United States Court of Appeals

FOR THE DISTRICT OF COLUMBIA CIRCUIT

Argued October 22, 2015 Decided June 3, 2016

No. 15-5166

SPECTRUM PHARMACEUTICALS, INC.,
APPELLANT

v.

SYLVIA MATHEWS BURWELL, IN HER OFFICIAL CAPACITY AS SECRETARY, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, ET AL.,
APPELLEES

Appeal from the United States District Court
for the District of Columbia
(No. 1:15-cv-00631)

Jessica L. Ellsworth argued the cause for appellant. With her on the briefs were *Susan M. Cook, Eugene A. Sokoloff,* and *Elizabeth Austin Bonner*.

Jonathan M. Ettinger was on the brief for *amicus curiae* National Organization for Rare Disorders in support of appellant.

Christopher M. O'Connell, Trial Attorney, U.S. Department of Justice, argued the cause for federal appellees.

With him on the brief were *Benjamin C. Mizer*, Principal Deputy Assistant Attorney General, *William B. Schultz*, General Counsel, Food and Drug Administration, and *Annamarie Kempic*, Deputy Chief Counsel, Litigation.

Douglas B. Farquhar argued the cause for intervenor-appellee Sandoz Inc. With him on the brief were *James P. Ellison* and *Jennifer M. Thomas*.

Before: GRIFFITH, KAVANAUGH, and WILKINS, *Circuit Judges*.

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

GRIFFITH, *Circuit Judge*: In this case, Spectrum Pharmaceuticals claimed that the Food and Drug Administration's approval of a cancer drug violated Spectrum's exclusive marketing rights. The district court granted summary judgment against Spectrum, and we affirm.

I

Levoleucovorin is better known by the brand-name Fusilev, which Spectrum has sold since 2008 for the purpose of counteracting liver damage during a type of chemotherapy known as methotrexate therapy (the "Methotrexate Indications"). Fusilev is an "orphan drug," so called because it is designed to treat a rare disease or condition that historically received little attention from pharmaceutical companies, and hence became "orphaned" because the comparatively small demand for treatment left little motive for research and development. Pub. L. No. 97-414, § 1(b), 96 Stat. 2049 (1983). Under the Orphan Drug Act amendments to the Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 360aa-ee, intended to increase incentives for companies to develop new

orphan drugs, Spectrum received exclusive marketing rights to the Methotrexate Indications for seven years. In other words, because Spectrum was the first to develop levoleucovorin as an orphan drug for methotrexate therapy, no other company could sell a generic version of the drug for that purpose until 2015.

In 2011, Spectrum received approval from FDA to market Fusilev for an altogether new use: helping patients with advanced colorectal cancer to manage their pain (the "Colorectal Indication"). Spectrum has exclusive marketing rights for the Colorectal Indication until 2018.

On March 7, 2015, Spectrum's exclusivity period expired for the Methotrexate Indications. Two days later, Sandoz Inc. received FDA approval to market a generic version of levoleucovorin for the Methotrexate Indications, having had its application expedited in 2012 to address a drug shortage. Unlike Fusilev, which is sold in a freeze-dried powder that must be mixed with another chemical before it can be used, Sandoz sells its generic drug in a ready-to-use form. Pursuant to FDA regulations, Sandoz's label contains only the Methotrexate Indications and makes no mention of the Colorectal Indication. Shortly after Sandoz launched its product, Spectrum filed suit to enjoin FDA's approval of Sandoz's drug.

Spectrum argued to the district court that Sandoz's sole intended use of the generic was to treat patients with colorectal cancer, even though the label provided for use only in patients undergoing methotrexate therapy. Spectrum urged that FDA was willfully blind to the fact that the generic drug would not be used for counteracting liver damage, but for managing pain, which is Spectrum's exclusive domain. This intended use made the agency's approval of the generic

unlawful, argued Spectrum, because it violated Spectrum's exclusive marketing rights for the Colorectal Indication.

Spectrum's argument focused largely on Sandoz's vial sizes. The record shows the standard dose of levoleucovorin for the Methotrexate Indications is 7.5 mg, although some patients need a 75 mg or 85 to 90 mg dose in certain rare situations. In contrast, the Colorectal Indication regularly requires a much larger dose of 150 mg. Spectrum sells Fusilev in 50 mg vials, but Sandoz sells its generic in 175 mg and 250 mg vials, sizes that Spectrum argues are intended to treat the Colorectal Indication despite being labeled for only the Methotrexate Indications.[1]

Spectrum also challenged FDA's approval on two additional grounds: Spectrum urged that the approval was arbitrary and capricious, in violation of the Administrative Procedure Act, because FDA changed its position on the safety and efficacy of large vials of levoleucovorin without explanation. Finally, Spectrum contended that it was entitled to notice before FDA expedited review of Sandoz's generic drug.

The district court granted summary judgment against Spectrum, holding that FDA's approval of Sandoz's generic drug was lawful. The district court reasoned that the Orphan Drug Act allows FDA to approve Sandoz's drug so long as the generic's label omits the Colorectal Indication. The district court rejected Spectrum's remaining arguments as well, holding that the agency did not improperly change

[1] In 2011, Spectrum received two additional FDA approvals to market Fusilev in larger vials of 175 mg and 250 mg, first for the Methotrexate Indications alone, and second for the Colorectal Indication. Spectrum later decided not to sell the larger vials at all.

positions without explanation, and any error in expediting the agency's review of the generic was harmless.

Spectrum appeals the judgment of the district court. We have jurisdiction under 28 U.S.C. § 1291.

II

Our review is de novo. *Purepac Pharm. Co. v. Thompson*, 354 F.3d 877, 883 (D.C. Cir. 2004) (reviewing the district court's grant of summary judgment); *Serono Labs., Inc. v. Shalala*, 158 F.3d 1313, 1319 (D.C. Cir. 1998) (reviewing the district court's statutory and regulatory interpretations). Because Spectrum challenges the decision of an administrative agency, de novo review means that we will "review directly the decision of the [agency]." *Purepac*, 354 F.3d at 883 (quoting *Lozowski v. Mineta*, 292 F.3d 840, 845 (D.C. Cir. 2002)). Accordingly, we will uphold FDA's approval of Sandoz's generic drug under the Administrative Procedure Act unless that decision was "'arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law.'" *Id.* (quoting 5 U.S.C. § 706(2)(A)).

A

Spectrum's primary argument on appeal is that FDA violated Spectrum's exclusive marketing rights by ignoring that doctors and patients would use Sandoz's generic for the Colorectal Indication.

i

The Food, Drug, and Cosmetic Act governs FDA's approval of a pharmaceutical drug. *AstraZeneca Pharm. LP v. FDA*, 713 F.3d 1134, 1136 (D.C. Cir. 2013). To secure FDA approval to market a new drug, a company files a new drug

application (NDA) that triggers a process through which FDA approves new drugs shown to be safe and effective. 21 U.S.C. § 355(a)-(j). In its application, the company specifies what the drug will be used for and the volume in which it will be sold. *Id.* § 355(b). FDA's approval of an NDA allows the company to sell the drug at the proposed volume and with a label indicating the proposed purpose. *Id.* § 355(a). The first drug to be approved for a particular use through the NDA process is called a "pioneer."

Recognizing that this process can be lengthy and expensive, due in part to the clinical trials required to determine a drug's safety and effectiveness, Congress crafted a statutory scheme that balances two interests: innovation and affordability. *Teva Pharm. Indus. Ltd. v. Crawford*, 410 F.3d 51, 54 (D.C. Cir. 2005). To promote innovation, Congress gave producers of pioneer drugs different periods of market exclusivity, depending in part on the type of drug they develop. 21 U.S.C. § 355(a)-(j). In 1983, Congress passed the Orphan Drug Act to lengthen the exclusive marketing period to seven years for drugs that treat rare diseases. *Id.* § 360cc(a). During that period, FDA may not, subject to certain exceptions not applicable here,[2] approve another company's application "for such drug for such disease or condition." *Id.*

Although market exclusivity promotes development of new drugs, it also risks increasing their price by eliminating competition. In an effort to hold down drug prices, Congress created a streamlined approval process for generic drugs in 1984. *See* Drug Price Competition and Patent Term Restoration Act (Hatch-Waxman Amendments), 21 U.S.C.

[2] FDA can cut short an exclusivity period if there is a drug shortage, provided the producer of the pioneer cannot supply the drug in sufficient quantities, or if the producer of the pioneer consents. 21 U.S.C. § 360cc(b).

§ 355(j); *Mead Johnson Pharm. Grp.*, *Mead Johnson & Co. v. Bowen*, 838 F.2d 1332, 1333 (D.C. Cir. 1988). Under that process, a company can file what is known as an abbreviated new drug application (ANDA) that relies on clinical research data for the pioneer rather than new studies for the generic. To secure FDA approval, an ANDA need show only that the generic drug is equivalent in all material respects to the pioneer drug. 21 U.S.C. § 355(j)(2)(A); *Mead Johnson*, 838 F.2d at 1333. FDA will not approve the generic until the exclusive marketing period for the pioneer expires.

A complication arises when a pioneer drug can be used for multiple purposes, and the exclusive marketing period for one use of the drug expires, while it continues for another. In this situation, FDA permits what is called a labeling "carve-out" that allows producers to sell a generic if they exclude from its label any indication that is still protected by exclusive marketing rights. 21 C.F.R. § 314.94(a)(8)(iv). Labeling carve-outs are so named because any exclusive use is carved out, *i.e.*, omitted, from the list of approved uses on the generic's label. FDA allows labeling carve-outs under the Orphan Drug Act just as it does for generics generally under the Food, Drug, and Cosmetic Act. No matter what use for the drug is described on the label, however, FDA does not prevent a doctor from prescribing a drug for some other use, called an "off-label" use. *See Bristol-Myers Squibb Co. v. Shalala*, 91 F.3d 1493, 1496 (D.C. Cir. 1996) ("[T]he new drug provisions apply only at the moment of shipment in interstate commerce and not to action taken subsequent[ly]." (quoting Legal Status of Approved Labeling for Prescription Drugs; Prescribing for Uses Unapproved by the Food and Drug Administration, 37 Fed. Reg. 16,503 (1972))). We have approved FDA's general approach to labeling carve-outs as an acceptable interpretation of the Food, Drug, and Cosmetic Act. *Id.* at 1499-1501.

Against this regulatory background, FDA approved Sandoz's generic drug with a label that says nothing about the Colorectal Indication. Spectrum argues that this labeling carve-out violates the Orphan Drug Act because of how Sandoz intends its generic to be used. According to Spectrum, FDA cannot approve an ANDA when the agency knows that the generic will be used for the carved-out purpose. Spectrum asserts that FDA's own files show that Sandoz intended doctors and patients to use the generic for the Colorectal Indication, citing statements by FDA officials associating large vials of levoleucovorin with the Colorectal Indication and small vials with the Methotrexate Indications. For example, Spectrum rests heavily on a statement by an FDA official made during a meeting about Fusilev in 2009 that the Methotrexate Indications do "not require single use vials larger than 50 mg." This statement, Spectrum suggests, shows that FDA knew that Sandoz's large vials of 175 mg and 250 mg are suitable for the Colorectal Indication and go well beyond the average dose of 7.5 mg needed for the Methotrexate Indications. FDA responds that it need look no further than the use indicated in Sandoz's ANDA to make certain the generic drug will not trench on the prior grant of exclusivity to Spectrum. We agree with FDA and find its interpretation of the Orphan Drug Act reasonable.

The Orphan Drug Act provides that once FDA approves a pioneer drug "designated . . . for a rare disease or condition," it may not approve another application "for such drug for such disease or condition" by another company for seven years. 21 U.S.C. § 360cc(a). Spectrum would have us read the phrase "for such disease or condition" to require the agency to consider the *intended* use of a drug, even if the drug is not "designated," or labeled, for that purpose. In Spectrum's

view, a drug is "for" a disease or condition if the producer intends it to be used for that disease or condition. FDA responds that "for such disease or condition" refers only to the uses included on a drug's label.

The statute does not unambiguously foreclose FDA's interpretation. Because Congress has not "directly spoken to the precise question at issue,"[3] we must determine whether the agency's interpretation is "a permissible construction" of the Orphan Drug Act. *Chevron U.S.A. Inc. v. Nat. Res. Def. Council, Inc.*, 467 U.S. 837, 842-43 (1984); *see also Teva Pharm. USA, Inc. v. Sebelius*, 595 F.3d 1303, 1315 (D.C. Cir. 2010) (applying *Chevron*). We conclude that it is.

First, FDA's reading of the statute closely hews to the text. *See Abbott Labs. v. Young*, 920 F.2d 984, 988 (D.C. Cir. 1990) (recognizing that the reasonableness of an agency's interpretation turns in part on "the construction's 'fit' with the statutory language"). As the Fourth Circuit reasoned in *Sigma-Tau Pharmaceuticals, Inc. v. Schwetz*, 288 F.3d 141 (4th Cir. 2002), the words "for such disease or condition" suggest Congress intended to make section 360cc "disease-specific, not drug-specific," and the rest of the statutory language focuses on protecting approved indications, not intended off-label uses. *See id.* at 145 (reasoning that the statutory language is "directed at FDA approved-use, not generic competitor intended-use"). The statute creates limits on the approval of an "application," which by implication

[3] We need not resolve whether the Orphan Drug Act answers the flipside of that question: whether the statute unambiguously *requires* FDA's interpretation. FDA has not pressed that argument before us and it is unnecessary to the resolution of this case. We therefore leave for another day the question whether FDA could permissibly adopt an alternative interpretation.

directs FDA to evaluate what is written on the application. 21 U.S.C. § 360cc. An application will necessarily include only stated indications, not intended off-label uses. *Id.* § 355(b).

Second, FDA's interpretation conforms to the statutory purposes of the Orphan Drug Act. *See Abbott Labs.*, 920 F.2d at 988 (recognizing that an interpretation's "conformity to statutory purposes" affects its reasonableness). Spectrum raises a number of policy arguments, urging primarily that the agency's approach would undermine the Orphan Drug Act's incentives for drug innovation. But, as described above, innovation was not Congress's only concern when it created the drug approval process. Congress also sought to promote *affordable* drugs. *Teva*, 410 F.3d at 54; *see also Abbott Labs.*, 920 F.2d at 985. FDA's interpretation accommodates both interests by allowing generic producers to enter the market for certain purposes while, at the same time, protecting a company's right to market its pioneer drugs for exclusive uses. *See* Orphan Drug Regulations, Final Rule, 57 Fed. Reg. 62,076, 62,077 (Dec. 29, 1992) ("FDA believes the final rule achieves the best balance possible between protecting exclusive marketing rights and fostering competition.").

To the extent FDA has discretion in choosing how best to implement the Orphan Drug Act, it is up to the agency to strike the balance between the congressional policy goals of drug affordability and innovation. We will not impose a choice on FDA that Congress did not require. *Cf. Bristol-Myers*, 91 F.3d at 1500 (concluding that Congress was indifferent as to whether the label for a generic drug lists every approved use of a brand-name drug). As the Supreme Court said in *Chevron*, an agency's "reasonable accommodation of conflicting policies that were committed to the agency's care by the statute" should control unless Congress would not have approved of its choice. 467 U.S. at

845 (quoting *United States v. Shimer*, 367 U.S. 374, 383 (1961)). Spectrum's policy concerns cannot supplant FDA's reasonable resolution of these issues, especially because we already rejected similar arguments that allowing labeling carve-outs at all under the Food, Drug, and Cosmetic Act undermines the exclusivity rights of producers of pioneer drugs. *See Bristol-Myers*, 91 F.3d at 1499-1501. There is nothing in the Orphan Drug Act that changes our view.

We also note that many of Spectrum's arguments simply do not apply here. Spectrum suggests the record unequivocally and objectively shows FDA *knew* that Sandoz's generic was intended for *only* the Colorectal Indication. But this is simply not the case. We can think of at least two reasons why a user could prefer Sandoz's generic to Fusilev for the Methotrexate Indications. First, Spectrum's 50 mg vial, unlike Sandoz's 175 mg and 250 mg vials, is insufficient to provide an entire dose for some patients who require 85 to 90 mg for the Methotrexate Indications. Second, Sandoz's drug is in a ready-to-use form, while Spectrum's must be mixed with another chemical before it can be used. Accordingly, we need not address whether our conclusion would differ were the record to show that a generic's off-label use is its *only* intended use.

iii

Spectrum argues that even if the Orphan Drug Act does not require FDA to consider a generic's intended off-label uses, the agency's own regulation does. This regulation bars FDA from approving a generic that is "intended" for the same use as the pioneer during its seven-year exclusivity period. 21 C.F.R. § 316.3(b)(12), (14). Spectrum urges that the regulation's use of the word "intended" required FDA to consider how Sandoz subjectively intended doctors and

patients to use its drug when FDA evaluated its ANDA. FDA responds that even if it must consider a generic's intended use, the agency can properly determine that purpose by looking solely to the labeled uses proposed in the application.

We agree with FDA and conclude that during the approval process, the agency can look solely to Sandoz's labeling claims to determine the intended use of its drug. FDA's approach here is consistent with how the agency has interpreted "intended use" outside of the ANDA approval context to mean "the objective intent of the persons legally responsible for the labeling of drugs." 21 C.F.R. § 201.128. Under that regulation, intent "is determined by such persons' expressions" or "*may* be shown by the circumstances surrounding the distribution" of the drugs. *Id.* (emphasis added). For example, intent may be shown by "labeling claims" or other statements by drug manufacturers. *Id.* To be sure, FDA recognizes that there may be situations in which it will look beyond just the manufacturer's statements, but nothing in its regulations requires FDA to do so. FDA's decision to look to Sandoz's labeling claims as an objective measure of Sandoz's intent is reasonable and consistent with FDA's regulations.

Spectrum resists this conclusion by urging that FDA cannot escape the overarching goal of drug regulation: to ensure that drugs are labeled accurately, with instructions that offer adequate guidance to the intended user. *See United States v. Regenerative Scis., LLC*, 741 F.3d 1314, 1323-24 (D.C. Cir. 2014) (recognizing that to satisfy the statutory requirement that a drug's label provide "'adequate directions for use,' a drug's label must provide 'directions under which the *layman* can use a drug safely and for the purposes for which it is intended'" (quoting 21 C.F.R. § 201.5)). We agree to a point. Nothing in our holding allows FDA to permit

Sandoz to promote misbranded drugs. But the ANDA approval stage is not the point in time at which FDA must evaluate a generic's purpose beyond that which is set forth in the ANDA itself. If Sandoz improperly deviates from that stated purpose by marketing its drug for the Colorectal Indication, FDA can pursue a later enforcement action to ensure the generic is labeled accurately. *See Wash. Legal Found. v. Henney*, 202 F.3d 331, 333 (D.C. Cir. 2000) (recognizing that a manufacturer's "direct advertising or explicit promotion of a product's off-label uses is likely to provoke an FDA misbranding or 'intended use' enforcement action").

Because FDA's interpretation of the Orphan Drug Act is reasonable, it is lawful. *See Glob. Crossing Telecomms., Inc. v. Metrophones Telecomms., Inc.*, 550 U.S. 45, 47-48 (2007).

B

Spectrum next seeks to overturn FDA's approval of Sandoz's generic drug on the ground that the approval entailed a policy change that the agency never justified. Spectrum argues that when FDA approved Sandoz's ANDA, the agency found that large vials of levoleucovorin are appropriate for the Methotrexate Indications, yet the agency had previously reached the opposite conclusion. To overcome an arbitrary and capricious challenge, an agency "must 'provide reasoned explanation for its action'" when it changes course, "which 'would ordinarily demand that it display awareness that it *is* changing position.'" *Nat'l Ass'n of Home Builders v. EPA*, 682 F.3d 1032, 1038 (D.C. Cir. 2012) (quoting *FCC v. Fox Television Stations, Inc.*, 556 U.S. 502, 515 (2009)). We reject Spectrum's argument because FDA never changed its position at all.

The record shows that FDA has always treated larger-than-necessary vials of levoleucovorin as appropriate for the Methotrexate Indications, meaning safe and effective. FDA's approval of a drug application shows that the agency concluded that the drug in its anticipated form is safe and effective for the indication sought. 21 U.S.C. § 355(d). Even though the average dose needed for the Methotrexate Indications is 7.5 mg, Spectrum has long sold an FDA-approved vial of 50 mg for these indications. And FDA approved Spectrum's own application to market 175 mg and 250 mg vials of levoleucovorin exclusively for those purposes, even though Spectrum ultimately chose not to sell the drug in those vial sizes.

Spectrum makes two efforts to identify an instance in which FDA concluded that large vials of levoleucovorin are *not* appropriate for the Methotrexate Indications, but both fall short. First, Spectrum points to an earlier FDA draft guidance document that cautioned against using vials containing excess volumes of pharmaceutical drugs because of safety risks from misuse. The agency warned that vial sizes "should be appropriate for the labeled use and dosing of the product."[4] Spectrum argues that FDA did not explain why it deviated from this guidance when it allowed Sandoz to market 175 mg and 250 mg vials of levoleucovorin despite the typical user requiring far less.

[4] FDA, DRAFT GUIDANCE FOR INDUSTRY: ALLOWABLE EXCESS VOLUME AND LABELED VIAL FILL SIZE IN INJECTABLE DRUG AND BIOLOGICAL PRODUCTS 4 (2014), *available at* http://www.fdanews.com/ext/resources/files/03/03-13-14-Guidance.pdf (last visited May 19, 2016).

Assuming FDA must explain a departure from this guidance document,[5] there was no departure that would demand explanation here. The guidance document at issue offers a general approach for pharmaceutical drugs, and such broad guidance must give way to more specific risk analysis by the agency. *Cf. Union of Concerned Scientists v. Nuclear Regulatory Comm'n*, 711 F.2d 370, 381 & n.26 (D.C. Cir. 1983) (discussing the "fundamental maxim" that "the terms of a more specific statute take precedence over those of a more general statute where both statutes speak to the same concerns"). Here, FDA considered and rejected the risks associated with excess quantities of *this* drug before approving Sandoz's ANDA. In 2014, Spectrum submitted a citizen petition requesting that FDA not approve any levoleucovorin ANDAs with 175 mg or 250 mg vials, with or without a labeling carve-out for the Colorectal Indication. Among other things, Spectrum argued that larger vials pose safety risks to patients from overdose or contamination when used for the Methotrexate Indications. FDA denied the petition, reasoning that the larger vials were safe and effective, and concluding that proper labeling would address safety risks.[6] Different drugs have different risks of overdose or misuse, and FDA carefully evaluated Spectrum's safety arguments in light of the minimal problems that have occurred with levoleucovorin.

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[5] At the time FDA approved Sandoz's ANDA, this guidance document was in preliminary draft form. We express no view whether FDA would have been required to acknowledge a change in position had the agency departed from its draft guidance document.

[6] Letter from Janet Woodcock, Director, Center for Drug Evaluation and Research, to Robert Church and David Fox, Hogan Lovells (Feb. 24, 2015) (denying FDA-2014-P-1649, Spectrum's citizen petition submitted to FDA).

Spectrum also argues that the record shows FDA consistently associated large vials of levoleucovorin with the Colorectal Indication and small vials with the Methotrexate Indications. Spectrum rests heavily on a statement by an FDA official made during a meeting about Fusilev in 2009 that the Methotrexate Indications do "not require single use vials larger than 50 mg." But this does not show that FDA's approval of Sandoz's ANDA constituted a change in position. FDA's concern when evaluating an ANDA is whether the generic is as safe and effective as the pioneer for the indication requested, not whether the proposed drug is packaged in the best possible form. *See* 21 U.S.C. § 355(j); 21 C.F.R. § 314.127(a)(7). Accordingly, whether large vials are necessary for the Methotrexate Indications is beside the point: FDA's statement to that effect says nothing about whether large vials are safe and effective for the Methotrexate Indications, which is the question FDA answered when it approved Sandoz's ANDA.

C

Spectrum's final contention is that FDA was required to give Spectrum notice and an opportunity to be heard before expediting Sandoz's ANDA in response to a drug shortage. Although the Orphan Drug Act allows FDA to abrogate market exclusivity in the case of a drug shortage, FDA must first give the producer of the pioneer an opportunity to show that it can meet market demand. 21 U.S.C. § 360cc(b)(1). Spectrum argues that it was not given that opportunity before FDA expedited consideration of Sandoz's ANDA in February 2012, even though at that point in time Spectrum had exclusive marketing rights for both the Methotrexate and Colorectal Indications. In other words, Spectrum reads the Orphan Drug Act to create a notice obligation even in

situations where FDA does not cut short a market exclusivity period. This argument has no basis in the statute.

The Orphan Drug Act creates a notice obligation only when FDA abrogates a pioneer drug's period of market exclusivity. Section 360cc(b) is titled "Exceptions" because it creates a process that FDA must follow when it makes exceptions to market exclusivity. The clear purpose of the notice obligation is to protect the rights of producers of pioneer drugs in the event FDA decides a drug shortage requires it to eliminate those rights. In contrast, the statute says nothing at all about notice requirements when FDA expedites its review of an ANDA or simply evaluates a drug shortage without more.

Spectrum argues that FDA's implementing regulation creates a notice obligation even if the Orphan Drug Act does not. *See* 21 C.F.R. § 316.36 (detailing process requirements to withdraw orphan-drug exclusivity). But the regulation does not change our conclusion. The regulation simply tracks the statute to create a notice obligation only in cases where FDA is "withdrawing the drug product's exclusive approval." *Id.* § 316.36(b); *see also id.* § 316.36(a) (discussing the notice obligations that apply "[u]nder section 527 of the act," *i.e.*, 21 U.S.C. § 360cc). The regulation speaks repeatedly in terms of the ultimate withdrawal decision. 21 C.F.R. § 316.36(b) ("Once withdrawn under this section, exclusive approval may not be reinstated for that drug."); *id.* ("An order withdrawing the sponsor's exclusive marketing rights may issue whether or not there are other sponsors that can assure the availability of alternative sources of supply."). The regulation, read as part of the overall statutory framework, does no more than elaborate on the procedural protections that FDA guarantees when making an exception to exclusivity. Because FDA did not cut short Spectrum's period of market exclusivity,

Spectrum was not entitled to notice and an opportunity to be heard before the agency approved Sandoz's ANDA.

III

We affirm the order of the district court granting summary judgment against Spectrum.