No. 2023-1186

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

JAZZ PHARMACEUTICALS, INC.,
Plaintiff-Appellant,

v.

AVADEL CNS PHARMACEUTICALS LLC,
Defendant-Appellee.

Appeal from the United States District Court for the District of Delaware in No. 21-691, Honorable Gregory B. Williams

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REPLY BRIEF FOR PLAINTIFF-APPELLANT JAZZ PHARMACEUTICALS, INC.

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January 20, 2023

CERTIFICATE OF INTEREST

Counsel for Jazz Pharmaceuticals, Inc., Steven J. Horowitz,

certifies the following:

1. **Represented Entities.** Provide the full names of all entities represented by undersigned counsel in this case. Fed. Cir. R. 47.4(a)(1).

   Jazz Pharmaceuticals, Inc.

2. **Real Party in Interest.** Provide the full names of all real parties in interest for the entities. Do not list the real parties if they are the same as the entities. Fed. Cir. R. 47.4(a)(2).

   None

3. **Parent Corporations and Stockholders.** Provide the full names of all parent corporations for the entities and all publicly held companies that own 10% or more stock in the entities. Fed. Cir. R. 47.4(a)(3).

   Jazz Pharmaceuticals plc.

4. **Legal Representatives.** List all law firms, partners, and associates that (a) appeared for the entities in the originating court or agency or (b) are expected to appear in this court for the entities. Do not include those who have already entered an appearance in this court. Fed. Cir. R. 47.4(a)(4).

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5. Related Cases. Provide the case titles and numbers of any case known to be pending in this court or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal. Do not include the originating case number(s) for this case. Fed. Cir. R. 47.4(a)(5).

Jazz Pharms., Inc. v. Avadel CNS Pharms., LLC, No. 1:22-cv-00941-GBW (D. Del.) (filed July 15, 2022).

6. Organizational Victims and Bankruptcy Cases. Provide any information required under Fed. R. App. P. 26.1(b) (organizational victims in criminal cases) and 26.1(c) (bankruptcy case debtors and trustees). Fed. Cir. R. 47.4(a)(6).

Not applicable

January 20, 2023

/s/ Steven J. Horowitz

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INTRODUCTION

The interpretive question at the center of this appeal is how best to understand the phrase "an approved method of using [a] drug" under the Federal Food, Drug, and Cosmetic Act (FDCA), a phrase which appears in a provision in parallel with the phrase "the drug for which the application was approved." 21 U.S.C. § 355(c)(3)(D)(ii)(I)(aa). In other words, what qualifies as an approved drug or an approved method of using a drug? The parties disagree not only as to the answer but also as to the framework for answering the question. But the statutory context and FDA's historical practice of regulation in this space easily resolve the framework dispute. FDCA law, as authoritatively interpreted by FDA, provides the framework for understanding what the FDCA means when it refers to an approved drug or an approved method of using a drug. And the latter, under FDA's controlling regulation, encompasses conditions of use, such as those claimed in the '963 patent. The district court was therefore wrong to order delisting.

Avadel asks this Court to bring a patent-law framework to bear on the question of what qualifies as an approved method of using a drug, and it emphatically rejects any suggestion that FDA can authoritatively

speak to the question. In Avadel's view, the delisting statute's use of the terms "patent" and "claim" invokes patent-law principles. This much is true and undisputed, and it explains why this Court has held that claims regarding improper patent listing involve substantial questions of patent law, satisfying the jurisdictional prerequisite of 28 U.S.C. § 1338. But the use of some patent-law terms in the FDCA does not transform the entire statute into patent law. Instead, "patent" and "claim" carry their patent-law meanings and decisional frameworks, while "the drug for which the application was approved" and "approved method of using [a] drug" carry their FDCA-law meanings and decisional frameworks—including a critical role for the FDA itself in clarifying the meaning of those terms.

The proper framework makes short work of this dispute. As a matter of FDCA law (including FDA regulations), Jazz was required to list the '963 patent in the Orange Book. At a minimum, Jazz was permitted to do so in 2014. And while Avadel disputes the relevance of changes in *listing* rules—as Avadel seeks to treat listing and delisting as involving different standards—Avadel does not dispute that the listing standards did change and that the changes were solely

prospective. Even if Avadel were right to insist that this appeal involves only patent-law questions, the decision below should be reversed because it is based on an erroneous claim construction.

ARGUMENT

I. WHAT QUALIFIES AS AN "APPROVED METHOD OF USING [A] DRUG" IS AN FDCA QUESTION—AND IT ENCOMPASSES THE CONDITIONS OF USE CLAIMED IN THE '963 PATENT.

The primary target of Avadel's response brief is an argument Jazz has never made. Jazz does not contend that delisting claims involve *no* patent-law questions. Nor would such a contention make any sense. What a patent claims involves a substantial question of patent law, which is why this Court concluded it had jurisdiction to address the claim in *Apotex, Inc. v. Thompson*, 347 F.3d 1335, 1343 (Fed. Cir. 2003). But the threshold dispute in this appeal is not about what the '963 patent claims. Instead, it is about the interpretation of "an approved method of using the drug" as that phrase is used in section 505 of the FDCA. *See* 21 U.S.C. § 355(c)(3)(D)(ii)(I)(bb). *That* question is an FDCA question, not a patent-law question. And its answer is informed by the broader statutory FDCA context and FDA's authoritative regulations. Based on that context, "an approved method of using the

drug" includes an approved condition of use, such as the elements of the REMS claimed by the '963 patent.

A. The FDCA—Not Patent Law—Governs What Counts as an "Approved Method of Using [a] Drug" Under the FDCA.

1. A defendant in a Hatch-Waxman case may seek delisting of an Orange Book-listed patent if "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). Courts evaluating delisting claims must therefore answer *two* distinct questions.

The first is a patent-law question: what does the patent claim? To answer that question, courts will use the tools and frameworks of patent law, such as claim construction and the standards for infringing a patent. *See Apotex*, 347 F.3d at 1343–44 (noting that listing dispute "turns *in part* on a question of patent law," insofar as it "requires what amounts to a finding of patent infringement, except that the 'accused product' is the drug that is the subject of the NDA and the 'accused method' is a method that is reasonably likely to be used by a hypothetical infringer" (emphasis added)). When this question is

disputed, courts can apply patent-law principles to answer it, and it would not be proper (or even possible) to "hand off that patent-law inquiry to the FDA." *Contra* Avadel Br. 5. After all, FDA disavows any "expertise to review patent information" and has declined to devote its "scarce resources" to "reviewing patent claims." *E.g.*, 59 Fed. Reg. 50338, 50343 (Oct. 3, 1994).

In this case, however, what the '963 patent claims turns out to be largely uncontroversial. As Jazz explained in its opening brief, Jazz Br. 38–39, the '963 patent claims 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.

The second question presented by the delisting statute, however, is the core issue in this appeal: is the patented invention (*i.e.*, whatever a court concludes the patent claims) either "the drug for which the application was approved" or—relevant here—"an approved method of using the drug"? What counts as the approved drug or an approved method of using a drug is emphatically *not* a patent-law question. It is a question of FDCA law, over which FDA has regulatory authority. *See* 21 U.S.C. §§ 371(a), 393. Indeed, while FDA does not review patent

claims to determine what they cover, FDA *does* have authority to promulgate rules and guidance to clarify what the approved drug *is* for purposes of patent listing. *See In re Lantus Direct Purchaser Antitrust Litig.*, 950 F.3d 1, 5 (1st Cir. 2020) (noting that FDA "provides further guidance . . . on what patents qualify as claiming a drug"). In doing so, FDA brings both its scientific expertise and its delegated policymaking authority to bear, as it attempts to "maintain[] a balance between the innovator companies' intellectual property rights and the desire to get generic drugs on the market in a timely fashion." 68 Fed. Reg. 36676, 36676 (June 18, 2003) (final rule clarifying "the types of patents that must and must not be submitted").

For its part, Avadel submits that what counts as an "approved method of using the drug" as used in section 505(c)(3)(D)(ii)(I) of the FDCA is exclusively a patent-law question for courts to resolve, without reference to FDA regulations.[1] *See* Avadel Br. 50. What is more, Avadel contends that the statutory categories (*i.e.*, approved drugs and

[1] Notably, Avadel does not actually suggest that determining whether a patent falls into the other relevant category ("the drug for which the application was approved") is exclusively a question of patent law.

approved methods of using a drug) are "unambiguous and need no further interpretation." *Id.* FDA apparently disagrees. *See, e.g.*, 68 Fed. Reg. 36,656, 36,681 ("'Drug' is an ambiguous term . . . .").

Consider two examples. First, is a patent claiming a different crystal form of the drug described in the NDA (a "polymorph") properly listed as a patent that claims "the drug for which the application was approved"? FDA says "yes," but only if the innovator "has test data . . . demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA." 21 C.F.R. § 314.53(b)(1); *see id.* § 314.53(b)(2)(i)–(v) (specifying the specific data required). Second, is a patent claiming the pharmacologically active substance that the drug described in the NDA becomes after it is ingested (a "metabolite") properly listed as a patent that claims "the drug for which the application was approved"? Here, FDA says "no," without exception. *See* 21 C.F.R. § 314.53(b)(1).

In both cases, FDA's regulation provides an authoritative interpretation of an ambiguous statute based on the agency's scientific expertise and its balancing of competing policy interests. On Avadel's view, however, FDA's interpretations of these *listing* requirements—

requiring listing for certain polymorph patents and prohibiting listing for metabolite patents—shed no light on whether patents claiming polymorphs or metabolites should be *delisted*. As a result, a court evaluating a request to delist a polymorph patent or metabolite patent can decide whether to issue a delisting order without even considering FDA's authoritative instructions.

That cannot be right. What counts as an approved drug is an FDCA question over which the FDA has regulatory authority, and FDA's views of what patents should be listed in the Orange Book are entitled to deference in delisting disputes. The same is true for what counts as an "approved method of using a drug," the parallel provision in the delisting statute. Both are FDCA questions, not patent-law questions. *See Erlenbaugh v. United States*, 409 U.S. 239, 244 (1972) ("[I]ndividual sections of a single statute should be construed together[.]").

2. Avadel relies heavily on the so-called "old-soil principle" to argue that the statute's use of the terms "patent" and "claim," "transplanted" from patent law, carry with them "patent-law principles that courts use in construing patent claims." Avadel Br. 29–32. The

horticultural metaphor is fine as far as it goes. A "term of art" which is "obviously transplanted from another legal source" typically carries the "cluster of ideas that [are] attached to *each borrowed word*," absent some contrary indication. *George v. McDonough*, 142 S. Ct. 1953, 1959 1963 (2022) (emphasis added). But the provenance of such borrowed terms does not spread like wildfire through the rest of a statute. "Patent" and "claim" may be transplanted from patent law, but "the drug for which the application was approved" or "an approved method of using the drug" are *not* patent-law terms of art, and the fact that the FDCA imports some patent-law terms cannot strip FDA of its regulatory authority or transform every FDCA issue into a patent-law issue.

Avadel's old-soil argument depends on just such faulty transitive logic, however. On Avadel's theory, because "patent" and "claim" are patent-law terms of art, a *different* word—"method," which Avadel does *not* argue is a clear transplant from patent law—must be given a patent-law meaning. *See* Avadel Br. 31–32. This theory finds no support in Avadel's cases, each of which interprets the obviously transplanted term of art (not some *other* term) based on the source from

which it is drawn. *See George*, 142 S. Ct. at 1959–60 (interpreting the phrase "clear and unmistakable error" based on the meaning developed by the Department of Veteran Affairs through decades of practice); *Taggart v. Lorenzen*, 139 S. Ct. 1795, 1801 (2019) (interpreting "operates as an injunction" in a bankruptcy-law provision as incorporating the courts' usual authority to enforce injunctions through civil contempt); *Stokeling v. United States*, 139 S. Ct. 544, 551 (2019) (interpreting "force or violence" in Title 18 as incorporating principles from the common law of robbery).

What is more, Avadel's theory plucks a single word ("method") from a statutory phrase ("approved method of using the drug"), stripping it of its FDCA context in a way that confuses rather than clarifies the interpretive inquiry. Whatever might be said of the isolated word "method," the phrase "approved method of using the drug" is not a patent-law term of art. Indeed, the phrase is peculiar to section 505 of the FDCA. To the best of Jazz's knowledge, it does not appear elsewhere in the FDCA or in any other federal statute. Its meaning is best elucidated by considering the context in which it appears, not by extracting one piece of it and treating that piece as a patent-law term

that, by extension, controls the meaning of the phrase as a whole. *See Deal v. United States*, 508 U.S. 129, 132 (1993) (noting "fundamental principle of statutory construction (and, indeed, of language itself) that the meaning of a word cannot be determined in isolation, but must be drawn from the context in which it is used").

At bottom, Avadel's theory goes something like this: Congress clearly borrowed two words ("patent" and "claim") from patent law; sandwiched a *different* but more generic word used both in patent law and elsewhere ("method") between modifiers to create a novel phrase ("approved method of using the drug"); placed that phrase in a non-patent statute (the FDCA); and paired it with another phrase that clearly invokes the FDCA ("the drug for which the application was approved")—all to "incorporate[] . . . by reference" only the patent-law sense of "method." Avadel Br. 32. "That is no way to do statutory construction." *Borden v. United States*, 141 S. Ct. 1817, 1829 (2021) (rejecting "term-of-art machinations" that ignored surrounding language).

3. The broader context of FDCA section 505 shows that the phrase "approved method of using the drug" should be understood to

include all of the "conditions of use" that FDA has approved for that drug. The new drug application process begins with the applicant proposing labeling for its drug. *See* 21 U.S.C. § 355(b)(1)(vi). FDA then evaluates whether the drug will be safe and effective "under the conditions of use" described in that labeling. *Id.*, § 355(d)(5). After approval, FDA must withdraw the drug if it is no longer considered safe or effective "under the conditions of use upon the basis of which the application was approved." *Id.*, § 355(e)(5).

The generic drug provisions work in parallel with the above requirements. Generic applicants may seek approval only for "conditions of use . . . previously approved" for the listed drug. *Id.*, §§ 355(j)(2)(A)(i), 355(j)(4)(B). Generic applicants must certify to each patent covering those conditions; they must certify to "each patent" in the Orange Book "which claims a use for [the] listed drug for which the applicant is seeking approval." *Id.*, § 355(j)(2)(A)(vii). If sued on the basis of such a certification, a generic applicant can ask the courts to order that a patent be delisted if it was improperly listed and does not claim "an approved method of using the drug." *Id.*, § 355(c)(3)(D)(ii)(I)(bb).

These various statutory provisions all work in concert to ensure that all patents related to the approved conditions of use that a generic applicant must duplicate are included in the Orange Book and may be included in litigation prior to approval. Excluding from the Orange Book patents that cover a pioneer drug's mandatory conditions of use will interfere with the proper functioning of the Hatch-Waxman scheme. Generic applicants will not have any notice of such patents and will not have the opportunity to obtain the clarity that Hatch-Waxman patent litigation provides—or, where possible, to avoid infringement with a "section viii statement" and proposed labeling that "carves out" the patented conditions of use. *Caraco Pharm. Lab'ys, Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 406 (2012).

4. FDA's operative regulation supports this reading. First, the regulation provides that sponsors must list patents in the Orange Book "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) (emphasis added).

Second, the regulation prohibits the submission of "[p]rocess patents." *Id.* That prohibition is proof that FDA does not interpret

"approved method of using a drug" with reference to patent-law principles. *All* patents that claim "methods" in the Title 35 sense are "process patents." *See* 35 U.S.C. § 100(b). If Title 35 were to control what qualifies as an approved method of using a drug, then sponsors would be both required to submit, and forbidden to submit, all such patents.

Avadel has no real response. Citing a journal article, Avadel contends that the reference to "process patents" was meant to cover only "patents claiming a manufacturing process," Avadel Br. 42 n.4, but the text of the regulation contains no such limitation. In any event, Avadel's reading of the regulation just proves Jazz's point: Everyone agrees that FDA does not give "process" the broad definition in 35 U.S.C. § 100(b), and that FDA's interpretation is authoritative. And that is unsurprising, as FDA is not engaging in a patent-law inquiry when it interprets the phrase "approved method of using [a] drug."

5. Neither *Apotex* nor *Caraco* holds otherwise. To begin with, *Apotex* predates the creation of the delisting counterclaim and was assessing this Court's jurisdiction to address the merits of Apotex's claim for an injunction that would direct FDA to delist an Orange Book

patent. *See Apotex*, 347 F.3d at 1344. The question, then, was whether Apotex's claim depended on a "substantial question of federal patent law." *Id.* at 1342. And the answer was "yes": whether a patent is properly listed turns at least "in part on a question of patent law." *Id.* at 1343. But the fact that the case involved a substantial patent-law question does *not* mean that *everything* to do with listing or delisting is a patent-law question.

Caraco also does not help Avadel. All agree that Congress intended for "courts to resolve" disputes about Orange Book listings. *Caraco*, 566 U.S. at 423–25. But it is at best misleading for Avadel to assert that "the Supreme Court [in *Caraco*] made clear that an Orange Book delisting counterclaim is a patent claim that should be resolved according to the principles of patent law." Avadel Br. 34–35. Avadel first tries to rely on a footnote addressing the jurisdictional question. *Caraco*, 566 U.S. at 412 n.5. The Supreme Court did not find jurisdiction based on the delisting statute. Quite to the contrary, the Supreme Court found jurisdiction because (as here) the underlying complaint included a claim for patent infringement. *See id.* (discussing 35 U.S.C. § 271(e)(2)(A)).

More broadly, the statutory analysis in *Caraco* did not involve the application of patent law. To be sure, the counterclaim in the FDCA includes the word "patent," as did the Court's opinion. But the issues before the Court were (1) whether the word "an" in the counterclaim should mean "any" or "a particular one," *see id.* at 413–14; (2) whether a Use Code constitutes "patent information" within the specific meaning of section 505(b)-(c) of the FDCA, *see id.* at 417–19; and (3) how to best give independent meaning to "correct" and "delete" in the counterclaim, *see id.* at 419–21. At no point did the Court state that patent law principles govern those questions, let alone the question presented by this case. To the contrary, the Court *did* repeatedly stress that the language of the counterclaim must be read in a way that maintains the integrity of the drug approval scheme in FDCA section 505. *See, e.g.*, *id.* at 404 ("The FDA regulates the manufacture, sale, and labeling of prescription drugs under a complex statutory scheme."); *id.* at 415 (evaluating how "the counterclaim naturally functions" within the "framework" of the FDCA); *id.* at 419 (relying on "the broader statutory context" of the FDCA). As discussed above, that statutory context and

FDA's regulation both teach that approved methods of using a drug must include all conditions of use that FDA has approved for that drug.

B. The '963 Patent Claims an "Approved Method of Using" Xyrem® Because It Claims Elements of an Approved Condition of Use.

A REMS falls comfortably within the ordinary meaning of "an approved method of using [a] drug," and the elements of a REMS clearly constitute approved conditions of use. Meanwhile, both Congress and FDA know that the Orange Book includes REMS patents—and they have chosen not to act on repeated calls to change the rules to exclude such patents.

1. A REMS is an "approved method of using [a] drug" under the plain meaning of the delisting statute. As the Supreme Court has explained, "use" is an "expansive" term that "sweeps broadly." *Smith v. United States*, 508 U.S. 223, 229 (1993). For example, the phrase "uses a firearm" clearly covers "using a firearm as a weapon." *Id.* at 230, 236 (citation omitted). But that doesn't mean that the phrase "*excludes* any other use." *Id.* at 230. To the contrary: "it is both reasonable and normal" to say that a person "uses" a gun by bartering it for contraband. *Id.* The same linguistic principles apply here. While "the

example of 'use' that most immediately comes to mind" might be administering a drug to a patient, that "does not preclude us from recognizing that there are other 'uses' that qualify as well." *Id.* "[O]ne can use a [drug] in a number of ways," *id.*—including by "deploy[ing]" it through a REMS, *The New Oxford American Dictionary* 1853 (2005) ("use" means "take, hold, or deploy (something) as a means of accomplishing a purpose").

Had Congress meant to limit the phrase "approved method of using [a] drug" to just how the drug is administered to a patient, it could have said so. In fact, Congress employed just such language elsewhere in section 505. Take the provision governing abbreviated new drug applications, where Congress required applicants to report the effects of a drug "when *administered* to patients." 21 U.S.C. § 355(j)(2)(A)(iv) (emphasis added). Congress chose different language in the delisting provision—forgoing narrower options in favor of the broad phrase "approved method of using [a] drug." "When Congress includes particular language in one section of a statute but omits it in another section of the same Act," courts "generally take the choice to be deliberate." *Badgerow v. Walters*, 142 S. Ct. 1310, 1318 (2022) (citation

omitted). And "this Court may not narrow a provision's reach by inserting words Congress chose to omit." *Lomax v. Ortiz-Martinez*, 140 S. Ct. 1721, 1725 (2020).

2. The '963 patent also is properly listed because it claims an approved "condition of use" within the meaning of FDCA section 505 and FDA's implementing regulations. There is no question that the '963 patent claims elements of an approved REMS or that the REMS is intended to ensure that Xyrem® can be safely prescribed by providers and safely used by patients. Jazz Br. 38–39. Indeed, Avadel does not even attempt to deny that the '963 patent claims elements of the approved REMS for Xyrem®.

As previously explained, the elements of an approved REMS are necessarily among the drug's approved conditions of use. *See* Jazz Br. 35–37. Individually, each REMS element is an essential part of FDA's determination that the therapeutic benefits of sodium oxybate will outweigh its risks to patients and others. *See* 21 U.S.C. § 355-1(a)(1) ("necessary to ensure that the benefits of the drug outweigh the risks of the drug"); 21 U.S.C. § 355-1(f)(1)(A) ("the drug . . . can be approved only if, or would be withdrawn unless, such elements are required").

Collectively, REMS elements are among the most important "conditions of use prescribed, recommended, or suggested in [a drug's] proposed labeling." 21 U.S.C. § 355(d)(5).

As explained above, FDA has interpreted the phrase "approved method of using the drug" to include any "conditions of use for which approval [was] sought." 21 C.F.R. § 314.53(b)(1). Importantly, Avadel does not address—let alone dispute—FDA's authoritative position that "uses in [a] REMS document" are conditions of use that "can be" listed in the Orange Book. Appx5307.

Instead, Avadel attempts to argue that unrelated "regulations make clear" that the "conditions of use" include only the "conditions of administering the drug." Avadel Br. 45. None of the cited regulations help Avadel, however. 21 C.F.R. § 310.3(h)(5) actually refutes Avadel's argument: it confirms that a drug may have "*other* condition[s] of use" apart from "dosage, or method or duration of administration or application." Avadel also cherry picks from two regulations addressing specific *veterinary* drugs. *See* Avadel Br. 45 (citing 21 C.F.R. §§ 522.1680(c) (conditions of use for oxytocin), 522.1192(e) (conditions of use for ivermectin)). Xyrem® is not a veterinary drug. To the extent

veterinary drugs are relevant at all, Avadel fails to acknowledge that there are hundreds of such regulations, each of which describes different conditions of use for one or more veterinary drugs. *See* 21 C.F.R. pts. 520–529. Avadel also ignores the fact that many such regulations expressly define the drug's "conditions of use" to include important risk-mitigation measures not directly related to the administration of the drug. *E.g.*, 21 C.F.R. § 522.90a(d)(1)(iii) ("conditions of use" for ampicillin trihydrate suspension include a prohibition on the slaughtering of treated animals "for food use" for a specific period of time "after the last treatment"), 522.90b(d)(2)(iii) (prohibition on human consumption of milk from cows treated with ampicillin trihydrate powder "for 48 hours (4 milkings) after the last treatment").

Finally, Avadel echoes the FTC by suggesting that although REMS elements are "condition[s] of FDA *approval*," they are not "condition[s] of the drug's *use*." Avadel Br. 45. The suggestion is contrary to the statute (which FTC has no authority to interpret). The parallel provisions of section 505(d) and 505(e) use the two phrases interchangeably, making clear that the conditions of FDA's approval

and the conditions of use in the drug's labeling are one and the same. *Compare* 21 U.S.C. § 355(d)(1) (approval required where FDA finds that a new drug "is safe for use under the conditions prescribed . . . in [its] proposed labeling"), *with id.*, § 355(e)(1) (withdrawal required if FDA finds that the drug "is unsafe for use under the conditions of use upon the basis of which the application was approved").

Because the '963 patent claims elements of a REMS that stand as "approved conditions of use" for, and "approved method[s] of using," sodium oxybate, the patent belongs in the Orange Book. The district court erred when it concluded otherwise.

3. REMS patents are nothing new. FDA began imposing risk-management measures as a condition of approval in 1992. *See* 21 C.F.R. pt. 314, Subpart H. Within the decade, drugmakers began listing patents related to those measures in the Orange Book. Congress then enacted the delisting statute in 2003 and the REMS statute in 2007. Yet neither statute curtailed the listing of REMS patents; nothing in the legislative history of either law suggests that Congress was worried about the listing of such patents; and the REMS statute

provided FDA with alternative authorities to address disputes about REMS patents. Jazz Br. 37–38.[2]

More recently, both Congress and FDA have faced calls to exclude REMS patents from the Orange Book. *See, e.g.*, *Lowering the Cost of Prescription Drugs: Reducing Barriers to Market Competition: Hearing Before the Subcomm. on Health of the H. Comm. on Energy & Com.*, 116th Cong. 68–69, 73 (Mar. 13, 2019), https://www.govinfo.gov/content/pkg/CHRG-116hhrg38120/pdf/CHRG-116hhrg38120.pdf (statement of Michael A. Carrier, Professor, Rutgers Law School) (proposing new legislation to "prohibit listing of REMS patents in Orange Book"); Michael A. Carrier, *Four Proposals to Enhance Generic Competition* (July 2017) (proposing an amendment to 21 C.F.R. § 314.53(b)(1)). But these proposals have not been enacted. Instead, when it became law in 2021, the OBTA merely ordered FDA to solicit public comments and submit a report on "the types of patent information that should be included [in], or removed from" the Orange

[2] Avadel would maintain that the "REMS legislation" supposedly "cuts *against* Jazz's position," Avadel Br. 46, but the provision on which it relies does not even mention patents. *See* 21 U.S.C. § 355-1(f)(8).

Book. Pub. L. No. 116-290, § 2(e), 134 Stat 4889, 4891 (Jan. 5, 2021). FDA did so, but the agency has so far declined to make any change. *See generally* FDA, *The Listing of Patent Information in the Orange Book*, *available at* https://www.fda.gov/media/155200/download. Further, while the case below was pending, a draft bill in Congress proposed to address REMS patents in the Orange Book by eliminating the 30-month stay, a position that assumes that REMS patents are and will remain in the Orange Book. *See Increasing Prescription Drug Competition Act*, S.4918, 117th Cong. (introduced Sept. 22, 2022).

Not content to wait for FDA or Congress to enact their preferred policy, Avadel and the FTC have tried to use the courts to bypass both. But legislation-by-litigation is "an invitation no court should ever take up." *Bostock v. Clayton Cnty*, 140 S. Ct. 1731, 1753 (2020). "Choosing between [policy] alternatives is a task for Congress [or FDA]," and "[i]f policy considerations suggest that the current scheme should be altered, Congress [or FDA] must be the one to do it." *Intel Corp. Inv. Pol'y Comm. v. Sulyma*, 140 S. Ct. 768, 778 (2020).

C. The Interpretation of the FDCA is Properly Before This Court.

Jazz preserved its argument regarding the proper interpretation of the FDCA by presenting it to the district court. There as here, Jazz argued that "using Xyrem® according to its approved REMS is . . . a 'condition of use' as required by the FDA," and "[a]s such, the '963 patent claims 'an approved method of using the drug.'" Appx840. And there as here, Jazz pointed to FDA's authoritative regulations. *See* Appx839; *see also* Appx3602 (advancing argument regarding "conditions of use," based on FDA regulation); Appx3610 (same). The FTC responded to Jazz's position by submitting an amicus brief arguing that—irrespective of claim construction—a patent that claims a REMS distribution system cannot be listed under the FTC's preferred interpretation of the statute. *See* Appx5667–5672.

In Avadel's view, this Court should not consider the parties' dispute over the interpretation of the FDCA because Jazz packaged its arguments differently below. In particular, Avadel takes issue with Jazz's framing on appeal that emphasizes the distinction between patent-law frameworks and FDCA-law frameworks. *See* Avadel Br. 39. But any difference in the packaging does not amount to a new theory.

Instead, it is simply an effort to help the Court and the parties focus on the core of the actual interpretive dispute. Jazz's position, and its basic argument, remains the same. New packaging does not amount to forfeiture. *See, e.g.*, *Citizens United v. Fed. Election Comm'n*, 558 U.S. 310, 330–31 (2010) ("Once a federal claim is properly presented, a party can make any argument in support of that claim; parties are not limited to the precise arguments they made below.") (cleaned up); *United States v. Abreu*, 32 F.4th 271, 275 (3d Cir. 2022) ("Parties are free to place greater emphasis and more fully explain an argument on appeal than they did in the District Court or even, within the bounds of reason, reframe their argument.") (cleaned up).

Avadel's forfeiture arguments depend in large part on a mistaken depiction of the history of the parties' dispute. Avadel asserts that Jazz has always insisted that claim construction was critical to the interpretation of the FDCA; indeed, Avadel says that Jazz "*never* argued . . . that the statutory scheme mandated treating the '963 patent as a 'method of using [a] drug' . . . irrespective of claim construction." Avadel Br. 39. The emphasis on "never" is Avadel's, both through its use of italics and through its repetition of the word "never" roughly ten

times throughout its brief. But Jazz argued in its very first brief on the subject that delisting was improper, independent of claim construction.

In particular, Jazz made three arguments in response to Avadel's first motion for judgment on the pleadings, which Jazz described as "independent" of one another. *See* Appx832–833. The first of those arguments was that Jazz was required to list the '963 patent because it claimed a "condition of use" under FDA regulations, and thus "an approved method of using the drug." Appx840. "On this basis alone," Jazz argued—before even turning to claim construction—"Avadel's motion should be denied." *Id.* Jazz then proceeded to its position regarding claim construction, contending that *Avadel's argument* (not Jazz's own lead argument) was "premised entirely" on "claim construction," which could not "be adjudicated on the [then-]current record." Appx840–841. The disputed claim construction was "another, *independent* reason why Avadel's motion should be denied." Appx841 (emphasis added). Jazz thus made the "never-made" argument at the first opportunity in the district court, emphasizing that the '963 patent was required to be listed under the FDCA and FDA regulations, "independent" of the claim-construction dispute. Even the FTC

recognized that Jazz was making the argument based on "conditions of use"—irrespective of claim construction, which the FTC did not address—in its amicus brief supporting Avadel's renewed motion for judgment on the pleadings. *See* Appx5669 & n.29.

To be sure, once the district court decided to put off the delisting question until claim construction, the briefing shifted in emphasis. But Jazz did not (as Avadel claims) "*expressly* contend[] that its mandatory-listing argument applied *only* if the district court 'rules that the '963 patent claims methods.'" Avadel Br. 40 (citing Appx3602) (first emphasis in original). The word "only" is Avadel's, not Jazz's. What Jazz said was that "*if*"—but not *only if*—"the Court rules that the '963 patent claims methods, then Jazz was *required* to list it in the Orange Book." Appx3809 (first emphasis added). That was true and remains so on appeal. But also, if the court adopted Jazz's arguments (advanced from the beginning) regarding "conditions of use," then, too, Jazz would have been required to list the patent.

Even if Jazz had not made the same arguments regarding the proper interpretation of the FDCA in the district court, two key factors counsel in favor of addressing it. *See Bagot v. Ashcroft*, 398 F.3d 252,

256 (3d Cir. 2005) (noting "discretionary power" to address issues not raised below). For one thing, Jazz's argument on appeal is, at a minimum, closely related to arguments advanced below. *See Tri-M Grp., LLC v. Sharp*, 638 F.3d 406, 417 (3d Cir. 2011) ("[A]n argument omitted before the district court may nevertheless be considered where it 'is closely related to arguments that [the parties] did raise in that court.'") (quoting *Bagot*, 398 F.3d at 256). For another, the disputed issue is purely legal. *Id.* at 418 ("'[W]e have been reluctant to apply the waiver doctrine when only an issue of law is raised' and no additional fact-finding is necessary.") (quoting *Huber v. Taylor*, 469 F.3d 67, 74 (3d Cir. 2006)); *cf. Barefoot Architect, Inc. v. Bunge*, 632 F.3d 822, 834–35 (3d Cir. 2011).

Jazz's arguments regarding the proper interpretation of the FDCA were advanced below. But even if they were not advanced, or at least not advanced in the same form, Jazz respectfully submits that this Court should consider them.

II. A Delisting Remedy is Not Available Against a Patent That Was Properly Submitted to FDA, Absent Clear Congressional Intent to Effect a Retroactive Change in the Listing Rules.

The law regarding what patents may be listed in the Orange Book has changed since 2014, when Jazz submitted the '963 patent. One critical change was enacted as part of the Orange Book Transparency Act of 2020 ("OBTA"), which provided for the first time that "[p]atent information that is not the type of patent information required by subsection (b)(l)(A)(viii) *shall not be submitted under this paragraph*." 21 U.S.C § 355(c)(2) (emphasis added). Jazz explained in its opening brief that this change was solely prospective, Jazz Br. 51–54—and Avadel offers no argument to the contrary.

Instead, Avadel urges this Court to interpret the *delisting* statute in isolation, without reference to changes in the law of patent *listing*. Above all, Avadel asks the Court to cast aside FDA's authoritative regulations regarding patent information that should be submitted to the agency under the FDCA. The Court should decline to do so.

Jazz was, at a minimum, *permitted* to list the '963 patent in 2014, and because any changes after 2014 were solely prospective, a delisting remedy is not available.

A. There is No Dispute That the Orange Book Transparency Act of 2020 Changed the Rules for Patent Listing—and Did So Prospectively.

The OBTA provided for the first time that patent information not specifically required to be submitted "shall not be submitted." 21 U.S.C § 355(c)(2). This new provision was set forth in its own separate subparagraph of the Act, *see* Pub. L. No. 116-290, § 2(b)(1)(D), and it should be interpreted to mean *something*. *See Nat'l Ass'n of Mfrs. v. Dep't of Def.*, 138 S. Ct. 617, 632 (2018).

For its part, Avadel does not even quote the operative language of the statute, much less offer an explanation of what effect the language has on its theory. But the provision's meaning is straightforward: it indicates—again, for the first time—that the patents that *must* be submitted to FDA for inclusion in the Orange Book are the only ones that *may* be submitted to FDA. Avadel does not dispute Jazz's interpretation of this provision, nor does Avadel dispute that the provision is purely prospective. Instead, Avadel (like the district court) believes that any change to the *listing* rules effected by the OBTA is "not relevant," because this case is about *delisting*. Avadel Br. 47, 49.

But the listing and delisting rules must be read together, as explained below.

B. A Delisting Remedy is Available Only for Patents That Should Not Have Been Listed in the First Place.

The district court's decision depends on treating the standards for patent listing and patent delisting in isolation from one another. The OBTA's changes to patent listing rules are said to be "not relevant" because the Act did not amend the language of the delisting provision. *Id.* But this blinkered approach cannot be right: the listing and delisting provisions are in the same section of the FDCA and mirror one another in substance and language. *Compare, e.g.*, 21 U.S.C. § 355(b)(1)(A)(viii)(II) (requiring listing of a patent that "claims a method of using such drug"), *with id.*, § 355(c)(3)(D)(ii)(I)(bb) (permitting delisting of patent that does not claim "an approved method of using the drug").

The polymorph example discussed above (*supra* page 7–8) demonstrates the point: FDA's authoritative regulation requiring the *listing* of certain polymorph patents (a reasonable interpretation within the bounds of *Chevron* deference) leaves no room for courts to conclude that such patents are subject to *delisting*. Or, more to the point, if

Congress passed a law tomorrow providing that metabolite patents should be listed as patents claiming the approved drug (*contra* 21 C.F.R. § 314.53(b)(1)), that law would plainly control in a delisting dispute involving a metabolite patent. When Congress changes what patents may be *listed*, it likewise affects what patents may be subject to *delisting*.

Avadel's position rejects this logic. On Avadel's view, a change to rules for patent *listing* is "not relevant" so long as the language of the *delisting* statute remains unchanged. *See* Avadel Br. 47, 49. This is not a plausible reading of the statute as a whole. If the OBTA changed the rules for patent listing—a point Avadel does not dispute—then it likewise changed the rules for patent delisting.

C. The FDA's Operative Regulations in 2014—Which Permitted the Listing of the '963 Patent—Are Entitled to Deference.

Because listing rules *are* relevant to delisting, and because Avadel does not dispute that the OBTA is solely prospective, the only question is whether Jazz was permitted to list the '963 patent in 2014.

Avadel's arguments on this score primarily reflect an effort to reject the relevance of FDA patent-listing regulations, addressed above.

Avadel Br. 49–51. But even apart from that, Avadel does not confront what the OBTA accomplished. The prospective prohibition on listing patents not expressly permitted should be construed to mean something. Its plain import is that Congress recognized, under existing FDA practice, that innovators were permitted to submit patents that did not fall into the "must list" or "must not list" categories. *See* 21 C.F.R. § 314.53(b)(1). The OBTA eliminated the practice of permissive listing on a going-forward basis. But based on the law in 2014, Jazz was (at a minimum) *permitted* to list the '963 patent. Delisting now would be improper.

III. EVEN IF PATENT LAW PROVIDED THE APPROPRIATE FRAMEWORK, THE '963 PATENT CLAIMS A METHOD.

Even as a matter of claim construction, "system" and "method" can be used interchangeably. *See, e.g.*, Appx2884 (defining "system" as a "formulated, regular, or special method or plan of procedure"). To be sure, a given system claim may sometimes be best read to be directed primarily or even solely to a "set of interrelated and/or interdependent components," as in, for example, the components of a stereo system. Avadel Br. 53. The '963 patent, however, is not directed solely to components but to *procedures* and *processes*. It recites requirements

involving, for example, reconciliation of inventory, identification of the payer, and notification to the physician of any misuse or abuse. Appx98–99. These requirements reflect something more than just components; they are inputs into a process or method.

Preambles of method claims routinely use words that refer to something beyond the concept of processes or procedures; for example, they may "recite the physical structures of a system in which the claimed method is practiced." *Microprocessor Enhancement v. Tex. Instruments, Inc.*, 520 F.3d 1367, 1374 (Fed. Cir. 2008). But the reference to a physical structure or a "system" does not mean a claim cannot be directed to a process. In light of the ordinary meaning of system and the structure of claim 1 as a whole, the claim is best understood to cover a method. Accordingly, the patent is properly listed in the Orange Book even on Avadel's interpretation of the FDCA.

CONCLUSION

The district court's delisting order should be reversed.

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Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limitations of Federal Rule of Appellate Procedure 32(a)(7)(B) and Federal Circuit Rule 32(b)(1). The brief contains 6,973 words, excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(f) and Federal Circuit Rule 32(b)(2).

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