified by Par did not reveal any discernible trend, let alone "a steady and inevitable" upward drift. *Id.* at *7. Regarding the second alleged fact, the court found that while the *release* specification alone required a pH range between 3.4–3.6 (i.e., up to 3.64 before rounding) only at the time of distribution, the *stability* specification imposed an additional constraint that Eagle's proposed product maintain a pH between 3.4–3.6 from the time of its distribution through the entirety of its shelf life. *Id.* at *9. Accordingly, the district court found that Par had not established infringement under § 271(e). *Id.* at *10–11. Because the district court found Par had not established Eagle's product would infringe, it also denied Par's request for declaratory judgment under § 271(a) and (b). *Id.* at 11 n.3. Par appeals. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

Par challenges the district court's findings as to infringement under § 271(e)(2) and § 271(a) and (b). As to § 271(e)(2), Par alleges the district court's finding is clearly erroneous because "actual, real-world evidence" shows that the pH of products released at the upper end of the pH range identified in Eagle's release specification will inevitably drift up into infringing territory. As to § 271(a) and (b), Par argues the same evidence establishes that a product manufactured and sold in accordance with Eagle's ANDA would infringe, and that Par is therefore entitled to declaratory judgment. We do not agree.

I

We review a district court's conclusions of law de novo and its factual findings for clear error. *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1303 (Fed. Cir. 2015). Under the clear-error standard, we defer to the district court's findings "in the absence of a definite and firm conviction

that a mistake has been made." *Scanner Techs. Corp. v. ICOS Vision Sys. Corp. N.V.*, 528 F.3d 1365, 1374 (Fed. Cir. 2008) (cleaned up). Infringement is a question of fact that, after a bench trial, we review for clear error. *Alzo Corp. v. Mylan Labs., Inc.*, 464 F.3d 1286, 1289 (Fed. Cir. 2006).

Under § 271(e)(2), it is an act of infringement to submit an ANDA seeking FDA approval to make and sell a patented drug. 35 U.S.C. § 271(e)(2); *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1358 (Fed. Cir. 2003). Because the characteristics of a proposed ANDA product may not be established until the ANDA is approved, to determine infringement under § 271(e)(2), courts must conduct an inquiry to determine whether the probable ANDA product would infringe once it is made, used, or sold. *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1569 (Fed. Cir. 1997). This inquiry is controlled by the ANDA specification itself. Because "drug manufactures are bound by strict statutory provisions to sell only those products that comport with the ANDA[]," if the ANDA "defin[es] a proposed generic drug in a manner that directly addresses the issue of infringement, [it] control[s] the infringement inquiry." *Abbott Labs. v. TorPharm, Inc.*, 300 F.3d 1367, 1373 (Fed. Cir. 2002). The ANDA "directly resolves the infringement question" if "it defines a proposed generic product in a manner that either meets the limitations of an asserted patent claim or is outside the scope of such a claim." *Ferring B.V. v. Watson Labs., Inc.-Fla.*, 764 F.3d 1401, 1409–10 (Fed. Cir. 2014). If the ANDA specification does not speak clearly and directly to the question of infringement, courts may look to other relevant evidence, such as data or samples the ANDA filer has submitted to the FDA, to assess whether a proposed product will infringe. *Id.* at 1409; *Glaxo*, 110 F.3d at 1568.

Here, the inquiry begins and ends with Eagle's ANDA specification. Both the release and stability specification directly and unambiguously address the pH range of Eagle's proposed product and thus speak directly to

infringement. Together, these specifications restrict the pH of the proposed product to a pH range between 3.4–3.6 at release and throughout the products' shelf life—outside the infringing range. J.A. 2927. Indeed, Par concedes that the range listed in Eagle's release and stability specifications does not overlap with its claimed range. Oral Arg. at 0:37–1:04.[1] Par attempts to avoid the implications of this concession by effectively ignoring the role of the stability specification in the § 271(e)(2) analysis, arguing that because the FDA cannot ensure that every product Eagle sells will comply with the stability specification it is irrelevant. Appellant's Br. at 45–48. Yet Par cites no evidence that Eagle would not comply with its stability specification. And Eagle acknowledges it is bound by its representations to the FDA and that its ANDA product must therefore have a pH between 3.4–3.6 throughout its shelf life, not just at release. Oral Arg. at 15:35–59, 21:53–23:42. Par's unsupported conjecture that Eagle will not abide by its representations is inadequate to establish infringement. *See In re Brimonidine Patent Litig.*, 643 F.3d 1366, 1378 (Fed. Cir. 2011) ("We cannot assume that [an ANDA filer] will not act in full compliance with its representations to the FDA."). The district court did not clearly err in finding that Eagle's ANDA defines a product outside the scope of Par's claims. Accordingly, we affirm its finding of no infringement under § 271(e)(2).

II

To facilitate certainty of obligations and efficient resolutions of potential disputes, a patentee may seek a declaratory judgment that a person will infringe in the future. *Glaxo*, 110 F.3d at 1570. To establish entitlement to declaratory relief, the patentee must show: (1) the alleged future infringer is engaged in activity directed toward an

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[1] *Available at* https://oralarguments.cafc.uscourts.gov/default.aspx?fl=21-2342_07072022.mp3.

infringing activity or is making meaningful preparation for such activity; and (2) has indicated a refusal to change its course of action in the face of acts by the patentee sufficient to create reasonable apprehension that a suit is forthcoming. *Id.* at 1571. We review a district court's decision to grant or deny declaratory relief for abuse of discretion. *Id.* at 1570; *Minn. Min. and Mfg. Co. v. Norton Co.*, 929 F.2d 670, 672–73 (Fed. Cir. 1991). Under an abuse-of-discretion standard, we review the district court's factual findings for clear error. *Minn. Min*, 929 F.2d at 673.

The district court denied Par's request for declaratory judgment under § 271(a) and (b) because Par failed to establish by a preponderance of the evidence that Eagle's product would infringe, and that Eagle was therefore not engaged in an activity directed toward an infringing activity. *Decision*, at *11 n.3. It based that conclusion on its § 271(e)(2) analysis of the ANDA specification and the post-release pH data Par alleged to show an upward drift. Par argues the district court erred by finding no discernable upward drift in pH and rejecting the relevance of even minor pH fluctuations. Appellant's Br. at 35–38. We do not agree.

The district court's finding that there was no upward pH drift in Eagle's post-release pH data was not clear error. The court thoroughly considered the post-release pH data Par cites, along with Eagle's expert testimony assessing that data, and found that, while the pH measurements fluctuated over time, there was no discernable trend—and certainly not an inevitable upward trend—in the fluctuations. *Id.* at *7, ¶ 29. Contrary to Par's assertions, Eagle's expert does not concede a clear upward pH drift. Eagle's expert testified only that there were fluctuations—both upward and downward—in the pH, which is entirely consistent with the district court's finding. J.A. 15450:7–61:25. We see no clear error in this finding.

Par further alleges that the district court erroneously focused on pH measurements of products made according to Eagle's optimized manufacturing processes (post-optimization data), which reduced the magnitude of pH fluctuations in Eagle's products. Appellant's Br. at 37–38 (citing *Decision*, at *7, ¶ 29). Par does not contest that products manufactured using the optimized process did not drift into the infringing range. Instead, it asserts the post-optimization data is less probative than the evidence of pH fluctuations in pre-optimized products because there was less testing on the post-optimization products. Par is simply challenging the district court's weighing of the evidence. Absent a clear conviction the district court erred, it is not our role to set aside the district court's factual findings. *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 789 F.3d 1335, 1339 (Fed. Cir. 2015). The district court's reliance on post-optimization data was not clear error.

Par also argues the district court overlooked the evidence of pH fluctuations because it ignored Eagle's release specification. Appellant's Br. at 37–38. According to Par, if the district court had not ignored the release specification, it would have found that if Eagle released a product at pH 3.64, any minor upward pH fluctuation would result in infringement. Par continues to erroneously view the release specification in isolation. Eagle's ANDA is not constrained by its release specification only—it is also limited by the stability specification and the manufacturing process. Oral Arg. at 15:35–59, 27:30–50. As noted above, Eagle is bound by its representations to the FDA that it will manufacture its products in accordance with the optimized process and that the pH of its products will remain between 3.4–3.6.

The district court did not clearly err in finding that Par failed to establish that Eagle was engaged in, or making meaningful preparation for, infringing activity. As there is no clear error in the district court's findings, the district

court did not abuse its discretion in denying Par's request for declaratory relief.

CONCLUSION

Because we conclude that Eagle's ANDA specification controls and defines a non-infringing product under § 271(e)(2), and that the district court did not abuse its discretion in denying Par's request for declaratory judgment under § 271(a) and (b), we affirm.

AFFIRMED

COSTS

Costs to Eagle.