United States Court of Appeals for the Federal Circuit

GALDERMA LABORATORIES, L.P., TCD ROYALTY SUB LP,
Plaintiffs-Appellants

v.

LUPIN INC., LUPIN LTD.,
Defendants-Appellees

2024-1664

Appeal from the United States District Court for the District of Delaware in No. 1:21-cv-01710-SB, Circuit Judge Stephanos Bibas.

Decided: December 6, 2024

GERALD J. FLATTMANN, JR., Cahill Gordon & Reindel LLP, New York, NY, argued for plaintiffs-appellants. Also represented by ANDREW COCHRAN.

WILLIAM A. RAKOCZY, Rakoczy Molino Mazzochi Siwik LLP, Chicago, IL, argued for defendants-appellees. Also represented by KATIE BODA, JOSEPH THOMAS JAROS, ADRIANNE C. ROSE.

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

MOORE, *Chief Judge*.

Galderma Laboratories, L.P., TCD Royalty Sub LP (Galderma) appeals a decision from the United States District Court for the District of Delaware finding Lupin Inc. and Lupin Ltd.'s (collectively, Lupin) abbreviated new drug application (ANDA) does not infringe U.S. Patent No. 7,749,532 or U.S. Patent No. 8,206,740 (the Asserted Patents). *Galderma Lab'ys L.P. v. Lupin Inc. & Lupin Ltd.*, No. 21-CV-1710, 2024 WL 1571686 (D. Del. Mar. 22, 2024) (*Decision*). For the following reasons, we affirm.

BACKGROUND

Galderma owns and markets Oracea® (doxycycline USP) 40 mg capsules as a treatment for papules and pustules associated with rosacea. Following FDA approval, Oracea® was added to the Orange Book, which identified the Asserted Patents as encompassing Oracea®. The Asserted Patents share a common specification[1] and are directed to a once-daily, oral pharmaceutical composition formulated as about 30 mg immediate release (IR), and about 10 mg delayed release (DR), doxycycline and methods of treatment using the composition. *See* '532 patent at claims 1, 15; '740 patent at claims 1, 19. The claimed composition results in steady state blood levels of doxycycline between 0.1 μg/ml and 1.0 μg/ml. *See* '532 patent at claims 1, 15; '740 patent at claims 1, 19.

Oracea® achieves the claimed steady state blood levels through this combination of IR and DR pellets in a once daily dose. The IR portion is designed to "release substantially all of the active ingredient on administration

---

[1] Unless otherwise noted, we cite to only the '532 patent specification for brevity.

with no enhanced, delayed or extended release effect." '532 patent at 4:5–8. The DR portion contains an enteric coating applied to the surface of the pellets such that "there is no substantial release of doxycycline in the acidic stomach environment of approximately below pH 4.5. The doxycycline becomes available when the pH-sensitive layer dissolves at the greater pH of the small intestine; after a certain delayed time; or after the unit passes through the stomach." *Id.* at 7:47–52. In short, the IR portion is designed to release its doxycycline immediately upon ingestion in the fasted stomach, and the DR portion is designed to release its doxycycline at a delayed time when it reaches an environment with a pH higher than 4.5.

The district court summarized the *in vivo* absorption of Oracea®. *Decision* at *1. To obtain the steady state blood levels required by the claims, some doxycycline is released right away, the IR portion, and some is released later, the DR portion. Upon ingestion, the capsule travels quickly to the fasted stomach where a low pH causes the IR portion to release its doxycycline. *Id.* The DR portion, however, designed to not release doxycycline until a higher pH, remains intact. *Id.* The composition then leaves the stomach and enters the small intestine, starting with the duodenum. *Id.* The duodenum has a higher pH, resulting in the DR portion beginning to release its doxycycline. *Id.*

Lupin filed an ANDA to market a 40 mg doxycycline product, claiming bioequivalence to Oracea®. Lupin's ANDA product is labeled as containing 22 mg IR and 18 mg DR. J.A. 6624.[2] The prescribing information also describes its product as a 40 mg capsule composed of 22 mg IR and 18 mg DR enteric coated pellets. J.A. 6635. Lupin's ANDA Product achieves its DR effect by coating a portion of the pellets with Eudragit L30-D55, the same polymer used in Oracea®, which is designed to dissolve at and above pH 5.5.

---

[2] "J.A." refers to the joint appendix.

The ANDA also contains comparative dissolution testing results at pH 1.1 HCl (Acid) and pH 4.5 Phosphate (Buffer) of Lupin's ANDA product and Oracea®. J.A. 6559.

Lupin submitted certifications under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) that the Asserted Patents are invalid or will not be infringed by Lupin's ANDA product. In response, Galderma sued Lupin under the Hatch-Waxman Act for infringement of the Asserted Patents. *Decision* at *2. Before trial, Galderma narrowed the case to four asserted claims: claims 1 and 16 of the '532 patent, and claims 1 and 20 of the '740 patent (the Asserted Claims). *Id.* Claim 1 of the '532 patent is representative:

> An oral pharmaceutical composition of doxycycline, which at a once-daily dosage will give steady state blood levels of doxycycline of a minimum of 0.1 µg/ml and a maximum of 1.0 µg/ml, the composition consisting of (i) an immediate release (IR) portion comprising a drug, wherein the drug consists of about 30 mg doxycycline; (ii) a delayed release (DR) portion comprising a drug, wherein the drug consists of about 10 mg doxycycline, in which the DR portion is in the form of pellets coated with at least one enteric polymer; and (iii) one or more pharmaceutically acceptable excipients.

The district court construed the term "immediate-release portion" to be "a functional limitation meaning any part of the claimed composition that releases drug immediately upon administration, with no enhanced, delayed or extended release effect." *Decision* at *2. The district court construed "delayed-release portion" to be "a functional limitation meaning any part of the claimed composition that delays release of a drug until a time other than immediately following oral administration, e.g., through coating, uncoated matrix, or other impediment to delay release." *Id.*

Galderma argued Lupin's ANDA Product infringed the 30 mg IR, 10 mg DR limitations of the Asserted Claims, despite Lupin's ANDA stating its product contained 22 mg IR and 18 mg DR, because about 8 mg of Lupin's ANDA product's DR portion was actually an IR portion, resulting in a 30 mg IR, 10 mg DR product. *Id.* Galderma posited this was due to a "weak enteric coat" in the DR portion of Lupin's ANDA Product, resulting in early release of some of the supposedly DR doxycycline. *Id.* at *3. Galderma explained that, while both Oracea® and Lupin's ANDA Product use the same enteric polymer to coat the DR portion of their products, Lupin's ANDA Product only has a pellet weight gain of 18% due to enteric coating, whereas Oracea® uses a 30% weight gain. *Id.*; J.A. 4873 at 104:7–9. Additionally, Galderma theorized Lupin's use of methylene chloride in the coating process resulted in a weaker coat. *Decision* at *3; J.A. 4860 at 71:14–16. To prove its theory, Galderma relied mainly on the testimony of its expert, Dr. Rudnic, a two-stage *in vitro* dissolution test taking place at pH 1.1 and pH 4.5 from Lupin's ANDA showing release of some doxycycline from its DR portion at pH 4.5, and bioequivalence data between Oracea® and Lupin's ANDA Product. *Decision* at *3; J.A. 6559, 6520–21. Dr. Rudnic testified the two-stage dissolution test was relevant to the claims because pH 4.5 is found in the stomach, and the test showed some of the DR portion of Lupin's ANDA Product would release its doxycycline immediately upon ingestion, resulting in a product with about 30 mg IR portion and 10 mg DR portion. J.A. 4901 at 132:7–19.

Lupin argued its ANDA Product did not infringe. *Decision* at *3–4. Lupin's Executive Vice President of Research and Development, Mr. Avachat, testified that any methylene chloride used in the manufacturing process evaporates away, J.A. 5115 at 346:17–18, and was not used to make the coating weak, J.A. 5113 at 344:14–19. Lupin's dissolution expert, Ms. Gray, testified the two-stage dissolution test was unreliable because the percentage of

dissolved doxycycline in the Oracea® tablets decreased over time and the results for Lupin's ANDA Product had a high relative standard deviation. *Decision* at *4; J.A. 5167 at 398:14–18, 5168 at 399:12–16. Ms. Gray also testified about a single-stage test Lupin performed during trial on a small batch of capsules (the "rebuttal batch") that showed Lupin's DR pellets did not dissolve at pH 4.5. *Decision* at *4; J.A. 5177 at 408:19–20. Lupin also presented testimony from Dr. Buckton, who disagreed with Dr. Rudnic's conclusions regarding Lupin's ANDA Product's coating weakness due to an 18% weight gain and the two-stage dissolution test results. *Decision*, at *4; J.A. 5306 at 537:16–18, 5294–95 at 525:5–526:20.

The district court, after a three-day bench trial, found Lupin did not infringe the Asserted Patents.[3] *Decision* at *8. Specifically, the district court found Dr. Rudnic did not provide any evidence of how many pellets would get a lighter coating or how Lupin's ANDA showed insufficient coating of the DR pellets. *Id.* at *5. The district court credited the testimony of Dr. Buckton, Lupin's expert, that the two-stage dissolution test was not representative of the *in vivo* behavior of Lupin's ANDA Product. *Id.* at *6. The district court also found that, even if the test did reflect *in vivo* behavior, evident flaws in the data called the reliability of the results into question. *Id.* This was confirmed by the single-stage test using a batch of capsules produced with a rebuttal expert report of capsules, which showed no release of doxycycline from the DR pellets at pH 4.5. *Id.*

The district court found Galderma had not shown infringement via the doctrine of equivalents under either the function-way-result test or the insubstantial differences test. *Id.* at *8. Finally, the district court held

---

[3] Lupin did not present any validity challenges in the district court. J.A. 222–41.

Galderma did not show contributory or induced infringement, because there was no finding of direct infringement. *Id.* Galderma appeals. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

Galderma argues on appeal the district court erred in four ways: (1) disregarding controlling data in Lupin's ANDA, specifically the two-stage dissolution test, (2) allowing into evidence the results of the single-stage test using the rebuttal batch, (3) imposing limitations not present in the claims, and (4) not finding infringement under the doctrine of equivalents. We do not agree.

I.

Following a bench trial, 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). Infringement is a question of fact we review for clear error. *Alza Corp. v. Mylan Labs., Inc.*, 464 F.3d 1286, 1289 (Fed. Cir. 2006). 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).

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). The "ANDA specification 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, 1408–09 (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.

Galderma argues the district court clearly erred in disregarding the two-stage dissolution test in Lupin's ANDA. Galderma argues the two-stage dissolution test proves Lupin's ANDA Product releases about 8 mg of doxycycline from the labeled DR portion at pH 4.5. J.A. 6559. For example, the test results show capsule 1 released 78% doxycycline at time 150 minutes in pH 4.5. *Id.* This translates to 78% of a total of 40 mg of doxycycline released, or about 30 mg. Galderma asserts pH 4.5 is relevant to infringement because evidence at trial showed pH 4.5 is present in the stomach at the time of administration of Lupin's ANDA Product. Therefore, any product released at pH 4.5 is functionally immediate release. Additionally, the specification of the Asserted Patents notes the claimed DR portion should not release at pH 4.5, making any release at pH 4.5 necessarily a component of the IR portion. Opening Br. 15 (citing '532 patent at 7:47–53).

Lupin responds the district court did not disregard the two-stage dissolution test. Instead, the district court considered Galderma's arguments, but found the second-stage pH of 4.5 in the test was not physiologically relevant for a fasted stomach. *Decision* at *6. Therefore, the district court correctly found "Galderma cannot draw valid conclusions about *in vivo* behavior by looking to the second-stage results at pH 4.5." *Id.* We see no clear error in the district court's findings.

The district court found Galderma improperly drew conclusions about *in vivo* behavior from the two-stage *in vitro* dissolution test. *Decision* at *5. Specifically, the district court found "the pH of a fasted stomach is between 1 and 2, though it could be slightly higher for a short time right after drinking water." *Id.* at *6. The district court credited the testimony of Dr. Buckton and a paper submitted by Galderma. *Id.* (citing J.A. 5255 at 486:8–13 ("1 to 2 is a fasting figure."); J.A. 5592 ("Median pH value was 2.4 twenty minutes after administration of water and stabilized to 1.7 at later time points.")). The district court also credited Dr. Buckton's testimony that pH 4.5 better approximates the pH of the duodenum, where the DR portion is supposed to release its doxycycline. *Id.* While Dr. Rudnic testified that upon ingestion of the water required with Lupin's ANDA Product the pH of a fasted stomach will rise to pH 4.5, J.A. 4839:10–22, the district court did not clearly err in crediting Dr. Buckton over Dr. Rudnic. *Anderson v. City of Bessemer City, N.C.*, 470 U.S. 564, 575 (1985) ("When findings are based on determinations regarding the credibility of witnesses, Rule 52(a) demands even greater deference to the trial court's findings."). Dr. Rudnic relied on a paper which explicitly states "[m]edian pH value was 2.4" after administration of water. J.A. 5592. The district court did not clearly err in finding Galderma did not prove the two-stage dissolution test represented *in vivo* behavior of Lupin's ANDA Product, and therefore Galderma did not prove its theory of infringement.

Galderma also disputes the district court's alternative finding that even if the two-stage dissolution test results represented *in vivo* conditions, "evident flaws" in the data show it is unreliable. *Decision* at *6–7. Because we find no clear error in the district court's finding that Galderma did not prove the two-stage dissolution test represented *in vivo* behavior of Lupin's ANDA Product, we need not reach the

district court's analysis regarding the reliability of the test's data.

II.

Galderma argues the district court abused its discretion in admitting evidence regarding the rebuttal batch and legally erred in relying on the evidence to find noninfringement. The district court, to the extent it relied on rebuttal batch evidence at all,[4] did so to support its finding that the data from the two-stage dissolution test was unreliable. *Decision* at *6. Because we affirm the district court's finding Galderma did not prove the two-stage dissolution test represented *in vivo* behavior of Lupin's ANDA Product, we need not reach this issue.

III.

Galderma argues the district court imposed limitations during its infringement analysis not required by the Asserted Claims. Lupin responds the district court did not impose any additional claim limitations, and Galderma merely takes issue with the district court's factual findings. We agree with Lupin.

Galderma argues the court imposed a pH limitation, based on the testimony of Dr. Buckton, and used this limitation to improperly differentiate between the IR and DR portions of Lupin's ANDA Product. The district court's reliance on pH ranges was limited to its analysis of whether the two-stage dissolution test represented *in vivo* behavior of Lupin's ANDA Product in its evaluation of Galderma's infringement theory. *See Decision* at *6. As

---

[4] As the district court noted in its denial of Galderma's emergency-injunction motion "even if it were error for me to consider the small batch, the testing on that batch merely reinforced the lack of patent infringement." J.A. 31.

already discussed, the district court's finding on this issue was not clearly erroneous.

For temporal limitations, Galderma argues the district court required an exact thirty-minute cutoff between the IR and DR portions. The district court did not impose this requirement. Instead, the district court used thirty minutes as an example of a possible distinction between immediate and delayed release, noting "if release is 'delayed' after thirty minutes, it is 'immediate' before then." *Decision* at *2. The district court also took issue with Galderma's explanation of the relevance of the time capsules spent at the different pH levels in the two-stage dissolution test. It explained "the first stage is not just a stress test: it represents the capsule's arriving in the stomach and spending time at pH 1.1." *Decision* at *6. This is a factual finding regarding Galderma's infringement theory, and not an imposition of any claim limitations. Finally, the district court stated that "if [it] credited that Capsule 1's behavior at [thirty] minutes into the second stage reflects *in vivo* behavior at that time in the stomach, Galderma would have shown infringement." *Decision* at *7. But the district court did not find a capsule's behavior thirty minutes into the second stage of the dissolution test reflected *in vivo* behavior. It found Galderma did not prove the two-stage dissolution test represented *in vivo* behavior. This finding, which was not clearly erroneous, foreclosed the use of the two-stage dissolution test at pH 4.5 to show infringement. The district court's statement did not, as Galderma argues, impose a strict thirty-minute cutoff between IR and DR.

Finally, Galderma argues the district court imposed unspecified structural limitations. Galderma takes issue with the district court's finding that Galderma "never explained how [the district court] can infer that a certain percentage of *pellets* will leak based on a certain percentage of *capsules* leaking." *Decision* at *7. The district court did not impose any structural claim

limitations, but was, again, explaining a factual issue with Galderma's theory of infringement based on the two-stage dissolution test.

IV.

Galderma also raises several factual disputes regarding the district court's analysis of infringement under the doctrine of equivalents. We see no clear error in the district court's findings.

The doctrine of equivalents is "limitation specific, not focused only on the claim as a whole." *VLSI Tech. LLC v. Intel Corp.*, 87 F.4th 1332, 1342 (Fed. Cir. 2023). The doctrine asks "whether a substitute element matches the function, way, and result of the claimed element," or whether there are only "insubstantial differences." *Warner-Jenkinson Co., Inc. v. Hilton Davis Chemical Co.*, 520 U.S. 17, 40 (1997).

The district court found Galderma did not show infringement under the doctrine of equivalents under either test. *Decision* at *7–8. Under the "function, way, result" test, the district court found Galderma did not show Lupin's ANDA Product released either 30 mg immediately or 10 mg after a delay. *Id.* at *8. The district court noted Galderma argued bioequivalence was enough, but that only went to the result portion of the test. *Id.* Under the "insubstantial differences" test, the district court found the evidence showed Lupin's ANDA Product has a 22 mg IR and 18 mg DR portion, which is substantially different from the Asserted Claims. *Id.* We see no clear error in these findings.

Galderma argues the two-stage *in vitro* dissolution test in combination with the *in vivo* bioequivalence data satisfies both tests. For the "function, way, result" test, Galderma argues the two-stage dissolution test shows at pH 4.5 Lupin's ANDA Product functions as a 30 mg IR, 10 mg DR product by releasing doxycycline from the DR

portion at pH 4.5, and performs in substantially the same way by having a Eudragit L30-D55 coating. For substantially the same result, Galderma argues this is satisfied because the FDA deemed Lupin's ANDA Products bioequivalent to Oracea®. Galderma argues this same data also satisfies the "insubstantial differences" test. Finally, Galderma argues the mean data from the two-stage dissolution test at pH 4.5 show Lupin's ANDA Product will result in IR and DR portions equivalent to the Asserted Claims.

We see no clear error in the district court's findings that this evidence does not prove infringement under the doctrine of equivalents. As discussed, *supra*, the district court did not clearly err in finding Galderma did not prove the two-stage dissolution test represented relevant *in vivo* conditions such that the data correlated to the Asserted Claims' requirements. That leaves only Galderma's evidence of bioequivalence, which at most showed substantially the same result. This is insufficient to meet either the "function, way, result" test or the "insubstantial differences" test.

CONCLUSION

We have considered Galderma's other arguments and find them unpersuasive. Because the district court did not clearly err in finding Lupin's ANDA Product does not infringe the Asserted Patents, we affirm.

AFFIRMED