In the

United States Court of Appeals

For the Seventh Circuit

No. 21-2840

GRIPUM, LLC,

Petitioner,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION,

Respondent.

On Petition for Review of a Final Marketing Denial Order by the
U.S. Food and Drug Administration.
No. PM0001689

ARGUED APRIL 20, 2022 — DECIDED AUGUST 29, 2022

Before WOOD, HAMILTON, and KIRSCH, *Circuit Judges*.

WOOD, *Circuit Judge*. Gripum, LLC, manufactures and distributes hundreds of flavored liquids for use in e-cigarette devices. Seeking to take its products to market, Gripum submitted a "premarket tobacco product application" to the federal Food and Drug Administration (FDA) in September 2021. But the agency denied the application, reasoning that Gripum had failed to demonstrate public-health benefits as required by the Family Smoking Prevention and Tobacco Control Act (the

Act), see 21 U.S.C. § 387j. We now deny Gripum's petition for review of the FDA's decision, finding that the agency's approach to adjudicating the application was both reasoned and consistent with the Act.

I

A

Commonly known as "e-cigarettes," electronic nicotine delivery systems (called ENDS in bureaucratese) vaporize nicotine-laden "e-liquid" for users to inhale. Users have a choice of devices that accomplish that function and thus allow "vaping." The delivery systems come in an open form, which takes refillable cartridges, and a closed form, which requires single-use cartridges. There is a huge number of flavor options for the cartridges. Some e-liquids mimic traditional cigarette flavors such as tobacco or menthol. Others, like the e-liquid products at issue in this case, taste like candy, fruit, or baked goods. All, however, are laced with nicotine.

Under the Act, manufacturers of a "new tobacco product"—defined as a product that was not on the market as of February 15, 2007—must receive authorization from the FDA prior to marketing that product. As concern grew over the dangerous health consequences of vaping and e-cigarette use, the FDA promulgated the "Deeming Rule" in May 2016. See 81 Fed. Reg. 28,974 (May 10, 2016). This brought all "tobacco" products, including e-cigarettes and their delivery systems, under the Act's premarket-authorization requirements.

Most relevant for our purposes is the Act's command that the Secretary of Health and Human Services "shall deny an application" to market a new tobacco product if the manufacturer fails to show that the product would be "appropriate for

the protection of public health." This is commonly referred to as the "APPH" standard, but in the interest of using plain English, we will call it the "appropriateness" standard. 21 U.S.C. § 387j(c)(2). To determine whether a product meets the appropriateness standard, the Secretary must consider "the risks and benefits to the population as a whole, including users and nonusers of the tobacco product." *Id.* That assessment, in turn, must take into account the "increased or decreased likelihood that":

(A) "existing users of tobacco products will stop using such products"; and
(B) "those who do not use tobacco products will start using such products."

Id. § 387j(c)(4). In other words, the Secretary must weigh a product's risks of hooking new users (typically youth) into the world of tobacco, broadly defined, against its potential to help existing users (typically adults) wean themselves from tobacco's unhealthier forms (namely, combustible cigarettes).

As a matter of enforcement discretion, the FDA specified in its 2016 Deeming Rule that manufacturers would be given two to three years to prepare market applications for the e-cigarette products already on the market. See 81 Fed. Reg. at 28,978. Soon thereafter, youth e-cigarette use exploded across the country. From 2017 to 2018, the number of high schoolers using e-cigarettes rose by over seventy-five percent. See FDA, *Results From 2018 National Youth Tobacco Survey Show Dramatic Increase in E-Cigarette Use Among Youth Over Past Year* (Nov. 15, 2018). With the urgency of the situation in mind, the FDA began around late 2017 to step up its enforcement efforts against products that targeted youth. See *Enforcement Priorities for Electronic Nicotine Delivery Systems (ENDS)*

and Other Deemed Products on the Market Without Premarket Authorization (Revised): Guidance for Industry 6–7 (Apr. 2020) (hereinafter 2020 Guidance).

In 2019, the FDA issued a guidance document to help manufacturers prepare applications. See *Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems: Guidance for Industry* (June 2019) (2019 Guidance). In that document, the FDA stated that it "understands that limited data may exist from scientific studies and analyses." *Id.* at 12. To address the paucity of data, it indicated that it "intends to review" "information on other products (*e.g.*, published literature, marketing information)" provided by an applicant, so long as the application also included "appropriate bridging studies" tying extant data to the applicant's own products. *Id.*

By 2020, nearly twenty percent of high-school students were active users of e-cigarettes, making e-cigarettes "the most widely used tobacco product among youth by far." FDA, *Technical Project Lead Review of PMTAs* (2020). The agency adjusted its enforcement priorities accordingly and publicized those changes in a guidance document issued that year. It announced that it planned to pay particular attention to flavored, cartridge-based e-cigarettes given their "extraordinary popularity" among youth. See 2020 Guidance at 13 (describing how ninety-three percent of e-cigarette users aged 12–17 reported that their first e-cigarette was a flavored product). The guidance document also recounted the many efforts undertaken by both the agency and manufacturers to reduce youth access. Regrettably, measures such as age-limited sale restrictions had failed to stem the tide, even after the FDA had sent over 6,000 warning letters and 1,000 civil monetary penalty complaints to retailers accused of illegal sales to minors.

See *id.* at 7. Because youths often obtain e-cigarettes from friends rather than by direct purchases, sales restrictions proved to be largely ineffective. The 2020 Guidance also clarified that the agency would "make enforcement decisions on a case-by-case basis" and that it "retains discretion to pursue enforcement action at any time against any deemed new tobacco product marketed without premarket authorization." *Id.* at 11.

B

Since 2013, petitioner Gripum has manufactured and distributed flavored e-liquids for use in open-system devices (that is, the refillable cartridges). It claims to have had 291 private label e-cigarette products under contract as of January 2022. On September 7, 2020, Gripum submitted a premarket application to the FDA seeking authorization to market hundreds of its flavored e-liquids, which carried colorful and evocative names such as "Peanut Butter Milk Pie," "Bad Monkey Giovanni," and "Sunshine Vape Dragon Berry Balls." In its application it included a review of the scientific literature and consumer surveys assessing trends in the use of e-cigarettes, though none of these materials discussed or referred to Gripum's own products.

About a year later, on September 8, 2021, the FDA issued a "marketing denial order" for Gripum's application, explaining that "the new products … lack sufficient evidence to demonstrate that the marketing of these products is appropriate for the protection of public health." The denial order went on to say that "robust and reliable evidence is needed regarding the magnitude of the potential benefit to adult smokers." Reliable evidence, the denial order explained, could have taken the form of a "randomized controlled trial and/or

longitudinal cohort study that demonstrated the benefit of your flavored ENDS products over an appropriate comparator tobacco-flavored ENDS." Although Gripum's application mentioned randomized controlled trials and longitudinal cohort studies of *other products*, Gripum never explained how or why its products were sufficiently similar to those other products so that the latter were relevant to its application. In other words, it failed to provide a "bridge" between the data about other products and its own proposed offering. In addition, the denial order concluded that the alleged public-health benefits of Gripum's products were too speculative to outweigh the risks of youth initiation. The agency thus concluded that it was required to deny Gripum's application in its entirety.

On October 8, 2021, Gripum timely filed its petition for review of the denial order pursuant to 21 U.S.C. § 387*l*(a)(1)(B). Seeking emergency relief from this court, Gripum filed a motion for a stay pending review on October 17, 2021. On November 4, 2021, we entered an order granting Gripum the requested relief.

Since Gripum lodged its petition, similar challenges to e-cigarette marketing denial orders have percolated across the courts of appeals. Not long after we entered our stay, the Sixth Circuit denied a stay pending review in one such case. See *Breeze Smoke, LLC v. FDA*, 18 F.4th 499, 503 (6th Cir. 2021). The Sixth Circuit petitioners then sought a stay from the Supreme Court, but that was denied. See *Breeze Smoke, LLC v. FDA*, 142 S. Ct. 638 (2021) (mem.). We are informed that Breeze Smoke has now voluntarily withdrawn its petition in the Sixth Circuit challenging its marketing denial order. In another case, the Fifth Circuit entered a stay of the marketing denial orders before it, see *Wages & White Lion Invs., LLC v. FDA*, 16 F.4th

1130 (5th Cir. 2021), but later the merits panel sided against the flavored e-cigarette manufacturers and upheld the agency's decisions, see *Wages & White Lion Invs., LLC v. FDA*, Nos. 21-60766 & 21-60800 (5th Cir. July 18, 2022). The Eleventh Circuit issued an opinion that was the mirror image of the Fifth Circuit's. In *Bidi Vapor LLC v. U.S. Food and Drug Admin.*, No. 21-13340 (11th Cir. Aug. 23, 2022), a panel majority vacated denial orders relating to six different companies, because it concluded that the agency had failed adequately to consider the companies' marketing and sale-access-restriction plans; the dissenting judge thought that the agency had said enough, and that in any event any error was harmless. Finally, the D.C. Circuit recently upheld FDA orders denying market authorization for certain flavored e-cigarette products. See *Prohibition Juice Co. v. FDA*, Nos. 21-1201, 21-1203, 21-1205 & 21-1207 (D.C. Cir. July 26, 2022). (There are also some additional pending challenges. See https://vaping360.com/vape-news/111563/vape-companies-challenging-fda-marketing-denials/.)

II

This case arises under section 912(a)(1)(B) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 387*l*(a)(1)(B)), which provides that any person adversely affected by the FDA's issuance of a marketing denial order may file a petition for review either in the D.C. Circuit or in the circuit in which the person resides or has its principal place of business. Gripum's principal place of business is in Skokie, Illinois, and so its challenge to the marketing denial order is properly before us.

Because denial orders are reviewed in accordance with section 706(2)(A) of the Administrative Procedure Act (APA),

an order may be held unlawful and set aside only if it is found to be "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A); see 21 U.S.C. § 387*l*(b). To meet the APA's arbitrary-and-capricious standard, "the agency must examine the relevant data and articulate a satisfactory explanation for its action including a rational connection between the facts found and the choice made." *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983); see also *FCC v. Prometheus Radio Project*, 141 S. Ct. 1150, 1158 (2021) ("The APA's arbitrary-and-capricious standard requires that agency action be reasonable and reasonably explained.").

Gripum advances three theories for why the FDA's adjudication of its application was arbitrary: (1) the agency failed to announce ascertainable standards prior to its adjudication of the application; (2) the agency quietly shifted the evidentiary standard after inviting reliance on an earlier, easier-to-meet standard; and (3) it failed to undertake an individualized approach to the application, instead applying generalized, and thereby arbitrary, presumptions.[1] We address these points in that order.

A

Gripum first argues that the FDA's failure to promulgate rules governing the premarket application process, or otherwise to announce ascertainable standards, rendered its

[1] We note in this connection that in our case Gripum did not present the argument that persuaded the Eleventh Circuit in *Bidi Vapor*, namely, that the FDA's analysis was flawed because it did not explain why it placed no weight on the companies' marketing and sales-access-restrictions. Gripum has thus waived, or at a minimum forfeited, this point.

adjudication of Gripum's application arbitrary. But the relevant standard applied by the agency—that benefits to adult users must outweigh the risk of fomenting youth use—flows directly from the Act, and the agency reasonably could have thought that no further elaboration on that point was needed. As the statute says, the FDA must evaluate "the risks and benefits to the population as a whole, including users and nonusers"; and to carry out that task, it must weigh "the increased or decreased likelihood that existing users of tobacco products will stop" against "the increased or decreased likelihood that those who do not use tobacco products will start." 21 U.S.C. § 387j(c)(4). That language expressly orders the agency to conduct the described balancing process and to consider both the risks and benefits attendant to each application that it adjudicates. The statute does not, contrary to Gripum's contention, obligate the agency to define threshold levels of likelihoods or the minimum number of users who must be aided for a product to pass muster. Indeed, bright lines of this sort would be difficult to square with the statute's comparative language.

Furthermore, Congress's intent to allow the FDA to develop its premarket policy through a flexible, case-by-case adjudicative approach is apparent in the structure of the Act. The statute delegates broad authority to the agency to regulate the marketing of tobacco products both through rulemaking, see 21 U.S.C. § 387g(a)(3), and through individual adjudications, see *id.* § 387j(c). It also obligates the agency to issue interpretative rules and regulations in some contexts. See, *e.g.*, 21 U.S.C. § 387e(j)(3)(B) (specifying that the FDA "shall issue regulations" with respect to the registration of tobacco manufacturers); *id.* § 387k(*l*)(1) (specifying that the FDA "shall issue regulations or guidance" with respect to the review of

"modified risk tobacco products"). But in the premarket-adjudication context of section 387j(c), there is no such obligation for the FDA to promulgate implementing regulations.

In a related vein, Gripum argues that the agency's adjudicative approach was inconsistent with the statutory appropriateness standard, and instead amounted to an ersatz "product-efficacy assessment" borrowed from the drug-review provision of 21 U.S.C. § 355(b)(1)(A)(i). Under such an "efficacy" standard, an applicant needs to show that a product is effective at meeting some fixed result (say, the killing of a bacterium at a minimum rate). But all the FDA required Gripum to do here is to show that its flavored e-cigarette products were *relatively better* at reducing rates of tobacco use than products already on the market. The agency properly applied the comparative standard mandated by the statute; Gripum simply failed to meet it.

B

Gripum next claims that the FDA changed course by requiring product-specific clinical studies to meet the appropriateness standard. It contends that in so doing, the agency failed to respect the reliance interests that manufacturers had in the administrative guidance they had received, and thus it acted arbitrarily. See *DHS v. Regents of the Univ. of Cal.*, 140 S. Ct. 1891, 1913 (2020) ("When an agency changes course, … it must be cognizant that longstanding polices may have engendered serious reliance interests that must be taken into account."); *FCC v. Fox Television Stations, Inc.*, 556 U.S. 502, 514–16 (2009). But like our sister circuits, we conclude that the FDA's e-cigarette guidance materials have consistently reflected that product-specific long-term data are required only

if existing studies are inadequately related to the proposed product.

In 2019, the FDA issued a nonbinding guidance document stating that "in general, FDA does not expect that applicants will need to conduct long-term studies to support an application." 2019 Guidance at 13. Gripum makes much hay of that sentence. But the broader document tells a more complicated story. It begins by describing how "[n]onclinical studies alone are generally not sufficient to support" the statutory showing. *Id.* at 12. It then describes how "in some cases, it may be possible to support a marketing order for an [e-cigarette] product without conducting new nonclinical or clinical studies," though that depends on whether "an established body of evidence … can be adequately bridged to [the] product, such as data from the published literature or government-sponsored databases." *Id.* at 46. This explanation underscores the case-by-case and open-ended nature of FDA review. Nowhere does it confer blanket permission to forego product-specific testing.

As the Sixth Circuit concluded, the agency indicated only that "it *might* accept evidence other than long-term studies, if that evidence had sufficient scientific underpinnings." *Breeze Smoke*, 18 F.4th at 506–07. So too the D.C. Circuit read the 2019 Guidance as "nowhere guarantee[ing] that unspecified other forms of evidence would necessarily be sufficient—only that they might be." *Prohibition Juice Co.*, Nos. 21-1201 etc. at 23. We conclude the same.

C

Gripum also argues that the agency failed to conduct a careful, individualized review of its evidence and instead

relied on a general presumption that e-liquids increase youth tobacco use. But according to Gripum, the belief that young people will be attracted to its e-liquids rests on a more tenuous base than the agency thinks, in part because evidence demonstrates that young users prefer closed-system devices to open-system ones.

Gripum's arguments rest on a questionable reading of both the agency's marketing denial order and the statutory burden. The Act requires the denial of an application unless the manufacturer can affirmatively demonstrate that it meets the appropriateness standard through the section 387j(c) comparative assessment. Even if Gripum is right when it asserts that young people are much less interested in e-liquids in open-system devices than they are in closed-system ones, the FDA reasoned that the marketing and sale of open-system devices still are responsible for *some portion* of youth initiation. To succeed under the appropriateness standard—a comparative one, as we have stressed—Gripum had the burden of demonstrating that its flavored e-liquids would "switch" some users of combustible cigarettes over to e-cigarettes. But as we already have noted, Gripum failed to provide evidence specific to its products. And though it did include studies of other products, those studies did not even compare tobacco-flavored e-cigarette products (which we will assume do have a "switching" effect) to flavored products resembling those Gripum wants to offer.

Before concluding, we have one unusual new item of business that requires our attention. Almost four months after the oral argument in this case, Gripum filed something it called an "Opposed Motion To Correct Administrative Record." In that motion, it asked us to re-open the underlying

administrative record and add a memorandum dated August 19, 2020, entitled "*Bundling and Bracketing Approach for Review of ENDS Open E-Liquid PMTAs*." This document, it contended, had just come to its attention when it was released by the FDA in response to a third party's freedom-of-information request. We invited the FDA to respond, which it has now done. Aside from remarking that, despite calling the motion "opposed," Gripum had not communicated with the agency before filing its motion, the FDA noted that Gripum has not identified anything that would undermine the presumption of regularity that attaches to an agency's certification of its record, see *Citizens to Preserve Overton Park, Inc. v. Volpe*, 401 U.S. 402, 415 (1971). On the merits, the FDA pointed out that Gripum's petition founders on the utter lack of evidence showing that the benefits of its products outweigh the harms. The further scientific review process described in the memorandum is triggered only for cases that pass that first threshold.

We agree with the FDA that the time has long passed for amendments or changes to the administrative record in the present case, and that the 2020 memorandum is in any event of dubious relevance. We therefore deny Gripum's motion.

* * *

In adjudicating Gripum's application, the FDA hewed to the statutory standard and issued a reasoned marketing denial order. Its determination that Gripum's products lack a clear benefit to current tobacco users was not arbitrary or unreasonable. We therefore DENY Gripum's petition for review.