NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

NOVARTIS PHARMACEUTICALS CORPORATION, NOVARTIS AG, NOVARTIS PHARMA AG, NOVARTIS INTERNATIONAL PHARMACEUTICAL LTD., LTS LOHMANN THERAPIE-SYSTEME AG,
Plaintiffs-Appellees

v.

WATSON LABORATORIES, INC., WATSON PHARMA, INC., nka ACTAVIS PHARMA, INC., ACTAVIS, INC., fka WATSON PHARMACEUTICALS, INC.,
Defendants-Appellants

2014-1799, 2014-1800

Appeals from the United States District Court for the District of Delaware in Nos. 1:11-cv-01112-RGA, 1:13-cv-00371-RGA, Judge Richard G. Andrews.

NOVARTIS PHARMACEUTICALS CORPORATION, NOVARTIS AG, NOVARTIS PHARMA AG, NOVARTIS INTERNATIONAL PHARMACEUTICAL LTD., LTS LOHMANN THERAPIE-SYSTEME AG,
Plaintiffs-Appellants

v.

PAR PHARMACEUTICAL INC.,
Defendant-Cross-Appellant

2015-1061, 2015-1062, 2015-1120, 2015-1121

Appeals from the United States District Court for the District of Delaware in Nos. 1:11-cv-01077-RGA, 1:13-cv-01467-RGA, Judge Richard G. Andrews.

PAR PHARMACEUTICAL, INC.,
Plaintiff-Appellee

v.

NOVARTIS PHARMACEUTICALS CORPORATION, NOVARTIS AG, NOVARTIS PHARMA AG, NOVARTIS INTERNATIONAL PHARMACEUTICAL LTD., LTS LOHMANN THERAPIE-SYSTEME AG,
Defendants-Appellants

2015-1141

Appeal from the United States District Court for the District of Delaware in No. 1:14-cv-00843-RGA, Judge Richard G. Andrews.

Decided: May 21, 2015

CHARLOTTE JACOBSEN, Fitzpatrick, Cella, Harper & Scinto, New York, NY, argued for plaintiffs-appellees in cases 2014-1799, 2014-1800. Also represented by CHRISTOPHER EARL LOH, NICHOLAS N. KALLAS.

GEORGE C. LOMBARDI, Winston & Strawn, LLP, Chicago, IL, argued for defendants-appellants in cases 2014-1799, 2014-1800. Also represented by MICHAEL KEENAN NUTTER; STEFFEN NATHANAEL JOHNSON, EIMERIC REIG-PLESSIS, Washington, DC.

CHRISTOPHER EARL LOH, Fitzpatrick, Cella, Harper & Scinto, New York, NY, argued for plaintiffs-appellants in cases 2015-1061, 2015-1062, 2015-1120, 2015-1121; defendants-appellants in case 2015-1141. Also represented by CHARLOTTE JACOBSEN, NICHOLAS N. KALLAS.

DANIEL BROWN, Latham & Watkins LLP, New York, NY, argued for defendant-cross appellant in cases 2015-1061, 2015-1062, 2015-1120, 2015-1121; plaintiff-appellee in case 2015-1141. Also represented by GABRIEL BELL, ROBERT J. GAJARSA, Washington, DC; ROGER J. CHIN, San Francisco, CA.

Before LOURIE, TARANTO, and HUGHES,
Circuit Judges.

LOURIE, *Circuit Judge.*

Watson Laboratories, Inc., Watson Pharma, Inc., and Actavis, Inc. (collectively, "Watson") appeal from the decision of the United States District Court for the District of Delaware finding the asserted claims of U.S. Patents 6,316,023 ("the '023 patent") and 6,335,031 ("the '031 patent") not invalid as obvious. *Novartis Pharm. Corp. v. Par Pharm., Inc.*, 48 F. Supp. 3d 733 (D. Del. June 18, 2014) ("*Watson Trial Opinion*"); 2014-1799, 2014-1800 Joint Appendix ("J.A.1") 1–4 (final judgment).

Novartis Pharmaceuticals Corp., Novartis AG, Novartis Pharma AG, Novartis International Pharmaceutical Ltd., and LTS Lohmann Therapie-Systeme AG (collectively, "Novartis") appeal from the decision of the United States District Court for the District of Delaware finding the '023 and '031 patents not infringed by Par Pharmaceutical Inc. ("Par")'s product, which is the subject of its Abbreviated New Drug Application ("ANDA"). *Novartis Pharm. Corp. v. Par Pharm., Inc.*, No. 11-cv-1077, 2014 WL 4364674 (D. Del. Aug. 29, 2014) ("*Par Trial Opinion*"); 2015-1061, 2015-1062, 2015-1120, 2015-1121 Joint Appendix ("J.A.2") 1–3, 4–6, 7–8 (final judgments).

In view of the fact that these appeals involve the same patents, related issues, and the same parties in the several cases, we decide them together in one opinion. Because the district court did not err in concluding that the patents are not invalid, and additionally did not clearly err in finding the patents not infringed by Par's ANDA product, we *affirm* the district court's judgments.

BACKGROUND

Novartis owns the '023 and '031 patents, which share a common specification. The patents are directed to transdermal pharmaceutical formulations of rivastigmine for the treatment of dementia related to Alzheimer's disease and Parkinson's disease. In 2007, Novartis received approval from the United States Food and Drug Administration (the "FDA") to market a transdermal rivastigmine patch in dosage strengths of 4.6 mg/24 hours ("4.6 mg dose") and 9.5 mg/24 hours ("9.5 mg dose"). In connection with the approved New Drug Application for its rivastigmine patch, Novartis listed the '023 and '031 patents as claiming the drug product in the FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly known as the "Orange Book") for each dosage strength.

In due course, Watson and Par each submitted ANDAs, seeking approval from the FDA to market generic versions of Novartis's rivastigmine patch (the "ANDA products"). Because Novartis at the time only had approval for the 4.6 mg and 9.5 mg doses, Par and Watson originally sought approval only for those two doses. Both ANDAs contained certifications that the patents listed in the Orange Book were invalid or would not be infringed by the ANDA products. After receiving notices of those certifications from Watson and Par in late 2011, Novartis filed suit, alleging infringement of the '023 and '031 patents by the 4.6 mg and 9.5 mg doses of Watson's and Par's ANDA products.

In 2012, Novartis received FDA approval for a dosage strength of 13.3 mg/24 hours ("13.3 mg dose"). After the Orange Book was updated to list the '023 and '031 patents for Novartis's newly approved third dosage strength, Par and Watson amended their ANDAs to seek approval of that dose as well. Novartis then filed new suits in 2013, asserting only the '031 patent against the 13.3 mg dose of Par's and Watson's ANDA products. Par filed suit against Novartis in 2014, seeking a declaratory judgment that its 13.3 mg dose also does not infringe the '023 patent.

In its suits against Watson and Par, Novartis asserted claims 2 and 7 of the '023 patent, and claims 3, 7, 13, 16, and 18 of the '031 patent, which are collectively directed to rivastigmine pharmaceutical compositions, transdermal devices comprising such compositions, and methods for stabilizing such compositions.

Claim 1 of the '031 patent, not asserted but included here because claims 3, 7, and 13 depend from it, reads as follows:

> 1. A pharmaceutical composition comprising:
>
> (a) a therapeutically effective amount of [rivastigmine];

> (b) about 0.01 to about 0.5 percent by weight of an antioxidant, based on the weight of the composition, and
>
> (c) a diluent or carrier.

'031 patent col. 8 ll. 14–21 (emphasis added). Claims 3 and 13 are dependent claims that recite additional limitations relating to the antioxidant.

Claim 7 of the '031 patent was the focus of the district court in the infringement analysis and reads as follows:

> 7. A transdermal device comprising a pharmaceutical composition as defined in claim 1, wherein the pharmaceutical composition is supported by a substrate.

Id. col. 8 ll. 49–51. Claims 2 and 7 of the '023 patent similarly recite a pharmaceutical composition and a transdermal device, respectively, comprising rivastigmine and an antioxidant. '023 patent col. 8 ll. 17–28, 43–50.

Claim 15 of the '031 patent, also not asserted but included here because claims 16 and 18 depend from it, reads as follows:

> 15. A method of stabilizing [rivastigmine], wherein the method comprises forming a composition by combining [rivastigmine] with an amount of *anti-oxidant* effective to stabilize [rivastigmine] from degradation.

'031 patent col. 9 ll. 10–16 (emphasis added). Claims 16 and 18 are dependent claims that recite additional limitations relating to the antioxidant.

Present in all asserted claims and important to the resolution of both the validity and the noninfringement issues is the "antioxidant" claim limitation. The district court construed the term "antioxidant" to mean an "agent that reduces oxidative degradation." J.A.1 48–50. The

district court then conducted separate bench trials on the Watson and Par suits.

I

At the Watson trial, the district court found that Novartis had proved infringement of the asserted claims by Watson's ANDA product and that Watson had not proved that the asserted claims were invalid.

Watson asserted that the prior art disclosed all of the limitations of the '023 and '031 patents. The district court agreed that U.K. Patent Application GB 2 203 040 A ("GB '040"), U.S. Patent 4,948,807 ("the '807 patent"), and Esther Elmalem et al., *Antagonism of Morphine-Induced Respiratory Depression by Novel Anticholinesterase Agents*, 30 Neuropharmacology 1059 (1991) ("the Elmalem article") were prior art, and that collectively they disclosed pharmaceutical compositions comprising rivastigmine and an antioxidant. *Watson Trial Opinion*, 48 F. Supp. 3d at 753. However, the court found that rivastigmine was not known to be susceptible to oxidative degradation at the time of the invention, and that the cited prior art did not teach otherwise. *Id.* Thus, it held, it would not have been obvious to add an antioxidant to a rivastigmine composition in a transdermal device.

Specifically, the district court first found that GB '040 disclosed all of the limitations of the asserted claims except the addition of an antioxidant, and therefore it "did not disclose or otherwise suggest that rivastigmine, in any formulation, was susceptible to oxidative degradation." *Id.* at 753–54. The court determined that one of skill in the art "would not have been motivated to include an antioxidant in any formulation unless there was evidence of oxidative degradation." *Id.* at 754. The court found that the compatibility of excipients like antioxidants in a given formulation is unpredictable without experimentation. Moreover, the court noted, there were many known types of degradation other than oxidation, and one of skill

in the art would only have been motivated to address known degradation problems. The court found that GB '040, however, was "silent" with respect to rivastigmine's instability. *Id.*

The district court similarly found that the '807 patent teaches the addition of an antioxidant to rivastigmine, but does not teach one of skill in the art that rivastigmine is susceptible to oxidative degradation. *Id.* at 754–55. The court acknowledged that the '807 patent states that antioxidants "can be incorporated as required." *Id.* at 755; '807 patent col. 7 ll. 45–53. However, the court considered the reference as a whole and found that nothing in the '807 patent suggests that rivastigmine requires an antioxidant, mentions any observed oxidative degradation of rivastigmine, or discloses any stability data. The court also noted that both the '807 patent and the U.S. counterpart of GB '040 were considered by the patent examiner during prosecution of the '023 and '031 patents. The court therefore found that the '807 patent "would not teach [one of skill] that an antioxidant was required to protect rivastigmine from oxidative degradation." *Id.*

The district court further found that the Elmalem article did not teach that rivastigmine is susceptible to oxidative degradation. *Id.* at 755–57. The most arguably relevant passage in the Elmalem article states, "All drugs were made up in sterile saline, which included an equal weight of [an antioxidant], to prevent oxidation." *Id.*; J.A.1 1876. Watson argued that this sentence discloses that rivastigmine was known to be susceptible to oxidative degradation, and that an antioxidant in the same amount as each test compound was added for the specific purpose of preventing oxidation of that test compound. Novartis responded that because it was well-known that physostigmine required an antioxidant in solution, all of the formulations being tested included an antioxidant to eliminate any variability added by the antioxidant.

The district court admitted that there "does not appear to be an objectively 'correct' reading; rather both arguments seem logical and are supported by highly qualified experts in the field." *Id.* at 757. Because the court credited Novartis's expert testimony as being more credible than Watson's and more consistent with the court's reading of the article, the court consequently interpreted the addition of the antioxidant to the other test formulations as a measure to reduce variability rather than a teaching that rivastigmine is susceptible to oxidative degradation. *Id.* at 756–57. The court determined that Watson failed to provide clear and convincing evidence that the Elmalem article should be understood otherwise. Despite the fact that the Elmalem article thus discloses a formulation with rivastigmine and an antioxidant, the court decided that the article "would not have motivated [one of skill in the art] to combine an antioxidant with the transdermal rivastigmine device disclosed by GB '040." *Id.* at 756.

Because the prior art did not teach that oxidative degradation of rivastigmine was a known problem, the district court thus found that it would not have been obvious to one of skill in the art to combine rivastigmine with an antioxidant, especially in a transdermal formulation. The court therefore held that Watson failed to prove obviousness by clear and convincing evidence.

II

At the Par trial, the district court found that Novartis did not prove that Par's ANDA product infringes claim 7 of the '031 patent. Novartis contended that the acetaldehyde impurities found in the adhesive used in Par's ANDA product met the claimed antioxidant limitation, but the court found that Novartis failed to put forth sufficient evidence to show that acetaldehyde is an antioxidant.

Although the district court agreed that some reducing agents can act as antioxidants by undergoing sacrificial oxidation, and that acetaldehyde is a reducing agent and therefore may be an antioxidant, the court credited Par's expert testimony that one of skill in the art would not have considered acetaldehyde to be an antioxidant, but that acetaldehyde could instead contribute to oxidative degradation. *Par Trial Opinion*, 2014 WL 4364674 at *3–4. The one piece of prior art that Novartis could point to as describing acetaldehyde as an antioxidant was a Chinese patent that Novartis produced shortly before trial, but the court excluded that because it found that allowing that into evidence would cause incurable prejudice to Par and would unnecessarily delay the trial.

The district court also discounted the evidence from testing conducted by Novartis's expert. *Id.* at *4–6. Novartis asserted that the test data showed that a test rivastigmine composition (not the transdermal formulation proposed in Par's ANDA) with acetaldehyde experienced less oxidative degradation than the composition without acetaldehyde. However, Par's expert detailed, and the court accepted, various concerns with the testing protocol and results that rendered the results unreliable. For example, Par's expert criticized the test for not properly modeling the conditions of a transdermal patch, much less simulating Par's ANDA product. As a result, the district court rejected that testing as too flawed to provide "usable evidence." *Id.* at *7.

Novartis's expert also presented calculations using three different analytical methods to support the statistical significance of the test results. However, another of Par's experts found fault with those methods. She provided a statistical analysis using a fourth method, which produced a lower confidence interval range that indicated that the differences shown in Novartis's data were not statistically significant. The district court accordingly found that Novartis failed to provide sufficient expert

testimony as to the statistical significance of its test results; as a result, the district court either could not rely on the test or would favor Par's expert testimony that the test results were inconclusive. *Id.* at *5.

The district court therefore found that Novartis failed to prove by a preponderance of the evidence that acetaldehyde is an antioxidant, and consequently failed to prove that Par's ANDA product contains an antioxidant.

In the declaratory judgment action, Par filed a motion for summary judgment of noninfringement of the '023 patent by the 13.3 mg dose of its ANDA product, based on collateral estoppel. The district court granted that motion.

The court accordingly entered final judgment in all of the cases, finding that the asserted claims are not invalid as obvious, and that Par's ANDA product does not infringe the '023 and '031 patents. Watson and Novartis timely appealed to this court. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

DISCUSSION

Following 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); *Alza Corp. v. Mylan Labs., Inc.*, 464 F.3d 1286, 1289 (Fed. Cir. 2006); *see also Polaroid Corp. v. Eastman Kodak Co.*, 789 F.2d 1556, 1559 (Fed. Cir. 1986) ("The burden of overcoming the district court's factual findings is, as it should be, a heavy one."). A district court also has broad discretion in determining witness credibility, and we give great deference to those determinations. *Energy Capital Corp. v. United States*,

302 F.3d 1314, 1329 (Fed. Cir. 2002); *Ecolochem, Inc. v. S. Cal. Edison Co.*, 227 F.3d 1361, 1378–79 (Fed. Cir. 2000) (citing *Anderson v. City of Bessemer City*, 470 U.S. 564, 575–76 (1985)).

This appeal raises questions of validity and infringement, but, unlike most such appeals, does not challenge the district court's claim construction. As we find no reason to disturb the district court's claim construction in these cases, we will proceed directly to the issues raised.

I

We first address Watson's argument that the district court erred by failing to hold the asserted claims of the '023 and '031 patents invalid as obvious under § 103.

A patent claim is invalid for obviousness if an alleged infringer proves that the differences between the claimed subject matter 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).* 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. __, 131 S. Ct. 2238, 2242 (2011).

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 level of ordinary skill in the pertinent art. *KSR Int'l Co. v. Tele-*

---

* Because the '023 and '031 patents were filed before the effective date of the America Invents Act, the earlier, pre-Act version of § 103(a) applies. *See* Leahy–Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284, 293 (2011).

flex Inc., 550 U.S. 398, 427 (2007); *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966); *Alcon Research, Ltd. v. Apotex Inc.*, 687 F.3d 1362, 1365 (Fed. Cir. 2012). "The presence or absence of a motivation to combine references in an obviousness determination is a pure question of fact." *Alza*, 464 F.3d at 1289.

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 for one of ordinary skill to combine prior art elements in the manner claimed. *Rolls Royce, PLC v. United Techs. Corp.*, 603 F.3d 1325, 1339 (Fed. Cir. 2010); *KSR*, 550 U.S. at 420. Even an obvious solution, however, does not render an invention obvious if the problem solved was previously unknown. *Mintz v. Dietz & Watson, Inc.*, 679 F.3d 1372, 1377 (Fed. Cir. 2012) ("Often the inventive contribution lies in defining the problem in a new revelatory way."); *Leo Pharm. Prods., Ltd. v. Rea*, 726 F.3d 1346, 1356–57 (Fed. Cir. 2013) (finding that the claimed invention would not have been obvious to try to persons of ordinary skill in the art "because they would not have recognized the problem"). These principles are relevant here.

Watson argues that the combination of rivastigmine with an antioxidant was disclosed by or suggested in both the '807 patent and the Elmalem article, and that the district court erred by requiring that an explicit motivation to combine be found in the prior art. More specifically, Watson contends that the district court incorrectly required specific examples of oxidative degradation associated with rivastigmine, even though the '807 patent illuminates the problem and proposes the solution. Watson also asserts that the Elmalem article expressly provides that motivation by teaching that oxidative degradation was a known problem for rivastigmine and that an antioxidant was the solution to that problem. Watson further argues that Novartis's interpretation of the Elmalem article renders the described experiment

unreproducible, and criticizes the district court's decision to rely on an expert's credibility instead of on scientific explanation to determine the appropriate interpretation of the prior art's teachings.

Novartis responds that there were no disclosures in the prior art that taught or reasonably suggested that rivastigmine was susceptible to oxidative degradation. Novartis asserts that one of skill in the art would not have expected that an antioxidant was required, either based on rivastigmine's chemical structure or without months of testing. Moreover, Novartis explains, both rivastigmine and the addition of an antioxidant were intended as solutions for the known degradation problems with physostigmine. Because oxidative degradation was not a known problem for rivastigmine, Novartis contends that the district court did not clearly err in finding that no motivation existed for adding an antioxidant. Novartis further asserts that Watson failed to show a motivation to combine an antioxidant with rivastigmine in a transdermal patch.

We agree with Novartis that the district court did not err in concluding that Watson failed to prove that the asserted claims are invalid as obvious. The district court also did not clearly err in finding that the prior art does not unambiguously identify oxidative degradation to be a known problem with rivastigmine, and that therefore one of skill would not have had a reason to add an antioxidant to the GB '040 transdermal formulation.

Although the addition of an antioxidant would have been an obvious solution for a formulation with known oxidation problems, here Watson failed to prove that a rivastigmine formulation was known to be susceptible to oxidative degradation. *See Leo Pharm.*, 726 F.3d at 1356–57 (finding that the invention was not obvious where stability problem not recognized or known). Without the knowledge of a problem, one of skill in the art would not

have been motivated to modify GB '040 with antioxidants as purportedly disclosed in the '807 patent or the Elmalem article.

The references upon which Watson primarily relies disclose rivastigmine formulations, but only with an antioxidant added either conditionally ('807 patent) or indiscriminately across the board (Elmalem), and, moreover, not in a transdermal patch. Merely finding each of the claimed elements in the prior art does not prove a composite invention obvious, however, because "claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *KSR*, 550 U.S. at 418–19.

The '807 patent specifically states that physostigmine is "chemically unstable" and "must be prepared in solution with an antioxidant," and thus one of that patent's objectives was to address a need for compounds with "greater chemical stability" than physostigmine. '807 patent col. 1 ll. 30–35, col. 3 ll. 37–39. Rivastigmine (as the racemate) is disclosed by the '807 patent as an alternative to physostigmine, with increased activity that may be due to greater chemical stability. *Id.* col. 11 ll. 23–29 (noting the racemate of rivastigmine, RA_7). As the district court noted, the '807 patent nowhere discloses evidence of oxidative degradation of rivastigmine. In the portion that Watson points to, the specification describes various types of formulations, such as tablets for oral administration and sterile solutions for parenteral administration. *Id.* col. 7 ll. 15–53. More specifically, the addition of buffers, preservatives, antioxidants, etc. is noted in the paragraph relating to sterile compositions for injection. *Id.* col. 7 ll. 45–50. Without prior knowledge as to whether a compound is susceptible to oxidative degradation, the statement that excipients like antioxidants can be incorporated "as required" is a mere generic qualification. The district court also credited evidence that one of skill in the art would not have been motivated to risk

incompatibility by including an antioxidant in a formulation without evidence of its necessity. We thus discern no clear error in the district court's finding that the '807 patent does not teach one of skill in the art that rivastigmine is susceptible to oxidative degradation, especially in a transdermal formulation.

The plain language of the Elmalem article appears to present a closer question. The district court, however, relied on the opinions of expert witnesses to provide analysis by persons of skill in the art, from whose perspective a court must view the prior art. Although the district court heard from highly qualified individuals in the relevant field who provided reasonable support for both parties' seemingly logical arguments, it found Novartis's expert's testimony more credible; we give great deference to such credibility determinations. *Ecolochem*, 227 F.3d at 1378–79.

Like the '807 patent, the Elmalem article contrasts the "low chemical stability" of physostigmine with the "greater chemical stability" of the test compounds, including rivastigmine. J.A.1 1875. Because oxidative degradation was a well-known problem with physostigmine in solution, we agree that the experimental procedure in the Elmalem article could reasonably be understood to add an antioxidant to the other test formulations for the purpose of negating an additional variable in the experiment. The district court thus did not clearly err in finding that the Elmalem article does not disclose that oxidative degradation was a known problem with rivastigmine.

The district court considered the parties' arguments and evidence, particularly their conflicting expert testimony as to how one of ordinary skill would have understood the prior art at the time of the invention. It made factual findings about the scope and content of the prior art, specifically, that rivastigmine was not known to be susceptible to oxidative degradation, and that the '807

patent and the Elmalem article do not teach otherwise. The district court also found that without an appreciation for rivastigmine's susceptibility to oxidative degradation, one of skill in the art would not have been motivated to patch together the prior art to add an antioxidant to a rivastigmine formulation, much less to a transdermal rivastigmine formulation. We owe those findings considerable deference on appeal, and we see no clear error based on the record before us.

In view of the foregoing, we therefore affirm the district court's holding that Watson failed to prove by clear and convincing evidence that the asserted claims of Novartis's '023 and '031 patents are invalid as obvious.

II

We next address the district court's holding that Par's ANDA product does not infringe claim 7 of the '031 patent.

After a bench trial, infringement is a question of fact that we review for clear error. *Alza*, 464 F.3d at 1289. Under the Hatch–Waxman framework, the filing of an ANDA constitutes an "artificial" act of infringement for purposes of creating case or controversy jurisdiction. 35 U.S.C. § 271(e)(2)(A); *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 676 (1990); *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1569 (Fed. Cir. 1997). Once jurisdiction is established, the ultimate infringement inquiry focuses on a comparison of the asserted patent claims against the ANDA product that is likely to be sold following FDA approval, under a traditional patent law analysis. *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1365–66 (Fed. Cir. 2003) (citing *Glaxo*, 110 F.3d at 1567–68). The burden of proving infringement by a preponderance of the evidence remains on the patentee, and we have rejected shifting that burden to the accused infringer. *Id.*

Additionally, we apply the law on evidentiary rulings and the general collateral estoppel principles of the regional circuit in which a district court sits. *Chimie v. PPG Indus., Inc.*, 402 F.3d 1371, 1376 (Fed. Cir. 2005); *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1295 (Fed. Cir. 2014) (citing *Pharmacia & Upjohn Co. v. Mylan Pharm., Inc.*, 170 F.3d 1373, 1381 n.4 (Fed. Cir. 1999)). The Third Circuit reviews a district court's decision to exclude evidence for abuse of discretion, considering the prejudice to the other party, ability to cure that prejudice, extent of disruption to the trial, and bad faith of the proffering party. *Glass v. Phila. Elec. Co.*, 34 F.3d 188, 191 (3d Cir. 1994); *Meyers v. Pennypack Woods Home Ownership Assoc.*, 559 F.2d 894, 904–905 (3d Cir. 1977). Collateral estoppel applies when an identical issue was previously adjudicated, the issue was actually litigated, the previous determination was necessary to the decision, and the party precluded from relitigating the issue was fully represented. *Jean Alexander Cosmetics, Inc. v. L'Oreal USA, Inc.*, 458 F.3d 244, 249 (3d Cir. 2006); *see also United States v. 5 Unlabeled Boxes, More or Less*, 572 F.3d 169, 173–74 (3d Cir. 2009) (distinguishing between res judicata and collateral estoppel).

Novartis argues that the district court clearly erred in not finding infringement because the acetaldehyde present in Par's ANDA product is an antioxidant. Novartis asserts that the district court erred in treating facts as opinions, and therefore subject to credibility determinations, rather than as objective scientific findings. Novartis emphasizes that the district court's construction does not define an antioxidant according to whether it is listed in pharmaceutical references or recognized by experts as one. The court abused its discretion in excluding the Chinese patent, Novartis argues, because the evidence was directly relevant to the issue of infringement and thus its probative value outweighed any prejudice, and allowing the evidence would not have been unduly disrup-

tive to trial because it supported an existing argument. Novartis also contends that the district court misunderstood how a reducing agent acts as an antioxidant, and wrongly accepted Par's expert testimony speculating, without any evidentiary basis, that acetaldehyde would increase oxidative degradation. Novartis explains that stress tests like the one conducted by its expert are commonly used to measure oxidative degradation, and argues that such a test can therefore be used to determine whether a compound reduces oxidative degradation. Novartis maintains that its testing data and statistical analyses prove that acetaldehyde reduces oxidative degradation of rivastigmine in oxidizing conditions and thus should suffice to meet its burden of proof.

Par responds that its ANDA product simply lacks an antioxidant, and that Novartis failed to prove that acetaldehyde is an antioxidant. Although Par's expert did not conduct his own testing, Par contends that the expert's testimony on how acetaldehyde could instead promote oxidative degradation was based on published material as well as his own expertise in chemistry, and thus had sound scientific footing. Par explains that reducing agents are not necessarily antioxidants, and Novartis failed to show that acetaldehyde actually acts as an antioxidant. Furthermore, Par criticizes Novartis's testing as lacking credibility and reliability, primarily because such a test had not been used before in such a manner and the expert failed to validate the test with compounds having known antioxidant characteristics. Par dismisses Novartis's later statistical analyses as post-hoc attempts to make the data fit a desired result. Par additionally asserts that, with respect to the 13.3 mg dose of Par's ANDA product, Novartis is collaterally estopped by the decisions on the lower dose products from relitigating whether acetaldehyde is an antioxidant.

We agree with Par that the district court did not clearly err in finding that Novartis failed to prove that

Par's ANDA product contains an antioxidant as required by the asserted claims. It appears that claim 7 of the '031 patent was the only claim addressed in the opinion, *see, e.g.*, *Par Trial Opinion*, 2014 WL 4364674 at *2, but the antioxidant limitation is present in all of the originally asserted claims of the '023 and '031 patents. The infringement evaluation of all the asserted claims is therefore properly focused on the presence or absence of an antioxidant in Par's ANDA product.

Under the district court's claim construction, which we do not disturb, it does not matter *how* a compound reduces oxidative degradation, but rather that it *does*. Experts for both parties agreed that not all reducing agents are antioxidants; simply because a reducing agent can reduce oxidative degradation by undergoing sacrificial oxidation does not necessarily mean that it actually does reduce oxidative degradation. Regardless whether acetaldehyde undergoes sacrificial oxidation or acts in other ways, the district court found that Novartis failed to prove that acetaldehyde reduces oxidative degradation. The court furthermore did not abuse its discretion in excluding the Chinese patent, as Novartis failed to show that not considering the reference was prejudicial error.

Novartis bore the burden of proving that acetaldehyde actually reduces oxidative degradation. Both parties proffered expert witnesses that testified on the basis of both scientific knowledge and experimental evidence, and the district court made factual findings based on the credibility of those witnesses. It was well within the district court's province to evaluate the validity of the data and the credibility of the corresponding testimony. The court made specific findings on the scientific soundness of Novartis's tests and concluded that the test results were unpersuasive. Additionally, the court determined which method to use for a statistical analysis based on the evidence presented at trial, and found that, even assuming that the test methodology were valid, the test results

were not statistically significant. These are all determinations of credibility, reliability, and weight, which are fully within the district court's purview. Because the district court found Novartis's expert's testing to be unreliable, Novartis provided no basis from which to draw any reliable inferences as to whether acetaldehyde acts as an antioxidant, regardless of the amount present.

Accordingly, the district court did not clearly err in finding that Par's ANDA product was not shown to infringe any asserted claim containing the antioxidant limitation. We find that, because the same key determination, dispositive of noninfringement, is at issue in the declaratory judgment action, the same conclusion must be arrived at there. *See Jean Alexander Cosmetics*, 458 F.3d at 249. Thus, the ruling on collateral estoppel was correct. The district court therefore did not err in granting final judgments of noninfringement in favor of Par for all three doses of its ANDA product. J.A.2 1–3, 4–6, 7–8.

CONCLUSION

We have considered the remaining arguments and conclude that they are without merit. For the foregoing reasons, we conclude that the district court did not err in holding that Watson failed to prove by clear and convincing evidence that the asserted claims of the '023 and '031 patents are invalid as obvious under 35 U.S.C. § 103, and we therefore affirm that judgment. We further conclude that the district court did not clearly err in finding that Novartis failed to prove by a preponderance of the evidence that Par's ANDA product infringes the '023 or '031 patents, and we also affirm those judgments.

AFFIRMED

COSTS

No costs.