United States Court of Appeals

FOR THE DISTRICT OF COLUMBIA CIRCUIT

Argued May 5, 2025 Decided June 27, 2025

No. 24-5262

JAZZ PHARMACEUTICALS, INC.,
APPELLANT

v.

ROBERT F. KENNEDY, JR., SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES, ET AL.,
APPELLEES

Appeal from the United States District Court
for the District of Columbia
(No. 1:23-cv-01819)

Kwaku A. Akowuah argued the cause for appellant. With him on the briefs was *Peter A. Bruland*. *Tobias S. Loss-Eaton* entered an appearance.

Brian J. Springer, Attorney, U.S. Department of Justice, argued the cause for appellees. With him on the brief was *Melissa N. Patterson*, Attorney.

Phillip J. Perry argued the cause for intervenor in support of appellees. With him on the brief were *Nicholas L. Schlossman*, *John R. Manthei*, *Andrew D. Prins*, *Peter E. Davis*, and *Richard Frohlichstein*.

Charles Duan was on the brief for *amici curiae* 12 Narcolepsy Patients, et al. in support of appellees.

Before: HENDERSON, WILKINS and PAN, *Circuit Judges*.

Opinion for the Court filed by *Circuit Judge* HENDERSON.

KAREN LECRAFT HENDERSON, *Circuit Judge*: This case involves a dispute about drug marketing exclusivity under the Orphan Drug Act (ODA or Act). The Food and Drug Administration (FDA) approved for marketing a drug containing oxybate produced by Avadel CNS Pharmaceuticals Inc. (Avadel) to treat narcolepsy during Jazz Pharmaceuticals, Inc.'s (Jazz) seven-year exclusivity period for a drug containing the same active ingredient approved for the same disease or condition.

The question before us is whether Avadel's and Jazz's drugs are the "same drug" within the meaning of the ODA so that Jazz's exclusivity period barred the FDA from granting marketing approval to Avadel's drug. *See* 21 U.S.C. § 360cc(a). We conclude they are not.

Under the FDA's longstanding regulatory definition of "same drug," a clinically superior drug is not the same as a drug that is otherwise the same. *See* 21 C.F.R. § 316.3(b)(14)(i). In 2017, the Congress amended the ODA's exclusivity provision, replacing the phrase "such drug" with "same drug." *See* 21 U.S.C. § 360cc(a). The statutory history, context and scheme show that, in doing so, the Congress incorporated the FDA's regulatory definition of "same drug." And it is undisputed on appeal that Avadel's drug, Lumryz, is clinically superior to Jazz's drug, Xywav.

Because the FDA did not act beyond its statutory authority when it approved Lumryz for marketing during the exclusivity period for Xywav, we affirm the district court's grant of summary judgment to the FDA and Avadel.

I. BACKGROUND

A. The 1983 Orphan Drug Act

The Congress enacted the ODA in 1983 as an amendment to the Federal Food, Drug, and Cosmetic Act of 1938 (FD&C Act). Orphan Drug Act, Pub. L. No. 97-414, §§ 1, 2, 5, 96 Stat. 2049, 2049–51, 2056–57 (1983) (codified as amended at 21 U.S.C. §§ 360aa–360ee). After having found that pharmaceutical companies needed financial incentives to make drug development for rare diseases economically feasible, the Congress determined it was in the public interest to provide such incentives.[1] *Id.* § 1(b).

To qualify for these incentives, the manufacturer or sponsor of a drug first requests that the FDA designate the drug as an orphan drug.[2] 21 U.S.C. § 360bb(a)(1). That designation provides benefits such as assistance with investigations and the approval process, monetary grants to defray drug development costs and tax credits. *See Eagle Pharms., Inc. v. Azar*, 952 F.3d

[1] A "rare disease or condition" is one that affects fewer than 200,000 people in the United States or that affects more than 200,000 people but for which there is no reasonable expectation that the cost of developing the drug and making it available domestically will be recovered from domestic sales. 21 U.S.C. § 360bb(a)(2).

[2] The Secretary of the U.S. Department of Health and Human Services (HHS) carries out responsibilities under the Act through the FDA Commissioner. *See* 21 U.S.C. § 393(d)(2). For brevity, this opinion refers simply to the FDA.

323, 325 (D.C. Cir. 2020) (citing 21 U.S.C. §§ 360aa, 360ee; 26 U.S.C. § 45C). Before any drug can be sold or marketed in interstate commerce, the FDA also must approve a drug application certifying the drug's safety and efficacy. 21 U.S.C. § 355(a)–(b). Once an orphan drug application is approved, the drug sponsor receives a seven-year period of marketing exclusivity. *Id.* § 360cc(a).

As originally enacted, subsection 360cc(a) provided that the FDA could not approve another section 355 application for "such drug for such disease or condition" for a sponsor other than the holder of the approved application during the seven-year exclusivity period. *Id.* (1983). The Congress provided two exceptions to the exclusivity period: if (1) the Secretary finds, after providing the exclusivity holder with notice and an opportunity to submit views, that the holder cannot ensure sufficient drug quantities; or (2) the holder consents to FDA approval of another section 355 application. *Id.* § 360cc(b).

Since 1992, FDA regulations have interpreted "such drug" to mean "same drug." *See* 21 C.F.R. § 316.31(a); Orphan Drug Regulations, 57 Fed. Reg. 62,076, 62,078 (Dec. 29, 1992) (1992 Rule). For a small-molecule drug like oxybate, the FDA has defined "same drug" to mean a drug that "contains the same active moiety" and is "intended for the same use" as a previously approved drug unless it is "clinically superior." 21 C.F.R. § 316.3(b)(14)(i); *see also* 1992 Rule, 57 Fed. Reg. at 62,077–80.

As relevant here, an "active moiety" roughly equates to an "active ingredient" or "drug substance," which forms part of the "drug product" or "finished dosage form." *Compare* 21 C.F.R. § 316.3(b)(2) (defining "active moiety" under the ODA), *with id.* § 314.3(b) (defining "active moiety," "active ingredient," "drug substance" and "drug product" under the

FD&C Act). The dosage form includes "design features that affect frequency of dosing." *Id.* § 314.3(b). For example, a drug may be formulated for immediate-, extended- or delayed-release. A drug is considered to be "[c]linically superior" if it "provide[s] a significant therapeutic advantage over" an approved drug that is otherwise the same, as shown by "[g]reater effectiveness," "[g]reater safety," or "[i]n unusual cases . . . a demonstration that the drug otherwise makes a major contribution to patient care." 21 C.F.R. § 316.3(b)(3). "[L]onger periods between doses" or a "change in drug delivery systems" (such as "innovative time-release delivery mechanisms") can constitute a "major contribution to patient care" on a "case-by-case basis." 1992 Rule, 57 Fed. Reg. at 62,079.

The FDA applies its clinical superiority scheme differently at two stages of the orphan-drug process. First, at the designation stage, the sponsor of a drug that is otherwise the same as an already-approved drug must present a "plausible hypothesis" that its drug is clinically superior to obtain orphan-drug designation. 21 C.F.R. §§ 316.20(a), 316.25(a)(3). Second, at the approval stage, the FDA will grant orphan-drug exclusivity after a drug has received marketing approval under 21 U.S.C. § 355 only if the sponsor "demonstrate[s]" that the drug is clinically superior. 21 C.F.R. § 316.34(c). The "post-approval clinical-superiority requirement" is intended to prevent a sponsor from obtaining serial exclusivity periods—known as "evergreening"—or securing exclusivity without providing an additional or different benefit to patients over a previously approved therapy. *See Eagle Pharms.*, 952 F.3d at 327 & n.4 (quoting Orphan Drug Regulations, 78 Fed. Reg. 35,117, 35,127 (June 12, 2013) (2013 Rule)).

In 2014, a district court determined that the plain language of the Act required the FDA to grant orphan-drug exclusivity

if the FDA has designated an orphan drug and approved the drug for marketing, precluding the FDA from applying the second step of its clinical-superiority requirement. *Depomed, Inc. v. HHS*, 66 F. Supp. 3d 217, 229–37 (D.D.C. 2014). We agreed with that interpretation in *Eagle Pharmaceuticals*, although we recognized our holding was superseded for approvals after 2017, when the Congress codified a clinical-superiority requirement in subsection 360cc(c) and made the change to subsection 360cc(a) that is the subject of this appeal. 952 F.3d at 325, 329 n.9.

B. The 2017 Amendments

The 2017 amendments altered the Act to make three changes relevant here. FDA Reauthorization Act of 2017, Pub. L. No. 115-52, § 607, 131 Stat. 1005, 1049–50 (2017 Act) (amending 21 U.S.C. § 360cc). First, in subsection 360cc(a), the Congress replaced "such drug for such disease or condition" with "the same drug for the same disease or condition," so the FDA "may not approve another application . . . for the same drug for the same disease or condition" for seven years from the orphan-designated drug's approval. *Id.* § 607(a)(1) (amending 21 U.S.C. § 360cc(a)). Second, the Congress similarly changed the language in the exclusivity exceptions from "such drug for such disease or condition" to "a drug that is otherwise the same," among other alterations not relevant here. *Id.* § 607(a)(2)(A) (amending 21 U.S.C. § 360cc(b)).

Third, the Congress codified a clinical superiority requirement for exclusivity. If a sponsor of an orphan-designated drug that is "otherwise the same" as an already-approved drug seeks exclusivity for the same rare disease or condition as the approved drug, the FDA is to require the sponsor to "demonstrate that such drug is clinically superior"

to the approved drug "that is the same drug." *Id.* § 607(a)(3) (adding 21 U.S.C. § 360cc(c)). The amended statute defines clinical superiority in line with FDA regulations to mean that a drug provides greater efficacy or safety or makes a major contribution to patient care. *Id.* It also grants the FDA authority to issue regulations to implement subsection 360cc(c) and "apply any definitions set forth in regulations that were [previously] promulgated" if not inconsistent with the amended statute. *Id.* (adding 21 U.S.C. § 360cc(d)). Finally, to assist in demonstrating clinical superiority, the FDA is to (1) notify the sponsor of the "basis for the [orphan-drug] designation," including the "plausible hypothesis" of clinical superiority offered by the sponsor and relied on by the FDA, and (2) publish a summary of the "demonstrate[ed]" "clinical superiority findings" upon granting exclusive approval under subsection 360cc(a). *Id.* (adding 21 U.S.C. § 360cc(e)).

C. Rival Orphan Drugs for Narcolepsy

Narcolepsy is a sleep disorder that, at the time the drugs at issue here received orphan-drug designation, affected around 180,000 people in the United States, making it a rare disease or condition.[3] The molecule oxybate is effective in treating narcolepsy symptoms. In 1994, Jazz's predecessor obtained orphan-drug designation for the active moiety of oxybate for treating narcolepsy. Jazz later received approvals and seven-year exclusivity periods for several different narcolepsy treatment indications of its first oxybate-based drug, Xyrem.[4]

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[3] Narcolepsy now affects over 200,000 people and is no longer considered a rare disease but that change in status is not a basis on which to revoke orphan-drug designation. 21 C.F.R. § 316.29(c).

[4] Xyrem had exclusivity periods from 2002 to 2009 to treat cataplexy associated with narcolepsy, from 2005 to 2012 to treat

In July 2020, the FDA approved Jazz's Xywav, an oxybate-based drug that the FDA determined was clinically superior to Xyrem because of its lower sodium content. Xywav was covered for orphan-drug designation by Jazz's designation of oxybate to treat narcolepsy and was entitled to orphan-drug exclusivity because it is clinically superior to Xyrem and, under Jazz's view, because exclusivity only bars approval of another sponsor's drug.

In January 2018, Avadel received orphan-drug designation for the active moiety oxybate for narcolepsy because it provided a plausible hypothesis that its proposed drug product's once-nightly dosing regimen from an extended-release formulation would make the drug clinically superior to Xyrem, which require patients to wake during the night to take a second dose.[5] Avadel then applied for marketing approval of Lumryz in December 2020, requiring the FDA to determine whether Xywav's exclusivity period until July 2027 blocked approval of Lumryz. Although Lumryz contains more sodium than Xywav, the FDA determined in May 2023 that the benefits of Lumryz's once-nightly dosing made a major contribution to

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excessive daytime sleepiness (EDS) associated with narcolepsy and from 2018 to 2025 to treat cataplexy and EDS in pediatric patients. Avadel seeks approval to treat cataplexy or EDS in adults and so Xyrem's exclusivity for the pediatric indication is not at issue.

[5] The Xywav drug product is an immediate-release calcium, magnesium, potassium and sodium oxybate oral solution whereas the Lumryz drug product is an extended-release sodium oxybate oral suspension. *See* 21 C.F.R. 314.3(b) (defining "drug product" as the finished dosage form that contains a drug substance—an active ingredient—along with other ingredients); *id.* (defining "dosage form" as the physical manifestation of a drug, including the (1) physical appearance, (2) physical form, (3) way it is administered and (4) design features affecting frequency of dosing).

patient care, rendering it clinically superior and therefore not the "same drug." Accordingly, the FDA concluded that Xywav's exclusivity did not bar marketing approval for Lumryz and that Lumryz was entitled to its own seven-year exclusivity period.[6]

In June 2023, Jazz sued in district court under the Administrative Procedure Act (APA) to challenge the FDA's approval of Lumryz, arguing that the FDA acted not in accordance with law and in excess of statutory authority by approving Lumryz in violation of subsection 360cc(a)'s exclusivity provision. *Jazz Pharms., Inc. v. Becerra*, No. 23-cv-1819, 2024 WL 4625731, at *10 (D.D.C. Oct. 30, 2024). Avadel intervened as a defendant and the district court granted summary judgment to the FDA and Avadel, reasoning that statutory text, history and purpose show that the Congress meant to ratify and incorporate the FDA's definition of "same drug" in subsection 360cc(a). *Id.* at *13. As a result, the FDA properly approved Lumryz during Xywav's exclusivity period because Lumryz's clinical superiority means it is not the "same drug" as Xywav. *Id.* at *17. In the alternative, the court determined that even if Lumryz is the "same drug" as Xywav, subsection (c)(1) nevertheless authorizes the FDA to grant

[6] In a letter submitted to the FDA before it approved Lumryz, Jazz conceded that the FDA could approve Lumryz if it was clinically superior to Xywav. J.A. 382–85; *see also* J.A. 145 n.118. Jazz does not renew on appeal its argument made in district court that FDA erred in finding that Lumryz is clinically superior to Xywav. Nevertheless, during this litigation Jazz has consistently maintained its position that the FDA may not approve Lumryz even if it is clinically superior. We of course have an "obligation to independently interpret the statute[]" to "determine the best reading." *Loper Bright Enters. v. Raimondo*, 603 U.S. 369, 373 (2024).

exclusive approval based on clinical superiority.[7] *Id.* at *17–18. Jazz timely appealed.

II. ANALYSIS

We review questions of statutory interpretation under the APA de novo. *See Loper Bright Enters. v. Raimondo*, 603 U.S. 369, 392 & n.4 (2024). "We start where we always do: with the text of the statute." *Bartenwerfer v. Buckley*, 598 U.S. 69, 74 (2023) (citation modified). It is also a "fundamental canon of statutory construction that the words of a statute must be read in their context and with a view to their place in the overall statutory scheme." *Util. Air Regul. Grp. v. EPA*, 573 U.S. 302, 320 (2014) (quotation omitted). "Statutory history is an important part of this context," including, in this case, considerations of incorporation and the old-soil canon. *United States v. Hansen*, 599 U.S. 762, 775 (2023); *see also id.* at 778–79.

A. The Statutory Text

Pursuant to the text, as amended, the Act prohibits the FDA from approving another application "for the same drug for the same disease or condition" as an orphan-designated and approved drug during the earlier drug's seven-year exclusivity period. 21 U.S.C. § 360cc(a). Jazz argues that "same" here means "the one previously referred to; aforesaid." *See Same*, *Collins English Dictionary* 1750 (12th ed. 2014).

For support, Jazz relies on the Eleventh Circuit's interpretation of "same" in this context to mean "being the one

[7] Because we affirm the district court's interpretation of subsection 360cc(a), we do not reach its alternative holding that subsection 360cc(c) created a third exception to exclusivity.

under discussion or already referred to." *Catalyst Pharms., Inc. v. Becerra*, 14 F.4th 1299, 1307–08 (11th Cir. 2021) (citing *Same*, *Merriam-Webster's Collegiate Dictionary Online*). But the Eleventh Circuit brushes past *Merriam-Webster's* first sense of the adjective "same," which defines it as "resembling in every relevant respect," and instead adopts the second definition of the term without explanation. *Id.* (citing *Same*, *Merriam-Webster's Collegiate Dictionary Online*). *Merriam-Webster's* first sense also fits with *Black's* contemporary definition. *Same*, *Black's Law Dictionary* 1541 (10th ed. 2014) ("Identical or equal; resembling in every relevant respect."). As a matter of ordinary meaning, a drug that is clinically superior to another drug does not resemble that drug in every relevant respect. Indeed, narcolepsy patients would most likely find it "relevant" that they no longer must wake up at night for a second dose of medication.

Even if the second sense were the better reading, it would remain to define the earlier referent. In Jazz's view, that referent is the "drug designated under section 360bb," which in this case is the active moiety of oxybate. For its part, Avadel points out that subsection 360cc(a) prohibits the FDA from approving another "application" after it approves an earlier "application," arguing as a result that the correct referent is instead the drug product. Thus, it is far from clear from plain meaning only what the correct referent would be—the active moiety (oxybate), the drug product (calcium, magnesium, potassium and sodium oxybate immediate-release oral solution) or something in between (including consideration of clinical superiority).

B. The Statutory History

"When Congress adopts a new law against the backdrop of a longstanding administrative construction, this Court

generally presumes the new provision should be understood to work in harmony with what has come before." *Monsalvo v. Bondi*, 145 S. Ct. 1232, 1242 (2025) (citation modified); *see also Bragdon v. Abbott*, 524 U.S. 624, 631 (1998) ("Congress' repetition of a well-established term carries the implication that Congress intended the term to be construed in accordance with pre-existing regulatory interpretations." (citations omitted)); *Wash. All. of Tech. Workers v. DHS*, 50 F.4th 164, 180 (D.C. Cir. 2022) ("If a statute uses words or phrases that have already received authoritative construction by a responsible administrative agency, they are to be understood according to that construction." (citation modified) (quoting A. Scalia & B. Garner, *Reading Law* 322 (2012)).

Jazz contends that changing "such drug" to "same drug" in subsection 360cc(a) was a "modest" alteration made simply to "clarify" the phrase and should be ascribed "no meaning." Appellant Br. 15–16; *see also id.* at 44. Jazz's argument conflicts with the Supreme Court's guidance that "when Congress amends legislation, courts must presume it intends the change to have real and substantial effect." *Ross v. Blake*, 578 U.S. 632, 641–42 (2016) (citation modified). We find more plausible that the Congress incorporated and ratified the FDA's longstanding regulatory definition of "same drug."

Granted, the Congress did not expressly incorporate that definition by cross-referencing in the statute the regulatory provision, as it has done in certain other provisions of the FD&C Act. *E.g.*, 21 U.S.C. § 355(c)(3)(E)(ii) ("active moiety (as defined by the Secretary in section 314.3 of title 21, Code of Federal Regulations (or any successor regulations))"). For Jazz, "Congress's failure to use such an express incorporation of prior regulations . . . cuts against the proposed inference" of incorporation. *New York v. EPA*, 413 F.3d 3, 19 (D.C. Cir. 2005), *cited by Env't Def. v. Duke Energy Corp.*, 549 U.S. 561,

576 (2007). But that is not the end of the inquiry. *New York*'s overall test asks whether there are "indications in the statutory language or history to infer that Congress intended to incorporate into a statute a preexisting regulatory definition." *Id.* Such indications abound here.

New York and *Environmental Defense* interpreted the Clean Air Act's (CAA) pollution control schemes regarding New Source Performance Standards (NSPS) and Prevention of Significant Deterioration (PSD). The NSPS provisions defined the term "modification" whereas the later PSD provisions employed that word "as defined in" the NSPS. *Env't Def.*, 549 U.S. at 566. Despite this cross-reference, implementing regulations promulgated by the Environmental Protection Agency (EPA) differed between the NSPS and PSD because the EPA interpreted the statutory definition differently in each context. The High Court was unconcerned by the incongruity. "Although we presume that the same term has the same meaning . . . in a single statute," we "also understand that most words . . . may be variously construed, not only when they occur in different statutes, but when used more than once in the same statute or even in the same section." *Id.* at 574 (citation modified). Because "[n]othing in the text or the legislative history . . . suggest[ed] that Congress had details of regulatory implementation in mind" when it added the cross-reference, the Supreme Court held that the EPA retained discretion to define the same term differently depending on the context in which it appeared. *Id.* at 576.

Of course, the Supreme Court has emphasized that "legislative history is not the law." *Azar v. Allina Health Servs.*, 587 U.S. 566, 579 (2019) (quotation omitted). But in any event neither the FDA nor Avadel relies on the threadbare *legislative* history here for their common reading of the statute. Instead, both the text and *statutory* history of the 2017

amendments demonstrate that the Congress "had details of regulatory implementation in mind" when it changed the Act. *Env't Def.*, 549 U.S. at 576; *see also* Scalia & Garner, *supra*, at 256 (explaining that statutory history forms part of the context of the statute and distinguishing it from legislative history). The changes the Congress *did* make also tell us more about the statute's meaning than the earlier failed bills Jazz cites. *See Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 422 (2012) (warning of "the perils of relying on the fate of prior bills to divine the meaning of enacted legislation").

The parties agree that the Congress made the 2017 amendments in large part to codify in statute the FDA's clinical superiority requirement and supersede *Depomed's* holding. Thus, the Congress had in mind the FDA's regulations, which in 2013 had codified in regulation the FDA's longstanding practice imposing a clinical-superiority requirement for orphan-drug exclusivity. 2013 Rule, 78 Fed. Reg. at 35,127, 35,132 (explaining the rationale for adding 21 C.F.R. § 316.34(c)). Equally, in subsection 360cc(d) the Congress granted the FDA authority to promulgate regulations to implement subsection 360cc(c), likewise making clear that it was thinking about regulatory implementation when it enacted the 2017 amendments. 21 U.S.C. § 360cc(d). This statutory context lends support to the view that the Congress's change from "such drug" to "same drug" incorporated the FDA's longstanding regulatory definition of that term and not that it was a mere housekeeping exercise.

This reading also fits with the old-soil canon of construction, despite Jazz's arguments to the contrary. "Where Congress employs a term of art 'obviously transplanted from another legal source, it brings the old soil with it.'" *George v. McDonough*, 596 U.S. 740, 746 (2022) (quoting *Taggart v. Lorenzen*, 587 U.S. 554, 560 (2019)). That other legal source

may be, for example, statute, regulation, common law, equity or court practice. *See, e.g.*, *Waetzig v. Halliburton Energy Servs.*, 145 S. Ct. 690, 697–98 (2025) (statute); *George*, 596 U.S. at 746 (regulation); *Hansen*, 599 U.S. at 778 (common law); *Taggart*, 587 U.S. at 560 (equity); *Kemp v. United States*, 596 U.S. 528, 538–39 (2022) (state procedural rules). The term's meaning in the first context must also be "'well-settled' before the transplantation." *Sackett v. EPA*, 598 U.S. 651, 683 (2023) (quoting *Kemp*, 596 U.S. at 539). Thus, "mere months" in the context of "rapidly changing . . . regulatory programs" is not enough, *id.* (quotation omitted), but "roughly 100 years" of regulatory history is, *George*, 596 U.S. at 744; *see also id.* at 746–47.

In *George*, where the Congress "used an unusual term that had a long regulatory history in th[at] very context"—namely "clear and unmistakable error"—it codified the doctrine as developed under earlier agency practice. 596 U.S. at 746. By contrast, in *Bruesewitz v. Wyeth LLC*, 562 U.S. 223, 233–35 (2011), a statute that spoke about "unavoidable" side effects did not incorporate a comment from the Second Restatement of Torts that carved out "unavoidably unsafe products" because "unavoidable" is "hardly a rarely used word" and there is no "special significance to the term 'unavoidable' standing alone." And in *Yellen v. Confederated Tribes of Chehalis Rsrv.*, 594 U.S. 338, 353 (2021), the Court rejected the notion that a 69-word definition of an Indian tribe was somehow longhand for the term of art "federally recognized tribe" in part because "recognized" is "too common and context dependent a word to bear so loaded a meaning." Finally, the Eleventh Circuit found the old-soil canon inapplicable to a statute otherwise similarly worded to a regulation because a one-word variation between them was "material" and thereby "suggest[ed] a variation in meaning." *CSX Corp. v. United States*, 18 F.4th 672, 681 (11th Cir. 2021) (quoting Scalia & Garner, *supra*, at 170).

This case is more like *George* than *Bruesewitz*, *Yellen* or *CSX*. First, the FDA has used the same definition of "same drug" in the ODA context since 1992—a quarter century before the amendments—which is more like *George*'s 100-year period of regulatory history than *Sackett*'s mere months in the context of rapid change. Second, Jazz's reliance on *Bruesewitz*, *Yellen* and *CSX* requires inconsistently defining the unit of analysis here as either broader or narrower than the FDA's reading. To draw support from *Bruesewitz* and *Yellen*, Jazz adopts a narrow reading, arguing that the Congress simply replaced "such" with "the same," which is too commonly used a word to support an inference of incorporation under the old-soil canon. But later referencing *CSX*, Jazz offers a broad reading, arguing for too much linguistic variation between the amended statute and the regulation. Jazz points out that the Congress replaced the entire phrase "such drug for such disease or condition" with "the same drug for the same disease or condition," 2017 Act, § 607(a)(1), 131 Stat. at 1049, which in turn varies from the FDA's regulations defining the scope of orphan-drug exclusive approval. *See* 21 C.F.R. § 316.31(a) (using the phrase "the same drug *for the same use or indication*" (emphasis added)); *id.* § 316.3(b)(12) (similar).

In *Bruesewitz*, the Supreme Court contrasted cases "putting a definitive gloss" on the Restatement comment at issue—which had used the adverbial "precise phrase 'unavoidably unsafe product'"—with the statute's use of the adjectival form "unavoidable." 562 U.S. at 234–35 (citing cases). Here, by replacing "such" with "same," the Congress created the precise phrase "same drug" used in the FDA's regulatory definition. And this case is far from *Yellen*'s implausible argument for retrofitting a 69-word-long definition into a three-word term of art. Equally, there is no incongruity with *CSX* because the term "same drug" does not vary across the statute or the relevant regulation.

Jazz also argues that the Congress would have changed "disease or condition" to "use or indication" if it wanted to incorporate the FDA's regulatory definition of "same drug" because several regulatory provisions employ the phrase "same drug for the same use or indication" not "same drug for the same disease or condition." However, the term "use or indication" appears in the FDA's regulatory definition of "exclusive approval" and its rule on the scope of orphan-drug exclusivity but not in its definition of "same drug." *Contrast* 21 C.F.R. §§ 316.3(b)(12) ("same drug for the same use or indication"), 316.31(a) (same), *with id.* § 316.3(b)(14) (defining "same drug"). And it makes sense that the Congress would retain the phrase "disease or condition" because the ODA is replete with that language rather than "use or indication."[8] *See generally* 21 U.S.C. §§ 360aa–ee.

Relatedly, Jazz's argument that a clinical superiority requirement in subsection 360cc(a) would render the phrase "same disease or condition" redundant fails because "disease or condition" has a different meaning from "use or indication." *Catalyst*, 14 F.4th at 1306; *see also id.* at 1302 n.2, 1310 (explaining that indication typically means intended use,

[8] The regulatory definition of "same drug" provides that being "intended for the same use" is one of the conditions for a drug to be the same as another drug. 21 C.F.R. § 316.3(b)(14). It follows that a drug intended for a different use would be different from a drug that is otherwise the same and therefore not barred by the latter's exclusivity period. *Catalyst* is not to the contrary. There, the parties agreed the two drugs were the "same drug" so the Eleventh Circuit interpreted only "same disease or condition," not "same drug." *See* 14 F.4th at 1301, 1306. Because the court determined that "same disease or condition" was unambiguous, it held that the FDA erred in interpreting that phrase to allow it to approve a drug for a different use or indication. *Id.* at 1306–13.

although approved indications may differ from intended off-label uses); *Caraco Pharm. Labs.*, 566 U.S. at 417 n.7 (explaining that an indication "refers generally to what a drug does" (citing 21 C.F.R. § 201.57(c)(2))).[9] In other words, the amended subsection 360cc(a) exclusivity test includes concepts of active moiety, intended use, clinical superiority—which together make up the regulatory definition of "same drug"—*and* disease or condition.

Thus, the Congress decided to incorporate fully the FDA's "same drug" regulatory definition and then made a second change from "such" to "the same" to retain the parallel sentence structure. Accordingly, the relevant unit of analysis is "same drug," which is a sufficiently "unusual term" with a "long regulatory history" to support inferring incorporation under the old-soil canon. *George*, 596 U.S. at 746.

C. Other Orphan Drug Act Provisions

The statutory context of the other section 360cc subsections and the statutory scheme as amended in 2017 further reinforce our interpretation. Taking each of the other subsections of section 360cc in turn, Jazz argues for the first time on appeal that the FDA's reading of the statute fits poorly with section 360cc(b)—enumerating exceptions to exclusivity—because it divests Jazz of its property interest in orphan-drug exclusivity without comparable process. Despite

[9] In this context, the disease or condition is narcolepsy and Lumryz's approved indication is the treatment of cataplexy or EDS in adults with narcolepsy. These are not coextensive—narcolepsy can occur without cataplexy, for example. And an indication can change over time, as evidenced by the subsequent approvals of Xyrem to treat cataplexy in adults, then EDS in adults and eventually cataplexy and EDS in children.

the FDA's contention otherwise, Jazz has not forfeited this argument by not raising it in district court. That is so because Jazz is not introducing a standalone due process challenge. Instead, in the context of the parties' narrow dispute over statutory interpretation, Jazz is offering another argument that the FDA's reading of subsection 360cc(a) is implausible because of an alleged incongruity with the amount of process provided in subsection 360cc(b). *See Yee v. City of Escondido*, 503 U.S. 519, 534 (1992) ("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." (citations omitted)). And despite the FDA's longstanding view that there is "no property right to exclusive approval under the Orphan Drug Act," 1992 Rule, 57 Fed. Reg. at 62,083, that is, at most, only persuasive authority and we must still independently interpret the statute, *Loper Bright*, 603 U.S. at 394 (citing *Skidmore v. Swift & Co.*, 323 U.S. 134, 140 (1944)).

Jazz's due process argument nevertheless fails because, even assuming that Jazz has a property interest in its exclusivity entitled to due process protections, it has not shown that the process available under subsection 360cc(a) or provided to it here is deficient. Due process requires "notice and opportunity for hearing appropriate to the nature of the case." *Mullane v. Ctrl. Hanover Bank & Trust Co.*, 339 U.S. 306, 313 (1950). To determine whether a hearing is required before instead of after the deprivation of a property interest, courts consider (1) the private interest affected, (2) the risk of erroneous deprivation of that interest and the probable value of additional procedures and (3) the government's interest, including the function involved and the burden and cost of additional procedures. *See Mathews v. Eldridge*, 424 U.S. 319, 333–35 (1976). The Supreme Court has often found that post-deprivation procedures are enough. *Gilbert v. Homar*, 520 U.S. 924, 930–

31 (1997) (collecting cases). At times, only a very limited pre-deprivation hearing is required, followed by a more comprehensive post-deprivation hearing. *Id.* at 929 (discussing *Cleveland Bd. of Educ. v. Loudermill*, 470 U.S. 532, 544–46 (1985)).

In declining to create by regulation a notice and hearing process for exclusivity holders before approving a drug that the FDA considers to be different, the FDA reasoned that exclusivity holders had enough post-approval process because they could petition the FDA under 21 C.F.R. § 10.30 or obtain post-decisional review in federal court. 1992 Rule, 57 Fed. Reg. at 62,083. Moreover, pre-decisional review would be time-consuming, could be used for delay and would present challenges due to the need to evaluate non-public information. *Id.* The enumerated exceptions in subsection 360cc(b) are distinguishable. As to the first exception, it makes sense to require notice and the opportunity to submit views before finding that an exclusivity holder cannot meet market needs because the holder best knows its manufacturing capacity and can assist the FDA's decisional process. 21 U.S.C. § 360cc(b)(1). The second exception in no way deprives an exclusivity holder of property rights because the holder consents to the approval of the other drug. *Id.* § 360cc(b)(2). In any event, here the FDA provided ample pre-decisional process by reviewing written submissions and hearing an oral presentation from Jazz's counsel before going on to address Jazz's arguments for 20 pages in determining that Xywav's unexpired exclusivity did not bar its approval of Lumryz.

Turning to other subsections of section 360cc, Jazz remarks that the phrase "clinical superiority" appears in subsections 360cc(c) and (e) but not (a) and (b). True enough. But the requirement to demonstrate clinical superiority in paragraph 360cc(c)(1) tracks closely the FDA's longstanding

regulation on "recognition of exclusive approval" requiring that a sponsor of a drug that is "otherwise the same" demonstrate clinical superiority. 21 C.F.R. § 316.34(c). And paragraph 360cc(c)(2) mirrors the FDA's regulatory definition of "clinical superiority." *Compare* 21 U.S.C. § 360cc(c)(2), *with* 21 C.F.R. § 316.3(b)(3). In turn, clinical superiority is used in the FDA's definition of "same drug." 21 C.F.R. § 316.3(b)(14)(i). Thus, the references to clinical superiority in other subsections only underscore that the Congress "plainly was aware" that the FDA's regulatory definition of "same drug" employed the concept of clinical superiority. *Hikvision USA, Inc. v. FCC*, 97 F.4th 938, 946 (D.C. Cir. 2024).

Jazz goes on to point out a redundancy in paragraph 360cc(c)(1) from interpreting the term "same drug" to include the concept of "clinical superiority." Under that paragraph, for exclusive approval a drug sponsor of a drug that is "otherwise the same" as an already approved drug must "demonstrate that such drug is clinically superior" to the already approved drug "that is the same drug." 21 U.S.C. § 360cc(c)(1). Granted, it would be redundant for "same drug" as used at the end of paragraph 360cc(c)(1) to include a concept of clinical superiority. And our "normal presumption" is that "when Congress uses a term in multiple places within a single statute, the term bears a consistent meaning throughout." *Allina Health*, 587 U.S. at 576 (citation omitted).

However, we "also understand that most words . . . may be variously construed . . . when used more than once in the same statute or even in the same section." *Env't Def.*, 549 U.S. at 574 (citation modified). In context, it is clear that "same drug" in paragraph 360cc(c)(1) refers back to the condition that a drug be "otherwise the same." Put differently, only a drug that is *otherwise* the same as another drug *and* is not clinically superior to the other drug is the same drug as the other drug.

Subsection (a) simply uses the term "same drug" without more, i.e., without breaking down sameness into "otherwise the same" and "clinical superiority." Thus, the Congress used a clinical superiority test in subsection (a) because clinical superiority *vel non* is part of what determines overall sameness, as demonstrated by subsection (c).

Jazz further argues that the requirement in subsection 360cc(d) that any existing regulatory definitions applied in implementing subsection 360cc(c) be consistent with the statute cuts against inferring incorporation. But if, as we conclude, the Congress incorporated the FDA's regulatory definition of "same drug" in subsection 360cc(a), it necessarily would be consistent with the statute. Finally, subsection 360cc(e) also weighs in favor of inferring incorporation. By adding reference to the FDA's longstanding requirement at the designation stage that a sponsor provide a plausible hypothesis of clinical superiority to an already approved drug, the 2017 amendments evince the Congress's intent to adopt the FDA's orphan-drug designation process set forth in 21 C.F.R. §§ 316.20, 316.25. Those regulations require a sponsor of a drug that is "otherwise the same" as an already approved drug to present a plausible hypothesis of clinical superiority, which is consistent with the FDA's and Avadel's reading of subsection 360cc(a), further revealing the Congress's familiarity with the regulations.

Beyond the context of the other subsections in section 360cc, Jazz's statutory interpretation fits poorly with the statutory scheme as amended in 2017. For Jazz, the Congress wanted to limit serial exclusivity or "evergreening" by superseding *Depomed* but also wanted to limit the FDA's practice of approving clinically superior drugs notwithstanding an exclusivity period for a drug that is otherwise the same. But as the district court pointed out, it makes little sense for the

Congress to take clear action to undo a district court's holding constraining the FDA's authority while *sub silentio* repudiating the FDA's longstanding regulations on the scope of exclusivity. *Jazz Pharms.*, 2024 WL 4625731, at *16.

Instead, the Congress acted both to prevent evergreening *and* to endorse the FDA's longstanding regulations allowing approval of a clinically superior drug during another drug's exclusivity period. That understanding of the Congress's action more plausibly balances its earlier findings both that more "promising orphan drugs" are needed and that "incentives" are needed to develop such drugs. Orphan Drug Act, § 1(b)(5), (6), 96 Stat. 2049. Under this scheme, sponsors are incentivized to develop innovative treatments for rare diseases by the prospect of an exclusivity period while, at the same time, other drugmakers that demonstrate their drug is more effective, safer or otherwise provides a major contribution to patient care are not blocked from entering the market either. That is the balance that the Congress ratified by incorporating the FDA's regulatory definition of "same drug" in subsection 360cc(a).

In sum, both the statutory context and the regulatory scheme that the 2017 amendments endorsed support the FDA's authorization to approve Lumryz's marketing despite the ongoing exclusivity period for Xywav.

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For the foregoing reasons, the judgment of the district court is affirmed.

So ordered.