FOR PUBLICATION

UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

LOTUS VAPING TECHNOLOGIES, LLC, *Petitioner*, v. U.S. FOOD & DRUG ADMINISTRATION, *Respondent*.	No. 21-71328 OPINION

NUDE NICOTINE INC., *Petitioner*, v. U.S. FOOD & DRUG ADMINISTRATION, *Respondent*.	No. 21-71321

On Petition for Review of an Order of the
Food & Drug Administration

Argued and Submitted August 11, 2022
San Francisco, California

Filed July 7, 2023

Before: Johnnie B. Rawlinson, Bridget S. Bade, and Daniel A. Bress, Circuit Judges.

Opinion by Judge Bade

SUMMARY*

Food and Drug Administration

The panel denied petitions for review challenging the denial of Petitioners' premarket tobacco product applications seeking Food and Drug Administration ("FDA") authorization to sell nicotine-containing e-liquids in the United States.

The FDA issued marketing denial orders for Petitioners' flavored products, finding that Petitioners' applications lacked sufficient evidence showing that their flavored products would provide a benefit to adult users that outweighs the risks such products pose to youth.

The panel held that the text of the Family Smoking Prevention and Tobacco Control Act (the "Tobacco Control

* This summary constitutes no part of the opinion of the court. It has been prepared by court staff for the convenience of the reader.

Act") plainly authorizes the FDA to require that manufacturers submit comparative health risk data, which necessarily includes comparisons of flavored e-liquids to tobacco-flavored e-liquids. The panel also held that the FDA did not arbitrarily or capriciously deny Petitioners' applications, and that any error the agency committed by failing to consider Petitioners' marketing plans was harmless.

First, Petitioners contended that the FDA exceeded its statutory authority by requiring comparative efficacy studies to demonstrate that their flavored products— electronic nicotine delivery systems ("ENDS")—better promote smoking cessation than comparable tobacco-flavored products. The panel joined the Second, Third, Fourth, Seventh, and D.C. Circuits in holding that the FDA had statutory authority to regulate as it did. The Tobacco Control Act expressly authorized the FDA's consideration of comparative evidence.

Second, Petitioners argued that that the FDA acted arbitrarily and capriciously by denying their applications to market flavored e-liquids. The panel rejected Petitioner's first argument that the FDA unfairly surprised them by demanding that they compare their flavored e-liquids to *tobacco*-flavored ones. Considering the Tobacco Control Act's purpose and the FDA's concern regarding the substantial increase in youth initiation prompted by *flavored* ENDS products, Petitioners cannot plausibly contend that the agency led them to believe a flavor-to-flavor comparison would meet the Act's requirements. The panel also rejected Petitioner's second argument—that the FDA purportedly stated that it would accept single-point-in-time studies, like consumer surveys, but ultimately required studies that followed consumers over long time periods. The panel held

that the FDA did not introduce a new evidentiary standard; rather, it consistently required evidence that evaluated the impacts of flavored versus non-flavored products on initiation and cessation. The FDA acted in conformity with its previous guidance and reasonably rejected Petitioners' applications because their other proffered evidence was not sufficiently reliable and robust. The panel held the agency did not act arbitrarily or capriciously by concluding that Petitioners' evidence fell short.

The panel next turned to Petitioners' contentions that the FDA's failure to consider their marketing and sales-access-restrictions plans was arbitrary and capricious. The panel assumed, without deciding, that the FDA erred in ignoring Petitioners' marketing plans, but concluded that any error was harmless. The Tobacco Control Act incorporates the Administrative Procedures Act's harmless error rule. Petitioners do not identify how their marketing measures were materially different from those the FDA had already said are insufficient. At the time the FDA reviewed Petitioners' applications, it had already concluded that eliminating marketing aimed at youth users and monitoring retailers' sales were ineffective in preventing youth use because children maintained a steady stream of access to the flavored products they desired through alternate means, like their friends and social networks. Accordingly, the panel concluded that, even if the agency erred by failing to consider Petitioners' marketing plans, any error was harmless, and it would not remand on this basis.

Finally, the panel addressed Petitioners' post-argument motions to supplement the administrative record and file supplemental briefing, and seeking judicial notice of a premarket tobacco product application deficiency letter, FDA internal memoranda, and FDA press releases. The

panel denied the motions to supplement the administrative record and file supplemental briefing and granted the motions for judicial notice.

COUNSEL

Eric N. Heyer (argued), Joseph A. Smith, and Jessica Tierney, Thompson Hine LLP, Washington, D.C., for Petitioner Lotus Vaping Technologies LLC.

Kate Talmor (argued), Lindsey Powell, Antonia Konkoly, and Joshua Koppel, Trial Attorneys, Civil Division; Eric B. Beckenhauer, Assistant Branch Director; Brian M. Boynton, Principal Deputy Assistant Attorney General; Julie Lovas, Senior Counsel, Office of Chief Counsel, Food and Drug Administration; Wendy S. Vicente, Acting Department Chief Counsel for Litigation, Food and Drug Administration; Daniel J. Barry, Acting General Counsel, Department of Health and Human Services; United States Department of Justice; Washington, D.C.; for Respondent.

J. Gregory Troutman, Troutman Law Office PLLC, Louisville, Kentucky, for Amici Curiae 38 National and State Electronic Nicotine Delivery System Product Advocacy Associations.

Mary G. Bielaska, Zanicorn Legal PLLC, New York, New York, for Amici Curiae Dr. David B. Abrams, Clive D. Bates, and Professor David T. Sweanor.

Jordan Raphael, Byron Raphael LLP, Los Angeles, California; Dennis A. Henigan and Connor Fuchs, Campaign for Tobacco-Free Kids, Washington, D.C.; for Amici Curiae Medical and Public Health Groups.

OPINION

BADE, Circuit Judge:

Congress has authorized the United States Food and Drug Administration ("FDA") to regulate the manufacture, marketing, and distribution of tobacco products. 21 U.S.C. § 387a. Exercising that authority, the FDA promulgated a final rule in 2016 that subjects e-cigarettes and their component e-liquids to the requirements outlined in the Family Smoking Prevention and Tobacco Control Act ("Tobacco Control Act" or the "Act"). *Id.* §§ 387–387t. The Act requires manufacturers to apply for authorization to sell new tobacco products, which the FDA permits only if the marketing of such products would be "appropriate for the protection of the public health." *Id.* § 387j(c)(2)(A).

Petitioners Lotus Vaping Technologies, LLC, and Nude Nicotine Inc. each submitted premarket tobacco product applications seeking FDA authorization to sell nicotine-containing e-liquids in the United States. The FDA issued marketing denial orders for Petitioners' flavored products, finding that Petitioners' applications lacked sufficient evidence showing that their flavored products would provide a benefit to adult users that outweighs the risks such products pose to youth. Petitioners seek review of these denial orders.[1]

We are asked to decide whether the FDA has statutory authority to require manufacturers to demonstrate that their flavored electronic nicotine delivery systems ("ENDS")

[1] We consolidated these cases for oral argument, and we keep them consolidated for disposition.

better promote smoking cessation than comparable tobacco-flavored products, and whether the agency arbitrarily or capriciously denied Petitioners' applications. We hold that the text of the Tobacco Control Act plainly authorizes the FDA to require that manufacturers submit comparative health risk data, which necessarily includes comparisons of flavored e-liquids to tobacco-flavored e-liquids. We also hold that the FDA did not arbitrarily or capriciously deny Petitioners' applications and that any error the agency committed by failing to consider Petitioners' marketing plans is harmless. In so holding, we join the majority of our sister circuits that have addressed the merits of the same issues in materially identical cases. *See Magellan Tech., Inc. v. FDA*, No. 21-2426, 2023 WL 4035722 (2d Cir. June 16, 2023); *Liquid Labs LLC v. FDA*, 52 F.4th 533 (3d Cir. 2022); *Avail Vapor, LLC v. FDA*, 55 F.4th 409 (4th Cir. 2022); *Gripum, LLC v. FDA*, 47 F.4th 553 (7th Cir. 2022); *Prohibition Juice Co. v. FDA*, 45 F.4th 8 (D.C. Cir. 2022). We deny the petitions for review.

I

A

The Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. §§ 301–399i, as amended by the Tobacco Control Act, *id.* §§ 387–387t, authorizes the Secretary of Health and Human Services to regulate the manufacture, marketing, and distribution of "tobacco products" through the FDA. *Id.* § 387a(a), (e). Congress's stated purpose in enacting the Tobacco Control Act was to, among other things, "ensure that the Food and Drug Administration has the authority to address issues of particular concern to public health officials, especially the use of tobacco by young people and dependence on tobacco" and "to promote cessation to reduce

disease risk and the social costs associated with tobacco-related diseases." Tobacco Regulation, Federal Retirement Reform, Pub. L. No. 111-31, § 3, 123 Stat. 1776, 1781–82 (2009); *see also Big Time Vapes, Inc. v. FDA*, 963 F.3d 436, 444 (5th Cir. 2020) ("Obviously, the [Tobacco Control Act's] purpose sounds in (1) protecting public health and (2) preventing young people from accessing (and becoming addicted to) tobacco products."). Congress immediately subjected "cigarettes, cigarette tobacco, roll-your-own tobacco," "smokeless tobacco," and "any tobacco product containing nicotine that is not made or derived from tobacco" to the FDA's tobacco-product authorities. 21 U.S.C. § 387a(b). But Congress delegated to the Secretary the power to determine whether "any other tobacco products" should be covered by the Act. *Id.* § 387a(b); *see id.* § 321(d).

Exercising this authority, the FDA promulgated a final rule in 2016 that extended the Tobacco Control Act to all products meeting the FDCA's definition of "tobacco product" under 21 U.S.C. § 321(rr)(1).[2] *See* Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act, 81 Fed. Reg. 28,973-01 (May 10, 2016) ("Deeming Rule"). The parties agree that ENDS generally, and Petitioners' products specifically, satisfy that statutory definition. *Id.* at 28,975–76.

Thus, under the Deeming Rule, Petitioners must comply with the Tobacco Control Act. This includes § 387j, which

[2] Under that definition, a "tobacco product" is "any product made or derived from tobacco, or containing nicotine from any source, that is intended for human consumption, including any component, part, or accessory of a tobacco product." 21 U.S.C. § 321(rr)(1).

requires that manufacturers obtain FDA authorization to market "new tobacco product[s]" in interstate commerce. 21 U.S.C. § 387j(a)(1)–(2). Premarket authorization can be obtained in three ways. Only one is relevant here: A manufacturer may submit a premarket tobacco product application ("PMTA") showing that the "product to be marketed would be appropriate for the protection of the public health." *Id.* § 387j(a)(2)(A), (c)(2)(A).

"The PMTA process is onerous, requiring manufacturers to gather significant amounts of information." *Big Time Vapes*, 963 F.3d at 439. Congress requires that applications include "full reports . . . concerning investigations which have been made to show the health risks of such tobacco product and whether such tobacco product presents less risk than other tobacco products," a full statement of the ingredients, and a full description of the manufacturing process, among other information. *See* 21 U.S.C. § 387j(b)(1).

When evaluating an application, the FDA must examine "the risks and benefits to the population as a whole, including [to] users and nonusers of the tobacco product." *Id.* § 387j(c)(4). This includes "the increased or decreased likelihood that existing users of tobacco products will stop using such products," and "the increased or decreased likelihood that those who do not use tobacco products will start using such products." *Id.* The Tobacco Control Act instructs that the FDA "shall deny" an application "if, upon the basis of the information submitted . . . and any other information before [the FDA]," the application does not show that the marketing of the product "would be

appropriate for the protection of the public health."[3] *Id.* § 387j(c)(2)(A). Otherwise, and if all other statutory requirements are met, the FDA must issue a marketing granted order. *Id.* § 387j(c)(1)(A).

When the Deeming Rule was promulgated, ENDS products were widely available in the United States. *See* Deeming Rule, 81 Fed. Reg. at 28,982. The FDA recognized that manufacturers of these products would need time to gather data and prepare the documents needed to receive market authorization.[4] *Id.* at 29,010–11. Thus, the FDA announced staggered compliance deadlines for newly deemed products that were marketed in the United States as of August 8, 2016. *Id.* at 28,974, 29,011.

The Deeming Rule originally set the PMTA submission deadline for August 8, 2018. *Id.* The FDA later extended the deadline to August 8, 2022. FDA, Enforcement Priorities for Electronic Nicotine Delivery Systems (ENDS) and Other Deemed Products on the Market Without Premarket Authorization (Revised): Guidance for Industry 5 (2020) ("2020 Guidance"). But, after a successful challenge

[3] In addition, the FDA must deny an application if: (1) "the methods used in, or the facilities or controls used for, the manufacture, processing, or packing of such tobacco product do not conform to the requirements of section 387f(e) of [the Tobacco Control Act]"; (2) "based on a fair evaluation of all material facts, the proposed labeling is false or misleading in any particular"; or (3) "such tobacco product is not shown to conform in all respects to a tobacco product standard in effect under section 387g of [the Tobacco Control Act], and there is a lack of adequate information to justify the deviation from such standard." 21 U.S.C. § 387j(c)(2)(B)–(D).

[4] Tobacco products that were on the market on or before February 15, 2007 were "grandfathered" and did "not require premarket authorization." Deeming Rule, 81 Fed. Reg. at 29,009.

by the American Academy of Pediatrics and other interested entities, a district court accelerated the deadline to May 11, 2020, *Am. Acad. of Pediatrics v. FDA*, 399 F. Supp. 3d 479, 480–81, 487 (D. Md. 2019), and then adjusted it to September 9, 2020 in response to the COVID-19 pandemic, *see* Order, *Am. Acad. of Pediatrics v. FDA*, No. 8:18-CV-883, Dkt. 182 (D. Md. Apr. 22, 2020); *id.*, Dkt. 201 at 1 (D. Md. April 15, 2022).

The FDA also implemented a twelve-month grace period after the PMTA submission deadline to afford the agency time to review the applications and issue appropriate orders. Deeming Rule, 81 Fed. Reg. at 28,978. The agency did not "intend to initiate enforcement action for failure to have premarket authorization" until after the entire compliance period expired on September 9, 2021. *Id.* at 29,011; Center for Tobacco Products, Deemed Product Review: A Conversation with the Office of Science 4 (June 11, 2021).

B

In advance of the submission deadline, the FDA issued nonbinding guidance and a proposed rule to assist ENDS-product manufacturers with their applications.

1

In June 2019, the FDA issued guidance outlining its then-current "thinking on the types of information an applicant should include in a PMTA to help show that permitting the new tobacco product to be marketed would be [appropriate for the protection of the public health]." FDA, Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems: Guidance for Industry 46 (2019) ("2019 Guidance"). That information included "well-controlled investigations"—i.e., investigations that "are

designed and conducted in such a way that minimizes or controls for bias, confounding variables, and other factors that may render the results unreliable"—or "other 'valid scientific evidence' if found sufficient to evaluate the tobacco product." *Id.* at 12 & n.21.

For example, the FDA "intend[ed] to review" "information on other products (e.g., published literature, marketing information)" if applicants provided "appropriate bridging studies." *Id.* at 12.[5] But the FDA cautioned that published literature reviews "are considered a less robust form" of evidence, *id.* at 47, and that "[n]onclinical studies alone are generally not sufficient to support" marketing authorization, *id.* at 12 & n.22, 46. Nonetheless, given the relative newness of the products, the FDA did "not expect that applicants [would] need to conduct long-term studies to support an application."[6] *Id.* at 13.

The 2019 Guidance also encouraged applicants to submit "data that adequately characterizes the potential impact of the new tobacco product on the health of both users and nonusers." *Id.* at 37. To that end, the FDA advised that

[5] The FDA further explained: "For clinical assessments, instead of conducting clinical studies that span months or years to evaluate potential clinical impact, applicants could demonstrate possible long-term health impact by including existing longer duration studies in the public literature with the appropriate bridging information (i.e., why the data used are applicable to the new tobacco product) and extrapolating from short-term studies." 2019 Guidance at 13; *see also id.* at 50.

[6] The 2019 Guidance mirrored the assertions made by the FDA at a public meeting in October 2018. *See* Center for Tobacco Products, Premarket Tobacco Product Application Content Overview 26 (Oct. 23, 2018) (stating that "[n]o specific studies are required for a PMTA" and that "it may be possible to support a marketing order for an ENDS product without conducting new nonclinical or clinical studies").

applicants include "[e]valuations of the likelihood of initiation among never-users and former users of tobacco products and cessation among current tobacco users." *Id.* at 38. Those behaviors could be addressed in "randomized clinical trials," but the FDA "believe[d] this would also be true of observational studies (perception, actual use, or both) examining cessation behaviors." *Id.*

Relatedly, the 2019 Guidance conveyed the FDA's recommendation that applicants compare their products to other tobacco products to demonstrate the risks and benefits of marketing. *Id.* at 13–14, 23–24. The FDA explained that, as part of its determination under § 387j(c)(4), it would "review[] the health risks associated with changes in tobacco product use behavior (e.g., initiation, switching, dual use, cessation) that are likely to occur with the marketing of the new tobacco product." *Id.* at 13. Thus, the FDA urged applicants to "compare the health risks of [their] product[s] to both products within the same category and subcategory, as well as products in different categories as appropriate." *Id.*

For e-liquids, the FDA recommended that "the product's health risks be compared to those health risks presented by other e-liquids used in a similar manner" and that manufacturers "include those characteristics (materials, ingredients, design, composition, heating source, or other features) that contribute to the new product presenting the same, less, or different health risks than other tobacco products of similar category and subcategory." *Id.* at 14. "This comparative health risk data," the FDA advised, would be "an important part of the evaluation of the health effects of product switching." *Id.* at 13.

2

In September 2019, the FDA issued a proposed rule to help "ensure that PMTAs contain sufficient information for [the] FDA to determine whether a marketing order should be issued." Premarket Tobacco Product Applications and Recordkeeping Requirements, 84 Fed. Reg. 50,566-01, 50,566 (Sept. 25, 2019) ("Proposed Rule"). The focus of the Proposed Rule's "content requirements [was] the threshold amount of information necessary for application filing" because the FDA was "still gaining experience in applying the authorization standard to PMTAs" and it believed that applicants had "some flexibility in the types of scientific information they [could] submit." *Id.* at 50,567.

The threshold information included a marketing plan "concerning at least the first year of marketing after an applicant receives a marketing order." *Id.* at 50,580. The Proposed Rule advised that marketing plans would aid the agency in assessing "whether permitting the marketing of the new tobacco product would be [appropriate for the protection of the public health] because they . . . provide input that is critical to [the] FDA's determination of the likelihood of changes in tobacco product use behavior, especially when considered in conjunction with other information contained in the application." *Id.* at 50,581.

Like the 2019 Guidance, the Proposed Rule did "not set requirements for specific studies that must be contained in every single PMTA." *Id.* at 50,599. The FDA similarly recognized that "long-term data is not available for all categories of products," and thus, it did "not expect that long-term clinical studies . . . [would] need to be conducted for each PMTA." *Id.* at 50,619. The Proposed Rule reinforced, however, that the FDA would rely "upon only

valid scientific evidence to determine whether the marketing of the new tobacco product would be [appropriate for the protection of the public health]." *Id.*

In addition, the Proposed Rule reiterated the FDA's "recommend[ation]" that an "applicant compare the health risks of its product to both products within the same category and subcategory, as well as products in different categories as appropriate." *Id.* at 50,600. And, echoing the 2019 Guidance, the Proposed Rule underscored that "comparative health risk data is an important part of the evaluation." *Id.*

3

In April 2020, the FDA issued guidance conveying its enforcement priorities for ENDS products. 2020 Guidance at 9. Relevant here, the FDA announced that it would prioritize enforcement against "flavored, cartridge-based ENDS products" to counteract "an alarming increase in the use of ENDS products by middle and high school students" driven by the "extraordinary popularity" of flavored products with minors and their "overwhelming[] prefer[ence]" for cartridge-based devices. *Id.* at 3, 6, 13, 15, 19–22.

Notably, the 2020 Guidance also compiled a list of measures that manufacturers had proposed as safeguards to limit youth access to ENDS products for both brick and mortar and online stores. *Id.* at 7. The safeguards included (1) age-verification requirements and technology; (2) contractual penalties for retailers that sold tobacco products to minors; and (3) restrictions on the quantity of ENDS products that consumers could purchase. *Id.* But the FDA reported that youth e-cigarette use continued to increase, *id.* at 8–9, and that youth continued to have access to such products even when those safeguards were in place, *id.* at 8–

9, 21. Thus, the FDA concluded "that focusing on how the product was sold would not appropriately address youth use of . . . flavored, cartridge-based products," *id.* at 21, and it advised the industry that "age verification alone" would not adequately address youth use of tobacco products "given the many sources of products available for youth access," *id.* at 44.

C

Lotus Vaping Technologies, LLC is an Idaho-based manufacturer of tobacco products. Lotus's nicotine-containing e-liquids are designed to be used in open-system devices[7] and come in a variety of flavors. Although such flavors include tobacco and menthol, Lotus's other flavored products[8]—e.g., "apple," "cinnamon candy," "juicy fruit," and "rootbeer"—are the ones at issue here.

Nude Nicotine Inc. is a California-based manufacturer of nicotine-containing e-liquids. Like Lotus's products, Nude Nicotine's e-liquids are also designed to be used in open-system devices. But unlike Lotus's products, Nude Nicotine's e-liquids are not sold with added flavors. Nevertheless, Nude Nicotine's products constitute "flavored

[7] E-cigarettes come in "open" and "closed" forms. Premarket Tobacco Product Applications & Recordkeeping Requirements, 86 Fed. Reg. 55,300-01, 55,317 (Oct. 5, 2021). An open device "includes a reservoir that a user can refill with an e-liquid of their choosing." *Id.* A closed device, by contrast, "includes an e-liquid reservoir that is not refillable . . . or that uses e-liquid contained in replaceable cartridges or pods that are not intended to be refillable." *Id.*

[8] We use the term "flavored products" to refer to products other than tobacco- or menthol-flavored products, which includes nonflavored products that are designed to have flavor added to them. Our definition is consistent with the nomenclature used by the FDA.

products" because they are designed to be suitable for flavor addition.

1

In September 2020, Lotus and Nude Nicotine submitted applications seeking marketing authorization for their flavored products. Lotus supported its application with a scientific literature review, a customer survey, and a coalition survey of thousands of participants. Nude Nicotine submitted product testing, an e-liquid stability study, and scientific literature.

Each Petitioner also submitted a marketing plan to describe the steps it would take to minimize unauthorized use of their products. Both Petitioners proposed age verification for sales of their products and age gating to restrict youth access to advertisements on outlets such as social media. Lotus also proposed individual purchase limits for online sales and maintained that product demonstrations or sampling would occur only at age-gated industry trade shows. Nude Nicotine outlined a program that would purportedly bind its retailers to comply with age gating requirements, certain marketing procedures, and other post-market monitoring practices. Petitioners also emphasized their commitment to post-market surveillance to ensure appropriate marketing of their products.

2

In July 2021, a few months before the FDA issued decisions on Petitioners' applications, the FDA circulated an internal memorandum that announced "a new plan to effectively manage" a subset of applications for flavored ENDS products and to "take final action on as many

applications as possible by September 10, 2021."[9] Under this new plan, the agency would conduct a "simple" fatal flaw review to identify whether the application contained "either a randomized controlled trial (RCT) or a longitudinal cohort study." If those studies were lacking, the application would "likely receive a marketing denial order."

One month later, the FDA circulated another internal memorandum that explained that the agency would broaden its inquiry to consider evidence from other types of studies if such studies "reliably and robustly assess behavior change." The memorandum cautioned that cross-sectional surveys, consumer perception studies, and general scientific literature would "not likely be sufficiently robust or direct in providing evidence as to the impact of the new ENDS on adult switching or cigarette reduction." The memorandum also advised that the FDA would not evaluate marketing plans "for the sake of efficiency." The FDA rescinded this memorandum within days of its circulation.

[9] The FDA initially believed that it would receive applications for a few thousand ENDS products. *See* FDA, Final Regulatory Impact Analysis Final Regulatory Flexibility Analysis Unfunded Mandate Reform Act Analysis 48 (May 2016). The agency ultimately received applications for more than 6.5 million newly deemed tobacco products, and the majority of those applications were for ENDS. *See* News Release, FDA, FDA Denies Marketing Applications for About 55,000 Flavored E-Cigarette Products for Failing to Provide Evidence They Appropriately Protect Public Health (Aug. 26, 2021); Center for Tobacco Products, Deemed Product Review: A Conversation with the Office of Science 17 (June 11, 2021); Statement, FDA, FDA Makes Significant Progress in Science-Based Public Health Application Review, Taking Action on Over 90% of More Than 6.5 Million 'Deemed' New Tobacco Products Submitted (Sept. 9, 2021).

In late August 2021, the FDA announced that it had issued the first marketing denial orders for ENDS products "after determining the applications for about 55,000 flavored ENDS products . . . lacked sufficient evidence that they have a benefit to adult smokers sufficient to overcome the public health threat posed by the well-documented, alarming levels of youth use of such products." News Release, FDA, FDA Denies Marketing Applications for About 55,000 Flavored E-Cigarette Products for Failing to Provide Evidence They Appropriately Protect Public Health (Aug. 26, 2021). Within a matter of weeks, then-Acting Commissioner of the FDA, Janet Woodcock, issued a statement conveying that the agency had acted on applications for over 6 million ENDS products. Statement, FDA, FDA Makes Significant Progress in Science-Based Public Health Application Review, Taking Action on Over 90% of More Than 6.5 Million 'Deemed' New Tobacco Products Submitted (Sept. 9, 2021). This action included the issuance of marketing denial orders "for more than 946,000 flavored ENDS products." *Id.*

3

In September 2021, the FDA issued marketing denial orders to Lotus and Nude Nicotine for their flavored e-liquids. The "key basis" for both orders was that Petitioners' applications did not include "a randomized controlled trial and/or longitudinal cohort study that demonstrated the benefit of [Petitioners'] flavored ENDS products over an appropriate comparator[:] tobacco-flavored ENDS," *and* that the applications otherwise lacked "reliabl[e] and robust[]" forms of "other evidence . . . evaluat[ing] the impact of the new flavored [versus] tobacco-flavored

products on adult smokers' switching or cigarette reduction over time."

Along with the orders, the FDA provided each Petitioner with a Technical Project Lead review ("TPL") that described the agency's reasoning in greater detail. The TPLs, which are materially identical, stressed the "exponential growth in youth ENDS use" and the "enduring prevalence of youth ENDS use in the U.S." The FDA found that "[t]he role of flavors in increasing the appeal of tobacco products to youth . . . is well-established in the literature." And although the agency acknowledged that "there is variability in the popularity of device types among youth," it determined that "the role of flavor is consistent." For example, the FDA pointed to a "substantial rise in use of *disposable* flavored ENDS" after it "changed its enforcement policy to prioritize *pod-based* flavored ENDS." Thus, in the FDA's view, the data established "that the removal of one flavored product option prompted youth to migrate to another ENDS type that offered the desired flavor options, underscoring the fundamental role of flavor in driving appeal."

In addition, the TPLs described the types of evidence capable of showing that flavored products are appropriate for the protection of the public health. For flavored products, "the magnitude of the likely benefit [to adult smokers] would have to be substantial enough to overcome the significant risk of youth uptake and use posed by [those] products." Thus, "strong direct evidence" demonstrating the potential benefit was required. Randomized controlled trials and longitudinal cohort studies were "most[] likely to demonstrate such a benefit," but "other types of evidence could be adequate if sufficiently reliable and robust." The FDA explained that evidence must be product specific, and the agency concluded that cross-sectional surveys (entailing

"a one-time assessment of self-reported outcomes"), consumer perception studies (evaluating intentions but not actual product use or behavior), and general scientific literature would not suffice.

The TPLs advised that the FDA had reviewed Petitioners' applications to assess whether they contained "a randomized controlled trial, longitudinal cohort study, or other evidence regarding the impact of the ENDS on switching or cigarette reduction that could potentially demonstrate the benefit of their flavored ENDS over tobacco-flavored ENDS" and concluded they did not. Because that "key evidence" was missing, the FDA did not "assess other aspects of the applications," including Petitioners' marketing plans.

Petitioners timely sought review in this court. *See* 21 U.S.C. § 387l(a).

II

"Under the Tobacco Control Act's judicial review provision, a party subject to a marketing denial order may petition for review either in [the D.C. Circuit] or in the circuit in which its principal place of business is located." *Prohibition Juice*, 45 F.4th at 17 (citing 21 U.S.C. § 387*l*(a)(1)(B)). We review such orders in accordance with the Administrative Procedure Act ("APA"), which requires us to "hold unlawful and set aside agency action, findings, and conclusions" that are "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A).

Under this "narrow standard of review," we do not substitute our own judgment for that of the agency. *DHS v. Regents of the Univ. of Cal.*, 140 S. Ct. 1891, 1905 (2020).

Instead, we assess only "whether the decision was based on a consideration of the relevant factors and whether there has been a clear error of judgment." *Marsh v. Or. Nat. Res. Council*, 490 U.S. 360, 378 (1989) (quotation omitted). Agency action must "be reasonable and reasonably explained." *FCC v. Prometheus Radio Project*, 141 S. Ct. 1150, 1158 (2021). And an agency "must defend its actions based on the reasons it gave when it acted," not with post hoc rationalizations. *Regents*, 140 S. Ct. at 1909.

III

Petitioners primarily assert two arguments on appeal. First, they contend that the FDA exceeded its statutory authority by requiring comparative efficacy studies. Second, Petitioners argue that the FDA's denial of their PMTAs was arbitrary, capricious, or otherwise unlawful. We begin with the FDA's statutory authority.

A

Petitioners maintain that the FDA exceeded the scope of its statutory authority by requiring applicants to demonstrate that their flavored products better promote smoking cessation than comparable tobacco-flavored products. We disagree and join the Second, Third, Fourth, Seventh, and D.C. Circuits in holding that the FDA had statutory authority to regulate as it did.[10] *See, e.g.*, *Magellan Tech., Inc.*, 2023 WL 4035722 at *7 ("The TCA expressly contemplates a comparative analysis among tobacco products in the context of evaluating whether the products are Appropriate."); *Liquid Labs*, 52 F.4th at 542 (explaining that the Act

[10] Because the Tobacco Control Act "is best read to support the FDA's action, we need not consider whether or how much deference to accord its interpretation." *Prohibition Juice*, 45 F.4th at 18.

"expressly asks for evidence concerning whether an applicant's tobacco product presents less risk than other tobacco products" (internal quotation marks and citations omitted)); *Avail Vapor*, 55 F.4th at 427 ("The [Act] explicitly contemplates that [the] FDA must embark on a comparative inquiry before allowing any marketing of a new tobacco product."); *Gripum*, 47 F.4th at 555 (explaining that the FDA is required under the Act to "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)"); *Prohibition Juice*, 45 F.4th at 19 (concluding that the Act "not only allows but expressly instructs the FDA" to compare a flavored ENDS product's effectiveness at promoting cessation of combustible cigarette use).

We start with the text of the Tobacco Control Act. *See Van Buren v. United States*, 141 S. Ct. 1648, 1654 (2021). The Act permits the FDA to authorize the marketing of a new tobacco product only if the manufacturer has established that it "would be appropriate for the protection of the public health." 21 U.S.C. § 387j(c)(2)(A). In making that determination, the FDA must consider "the *increased or decreased likelihood* that existing users of tobacco products will *stop* using such products," as well as "the *increased or decreased likelihood* that those who do not use tobacco products will *start* using such products." *Id.* § 387j(c)(4) (emphases added). These considerations are inherently comparative. *See Avail Vapor*, 55 F.4th at 428.

The textual support for the FDA's authority does not end there. Congress also directed applicants seeking to market a new tobacco product to include in their applications "full reports of all information . . . concerning investigations

which have been made to show the health risks of such tobacco product and *whether such tobacco product presents less risk than other tobacco products*." 21 U.S.C. § 387j(b)(1)(A) (emphasis added). Section 387j(c) provides, in turn, that the FDA "shall deny an application . . . if, upon the basis of the information submitted"—which would necessarily include any comparative reports submitted in accordance with § 387j(b)(1)(A)—"and any other information before the [FDA]," the agency finds that the applicant did not show "that permitting [the] tobacco product to be marketed would be appropriate for the protection of the public health." *Id.* § 387j(c)(2)(A). Put differently, the FDA must weigh the risk of hooking new users on tobacco products against a product's potential to help existing users switch from unhealthier forms of tobacco—i.e., combustible cigarettes. *See Gripum*, 47 F.4th at 555.

Perhaps realizing that the Tobacco Control Act expressly authorizes the FDA's consideration of comparative evidence,[11] Petitioners contend that the term "risk," as used in § 387j(b)(1)(A), refers only to "physiological *health* risks" and "not some broader concept of risk that encompasses initiation and cessation behaviors." We find this contention wholly unpersuasive. As the D.C. Circuit aptly explained: "The degree to which a harmful product entices and addicts new users is inarguably a component of the 'health risk' it poses." *Prohibition Juice*, 45 F.4th at 19–20.

[11] Indeed, Nude Nicotine "acknowledged fully" at oral argument that "it is a fair application of the statutory standard" for the FDA to require that manufacturers of flavored ENDS compare their products to tobacco-flavored products to obtain marketing authorization.

We therefore conclude that the Tobacco Control Act expressly authorizes the FDA to consider comparative evidence, and we agree with our sister circuits that "[t]he FDA acted well within [Congress's] statutory directive when it compared the claimed cessation benefits of flavored and non-flavored products."[12] *Id.* at 19; *Gripum*, 47 F.4th at 558 ("Th[e] [statutory] 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."); *Liquid Labs*, 52 F.4th at 543 (finding that "the statute and June 2019 Guidance are clear about comparative analysis"); *Avail Vapor*, 55 F.4th at 427–28 (same); *Magellan Tech., Inc.*, 2023 WL 4035722 at *7 (same).

B

We turn now to Petitioners' remaining challenge: that the FDA acted arbitrarily and capriciously by denying their applications to market flavored e-liquids.

In their opening briefs, Petitioners advance virtually identical arguments to those asserted by the ENDS manufacturers in *Prohibition Juice*, *Gripum*, *Liquid Labs*, *Avail Vapor*, and *Magellan*. Petitioners insist that the FDA pulled a "surprise switcheroo" by requiring manufacturers to submit evidence of comparative efficacy through a randomized controlled trial, longitudinal cohort study, or other long-term study, while also rejecting evidence that the agency had previously recommended manufacturers submit, including published scientific literature and observational

[12] We reject Petitioners' arguments premised on 21 U.S.C. §§ 355 and 387k for the same reasons articulated by the D.C. Circuit in *Prohibition Juice*, 45 F.4th at 20. Similarly, we need not evaluate whether injunctive relief is appropriate because we deny the petitions for review.

studies. Petitioners also maintain that the FDA acted arbitrarily and capriciously by ignoring their marketing plans, rejecting the evidence they submitted in support of their applications, "imposing an evidentiary double standard," failing to consider allegedly material distinctions between different kinds of ENDS products, and failing to offer less drastic alternatives to marketing denial orders. Nude Nicotine additionally contends that the FDA's review resulted in disparate outcomes for similarly situated applicants. The D.C. Circuit rejected each of these arguments days before we held oral argument in these consolidated cases. *See Prohibition Juice*, 45 F.4th at 20–24.

Ostensibly in response to our sister circuit's decision, Petitioners refocused their arbitrary and capricious challenge at oral argument, advocating primarily that the FDA did not provide sufficient notice of the "substantive evidentiary standard" governing PMTAs.[13] We therefore take Petitioners to raise two principal arguments in support of their arbitrary and capricious claim. We find neither persuasive.

1

The first argument proceeds as follows: Although the 2019 Guidance informed ENDS manufacturers to "compare the health risks of [their] product[s] to both products within the same category and subcategory, as well as products in

[13] Petitioners were likely also influenced by the Fifth Circuit's rejection of these arguments, also shortly before argument in these cases. *See Wages & White Lion Invs., LLC v. FDA* (*Triton II*), 41 F.4th 427 (5th Cir. 2022), *reh'g en banc granted*, *vacated by* 58 F.4th 233 (5th Cir. 2023).

different categories," 2019 Guidance at 13, Petitioners believed that they had unfettered discretion to choose a relevant comparator. Under Petitioners' theory, it would have been adequate for a manufacturer of flavored ENDS to, for example, compare its flavored e-liquids to other flavored e-liquids. Petitioners thus contend that the FDA unfairly surprised them by demanding that they compare their flavored e-liquids to *tobacco*-flavored ones.

We, like the D.C. Circuit, find this argument to be "far off base." *Prohibition Juice*, 45 F.4th at 23. As discussed, the FDA may authorize the marketing of a new tobacco product only if an applicant demonstrates that it "would be appropriate for the protection of the public health." 21 U.S.C. § 387j(c)(2)(A). To facilitate that inquiry, Congress directed manufacturers to include in their applications reports concerning "whether [the] tobacco product presents less risk than other tobacco products." *Id.* § 387j(b)(1)(A). And, as Petitioners admitted at oral argument, the FDA told ENDS manufacturers to compare the health risks of their products to "products within the same category and subcategory, as well as products in different categories." 2019 Guidance at 13.

Moreover, as the D.C. Circuit explained, "[a] core objective of the Tobacco Control Act is to 'ensure' tobacco products will not be 'sold or accessible to underage purchasers,'" *Prohibition Juice*, 45 F.4th at 12 (quoting P.L. No. 111-31, § 3(7)), and at the time Petitioners were preparing their PMTAs, they knew the FDA was focusing on the desirability of flavored products to youth users. *See, e.g.*, 2019 Guidance at 42; 2020 Guidance at 11–17. Considering the Act's purpose and the FDA's concern regarding the substantial increase in youth initiation prompted by *flavored* ENDS products, Petitioners cannot plausibly contend that

the agency led them to believe a flavor-to-flavor comparison would meet the Act's requirements.

Indeed, Petitioners do not explain how a flavor-to-flavor comparison would provide any meaningful information to the FDA. For example, demonstrating that "apple" flavored ENDS products are less risky than "cinnamon candy" flavored products would not provide the FDA with useful information about whether Petitioners' flavored tobacco products on the whole are less harmful to existing users than their tobacco-flavored counterparts, or whether flavored products draw existing users away from combustible cigarettes or help them otherwise quit smoking—benefits that could counterbalance the risk of youth use. We therefore conclude that the FDA did not act arbitrarily or capriciously in requiring a comparison between flavored products and tobacco-flavored products. *See Prohibition Juice*, 45 F.4th at 23 (because the FDA had identified flavor as a driver of youth use, "Petitioners' own unflavored or tobacco-flavored e-liquids were an obvious, otherwise-similar comparator against which to gauge whether the added risks of their flavored e-liquids are overcome by those products' added benefits to adult smokers").[14]

[14] After oral argument and in subsequent motions to this court, Petitioners have seemingly attempted to renew their contention that the FDA failed to meaningfully consider the distinction between cartridge-based or disposable ENDS products and bottled e-liquids. We join our sister circuits in rejecting this argument. First, the FDA acknowledged that "there is variability in the popularity of device types among youth, suggesting there may be differential appeal of certain product styles," but "reasonably explained that it nonetheless found the scientific literature about public health risks to youth applicable to petitioners' products, because 'across these different device types, the role of flavor

2

Petitioner's second argument—that the FDA purportedly stated that it would accept single-point-in-time studies, like consumer surveys, but ultimately required studies that followed consumers over long time periods—fares no better.

Again, we agree with our sister circuits who have held that the FDA did not introduce a new evidentiary standard; rather, it consistently required evidence that evaluated the impacts of flavored versus non-flavored products on initiation and cessation. The FDA repeatedly used conditional language indicating that it *might* accept evidence other than long term studies *if* such evidence was sufficiently reliable and robust. *See, e.g.*, *Gripum*, 47 F.4th at 559–60 (explaining that the FDA stated that "'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'" (quoting 2019 Guidance at 46) (alterations in original)); *Prohibition Juice*, 45 F.4th at 21 (explaining that the FDA provided that "randomized

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is consistent.'" *Prohibition Juice*, 45 F.4th at 26 (citation omitted). The "FDA's original focus on *enforcement* against cartridge-based ENDS products did not foreclose it from denying a marketing order for [Petitioners'] e-liquids, especially in light of the growing evidence that the role of flavors in driving youth initiation was consistent across products." *Avail Vapor*, 55 F.4th at 427; *see also Liquid Labs*, 52 F.4th at 544–45 (same). The FDA supported its determination with evidence including "large, national surveys and longitudinal cohort studies" that "consistently demonstrated" the "preference for use of flavored ENDS among youth." Thus, the FDA did not arbitrarily disregard distinctions between open and closed ENDS products.

controlled trials or longitudinal studies would not be necessary if applicants submitted similarly rigorous 'valid scientific evidence'" and "[t]he FDA nowhere guaranteed that unspecified other forms of evidence would necessarily be sufficient—only that they might be" (quoting 2019 Guidance at 12–13)); *Magellan Tech., Inc.*, 2023 WL 4035722 at *5 (same).

As the Fourth Circuit explained: the "FDA never guaranteed that manufacturers could carry their evidentiary burden under the [Act] without providing long-term data." *Avail Vapor*, 55 F.4th at 422. And by focusing on isolated statements in the 2019 Guidance that the FDA did not expect applicants would need to conduct long-term studies, Petitioners "failed to look at the 2019 guidance in any depth," as "[t]he agency made quite clear that it was interested in receiving information about long-term *impact*, even if that information did not necessarily come from a long-term *study*." *Id.* at 422–23.

Here, the FDA acted in conformity with its previous guidance and reasonably rejected Petitioners' applications because their other proffered evidence was not sufficiently reliable and robust. *See id.* at 422 (concluding that the FDA "did not reject Avail's application because it failed to include certain long-term studies, but rather due to a lack of *any* 'valid scientific evidence' substantial enough to outweigh the known risks to youth of flavored products"). Specifically, Petitioners stumbled at the initial hurdle of providing useful comparative evidence demonstrating the risks and benefits of initiation and cessation. Lotus failed to even include product-specific evidence. And, although Nude Nicotine offered some product-specific evidence—for example, in the form of a Harmful and Potentially Harmful Constituents analysis—the FDA adequately explained that

such evidence did not, standing alone, "demonstrate that current smokers are likely to start using the new product exclusively or predominantly." Therefore, Petitioners could not show a sufficient benefit to adult users relative to the risk to youth users.

Lotus points to cross-sectional surveys, literature reviews, and a coalition survey, and Nude Nicotine contends that its PMTA contained abuse liability studies, a cross-sectional actual use survey, and a consumer perception studies review. But the FDA reasonably explained in the Marketing Denial Orders and TPLs that cross-sectional surveys are not sufficiently robust for flavored products because they "entail a one-time assessment of self-reported outcomes" and that "single data collection does not enable reliable evaluation of behavior change over time." Similarly, consumer perception studies, like surveys or experiments, are not sufficiently rigorous because they "are not designed to directly assess actual product use behavior." Petitioners do not contend that they offered any other forms of robust evidence that could overcome a lack of randomized controlled trials or longitudinal cohort studies.

Thus, the FDA did not act arbitrarily or capriciously in finding Petitioners' "other evidence" insufficient. *See, e.g.*, *Liquid Labs*, 52 F.4th at 539–43 (explaining that "the FDA did not newly require those specific types of [long-term] studies but instead found that Liquid Labs' other evidence was inadequate"); *Avail Vapor*, 55 F.4th at 422 (explaining that "Avail failed to include" "the type and quality of evidence" the FDA required, and "this failure, rather than the absence of certain [long-term] studies in its PMTAs, resulted in FDA issuing a marketing denial order"); *Gripum*, 47 F.4th at 558–61 (explaining that because Gripum did not (1) provide robust, product specific evidence that "the

benefits to adult users . . . outweigh[ed] the risk of fomenting youth use," or (2) offer sufficient explanations to bridge the data between long-term studies of other products and its own products, the FDA did not act arbitrarily and capriciously when it denied Gripum's application); *see also Magellan Tech., Inc.*, 2023 WL 4035722 at *5 ("Consistent with its position, the FDA considered Magellan's weak scientific evidence and found it insufficient to support an Appropriate finding."); *Prohibition Juice*, 45 F.4th at 22 (explaining that the FDA reasonably drew differing conclusions from evidence of differing strength). *But see R.J. Reynolds Vapor Company v. FDA*, 65 F.4th 182, 190 (5th Cir. 2023) (concluding that the FDA acted arbitrarily and capriciously when it previously "represented that long-term studies were likely unnecessary" and never told applicants that switching evidence would be required for menthol-flavored products).

We are not tasked with determining whether we agree with the FDA's decision, made within its area of expertise, that Petitioners' proffered evidence was insufficient. Instead, we join the Second, Third, Fourth, Seventh, and D.C. Circuits in determining that the agency consistently advised that, in the absence of long-term data, it might rely upon sufficiently robust and reliable other evidence. The agency did not act arbitrarily or capriciously by concluding that Petitioners' evidence fell short of that standard.

3

We now turn to Petitioners' contentions that the FDA's failure to consider their marketing and sales-access-restrictions plans was arbitrary and capricious. We assume, without deciding, that the FDA erred in ignoring Petitioners' marketing plans, but we conclude that any error was harmless.

The Tobacco Control Act incorporates the APA's harmless error rule. *See* 21 U.S.C. § 387*l*(b); 5 U.S.C. § 706 ("[D]ue account shall be taken of the rule of prejudicial error."). An error is harmless if it "had no bearing on the procedure used or the substance of [the] decision reached." *Cal. Wilderness Coal. v. U.S. Dep't of Energy*, 631 F.3d 1072, 1092 (9th Cir. 2011) (alteration in original) (quoting *Paulsen v. Daniels*, 413 F.3d 999, 1006 (9th Cir. 2005)). "[T]he burden of showing an agency's deviation from the APA was not harmless rests with the petitioner." *Id.* Generally, this court "must judge the propriety of [agency] action solely by the grounds invoked by the agency." *SEC v. Chenery Corp.*, 332 U.S. 194, 196 (1947). But "*Chenery* does not require that [courts] convert judicial review of agency action into a ping-pong game." *N.L.R.B. v. Wyman-Gordon Co.*, 394 U.S. 759, 766 n.6 (1969) (plurality opinion).

In the 2020 Guidance, the FDA identified the measures that manufacturers had proposed to restrict minors' access to ENDS products sold online and at brick-and-mortar stores. These measures included: (1) age-verification technology for online sales; (2) enhanced monitoring for retailer compliance with age-verification requirements; (3) contractual penalties for retailers selling tobacco products to minors; and (4) restrictions on the quantity of ENDS products customers can purchase within a period of time. Despite those efforts, youth e-cigarette use continued to increase. Consequently, the 2020 Guidance reported the FDA's conclusion that "age verification alone is not sufficient" and that "focusing on how the product was sold would not be sufficient to address youth use of these products given the many sources of products available for youth access."

We are persuaded by the Second, Third, Fourth, and D.C. Circuits' analysis on this issue. In each of the cases decided by these courts, "the manufacturers were unable to identify any prejudice they suffered from the FDA's lack of individualized review of their plans to prevent youth access to their flavored e-liquids," because the proffered marketing plans contained materially identical measures to those that the FDA had already described as insufficient. *Prohibition Juice*, 45 F.4th at 24; *see also Liquid Labs*, 52 F.4th at 544 (concluding that Liquid Labs did not show that its marketing plans would have changed the result because its "age verification measures," "mystery shopper program," and "prohibition on marketing material" targeting youth were "similar, if not identical, to the kinds of approaches the FDA found did not address this serious problem," and such plans could not, in any case, have rectified the other scientific deficiencies in its applications); *Avail Vapor*, 55 F.4th at 425–26 (same); *Magellan Tech., Inc.*, 2023 WL 4035722 at *6 (same). Here, Petitioners' marketing plan arguments fail for the same reason.

Petitioners do not identify how their marketing measures are materially different from those the FDA has already said are insufficient. For example, Lotus' marketing plan provides that its products "will continue to be strictly marketed and sold to adults in adult-only retailers and through age-verified online websites," and that the products "will not be promoted by Lotus partners, sponsors, influencers, bloggers, or brand ambassadors on non-age-gated social media, radio or television." Nude Nicotine's marketing plan similarly provides for "using and requiring age-gating and age verification for sales of all Nude Nicotine products," requiring distributors and retailers to register as licensed or authorized resellers, contractually binding its

authorized retailers to use age-gating marketing procedures, and engaging in post-marketing surveillance.

At oral argument, Lotus was asked to identify how its marketing plan differed from the marketing plans in *Prohibition Juice*. Counsel identified the following differences: limiting consumer engagement to trade shows, age-gated social media, no use of social media influencers, quantity restrictions for online sales, and contractual penalties. But these measures track those that the FDA found were ineffective to counterbalance the risk of youth use, *see* 2020 Guidance at 6–8, 21–22, 44–45, and Petitioners did not otherwise argue that any of their marketing tactics were novel. *Cf. Prohibition Juice*, 45 F.4th at 16 (recognizing that some "e-cigarette companies are developing novel technologies, such as requiring age verification *assisted by facial recognition software* to unlock their products, which they assert could prevent underage use" (emphasis added)); *Bidi Vapor LLC v. FDA*, 47 F.4th 1191, 1205 (11th Cir. 2022) (finding the FDA acted arbitrarily and capriciously by not reviewing the tobacco companies' marketing plans, which "included measures not specifically mentioned in the 2020 Guidance," such as "Trace/Verify technology" and counterfeit prevention systems); *Avail Vapor*, 55 F.4th at 418, 425–26 (explaining that "[w]hile some other ENDS manufacturers were exploring innovative 'access restriction' technology, whereby, for example, an ENDS product is tied to the thumb print of the purchaser, Avail's marketing plan included only garden variety restrictions," including non-descriptive product names and age-verification services). We therefore join the Second, Third, Fourth, and D.C. Circuits in concluding that the FDA's failure to consider Petitioners' marketing plans, if erroneous, was harmless error.

We acknowledge that in *Bidi Vapor*, the Eleventh Circuit reached a different conclusion, *see* 47 F.4th at 1205, but we do not understand our decision to conflict with that case. There, the Eleventh Circuit noted that the petitioners had submitted marketing plans containing novel restrictions designed to limit youth access. *See id.* at 1205 (discussing marketing plans that "conformed with the recommendations . . . , directly addressed the concerns of youth access . . . , and included measures not specifically mentioned in the [FDA's] 2020 Guidance"); *see also id.* at 1206 (describing "novel marketing and sales-access-restriction plans"). So, although the Eleventh Circuit concluded that the FDA's error was not harmless in *Bidi Vapor*, it did so on a materially different record.

In sum, at the time the FDA reviewed Petitioners' applications, it had already concluded that eliminating marketing aimed at youth users and monitoring retailers' sales were ineffective in preventing youth use because children maintained a steady stream of access to the flavored products they desired through alternate means, like their friends and social networks. *See* 2020 Guidance at 44–45; *Prohibition Juice*, 45 F.4th at 24–25 ("When an agency's mistake plainly had no bearing on the substance of its decision, we do not grant a petition for review based on that mistake" and "[w]here a petitioner had ample opportunity yet failed to show that an agency error harmed it, vacatur and remand to give the agency an opportunity to fix the error is unwarranted." (internal quotation marks and citation omitted)). Therefore, even if the agency erred by failing to consider Petitioners' marketing plans, any error was harmless, and we will not remand on this basis.

IV

Finally, we address Petitioners' post-argument motions to supplement the administrative record and file supplemental briefing and seeking judicial notice of PMTA deficiency letters, FDA internal memoranda, and FDA press releases. We deny the motions to supplement the administrative record and file supplemental briefing and grant the motions for judicial notice.

First, Petitioners filed motions to supplement the administrative record with an internal FDA Memorandum, dated August 19, 2020, and for leave to file supplemental briefing.[15] The memorandum describes a "bundling and bracketing" procedure to expedite review of PMTAs. Petitioners argue that the August 2020 Memorandum demonstrates that the FDA was using a "holistic review approach" at the time Petitioners submitted their PMTAs that "made no reference whatsoever to requiring randomized controlled trials, longitudinal cohort studies, or 'other evidence' comparing flavored bottled e-liquids to tobacco-

[15] The general rule is "that courts reviewing an agency decision are limited to the administrative record." *Lands Council v. Powell*, 395 F.3d 1019, 1029 (9th Cir. 2005) (citing *Fla. Power & Light Co. v. Lorion*, 470 U.S. 729, 743–44 (1985)). Although "[r]eview may . . . be expanded beyond the record if necessary to explain agency decisions," we have only allowed extra-record materials in limited circumstances that do not apply here. *See Sw. Ctr. for Biological Diversity v. U.S. Forest Serv.*, 100 F.3d 1443, 1450 (9th Cir. 1996) (explaining that the administrative record may be supplemented "(1) if necessary to determine whether the agency has considered all relevant factors and has explained its decision, (2) when the agency has relied on documents not in the record, . . . (3) when supplementing the record is necessary to explain technical terms or complex subject matter," or (4) when "plaintiffs make a showing of agency bad faith" (internal quotation marks and citations omitted)).

flavored bottled e-liquids in terms of their ability to promote reduction or cessation of use of combustible cigarettes." Petitioners then argue that this "holistic" approach was subsequently, and without notice, replaced by a different and more demanding evidentiary requirement. Petitioners argue from a negative—that is, because the memorandum does not state that comparative studies are required, the FDA must have been using an approach that did not require such studies and shifted the review criteria only after Petitioners submitted their PMTAs.

The FDA responds that there is no reason to supplement the record because the memorandum prescribes procedures for a stage of review that Petitioners' PMTAs never reached and therefore is "inapplicable in these circumstances." Additionally, the FDA contends that this "wholly internal memo" could not have created reliance interests, and that it is merely "a procedural document discussing an approach for streamlining a narrow aspect of the review of certain products in further scientific review."

The agency's final argument is sufficient to demonstrate that the motion to supplement is not well taken: the August 2020 Memorandum is procedural in nature—it does not describe the *standards* that would apply to the review of the data; rather, it offers *procedural* instructions to increase the efficiency of reviewing thousands of PMTAs at the outset—and therefore it is irrelevant to the substantive issues presented here. *See Gripum*, 47 F.4th at 560–61 (finding the same memorandum "of dubious relevance"). "Bundling and bracketing," as procedural tools, say nothing about how the agency substantively reviews the applications. Even assuming that Petitioners' PMTAs were bundled and bracketed, that does not mean that their applications would have been granted. Indeed, simply using bundling and

bracketing procedures cannot change the results of the review process if the PMTAs failed to include the necessary comparative studies contemplated in the Tobacco Control Act. Because a memorandum describing a procedure to streamline the review of data (either before or during scientific review) is irrelevant to the issues presented in this appeal, Petitioners' motions to supplement and for leave to file supplemental briefs are denied.[16]

Second, Lotus filed three motions asking the court to take judicial notice of various documents. In one motion, Lotus seeks judicial notice of two PMTA deficiency letters issued by the FDA in other matters: *Logic Technology Development LLC v. FDA*, No. 22-3030, (June 26, 2020), and *R.J. Reynolds Vapor Company v. FDA*, No. 23-60037. In a second motion, Lotus seeks judicial notice of two FDA internal memoranda: *Development of the Approach to Evaluating Menthol-Flavored ENDS PMTAs* (Oct. 25, 2022); and *Process for Evaluating Menthol-Flavored ENDS PMTAs* (Oct. 25, 2022). In a third motion, Lotus seeks judicial notice of an October 26, 2022 FDA press release: *FDA Denies Marketing of Logic's Menthol E-Cigarette Products Following Determination They Do Not Meet Public Health Standard*, FDA (Oct. 26, 2022) ("October Press Release").

Rule 201(b) of the Federal Rules of Evidence provides that we may take judicial notice of "a fact that is not subject to reasonable dispute because it . . . can be accurately and readily determined from sources whose accuracy cannot

[16] In any event, for the reasons we have already given, supplementing the record to include this memorandum would not change the result in this case, and the parties effectively briefed the memorandum through their submissions on Petitioners' motions to supplement.

reasonably be questioned." These are published materials representing the considered views of the FDA, and the FDA does not contest their accuracy here. Therefore, we take judicial notice of the FDA's deficiency letters, internal memoranda, and press release. But, as we explain next, they do not alter our analysis.

Based on the additional PMTA deficiency letters, Lotus raises the same "surprise switcheroo" argument we rejected in Section IV.B., *supra*. Specifically, Lotus argues that the FDA indicated that scientific evidence was needed to demonstrate whether flavored ENDS products facilitate adult smokers switching from combustible cigarette use at a rate exceeding that of tobacco-flavored or menthol-flavored products *after* Lotus submitted its own PMTA. This argument fails for the reasons we have previously discussed. The FDA has consistently required sufficiently robust, product-specific evidence demonstrating that flavored ENDS products are appropriate for protection of the public health, which necessarily requires evidence of their effects on switching product use.

Lotus similarly argues that the agency's internal memoranda establish that the FDA's Office of Science preliminarily recommended that the FDA grant marketing authorization of menthol-flavored products, and that recommendation was later overruled. In Lotus's view, these memoranda demonstrate that the FDA "adopted the evidentiary standard it would ultimately apply to grant marketing authorization well after the applications were submitted." We disagree.

As an initial matter, the October 2022 memoranda address menthol-flavored ENDS products (which are not at issue here) and address the status of the review process long

after Petitioners' PMTAs were denied in September 2021. Moreover, the internal memoranda simply reflect the process by which the FDA considered the available evidence and concluded that menthol-flavored ENDS products should be treated the same as other flavored ENDS products (e.g., fruit, sweets, and mint)—that is, "the products could be found to be [appropriate for the protection of the public health] only if the evidence showed that the benefits of the menthol-flavored ENDS were greater than tobacco-flavored ENDS, which pose lower risk to youth." *See Development of the Approach to Evaluating Menthol-Flavored ENDS PMTAs* at 2–3. These memoranda do not demonstrate that the FDA engaged in a "surprise switcheroo."

Finally, Lotus argues that the FDA press release discusses the first menthol-flavored ENDS products to receive a full scientific review, and the FDA issued marketing denial orders because the applications did not demonstrate that these products are "more *effective* at promoting complete switching or significant cigarette use reduction relative to tobacco-flavored [ENDS] among adult smokers." Lotus argues that this statement is relevant to evaluating FDA's claims that its analysis of Lotus' application focused on "benefits," not "efficacy," and that it has never "required" smoking cessation studies.

But the FDA's statements in the press release simply bolster the position that it has maintained throughout this litigation: the FDA "evaluat[es] new tobacco products based on a public health standard that considers the risks and benefits of the tobacco product to the population as a whole" by assessing whether the flavored ENDS product is likely to reduce combustible cigarette use among adults as compared to tobacco-flavored ENDs products, so as to justify the risk flavored products pose to youth. October Press Release; *see*

also, e.g., *Gripum*, 47 F.4th at 559 (explaining, in response to the argument that the FDA's approach amounted to a "product-efficacy assessment," that "all the FDA required Gripum to do [was] to show that its flavored e-cigarette products were *relatively better* at reducing rates of tobacco use than products already on the market" and concluding the FDA "properly applied the comparative standard mandated by the statute; Gripum simply failed to meet it"). Therefore, while we grant Lotus's motions seeking judicial notice, these documents do not change our analysis.

V

The FDA acted within its statutory authority under the Tobacco Control Act to require Petitioners to demonstrate that their flavored ENDS products are comparatively better at promoting smoking cessation than tobacco-flavored products. Moreover, the agency's denial of Petitioners' PMTAs was not arbitrary and capricious. The FDA did not impose a new evidentiary standard or unfairly surprise Petitioners in requiring comparative evidence and, even assuming the FDA erred in failing to assess Petitioners' marketing plans, any error was harmless.

PETITIONS FOR REVIEW DENIED.