IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

JAZZ PHARMACEUTICALS, INC., Plaintiff, v. AVADEL CNS PHARMACEUTICALS, LLC, Defendant.	C.A. No. 21-691-MN

REPLY BRIEF IN SUPPORT OF DEFENDANT'S RENEWED MOTION FOR PARTIAL JUDGMENT ON THE PLEADINGS

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I. INTRODUCTION

Jazz's Opposition is an exercise in distraction. A federal statute enacted in 2003 expressly grants defendants like Avadel the right to bring a counterclaim "seeking an order requiring [an NDA holder] to correct or delete the patent information" in the Orange Book "on the ground that the patent does not claim either—(aa) the drug for which the application was approved; or (bb) an approved method of using the drug." 21 U.S.C. § 355(c)(3)(D)(ii)(I). That is all Avadel must prove to prevail—that the '963 patent does not fall into one of those two categories. The Supreme Court's *Caraco*,[1] decision confirms the simplicity and availability of this counterclaim:

> The provision authorizes an [] applicant sued for patent infringement to
>
> > "assert a counterclaim seeking an order requiring the [brand] to correct or delete the patent information submitted by the [brand] under subsection (b) or (c) [of §355] on the ground that the patent does not claim either—"(aa) the drug for which the [brand's NDA] was approved; or "(bb) *an approved method of using the drug*."
> >
> > 21 U. S. C. §355(j)(5)(C)(ii)(I).
>
> The counterclaim thus enables a generic competitor to obtain a judgment directing a brand to "correct or delete" certain patent information that is blocking the FDA's approval of a generic product.

Caraco Pharm. Lab'ys., Ltd. v. Novo Nordisk A/S, 566 U.S. 399, 408-09 (2012).[2]

There is no dispute that the '963 patent does not claim a drug. Thus, the *only* question before the Court is whether the '963 patent claims "an approved method of using the drug." Whether Jazz could or should have listed the '963 patent in the past, or whether *other* statutory language is or is not retroactive is of no moment. Whatever the propriety of Jazz's original listing

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[1] As Avadel previously addressed, *Caraco* cites to 21 U.S.C. § 355(j)(5)(C)(ii)(I) as the source of the above-referenced counterclaim for ANDA applicants. Avadel's motion relies on 21 U.S.C. § 355(c)(3)(D)(ii)(I), which is the parallel provision applicable to 505(b)(2) NDA applicants like Avadel. Because the two parallel portions of the statute use the same substantive language, *Caraco's* analysis applies equally here. D.I. 118 at 5 n.5.

[2] Emphasis added unless otherwise noted.

decision (which was in fact improper), the law gives Avadel a present right to seek an order requiring Jazz to delist the '963 patent from the Orange Book.

Turning to the statutory test, the '963 patent should be delisted because it does not claim an approved method of using a drug under either party's proposed claim construction. Under Avadel's proposal, the '963 patent claims are directed to systems, not methods. D.I. 118 at 6-7. Under Jazz's proposal, the claims recite "methods of using a computer-implemented system to safely *distribute* gamma-hydroxybutyrate," (D.I. 145 at 7) which is not a method of *using the drug* any more than a patent directed to distributing GHB using vehicles with biometric locks to minimize theft risks would be a method of using the drug. Jazz's inclusion of the phrase "for treatment of a narcoleptic patient" in its proposal does nothing to transform the claims into a method of using the drug, any more than would appending those words to such a biometric lock patent. D.I. 118 at 2, 9-10.

Jazz's new argument that it was somehow "permitted" to list the '963 patent in the Orange Book even if it does not claim a method of using a drug is yet another attempt to distract the Court from the real issue at hand. The Hatch-Waxman Act authorizes NDA applicants to submit patents that fall into one of the enumerated categories in 21 U.S.C. § 355(b)(1)(A)(viii) for listing in the Orange Book. The delisting statute authorizes this Court to order ineligible patents to be delisted pursuant to its terms. That statute, and case law interpreting it from the Supreme Court and the First Circuit Court of Appeals, would be rendered superfluous under Jazz's interpretation. Indeed, if Jazz believed that *any* patent is *permitted* to be listed in the Orange Book without risk of delisting, one wonders why it bothered to urge this Court to construe the '963 patent claims directed to "computer-implemented systems" as "methods"? That question answers itself.

Jazz's arguments continue to change, but its efforts to delay do not. Enough is enough. The sole question for the purpose of Avadel's delisting counterclaim is whether the '963 patent claims recite "an approved method of using the drug." Avadel respectfully submits that the answer is a resounding "no."

II. ARGUMENT

A. The '963 Patent Should Be Delisted Under Avadel's Construction Because The Claims Are Directed To Systems, Not Methods, As The Statute Requires

Construing the claims of the '963 patent in Avadel's favor is dispositive of the present motion. As Avadel detailed in the Joint Claim Construction Brief (D.I. 132), the '963 patent claims are directed to systems, not methods, and therefore do not claim a "method of using [a] drug."[3] 21 U.S.C. § 355(c)(3)(D)(ii)(I); 21 U.S.C. § 355(b)(1)(A)(viii). Accordingly, Jazz should be required to request that the FDA remove the '963 patent from the Orange Book. *Id.*; *see also* D.I. 118 at 9, 11.

Jazz argues that even if the '963 patent claims are directed to systems, the '963 patent was properly listed in the Orange Book when it issued because § 355(b)(1)(A)(viii) only *required* certain patents be listed in the Orange Book, but did not *prohibit* other patents from being listed. D.I. 153 at 14-18. This argument finds no support in the statute or the governing case law.

First, Jazz's assertion contradicts the unambiguous language of the delisting statute, which plainly states that patents that do not fall into one of two specific categories should be delisted. The statute does not require an inquiry into whether the NDA holder was authorized to list the patent in the first instance. The '963 patent is subject to delisting because it "does not claim . . .

[3] It is undisputed that the '963 patent is not directed to a drug substance or drug product, the other two categories of Orange Book-listable patents. 21 U.S.C. § 355(b)(1)(A)(viii).

an approved method of using the drug." 21 U.S.C. § 355(c)(3)(D)(ii)(I). That is the beginning and end of the statutory inquiry.

As the Supreme Court recognized in *Caraco*, an NDA applicant sued for patent infringement may "assert a counterclaim seeking an order requiring the [brand] to correct or delete the patent information submitted by the [brand] under subjection (b) or (c) of § 355 on the ground that the patent does not claim either" a "drug" or "an approved method of using the drug." 566 U.S. at 408-09 (citing 21 U.S.C. § 355(j)(5)(C)(ii)(I)). Thus, Jazz's unsupported assertion that it was "permitted to list the '963 patent in the Orange Book under the statute and regulations that were applicable at the time of its listing" is directly at odds with the unambiguous language of 21 U.S.C. § 355(c)(3)(D)(ii)(I). D.I. 153 at 17.

Second, Jazz's assertion is also at odds with the most natural reading of the Hatch-Waxman Act, and the one understood by courts addressing this statutory provision: *only* the enumerated categories of patents—to a drug substance, drug product, or method of using the drug—can be listed in the Orange Book. *In re Lantus Direct Purchaser Antitrust Litig.*, 950 F.3d 1, 4 (1st Cir. 2020) ("[T]he agency requires the manufacturer to declare that the submitted patent claims the 'drug substance,' 'drug product (composition/formulation),' or 'one or more methods of using' the drug for which it is listed.") (internal citation omitted). The *Lantus* court's understanding reflects the sensible conclusion that the statute's requirement that NDA applicants "*shall*" list each patent that claims a drug or "a method of using [a] drug" is meant to be an exclusive list. *See, e.g.*, *Carcieri v. Salazar*, 555 U.S. 379, 391-92 (2009) (holding that where Congress directed that the definition of "Indian" for purposes of the Indian Reorganization Act "shall" include persons meeting three discrete qualifications, Congress "explicitly and comprehensively defined the term"

by reference to those qualifications). Jazz's argument to the contrary should be rejected.[4]

Third, Jazz's permissive listing theory is a paradigmatic example of what prompted Congress to enact the delisting statute in 2003. Congress conferred the ability to adjudicate such counterclaims on district courts in response to the "abuses" Congress observed by brands improperly listing patents in the Orange Book. *Caraco*, 566 U.S. at 408. Congress specifically enacted that counterclaim to address situations where "a brand whose original patent on a drug was set to expire listed a new patent ostensibly extending its rights over the drug, but in fact covering neither the compound nor any method of using it," because the FDA is not in a position to review patent scope, or otherwise police such malfeasance. *Id*. If Jazz were correct, the statutory delisting counterclaim—along with the Supreme Court's discussion in *Caraco*—would be superfluous. That cannot be correct. *See Nat'l Ass'n of Mfrs v. Dep't of Defense*, 138 S. Ct. 617, 632 (2018) (rejecting "an interpretation of the statute that would render an entire subparagraph [of the statute] meaningless"). Jazz offers no explanation for the irreconcilable statutory conflict presented by its novel theory. Nor does it explain why, if it is correct, the delisting statute exists.

Fourth, Jazz's extended discussion as to whether the Orange Book Transparency Act ("OBTA") applies retroactively is irrelevant for the same reason. The instant counterclaim arises under the delisting statute, and is in no way "premised" on application of the OBTA. *See* D.I. 153 at 14; D.I. 118 at 5, 11; *supra* at 1-2. While Avadel cited the OBTA as supplemental support for why Jazz was not "required" to list the '963 patent, that explanation is not a necessary foundation to Avadel's delisting claim. D.I. 118 at 8. Even if the Court agreed entirely with Jazz's analysis

[4] Jazz's corollary assertion that "[a]t that time, the FDA was clear [as to] the only patents that 'must not be submitted to FDA' for listing in the Orange Book" (D.I. 153 at 15), is likewise flawed. The FDA's guidance cannot alter the plain import of the Hatch-Waxman Act, and to the extent Jazz suggests otherwise, it would conflict with the statute and therefore could not be applied. *See United Airlines v. Transp. Sec. Admin.*, 20 F.4th 57, 63 n.3 (D.C. Cir. 2021).

on this point, it would not change the correct outcome of Avadel's delisting motion.

In any event, the OBTA—stating that patent information "that is not the type of patent information required by subjection (b)(1)(A)(viii) shall not be submitted"—merely clarified what the Hatch-Waxman Act already conveyed: that "[t]he statute and applicable regulations call for the listing of *only* patents that claim the pertinent drug or a method of using the drug." *Lantus*, 950 F.3d at 7. Indeed, *Lantus* also involved patents submitted to the FDA *prior* to the passage of the OBTA, and the *Lantus* court (like Avadel) relied on 21 C.F.R. § 314.53(b)(1) to find that the Hatch-Waxman Act *only* allows for listing of patents that claim drugs or methods of using a drug. *Id*.; *see also id*. at 10. Based on this understanding, the First Circuit concluded that the patent at issue did not claim a "drug product" or method of using a drug and thus did "not qualify for listing in the Orange Book." *Id*. at 9. And like *Lantus*, *Caraco* issued before the OBTA was passed. Accordingly, Jazz's suggestion that the Hatch-Waxman Act became exclusionary as to which patents may be listed *only* after the OBTA was passed fails in light of both *Caraco* and *Lantus*.

Thus, even if Jazz's listing of the '963 patent in the Orange Book in 2014 were proper, that does not now immunize the '963 patent from delisting. As *Caraco* made clear, accused infringers can bring a counterclaim to delete patent information on the ground that it does not cover a drug or method of using the drug. *Caraco*, 566 U.S. at 408-09. *Caraco* and *Lantus* therefore establish that patents falling outside the categories described in § 355(b)(1)(A)(viii) may be delisted without regard to whether they were properly listed under the Hatch-Waxman Act in the first place.

If the Court determines the '963 patent is directed to a system, Avadel's motion should be granted. Jazz's argument that the Hatch-Waxman Act allows any patent to be listed in the Orange Book is a desperate attempt to introduce confusion into the straightforward question of whether a patent directed to a computer system should be delisted from the Orange Book. It should.

B. The '963 Patent Should Be Delisted Even Under Jazz's Proposed Construction Because The Claims Are Not Directed To A Method Of Using A Drug

Even if the claims cover "methods of using a computer-implemented system to safely distribute [GHB] for treatment of a narcoleptic patient" as Jazz contends, the '963 patent should still be delisted. D.I. 145 at 7. The Court need not look any further than the plain language of Jazz's proposed construction. A method "of *using a computer-implemented system to safely distribute* [GHB] for treatment of a narcoleptic patient" is not a method of "using [a] drug," as is required for Orange Book listing. *See Lantus*, 950 F.3d at 7 (finding it at first "readily apparent" from the pleadings that the asserted patent should not be listed in the Orange Book).

The distinction between "distribution" and "use" is reflected in Jazz's document and the Federal Register. "Use" involves the manner and medical purpose for which medical professionals administer, or direct patients to self-administer, a drug product. *See, e.g.*, D.I. 153 at Ex. A, 1 ("This new drug application provides for the *use* of Xyrem® Oral Solution for the treatment of cataplexy associated with narcolepsy."). "Distribution" involves the manner in which a drug is (or is not) made available to medical providers and patients. *See, e.g.*, 21 C.F.R. § 203.3(h) ("Distribute means to sell, offer to sell, deliver, or offer to deliver a drug…."). Jazz's reliance on restrictions governing marketing activities (D.I. 153 at 4-5) and the requirement that "Xyrem is available only through a restricted distribution program called the XYWAV and XYREM REMS," (*id*. at 5) does nothing to establish that the '963 patent involves *use* of a drug—it merely describes restrictions on the *distribution* of the drug to avoid misuse. *Id*. at 5. Jazz's arguments in opposition all devolve to the circular and conclusory assertion that a method of using a computer-implemented system to safety distribute GHB is a method of using a drug, and thus fail.[5]

[5] Jazz also contends that Avadel has argued that 21 U.S.C. § 355-1(f)(8), which prohibits the use of REMS patents to block or delay approval of an application to market a drug product, prohibits

For example, Jazz doubles down on its argument that it was "required" to list the '963 patent, because it covers a REMS that is a condition of Xyrem's use and is described in the labelling of the drug product. *Id*. at 9-10. Jazz ignores that the very regulation it cites requires more than the listed patent claim a "condition[] of use that [is] described in the pending or approved applications"; *it also requires that the patents claim a method of using a drug. See id*. at 9 (citing 21 C.F.R. § 314.53(b)(1) (2011)). As it did in its Opposition to Avadel's original motion, Jazz simply ignores this threshold listing requirement set out in the regulation (and statute). *See* D.I. 118 at 7-8 (explaining why Jazz was not required to list the '963 patent in the Orange Book). And even if Jazz's characterization of the regulation were somehow correct, the regulation would then conflict with the statute, and therefore could not be applied in any event. *See United Airlines*, 20 F.4th at 63 n.3. ("To the extent that the [regulation] . . . may conflict with the statute, the statute clearly controls.") (internal citation omitted).

Jazz next asserts that the FDA "rejected" Avadel's argument that the '963 patent does not claim a method of using a drug on the grounds that Avadel was required to certify against the '963 patent. That is yet another red herring. *Courts* adjudicate patent delisting counterclaims, not the FDA. *See Caraco*, 566 U.S. at 406-07. In any event, the FDA's certification determination only compared Avadel's proposed REMS to the self-serving *use code* that Jazz submitted for the '963 patent (which the FDA takes at face value): a "method of treating a patient with a prescription drug using a computer database in a computer system for distribution." *See* D.I. 153 at Ex. F, 9-12. This does not amount to a determination by the FDA that the *claims* of the '963 patent cover

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"patent owners from asserting REMS patents or the FDA from requiring" 505(b)(2) filers to submit Paragraph IV certifications. D.I. 153 at 13. That is not Avadel's argument. Avadel merely pointed out that Congress, the FDA, and academic commentators have expressed concerns of abuse by brand holders by listing REMS patents in the Orange Book. D.I. 118 at 10-11. These concerns are informative as to whether Congress intended REMS patents to be Orange Book-listable.

methods of using a drug.[6] In fact, Jazz's proposed claim construction does not even align with the use code it provided to the FDA for the '963 patent:

- Jazz's Use Code for the '963 patent submitted to FDA: method of *treating a patient* with a prescription drug using a computer database in a computer system for distribution. D.I. 153 at 12.
- Jazz's proposed construction of the '963 patent claims submitted to this Court: method of *using a computer-implemented system* to safely distribute [GHB] for treatment of a narcoleptic patient. D.I. 132 at 46.

Accordingly, the FDA's determination regarding whether Avadel's REMS falls within Jazz's *use code* is entirely immaterial to the question of whether Jazz's *proposed construction* describes a "method of using [a] drug." The FDA, by its own admission, "lacks both [the] expertise and [the] authority" to evaluate the claims of the '963 patent." *See Caraco*, 566 U.S. at 406-07 (citation omitted); D.I. 153 at Ex. F, 9 n. 34 ("Consistent with its ministerial role, FDA has not evaluated what the '963 patent actually covers or whether the use code published in the Orange Book accurately reflects what is covered by the '963 patent."). Indeed, the FDA is clear that it takes the use code provided by a brand "as a given" and "does not independently assess the patent's scope or otherwise look behind the description authored by the brand." *Id.* at 406. Instead, "the courts are the appropriate mechanism for the resolution of disputes about the scope and validity of patents." *Id.* (internal citations omitted). Thus, Jazz's argument again takes for granted the exact issue in dispute: whether the '963 patent actually claims methods of using a drug.

[6] The FDA's indication that "a method-of-use patent that claims a use other than an indication may be submitted for listing in the Orange Book" (D.I. 153 at 12) refers to approved versus unapproved indications. It does not demonstrate that Jazz's listing of the '963 patent in the Orange Book was proper, or that delisting is improper. The FDA did not state that a method of using a drug extends to methods of using a computer system to distribute a drug.

In sum, the claims of the '963 patent—under either party's construction—do not fall within an Orange Book-listable category. None of Jazz's arguments change the fact that "methods of using a computer-implemented system to safely distribute [GHB] for treatment of a narcoleptic patient" are methods of *distributing* a drug, not methods of using a drug.

C. Jazz Is Not Entitled To A 30-Day Delay To Delist The '963 Patent

In yet another attempt at delay, Jazz argues that it "has 30 days to correct any patent listing that is affected by order of a District Court," citing 21 C.F.R. § 314.94(a)(12)(vi)(A)(3). D.I. 153 at 18. Not only does Jazz cite to a regulatory provision specific to ANDA applicants,[7] which Avadel is not, it also ignores the regulatory mandate that NDA holders ordered by a court to withdraw a patent from the Orange Book must request that the FDA remove the patent within 14 days. 21 C.F.R. § 314.53(f)(2)(i). That is precisely the relief Avadel is seeking. *See* D.I. 118 at 11; Ex. C at 2 (ordering plaintiff to request removal of an improperly listed patent based on the delisting statute). Moreover, there is no "correction" that Jazz could make short of delisting the '963 patent that could resolve the issue at hand, and Avadel is entitled to the form of relief it requested. If the Court grants Avadel's motion, the remedy outlined in the statute is that Jazz must request removal of the '963 patent within 14 days. *Id.*

III. CONCLUSION

Avadel respectfully requests that the Court grant its renewed motion for judgment on the pleadings, and order Jazz to request that the FDA delist the '963 patent within 14 days of the Court's order.

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[7] The parallel provision specific to 505(b)(2) applicants, 21 C.F.R. § 314.50(i)(4)(i)(C), only applies when a decision by a federal court alters the construction of method-of-use patent claims, and allows patent holders 30 days to revise their patent information (*i.e.*, amend their use code) in accordance with said claim construction. 21 C.F.R. § 314.50(i)(4)(i)(C). Avadel's motion requests an order requiring Jazz to delist the '963 patent. Thus, only 21 C.F.R. § 314.53(f)(2)(i) applies.

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