United States Court of Appeals for the Federal Circuit

FERRING B.V.,
Plaintiff-Appellee,

v.

WATSON LABORATORIES, INC. – FLORIDA,
Defendant-Appellant,

AND

APOTEX, INC., AND APOTEX CORP.,
Defendants.

2014-1416

Appeal from the United States District Court for the District of Nevada in Nos. 3:11-cv-0481-RCJ-VPC, 3:11-cv-0853-RCJ-VPC, and 2:12-cv-1935-RCJ-VPC, Judge Robert Clive Jones.

Decided: August 22, 2014

PAUL W. BROWNING, Finnegan, Henderson, Farabow, Garrett & Dunner, LLP, of Washington, DC, argued for plaintiff-appellee. With him on the brief were JAMES B. MONROE, JUSTIN J. HASFORD, and MARY E. CHLEBOWSKI.

B. JEFFERSON BOGGS, JR., Merchant & Gould P.C., of Alexandria, Virginia, argued for defendant-appellant. With him on the brief were MATTHEW L. FEDOWITZ; CHRISTOPHER J. SORENSON and RACHEL C. HUGHEY, of Minneapolis, Minnesota.

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

LOURIE, *Circuit Judge.*

Watson Laboratories, Inc. – Florida ("Watson") appeals from the decisions of the United States District Court for the District of Nevada (i) holding that the subject matter of the asserted claims of Ferring B.V.'s ("Ferring") U.S. Patents 7,947,739 (the "'739 patent"), 8,022,106 (the "'106 patent"), and 8,273,795 (the "'795 patent") would not have been obvious under 35 U.S.C. § 103, (ii) finding that Watson's generic tranexamic acid product infringed those claims under 35 U.S.C. § 271, consequently (iii) ordering the U.S. Food and Drug Administration ("FDA") to reset the approval date of Watson's Abbreviated New Drug Application ("ANDA") 20-2093 and (iv) permanently enjoining the manufacture, use, sale, or offer for sale of Watson's generic product. *See Ferring B.V. v. Watson Labs., Inc. – Fla.*, No. 11-0481 (D. Nev. Apr. 14, 2014), ECF No. 524 ("*Final Order*"); J.A. 325–27. We conclude that the district court did not err in holding that the subject matter of the claims of Ferring's '739, '106, and '795 patents would not have been obvious. However, we conclude that the district court's judgment that Watson's generic product infringed the asserted claims of Ferring's patents was not in accordance with law. Accordingly, we affirm in part, reverse in part, and vacate both the district court's resetting order and injunction.

BACKGROUND

Ferring owns the '739, '106, and '795 patents, which are directed to modified release formulations of *trans*-4-(aminomethyl)cyclohexanecarboxylic acid, also known as tranexamic acid, the active ingredient in the drug marketed as a treatment for heavy menstrual bleeding, or menorrhagia, under the brand name Lysteda®. The claims of those patents are drawn to oral dosage forms or formulations and methods of treating menorrhagia and require three elements: (1) about 650 mg of tranexamic acid; (2) a so-called modified release material that comprises either about 10% to about 35% or about 5% to about 50% by weight of the formulation; and (3) a specified dissolution release rate of the tranexamic acid in water as measured by a particular United States Pharmacopeia ("USP") method. Claim 1 of the '739 patent is representative and reads as follows:

> 1. A tranexamic acid tablet formulation, comprising:
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> tranexamic acid or a pharmaceutically acceptable salt thereof; and
>
> a modified release material, wherein the modified release material comprises a polymer selected from the group consisting of hydroxyalkylcelluloses, alkylcelluloses, cellulose ethers, partial esters thereof, and mixtures thereof;
>
> wherein the modified release material is present in the formulation in an amount from about 10% to about 35% by weight of the formulation;
>
> wherein the formulation provides an in-vitro dissolution release rate of the tranexamic acid or pharmaceutically acceptable salt thereof, when measured by the USP 27 Apparatus Type II Paddle Method @ 50 RPM in 900 ml water at 37±0.5ºC., of less than about 70% by weight tranexamic acid or pharmaceutically acceptable

> salt thereof released at about 45 minutes, and about 100% by weight tranexamic acid or pharmaceutically acceptable salt thereof released by about 120 minutes; and
>
> wherein each tablet of the formulation provides a dose of about 650 mg of tranexamic acid.

'739 patent col. 69 ll. 46–67. Both claim 1 of the '106 patent and claim 1 of the '795 patent are similar but require a dissolution release rate of tranexamic acid of less than about 40% at about 15 minutes, less than about 70% at about 45 minutes, and not less than about 50% by about 90 minutes. '106 patent col. 69 ll. 8–19; '795 patent col. 35 ll. 37–48. Various dependent claims include additional limitations drawn to amount of tranexamic acid, amount or type of modified release material, water dissolution release rates measured by the USP test, pharmacokinetic requirements, and kind of dosage form. For example, claim 5 of the '739 patent and claim 19 of the '106 patent each limit the modified release material to hydroxypropylmethylcellulose, which is also known as hypromellose. '739 patent col. 70 ll. 20–22; '106 patent col. 70 ll. 62–64.

It is undisputed that the product Lysteda® is an embodiment of the claims in Ferring's '739, '106, and '795 patents. J.A. 938. Pursuant to the Hatch-Waxman Act, 21 U.S.C. § 355(b)(1), those patents are listed as referenced to Lysteda® in the FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* publication (commonly known as the "Orange Book"). In approving Lysteda®, the FDA recognized that the drug was intended for the treatment of a serious or life-threatening disease or condition that demonstrated the potential to address unmet medical needs. On that basis, the FDA granted the Lysteda® New Drug Application ("NDA") "fast track" status under 21 U.S.C. § 356(b)(1), which provided for expedited review. J.A. 18449–63. Lysteda® is the first

tranexamic drug approved by the FDA for treating menorrhagia in the United States.

Almost a year before the first of Ferring's patents issued, Watson filed ANDA 20-2093 seeking FDA approval to market tranexamic acid tablets as generic versions of Lysteda®. As specified in its ANDA, Watson's generic tablets are made of a so-called "core" mixture comprising 650 mg of tranexamic acid and various excipients including 6.52% by weight hypromellose, which is described as a binder. J.A. 13800.

Watson's initially-filed ANDA specified that the hardness of the cores was 13–20 kp; "kp" is an abbreviation for kiloponds, which is a measure of hardness compression. J.A. 13885. In an amendment submitted to the FDA dated August 29, 2012 and approved December 27, 2012, Watson modified its ANDA specification to require a core hardness of 13–17 kp. J.A. 13789, 13912, 13920. The cores are surrounded by a pH-dependent film coating comprising various agents including 1.86% Opadry® YS-1-7006, which itself is a mixture consisting of hypromellose and polyethylene glycol. J.A. 13800–02, 14074. The film coating is 2.91% by weight of the total weight of the composed tablet; it is designed to resist degradation in water, such as the mouth and the esophagus, but to dissolve immediately in acidic conditions, such as the stomach. *Id.*

Watson maintains that its ANDA contains no specification that addresses the manner in which its product dissolves in water. Appellant's Br. 24; J.A. 1598, 2080. However, biobatch data submitted in Watson's ANDA demonstrate that the dissolution release rate of tranexamic acid from its coated generic 650 mg tablets as measured by the USP 27 Apparatus Type II Paddle Method at 50 revolutions per minute in 900 mL of water at 37°C is as follows: 5% at 15 minutes, 16% at 45 minutes, 29% at 90 minutes, and 37% at 120 minutes. J.A. 14074.

In 2011, Watson submitted to Ferring a notice of certification pursuant to 21 U.S.C. § 355(j)(2)(B)(ii) and 21 C.F.R. § 314.95(c) regarding its proposed generic tranexamic acid product as specified in its ANDA. Ferring then initiated the instant suit, asserting that Watson's ANDA submission constituted an act of infringement of claims 1, 4, 5, 8–10, 12, and 13 of the '739 patent; claims 1, 5–8, 15, 16, 18, 19, and 30–37 of the '106 patent; and claims 1, 5, 6, and 8–10 of the '795 patent according to 35 U.S.C. § 271(e)(2)(A).* Ferring alleged that both Watson's uncoated cores and finished, coated commercial tablets infringed the asserted patent claims. After receiving FDA approval of its ANDA on December 27, 2012, Watson launched its generic tranexamic acid product at risk, which Ferring did not move to enjoin. J.A. 14848–51.

During discovery, Ferring and Watson each conducted dissolution testing of samples provided by Watson. Of the hundreds of coated commercial products tested by the claimed USP method, only about four individual coated tablets released more than 50% of their tranexamic acid at 90 minutes, but none of them released more than about 79% by 120 minutes. J.A. 14218–76, 14751–53, 14768–69, 18290, 18424, 18427, 18443. The data collected by both parties showed that, in the majority of the samples tested, only about 27% to 44% of the tranexamic acid was released from the individual coated tablets at 90 minutes and only about 33% to 52% was released at 120 minutes,

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* Ferring also sued Apotex, Inc. and Apotex Corp. (collectively "Apotex"), alleging that Apotex's ANDA product consisting of a generic version of Lysteda® would infringe the same patents at issue here. In the appeal from that case, 2014-1377, we today affirm the district court's judgment that the product specified in both Apotex's original and amended ANDAs would not infringe the asserted claims.

consistent with the biobatch data reported in Watson's ANDA itself. *Id.*

At trial, Ferring also relied on test data reported in a Watson document labeled PTX 381 to prove infringement. Appellee Br. 22; J.A. 991–93, 2003–11. Those data show dissolution profiles in water of experimental, uncoated 650 mg tranexamic acid cores of various specified hardness, as measured by the USP method, which Watson recorded in the development of its generic product formulation prior to submitting its ANDA to the FDA. J.A. 1617–19, 2070–72, 14840. The data show that the amount of tranexamic acid released in Watson's uncoated cores with a hardness of 13 kp is 96% at 15 minutes and 100% at 45 minutes; those with a hardness of 16 kp release 44% at 15 minutes and 95% at 45 minutes; those with a hardness of 17 kp release 27% at 15 minutes and 71% at 45 minutes; those with a hardness of 18 kp release 35% at 15 minutes and 76% at 45 minutes; and those with a hardness of 20 kp release 31% at 15 minutes and 77% at 45 minutes. J.A. 14840.

Following a *Markman* hearing, the district court construed the term "modified release material" to mean "a material that modifies the release of the active pharmaceutical ingredient" in water. *Ferring B.V. v. Watson Labs., Inc. – Fla.*, No. 11-0481 (D. Nev. Feb. 6, 2013), ECF No. 295; J.A. 195–96, 204. The court also construed the term "about" to mean "approximately." *Id.*; J.A. 204. After a bench trial, the court found that the asserted claims would not have been obvious because "[n]one of the prior art discusses [a dosage of 650 mg tranexamic acid], nor does any of the prior art motivate to a higher dosage. In fact, it motivates just the opposite direction." J.A. 2308–10. The court also found that both the uncoated cores of Watson's generic tranexamic acid product and the finished, coated commercial tablets with a core hardness of 17 kp and greater infringed the asserted claims under

§ 271(e)(2)(A) and § 271(a). J.A. 2307, 2311, 2315; *Final Order* at 1.

On the one hand, the district court considered Watson's submission of the ANDA itself to be an act of infringement and ostensibly refused to consider all FDA-approved amendments to the ANDA specification in its infringement analysis. J.A. 2249–56, 2316. On the other hand, based on its finding that only uncoated cores or finished, coated commercial tablets with a core hardness of 17 kp or greater infringed, the court suggested at the close of trial that Watson could avoid infringement by submitting a "change" of its ANDA to the FDA. J.A. 2316–17 ("It looks like, if you avoid or can get away from the 17 Kp, even as low as 16 with a mandatory, you're probably okay."). Consistent with the court's suggestion, Watson filed an amendment to its ANDA on February 11, 2014, further narrowing its specification to require a hardness range of 13–16.5 kp, which the FDA approved on March 3, 2014. J.A. 243–46, 255–57.

The district court nevertheless issued a final judgment permanently enjoining the manufacture, use, sale, or offer for sale of Watson's generic tranexamic acid product. *Final Order* at 1–2. The court further ordered the FDA to reset the approval date of Watson's ANDA 20-2093 pursuant to § 271(e)(4)(A) to a date no earlier than the expiration of Ferring's asserted patents, *viz.*, March 4, 2025. *Id.* at 2.

Watson appealed. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1). On Watson's motion, we stayed the district court's resetting order and injunction pending disposition of the appeal.

DISCUSSION

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 this case, 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 invalid for obviousness under § 103.

Following a bench trial, we review the district court's conclusions of law without deference 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 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).

Watson contends that each limitation of Ferring's claims was disclosed or suggested in the prior art. Watson relies on a July 27, 2000 report by the European Agency for the Evaluation of Medicinal Products Committee for Proprietary Medicinal Products ("EMA report") that evaluates the safety and efficacy of a 500 mg tranexamic acid product comprising the excipient hydroxypropylcellulose, which was indicated throughout Europe for the treatment of menorrhagia. J.A. 13629–37. According to Watson, it would have been obvious to increase the amount of tranexamic acid to 650 mg and to package the drug in a modified oral dosage form because U.S. Patent 5,858,411 of Nakagami described tranexamic acid as one of many medicinal ingredients that could be used with proposed sustained release granular preparations containing binders such as hydroxypropylcellulose and hypromellose. Ferring responds that there were no disclosures in the prior art that either taught or suggested 650 mg tranexamic acid formulations containing modified release materials with specified dissolution limitations, and that the prior art actually taught away from using

such a high dose. Ferring also argues that secondary considerations support the district court's conclusion of nonobviousness.

We agree with Ferring and the district court that Watson failed to prove that the subject matter of the asserted claims would have been obvious under § 103. A claim is invalid for obviousness if, to one of ordinary skill in the pertinent art, "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made." 35 U.S.C. § 103(a) (2006); *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406–07 (2007). Obviousness is a legal conclusion based on underlying factual findings, including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the pertinent art; (3) the differences between the claimed invention and the prior art; and (4) objective evidence such as commercial success, long-felt but unsolved need, and the failure of others. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966). Furthermore, 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.*, 564 U.S. __, 131 S. Ct. 2238, 2242 (2011).

In this case, the cited prior art references neither set forth the limitations required by the asserted claims, nor provided any reason or motivation to combine those teachings to derive the claimed formulations with specific dissolution profiles. Accordingly, the asserted claims have not been shown to be invalid under § 103.

First, the references disclose 500 mg tranexamic acid formulations, but no higher tablet strengths, and particularly not the claimed 650 mg formulation. The EMA report upon which Watson relies specifically notes that an increased dose of tranexamic acid results in a concomitant dose-dependent increase in gastrointestinal side effects.

J.A. 13631, 13635. Secondly, the references do not disclose the claimed amounts of modified release polymers. The EMA report merely recites hydoxypropylcellulose, a species of hydroxyalkylcellulose, among a list of a dozen other excipients, but does not specify an amount present in the formulation of that polymer or any other inactive ingredient. J.A. 13636. Nakagami likewise lists tranexamic acid as one of more than eight orally dosable medicinal ingredients suitable for a sustained-release granular preparation, but teaches that binders such as hydroxypropylcellulose and hypromellose may only be added in an amount from 1% to 5% by weight of the preparation, and does not teach any example of a tranexamic acid formulation. J.A. 14481–82. Third, Watson did not identify any prior art references disclosing the critical dissolution limitations of the patented claims, but merely asserted in a conclusory manner that those limitations would have been obvious or could have been predicted while failing to address why one of ordinary skill in the art would choose the specific release profiles claimed. Moreover, supporting evidence demonstrated that there was a long-felt and unmet need for a treatment for menorrhagia that avoided adverse events, as the FDA recognized in granting "fast track" status under 21 U.S.C. § 356(b)(1) to the NDA covering Lysteda®, which is the undisputed commercial embodiment of Ferring's asserted claims. *See* J.A. 13879, 18449–63.

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 Ferring's '739, '106, and '795 patents are invalid as obvious under § 103.

II

We next address the district court's holdings that Watson's ANDA submission and generic tranexamic acid product infringed the asserted claims.

Watson argues that the district court erred in finding infringement because the accused products do not meet the claimed *in vitro* dissolution release rate profile. Watson contends that its finished, commercial tablets with the pH-dependent coating dissolve far slower in water than the limitations set forth in the asserted claims. Watson asserts that the data showing dissolution rates of uncoated cores with different levels of hardness compression reported in document PTX 381 fall within the experimental use privilege afforded by 35 U.S.C. § 271(e)(1) for developmental work done to support an ANDA application. Watson further asserts that the accused products do not have the claimed amount of modified release material.

In response, Ferring maintains that both Watson's uncoated cores and coated tablets infringe the asserted claims because they both contain the requisite amount of a modified release material and because they both meet the claimed dissolution limitations. Ferring argues that Watson's ANDA specifies that a blend of polymers and other inactive ingredients, including hypromellose, makes up 32.87–34.83% of the accused tablets and asserts that the ANDA describes how Watson chose the type and amount of such inactive ingredients in its uncoated cores "such that they would release the tranexamic acid '[n]either too fast [n]or too slow.'" Appellee Br. 33 (citing J.A. 972–83, 13880–82) (alterations in original).

Infringement is a question of fact that we review for clear error. *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1339 (Fed. Cir. 2003). 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). The district court here thus erred to the extent that it read § 271(e) to mean that Watson's

act of filing an ANDA, by itself, established infringement sufficient to preclude consideration of the ANDA specification and any amendments before the FDA. The filing only constituted a technical act of infringement for jurisdictional purposes. J.A. 2192–93, 2248–56, 2316. As we have explained, once jurisdiction is established, the ultimate infringement inquiry provoked by such filing is focused on a comparison of the asserted patent claims against the product that is likely to be sold following ANDA approval and determined by traditional patent law principles. *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1365 (Fed. Cir. 2003); *Abbott Labs. v. TorPharm, Inc.*, 300 F.3d 1367, 1373 (Fed. Cir. 2002); *Bristol-Myers Squibb Co. v. Royce Labs., Inc.*, 69 F.3d 1130, 1135 (Fed. Cir. 1995). "The plain language of [§ 271(e)(2)(A)] does not alter a patentee's burden of proving infringement" by a preponderance of the evidence, and we have rejected shifting that burden to the accused infringer to disprove infringement. *Glaxo*, 110 F.3d at 1567–68.

The infringement determination is thus based on consideration of all the relevant evidence, and "[b]ecause drug manufacturers are bound by strict statutory provisions to sell only those products that comport with the ANDA's description of the drug," the ANDA itself dominates the analysis. *Abbott*, 300 F.3d at 1373; *see also Alcon Research Ltd. v. Barr Labs.*, 745 F.3d 1180, 1186–87 (Fed. Cir. 2014). In some cases, the ANDA specification directly resolves the infringement question because 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. *See Sunovion Pharm. v. Teva Pharm. USA, Inc.*, 731 F.3d 1271, 1279–80 (Fed. Cir. 2013) (proposed generic product infringed because the ANDA specification described an amount of stereoisomer within the scope of the asserted patent claim); *Bayer AG v. Elan Pharm. Research Corp.*, 212 F.3d 1241, 1248–50 (Fed. Cir. 2000) (proposed generic product did not infringe

because the ANDA specification required a surface area outside of the range claimed by the asserted patent). In cases in which the ANDA specification does not resolve the infringement question in the first instance, we have endorsed the district court's reference to relevant evidence, including biobatch data and actual samples of the proposed generic composition that the ANDA filer had submitted to the FDA. *See Glaxo*, 110 F.3d at 1569 (proposed generic product did not infringe because the ANDA specified only one crystalline form with certain purity, but did not reveal whether a different crystalline form claimed by the asserted patents would be present at all).

This case is more like *Glaxo* than either *Sunovion* or *Bayer* because Watson's ANDA specification does not itself resolve the question of infringement. There is no specification that calls for measuring the dissolution of its finished, coated commercial product in water; but silence does not answer the question of infringement. The focus that both Ferring and the district court thus gave to infringement by the uncoated cores of Watson's generic product is misplaced. The infringement evaluation is concerned only with the final, coated commercial tranexamic acid tablets for which Watson sought and was granted FDA approval to market as a generic version of a treatment of menorrhagia. *Id.* Watson cannot sell the uncoated cores alone because it would not comply with its ANDA specification; to do so would be to sell both an unapproved and adulterated drug in violation of the law. *See* J.A. 1465.

The independent claims of the '106 and '795 patents require "not less than about 50% by weight of the tranexamic acid or pharmaceutically acceptable salt thereof released at about 90 minutes." '106 patent col. 69 ll. 16–19; '795 patent col. 35 ll. 47–48. The independent claim of the '739 patent requires "about 100% by weight tranexamic acid or a pharmaceutically acceptable salt thereof

released by about 120 minutes." '739 patent col. 69 ll. 63–65. The dissolution data collected by both parties during discovery showed that, in an overwhelming majority of the samples tested by the claimed USP method, only about 27% to 44% of the tranexamic acid was released from the individual coated tablets at 90 minutes and only about 33% to 52% was released at 120 minutes, consistent with the biobatch data reported in Watson's ANDA itself. J.A. 14074, 14218–76, 14751–53, 14768–69, 18290, 18424, 18427, 18443. These data show the samples to be outside the scope of the asserted claims. Of the hundreds of coated commercial products tested, only about four individual tablets released more than 50% of their tranexamic acid at 90 minutes, and none of those released more than about 79% by 120 minutes. *Id.*

Ferring's argument that Watson's own expert conceded in deposition testimony that those results showed that Watson's coated tablets met the dissolution limitations of the asserted claims conveniently ignores that the same expert also testified at trial that those outliers were not representative of Watson's ANDA product. Appellee Br. 43; J.A. 1694–95, 17611–15. The expert, who personally oversaw the testing and specifically observed the dissolution tests at issue, testified that "there was something incomplete about the coating. It lacked coating integrity. The coating on the tablet sort of came apart and opened up. It was very atypical and aberrant relative to all of the other 176 tablets that were examined." J.A. 1694–95. We accordingly do not agree with Ferring or the district court that reliance on such anomalies proves infringement by a preponderance of the evidence in this case. *See In re Omeprazole Patent Litig.*, 84 F. App'x 76, 83 (Fed. Cir. 2003) ("For infringement, the record need only reflect proof by preponderant evidence.").

Furthermore, the district court in fact found that Watson's accused products would not infringe at a core hardness level of less than 17 kp. When all materials are

considered, including amendments, there is no support for the district court's inconsistent finding of infringement under either § 271(e) or § 271(a) because there was no evidence that Watson either did or will manufacture, use, or sell any commercial products with a core hardness of 17 kp or greater. J.A. 1408, 1435, 1464, 2317, 14186. Pursuant to the amendment suggested by the district court at the close of trial, Watson's FDA-approved ANDA specification now only permits it to make, use, and sell tablets with cores that have a hardness of 13–16.5 kp. J.A. 243–46, 255–57.

Ferring acknowledges that the only other data on which it relied at trial and on appeal to prove infringement was Watson's own internal project document labeled PTX 381. Appellee Br. 22. That document reported dissolution profiles in water of experimental, uncoated tranexamic acid cores of specified hardness, as measured by the USP method, which Watson recorded in the development of its generic product formulation prior to submitting its ANDA to the FDA. J.A. 991–93, 1617–19, 2003–11, 2070–72. Those data show that 95% to 100% of the tranexamic acid is released at 45 minutes from uncoated cores compressed to a hardness of 13 kp and 16 kp but that cores with a hardness of 17 kp or greater release 71% to 77% of the tranexamic acid at 45 minutes. J.A. 14840. And it was on that basis that the district court found that both the uncoated cores of Watson's generic tranexamic acid product and the final, coated commercial tablets with a core hardness of 17 kp and greater infringed Ferring's asserted claims, which require that less than about 70% of the tranexamic acid to be released at about 45 minutes. J.A. 2307–17. But Watson's PTX 381 document is not relevant to the question of infringement because it does not provide any data for the dissolution release rate of tranexamic acid from Watson's finished, coated commercial tablets. The data in PTX 381 therefore were not evidence that Watson's ANDA product would infringe the

asserted claims. Thus, although those data were not part of the ANDA, either as filed or as finally approved, we need not address the applicability to them of the experimental use provision of § 271(e)(1).

The asserted independent claims also require that the accused product contain a certain amount of "modified release material," ranging from about 5% to about 50% by weight of the formulation in the '795 patent and about 10% to about 35% by weight of the formulation in the '106 and '739 patents. '795 patent col. 35 ll. 31–33; '106 patent col. 69 ll. 5–7; '739 patent col. 69 ll. 54–56. The district court construed the term "modified release material" to mean "a material that modifies the release of the active pharmaceutical ingredient." *Ferring B.V. v. Watson Labs., Inc. – Fla.*, No. 11-0481 (D. Nev. Feb. 6, 2013), ECF No. 295; J.A. 195–96, 204. But under that construction, which we do not disturb, just because a certain material *can* modify release of the active pharmaceutical ingredient tranexamic acid, does not necessarily mean that it actually *does*. Experts for both parties agreed that testing is required to measure whether a particular excipient actually functions to modify the release of tranexamic acid in a given formulation and therefore qualify as a modified release material. J.A. 1151–52, 1260–61, 1684, 1897–98, 2102–09. Here, however, Ferring did not conduct any such testing and thus provided no basis from which to draw any reliable inferences regarding whether any of the inactive ingredients in Watson's ANDA product would modify the release of the tranexamic acid, regardless of the amount present.

Moreover, although it is not readily discernable from the record that the district court applied its stated construction in its infringement analysis, the only way for the court to have found that Watson's finished, coated commercial tablets infringed the asserted claims would have been for the court to have determined, as it suggested during trial, that a modified release material was any

material that causes tranexamic acid to behave differently in some way than in water alone. J.A. 1771–73, 1885–87. That alone would constitute reversible error as it would not follow its own claim construction.

We have considered Ferring's remaining arguments regarding infringement and find them unpersuasive. Because we hold that the asserted independent claims of Ferring's patents are not infringed, the asserted dependent claims are likewise not infringed. *Becton Dickinson & Co. v. C.R. Bard, Inc.*, 922 F.2d 792, 798 (Fed. Cir. 1990); *Wahpeton Canvas Co. v. Frontier, Inc.*, 870 F.2d 1546, 1552 n.9 (Fed. Cir. 1989) ("One who does not infringe an independent claim cannot infringe a claim dependent (and thus containing all the limitations of) that claim."). We thus conclude that the district court erred in finding that Ferring proved by a preponderance of the evidence that Watson's finished, coated commercial tranexamic acid ANDA product infringed the asserted claims. Therefore, there is no basis for the district court's order resetting the FDA approval date of Watson's ANDA or the court's grant of a permanent injunction against the manufacture, use, sale, or offer for sale of Watson's generic tranexamic acid product, and we accordingly vacate both.

CONCLUSION

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 Ferring's '739, '106, and '795 patents are invalid as obvious under 35 U.S.C. § 103 and we therefore affirm that judgment. We also conclude that the district court's finding that Watson's generic tranexamic acid product infringes Ferring's asserted claims was not in accordance with law and therefore reverse that judgment. Accordingly, we vacate the district court's order resetting the FDA approval date of Watson's ANDA 20-2093 and vacate the district court's permanent injunction of the manufacture,

use, sale, or offer for sale of Watson's generic tranexamic acid product.

AFFIRMED IN PART, REVERSED IN PART, and VACATED IN PART

COSTS

Costs to Watson.