United States Court of Appeals for the Federal Circuit

JAZZ PHARMACEUTICALS, INC.,
Appellant

v.

AVADEL CNS PHARMACEUTICALS, LLC,
Appellee

2023-1186

Appeal from the United States District Court for the District of Delaware in No. 1:21-cv-00691-GBW, Judge Gregory Brian Williams.

Decided: February 24, 2023

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

LOURIE, *Circuit Judge*.

Jazz Pharmaceuticals, Inc. ("Jazz") appeals from an order of the United States District Court for the District of Delaware granting a motion for an injunction brought by Avadel CNS Pharmaceuticals, Inc. ("Avadel"). *See Jazz Pharms., Inc. v. Avadel CNS Pharms., LLC,* No. 21-cv-00691, 2022 WL 17084371 (D. Del. Nov. 18, 2022) ("*Decision*"). The injunction directed Jazz to take measures to delist U.S. Patent 8,731,963 ("the '963 patent") from the U.S. Food and Drug Administration's ("the FDA's") Approved Drug Products with Therapeutic Equivalence Evaluations publication, more colloquially known as the "Orange Book." For the following reasons, we lift our stay of the injunction and affirm.

BACKGROUND

Jazz holds an approved New Drug Application ("NDA") for the narcolepsy drug Xyrem®. J.A. 1445. Xyrem's active ingredient is sodium gamma-hydroxybutyrate ("GHB"), which is also known as sodium oxybate. *Id.* GHB exerts a heavily sedating effect, which is theorized to grant deepened nighttime sleep, resulting in improved daytime wakefulness. GHB is prone to heavy misuse and is infamously known as a date-rape drug. Given that misuse, the FDA conditioned approval of Jazz's NDA upon development of Risk Evaluation and Mitigation Strategies ("REMS"), which include protocols that must be followed prior to

prescribing or dispensing Xyrem. *Id.* Xyrem's REMS originally restricted distribution to a single-pharmacy system, although the FDA waived that requirement in 2017. J.A. 5660.

The '963 patent relates to Jazz's single-pharmacy distribution system, which controls access to abuse-prone prescription drugs prescribed to narcolepsy patients through a central pharmacy and computer database by tracking prescriptions, patients, and prescribers. Representative claims 1 and 6 are presented below:

> 1. A computer-implemented system for treatment of a narcoleptic patient with a prescription drug that has a potential for misuse, abuse or diversion, comprising:
>
> one or more computer memories for storing a single computer database having a database schema that contains and interrelates prescription fields, patient fields, and prescriber fields;
>
> said prescription fields, contained within the database schema, storing prescriptions for the prescription drug with the potential for abuse, misuse or diversion, wherein the prescription drug is sold or distributed by a company that obtained approval for distribution of the prescription drug;
>
> said patient fields, contained within the database schema, storing information sufficient to identify the narcoleptic patient for whom the company's prescription drug is prescribed;
>
> said prescriber fields, contained within the database schema, storing information sufficient to identify a physician or other prescriber of the company's prescription drug

and information to show that the physician or other prescriber is authorized to prescribe the company's prescription drug;

a data processor configured to:

process a database query that operates over all data related to the prescription fields, prescriber fields, and patient fields for the prescription drug; and

reconcile inventory of the prescription drug before the shipments for a day or other time period are sent by using said database query to identify information in the prescription fields and patient fields;

wherein the data processor is configured to process a second database query that identifies that the narcoleptic patient is a cash payer and a physician that is interrelated with the narcoleptic patient through the schema of the single computer database;

said identifying that the narcoleptic patient is a cash payer by said second database query being an indicator of a potential misuse, abuse or diversion by the narcoleptic patient and being used to notify the physician that is interrelated with the narcoleptic patient through the schema of the single computer database.

'963 patent at col. 8 l. 39–col. 9 l.13 (emphasis added).

6. The system of claim 1 wherein the prescription drug comprises gamma hydroxyl butyrate (GHB).

Id. col. 9 ll. 27–28.

Under the Hatch-Waxman Act ("the Act"), when a drug developer files an NDA, information on each patent "for which a claim of patent infringement could reasonably be asserted" must be submitted to the FDA if the patent claims either (i) the drug submitted for approval, or a formulation or composition thereof, or (ii) "a method of using such drug for which approval is sought or has been granted in the application." 21 U.S.C. § 355(b)(1)(A)(viii). For "patents that claim a method of use, the applicant must submit information only on those patents that claim indications or other conditions of use for which approval is sought or has been granted in the NDA." 21 C.F.R. § 314.53(b)(1). The FDA publishes that information in the Orange Book, arming the patent owner with the ability to trigger a presumptive, thirty-month suspension of the FDA's approval of a competitive product.

In 2014, Jazz listed the '963 patent in the Orange Book as covering a method of using Xyrem. In 2017, three of the '963 patent's 28 claims were found unpatentable in an *inter partes* review proceeding. *See Amneal Pharms. LLC v. Jazz Pharms., Inc.*, No. IPR2015-01903, 2017 WL 1096638 (P.T.A.B. Mar. 22, 2017). The remaining claims expired in December 2022. Because Jazz received a grant of pediatric exclusivity, however, the '963 patent prevents the FDA from approving follow-on products until June 2023. *Decision* at *1; J.A. 6350.

The Orange Book was intended to meet the conflicting goals of generic applicants who wish to market approved products via an abbreviated approval pathway and holders of NDAs who own patents claiming approved products and their uses. *See* H.R. Rep. No. 98-857, pt. 1, at 14–15, 27–28, 32–33 (1984), reprinted in 1984 U.S.C.C.A.N. at 2647–48, 2660–61, 2665–66, 1984 WL 37416 (Leg. Hist.); *see also* 21 U.S.C. § 355(j) (describing Abbreviated New Drug Applications ("ANDAs")); *id.* § 355(b)(2) (describing

§ 505(b)(2)[1] NDAs, which differ from stand-alone NDAs in that at least some of the information required for approval comes from studies not conducted by or for the applicant or for which the applicant has a right of reference or use). Under the Act, a § 505(b)(2) applicant must file a certification with respect to each patent listed in the Orange Book that claims the drug or method of using the drug for which the applicant seeks approval. *See* 21 U.S.C. § 355(b)(2)(A).

In December 2020, Avadel submitted an NDA for GHB-based drug FT218, along with amendments pursuant to § 505(b)(2) and a proposed REMS. Unlike Xyrem, which requires the patient to wake up a few hours into the night to ingest a second dose, FT218 is dosed once nightly. *Decision* at *1. FT218's REMS also uses multiple pharmacies and databases for ensuring proper drug handling. Despite these differences, and the fact that Avadel had filed an NDA, not an ANDA, the FDA required Avadel to file a certification regarding the '963 patent's single-pharmacy system. Jazz subsequently sued Avadel for infringement of the '963 patent. Avadel contemporaneously sued the FDA, alleging that it violated the Administrative Procedure Act ("APA") by requiring certification over the '963 patent. Notably, the FDA does not verify that submitted patents actually meet statutory listing criteria, nor does the FDA proactively remove improperly listed patents. *See Apotex, Inc. v. Thompson*, 347 F.3d 1335, 1347 (Fed. Cir. 2003)

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[1] This number refers to the original section number from the Federal Food, Drug, and Cosmetic Act of 1938, Pub. L. No. 75-717 (codified as amended at 21 U.S.C. § 301 et seq.) ("FDCA"), which has been superseded by 21 U.S.C. § 355(b)(2). The industry continues to refer to this type of abbreviated application using the original FDCA section number. We will also.

("[T]he FDA's . . . duties with respect to Orange Book listings are purely ministerial.").

Another remedy for an improper listing is for an accused infringer to counterclaim when it is sued, seeking an order requiring the patent owner to correct or delete a listing under 21 U.S.C. § 355(c)(3)(D)(ii)(I) for NDA filers and under § 355(j)(5)(C)(ii)(I) for ANDA filers. Avadel's suit against the FDA was accordingly dismissed after the district court identified that § 355(c)(3)(D)(ii)(I) provided Avadel with a separately available and adequate remedy for its alleged harms. *See Avadel CNS Pharms., LLC v. Becerra*, No. 1:22-cv-02159, 2022 WL 16650467, at *6–9 (D.D.C. Nov. 3, 2022).

Avadel thus responded to Jazz's infringement assertions with a counterclaim seeking delisting of the '963 patent for failure to claim a drug or method of use. In evaluating the counterclaim, the district court found that, as a matter of claim construction, the '963 patent claims a system and thus does not claim an approved method of use. The district court subsequently ordered Jazz to ask the FDA to delist the '963 patent. Jazz filed a notice of appeal and moved the district court and this court to stay the injunction pending appeal. On November 29, 2022, we issued a temporary stay pending resolution of the concurrent district court motion. After the district court denied Jazz's stay motion on December 5, 2022, we extended the stay until the issues on appeal could be evaluated by this court on the merits. We have jurisdiction under 28 U.S.C. § 1292(c)(1).

DISCUSSION

We review a district court's grant of a permanent injunction for abuse of discretion. *Novo Nordisk A/S v. Caraco Pharm. Lab'ys, Ltd.*, 688 F.3d 766, 767 (Fed. Cir. 2012). An abuse of discretion may be established by showing that the court either made a clear error of judgment in weighing relevant factors, or exercised its discretion based on an

error of law or on findings that were clearly erroneous. *Joy Techs., Inc. v. Flakt, Inc.*, 6 F.3d 770, 772 (Fed. Cir. 1993).

Jazz contends that the district court abused its discretion in finding that the '963 patent is not a method-of-use patent for listing and delisting purposes under the FDCA. It further contends that, even if the '963 patent was not a method-of-use patent, the court abused its discretion in determining that § 355(c)(3)(D)(ii)(I) provides a delisting remedy. We address each argument in turn.

I.

First, we consider whether the district court erred in determining that the '963 patent is not a method-of-use patent under the FDCA. Jazz asserts that this inquiry involves asking two questions: (1) what does the patent claim, and (2) is the patented invention either "the drug for which the application was approved" or "an approved method of using the drug"? We address each question in turn.

A.

We first address whether the district court erred in determining what the '963 patent claims in the context of a listing/delisting inquiry. Jazz contends that patent law does not provide the correct framework for determining whether a patent should be listed in the Orange Book. Appellant's Br. at 27 ("[T]he disputed phrase in the FDCA is not directed to a patent-law question at all[.]"); *id.* at 29 ("[T]he Orange Book listing rules codified in the FDCA have nothing to do with . . . patent-law problems.").

The listing requirements set forth in 21 U.S.C. § 355(b) concern whether, *inter alia*, a patent "claims a method of using [the] drug for which approval is sought or has been granted in the application." Similarly, the listing requirements set forth in 21 C.F.R. § 314.53(b)(1) concern patents that "claim[] the drug or a method of using the drug," setting forth additional requirements "[f]or patents that claim

a method of use" and for when "the method(s) of use claimed by the patent do[] not cover an indication or other approved condition of use in its entirety." An inquiry into whether a patent may be properly listed or delisted from the Orange Book therefore clearly requires a determination of what that patent claims.

Jazz has acknowledged that analyzing a patent in that context involves asking the question, "what does the patent claim," and that the answer should be derived using the tools and framework of patent law, including claim construction. Appellant's Reply Br. at 4. It therefore seems undisputed that these statutes and regulations involve determining what a patent claims and that this determination raises issues of patent law. *Apotex*, 347 F.3d at 1344; *Caraco Pharm. Lab'ys, Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 405 (2012).

Jazz further asserts that "what the '963 patent claims turns out to be largely uncontroversial," describing the claims as reciting "elements of a REMS-based procedure to ensure that Xyrem® can be safely prescribed by doctors and safely used by patients. Avadel does not appear to disagree." Appellant's Reply Br. at 5; *see also* Appellant's Br. at 6 ("The '963 patent, properly construed, claims a method."); *id.* at 26 ("In short, the patent claims a method."); *id.* at 55–58. Avadel, of course, does disagree. Appellee's Br. at 52–55. We do also.

Claim construction is a question of law that we review *de novo*. *Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1454 (Fed. Cir. 1998) (en banc). "It is a 'bedrock principle' of patent law that 'the claims of a patent define the invention[,] which the patentee is entitled . . . to exclude.'" *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc) (quoting *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1115 (Fed. Cir. 2004)); *see also Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996) ("[W]e look to the words of the claims

themselves . . . to define the scope of the patented invention.").

The district court determined that the '963 patent claims recite systems, not methods. *Decision* at *2–3. Jazz contends that the word "system" as it appears in the '963 patent claims is, essentially, a synonym for "method." Appellant's Br. at 56–58. But method claims require the performance of steps; claims that describe physical components of a whole are system, or apparatus, claims. *See Finjan, Inc. v. Secure Computing Corp.*, 626 F.3d 1197, 1204 (Fed. Cir. 2010); *In re Kollar*, 286 F.3d 1326, 1332 (Fed. Cir. 2002) (noting the "distinction between a claim to a product, device, or apparatus, all of which are tangible items, and a claim to a process, which consists of a series of acts or steps").

Each of the '963 patent's three independent claims describes a "computer-implemented system" that comprises "one or more computer memories" and a "data processor." '963 patent at col. 8 l. 39–col. 9 at l. 13 (independent claim 1); *id.* col. 10 l. 27–col. 11. l. 6 (independent claim 23); *id.* col. 11 l. 7–col. 12 l. 10 (independent claim 24). As the district court correctly analyzed in its *Markman* Order, these claims recite "an assemblage of components," defining a system. J.A. 5723. Jazz has not identified any description in the patent specification or prosecution history to alter that conclusion. The claims to a system comprising computer memories and a data processor are not claims to a method.

That the claimed systems can be used in the course of treating patients suffering from narcolepsy does not alter the fact that these are system claims. *See MasterMine Software, Inc. v. Microsoft Corp.*, 874 F.3d 1307, 1315–16 (Fed. Cir. 2017) (finding that the inclusion of active verbs and other functional language describing the capabilities of a claimed system does not transform a system claim into a method claim); *see also HTC Corp. v. IPCom GmbH & Co.*,

667 F.3d 1270, 1277 (Fed. Cir. 2012). We therefore find that the claims of the '963 patent were properly construed by the district court as system claims, not method claims.

B.

We next turn to whether the system claimed in the '963 patent is "an approved method of using the drug" under 21 U.S.C. § 355(c)(2) and § 355(c)(3)(D)(ii)(I).

According to Jazz, FDA regulation 21 C.F.R. § 314.53(b)(1), which describes listing patents that "claim conditions of use," informs the analysis of whether a patent claims "an approved method of using the drug" under § 355. Jazz contends that this regulation yields a broader definition of "method" than permitted by the language of patent law and that this broader definition encompasses the claims of the '963 patent. More specifically, it contends that Xyrem prescribers were bound to follow the approved REMS; that is, the use of Xyrem, including using it to treat patients with narcolepsy, was *conditioned on* following the REMS. Because Xyrem's approved REMS involved the single pharmacy system that is described in the '963 patent, the '963 patent describes a listable condition of use for which approval had been granted in the NDA. Jazz thus contends that the district court erred by ending its analysis after construing the '963 patent claims as system claims, rather than further inquiring into whether § 314.53(b)(1) nevertheless allows these system claims to be listed as method-of-use claims.

Avadel responds in part by asserting that Jazz forfeited this argument. We need not address forfeiture because we conclude that, regardless of forfeiture, Jazz misreads the regulation describing method-of-use patents. Section 314.53 does not broaden the term "method" such that reciting a condition of use turns a system patent into a listable method-of-use patent. Rather, this regulation narrows that category of listable patents to those that (1) claim methods of use, wherein (2) those methods of use are

directly relevant to the NDA in question. *See* 21 C.F.R. § 314.53(b)(1) ("For patents that claim a method of use, the applicant must submit information only on those patents that claim indications or other conditions of use for which approval is sought or has been granted in the NDA."). The fact that the '963 patent claims recite a system that was, at least prior to 2017, implicated in a condition of using Xyrem, does not disturb the determination that the claims do not recite a listable method of use, which makes this regulatory provision inapplicable.

Jazz also points to subsections of 21 U.S.C. § 355 that use the phrase "conditions of use," in an attempt to establish that this term is inclusive of all patents claiming elements of an approved REMS. Appellant's Br. at 34–36. We are not persuaded. The subsections to which Jazz points (*e.g.*, § 355(d)(5), 355(e)(5), and 355(j)(2)) describe conditions of use evaluated for efficacy, implicating "relevant science," "clinical investigations," as well as "establishing effectiveness" and determining whether a "new drug can be expected to have the same therapeutic effect as the listed drug when administered" according to the approved "conditions of use prescribed, recommended, or suggested in the labeling." The scope of "conditions of use" in those provisions, however, does not expand the meaning of "method of using the drug" in the statutory provision at issue here, which must take its meaning from the patent laws.

Jazz asserts that, to the extent these listing statutes are ambiguous, deference should be given to the FDA's interpretation reflected in regulation § 314.53 under *Chevron, U.S.A., Inc. v. Natural Resource Defense Council, Inc.*, 467 U.S. 837 (1984). As explained above, we do not find § 314.53 to be an interpretation of the distinct statutory delisting provision at issue here, which we think must be interpreted to borrow the patent-law meaning of "method" in its reference to claiming methods of using a drug. Moreover, even if we thought the delisting language ambiguous as to that question, which we do not, *Chevron* deference

cannot be given here because the FDA has not definitively answered the question whether REMS patents more broadly should or can be listed in the Orange Book. Although the FDA has opened several notice-and-comment inquiries into whether REMS patents belong in the Orange Book, it has never proclaimed an official agency stance on that issue, instead proclaiming that "its duties with respect to Orange Book listings are purely ministerial." *Apotex*, 347 F.3d at 1347; *see also* J.A. 3986 n.34 ("Consistent with its ministerial role, FDA has not evaluated what the '963 patent actually covers or whether the [method] use code published in the Orange Book accurately reflects what is covered by the '963 patent.").

Avadel also highlights that the FDA only requires listing patents "for which a claim of patent infringement could reasonably be asserted," and that Congress explicitly prohibited companies from using REMS requirements to "block or delay" ANDA and § 505(b)(2) approvals. 21 U.S.C. § 355-1(f)(8). Although § 355-1(f)(8) does not expressly provide that a REMS patent may not be asserted against potential infringers, Avadel suggests that listing a REMS patent would allow a patent owner to "block or delay" ANDA and § 505(b)(2) filers in violation of that statute. Appellee's Br. at 46; *see also* Appellant's Br. at 10 (recognizing that "submission of an application under Section 505(b)(2) for a drug claimed in a patent or the use of which is claimed in a patent listed in the Orange Book is a statutory act of infringement"). Because we find that the district court did not err in concluding that the '963 patent must be delisted, we need not address Avadel's broader arguments about REMS patents, more generally.

II.

We finally consider Jazz's argument that 21 U.S.C. § 355(c)(3)(D)(ii)(I) is not available to provide Avadel with a delisting remedy for the '963 patent.

Jazz asserts that, in 2014, the regulatory framework permitted Jazz to list the '963 patent, which, it says, at a minimum fell into a category of patents neither required nor forbidden to be listed. According to Jazz, because it was permissive to list the '963 patent in 2014, § 355(c)(3)(D)(ii)(I) does not provide Avadel with the power to request an order to delist it now. We disagree.

As the district court correctly analyzed, the delisting statute does not require us to consider whether the patent holder violated the law by listing the patent in the first instance. It simply provides that those accused of infringing a listed patent may request an order requiring the patent holder to correct or delete listings for patents that do not claim the drug or a method of using the drug. As the '963 patent claims neither and has been asserted in a patent infringement action against Avadel, § 355(c)(3)(D)(ii)(I) provides Avadel with a delisting remedy. The district court therefore correctly ordered Jazz to seek delisting of the '963 patent from the Orange Book.

CONCLUSION

We have considered Jazz's remaining arguments and find them unpersuasive. For the foregoing reasons, we affirm and lift our stay of the injunction requiring Jazz to ask the FDA to delist the '963 patent. As the original date to comply with the injunction has expired, we modify the injunction insofar as restarting the 14-day period for compliance prescribed by 21 C.F.R. § 314.53(f)(2)(i) to be within 14 days of this decision.

AFFIRMED