No. _____

In the

Supreme Court of the United States

LOTUS VAPING TECHNOLOGIES, LLC,
Petitioner,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION,
Respondent.

On Petition for Writ of Certiorari to the United States Court of Appeals for the Ninth Circuit

PETITION FOR WRIT OF CERTIORARI

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QUESTION PRESENTED

Petitioner is an Idaho-based small business that makes bottled "e-liquid"—a liquid that contains nicotine for use in electronic nicotine delivery systems (also known as "ENDS" and "e-cigarettes"). Petitioner's case presents a circuit split on whether the Food and Drug Administration's denial of hundreds of thousands of marketing applications for ENDS products, including Petitioner's applications, was arbitrary and capricious under the Administrative Procedure Act. FDA denied the applications, all of which were for "flavored" products (*i.e.*, flavored to taste like something other than tobacco) solely because the applications did not include certain types of studies showing that flavored ENDS are more effective than tobacco-flavored ENDS in helping cigarette smokers quit or reduce smoking. But FDA, despite providing extensive guidance on the recommended contents of these applications, had not previously informed Petitioner (or the public) that such studies were required. Moreover, for the "sake of efficiency," FDA ignored other evidence in Petitioner's applications—detailed plans to limit youth exposure and access to the products—that FDA previously said would be "critical" for its marketing authorization determinations. Although the court below (and several other circuits) have found FDA's actions were not arbitrary and capricious, the Fifth Circuit (en banc) and the Eleventh Circuit have found FDA's actions were arbitrary and capricious.

The question presented is:

Whether FDA's denial of Petitioner's marketing applications for flavored ENDS was arbitrary and

capricious where FDA based the denial solely on a previously unannounced requirement for certain types of studies and where FDA ignored other evidence in the applications that FDA previously said was "critical" for marketing authorization.[1]

[1] This is the same question presented in *Magellan Technology, Inc. v. Food and Drug Administration*, Case No. 23-799 (petition for certiorari filed on January 22, 2024; FDA's response due on March 25, 2024). Undersigned counsel of record is also counsel of record for the petitioner in *Magellan*.

CORPORATE DISCLOSURE STATEMENT

Pursuant to Supreme Court Rule 29.6, the undersigned counsel of record certifies that Petitioner Lotus Vaping Technologies, LLC has no parent corporation and that no publicly held company owns 10 percent or more of the stock of the Petitioner. There is no other publicly held corporation or other publicly held entity that has a direct financial interest in the outcome of this case.

PARTIES TO THE PROCEEDINGS

Petitioner Lotus Vaping Technologies, LLC was the sole petitioner in the court of appeals.[2]

Respondent United States Food and Drug Administration was the sole respondent in the court of appeals.

RELATED PROCEEDINGS

United States Court of Appeals (9th Cir.), *Lotus Vaping Technologies, LLC v. United States Food and Drug Administration*, No. 21-71328 (judgment entered on July 7, 2023; petition for panel rehearing, or, in the alternative, rehearing en banc, denied on September 14, 2023).

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[2] The court below consolidated this case with *Nude Nicotine, Inc. v. FDA*, Case No. 21-71321, for oral argument and disposition. *See* App. 7. Nude Nicotine was the sole petitioner and FDA was the sole respondent in Case No. 21-71321; Nude Nicotine is not a party to this petition for certiorari and its time for filing a petition for certiorari has expired.

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INTRODUCTION

As the Fifth Circuit recently recognized in an en banc opinion, "[o]ver several years, the Food and Drug Administration ("FDA") sent manufacturers of e-cigarette products on a wild goose chase."[3]

Before a court-ordered deadline for applicants to submit premarket tobacco product applications ("PMTAs") to keep their ENDS products on the market, FDA set forth its expectations for PMTAs at public meetings, in guidance documents, and in a proposed rule. Starting approximately one year after that deadline, FDA denied hundreds of thousands of PMTAs for flavored ENDS, including Lotus's PMTAs. Moreover, "FDA has not approved a single PMTA for a single one of the more than 1,000,000 flavored e-cigarette products submitted to the agency."[4]

How is it that not a single applicant for a flavored ENDS got it right? Well, *after* Lotus and the other applicants submitted their PMTAs, and with *no notice to the public*, FDA decided that it would authorize the marketing of a flavored ENDS only if the flavored ENDS is more effective than a tobacco-flavored ENDS in helping combustible cigarette smokers quit or reduce smoking. And FDA decided that this new standard would have to be met through a randomized controlled trial, longitudinal cohort study, or some other study similarly conducted "over time," even though FDA had previously stated that it

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[3] *Wages & White Lion Investments, LLC v. FDA*, 90 F.4th 357, __, 2024 U.S. App. LEXIS 133, *1 (5th Cir. 2024) (en banc).

[4] *Id.* at *22-23.

did "not expect that applicants will need to conduct long-term studies to support an application." To make matters worse, FDA decided that it would not review applicants' plans to limit youth exposure and access to their products, even though FDA had previously stated that such plans would be "critical" for making marketing authorization determinations.

Relying on decisions from other circuits, the court below found that FDA did not act in an arbitrary or capricious manner by denying Lotus's applications based on a lack of the above-mentioned comparative efficacy studies, and that any error in FDA's failure to review Lotus's plans to limit youth access was harmless. But the decision below conflicts with decisions from the Fifth Circuit (sitting en banc) and the Eleventh Circuit.

The Fifth Circuit has correctly found that FDA's denial of PMTAs for flavored ENDS was arbitrary and capricious because the agency did not give the ENDS industry fair warning that PMTAs for flavored ENDS would need to include studies comparing those products to tobacco-flavored ENDS, let alone randomized controlled trials, longitudinal cohort studies, or other similar studies conducted "over time." The Fifth Circuit has also correctly found that FDA's denial of the PMTAs was arbitrary and capricious because the agency failed to take into account applicants' reasonable reliance on FDA's previous public statements that the above-mentioned studies would not be required, and that other types of studies could adequately support PMTAs. Both the Fifth Circuit and the Eleventh Circuit have correctly found that FDA's denial of PMTAs for flavored ENDS

was arbitrary and capricious because the agency did not bother to review the applicants' plans for limiting youth exposure and access, and that FDA's failure to review the plans was not harmless.

This Court should grant the instant petition to resolve the circuit split on whether FDA's denial of PMTAs for flavored ENDS was arbitrary and capricious under the APA.

OPINION BELOW

The Ninth Circuit's opinion (App. 1) is reported at 73 F.4th 657. The opinion denied a petition for review of a marketing denial order that FDA issued to Lotus on September 17, 2021 (App. 49).

JURISDICTION

The judgment of the court of appeals was entered on July 7, 2023. The court of appeals denied Lotus's petition for panel rehearing, or, in the alternative, rehearing en banc, on September 14, 2023. Justice Kagan extended the deadline for petitioning for writ of certiorari to February 11, 2024. The jurisdiction of this Court is invoked under 28 U.S.C. § 1254(1).

STATUTORY PROVISIONS INVOLVED

Pertinent statutory provisions are reproduced in the appendix as follows:

A. **5 U.S.C. § 706(2).** App. 103.

B. **21 U.S.C. § 387j.** App. 103.

C. **21 U.S.C. § 387*l*(b).** App. 105.

STATEMENT OF THE CASE

I. FDA's Regulatory Authority Over ENDS

Under the Federal Food, Drug, and Cosmetic Act ("FDCA"), as amended by the Family Smoking Prevention and Tobacco Control Act of 2009 ("TCA"), anyone wishing to market a "new tobacco product" in interstate commerce must file a premarket tobacco product application with FDA establishing that the marketing of the product "would be appropriate for the protection of the public health." 21 U.S.C. § 387j(c)(2)(A).

The FDCA requires FDA's determination on whether a new tobacco product is appropriate for the protection of the public health ("APPH") to be based on "the risks and benefits to the population as a whole, including users and nonusers of the tobacco product." 21 U.S.C. § 387j(c)(4). When making that determination, FDA must consider "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." 21 U.S.C. § 387j(b)(4)(A)-(B). FDA's APPH determination may be based on "well-controlled investigations," including "clinical investigations," as well as "other valid scientific evidence." 21 U.S.C. § 387j(b)(5).

The FDCA's tobacco provisions originally applied only to some traditional tobacco products (*e.g.*, cigarettes). 21 U.S.C. § 387a(b). In 2016, FDA adopted a rule extending those provisions to all tobacco products, including electronic nicotine delivery

systems. *See* FDA, *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. 28973 (May 10, 2016).[5]

Unlike traditional (combustible) cigarettes, ENDS do not contain tobacco leaf that is burned to create smoke that the user inhales. Instead, ENDS use an "e-liquid" containing nicotine that is heated to create an aerosol that the user inhales. According to FDA, "[c]urrent scientific literature demonstrates that ENDS are generally likely to have fewer and lower concentrations of harmful and potentially harmful constituents (HPHCs) than combustible cigarettes, and biomarker studies demonstrate significantly lower exposure to HPHCs among current exclusive ENDS users than current smokers." App. 77.

Some ENDS are "flavored," meaning that they have a flavor other than tobacco (such as fruit), while other ENDS are tobacco flavored. App. 67, n.xi. According to FDA, tobacco-flavored ENDS are far less popular than flavored ENDS, not only among youth, but among adult ENDS users as well. *See id.* (noting that only 22.3% of adult ENDS users and 13.3% of youth ENDS users use tobacco-flavored ENDS and that the remainder of both groups use flavored ENDS).

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[5] *But see Cigar Ass'n of Am. v. FDA*, No. 16-cv-1460, 2023 U.S. Dist. LEXIS 139035, *9 (D.D.C. Aug. 9, 2023) (vacating rule as it applies to premium cigars because FDA "ignored relevant data in the record" with respect to those products), appeal filed (Sept. 29, 2023).

By the time FDA extended the FDCA's tobacco provisions to ENDS in 2016, millions of ENDS products were already on the market. Rather than immediately remove those products from the market for lack of FDA authorization, FDA implemented an "enforcement discretion" policy under which it would not take action against unauthorized products that were on the market by August 8, 2016, so long as the manufacturer submitted a corresponding PMTA by a certain deadline (later set at September 9, 2020) and so long as that PMTA remained under FDA review. *See* 81 Fed. Reg. at 29009-15; *Vapor Technology Ass'n v. FDA*, 977 F.3d 496, 497-502 (6th Cir. 2020).

II. FDA's Instructions for PMTAs

Over a two-year period leading up to the September 2020 deadline for PMTAs, FDA provided the public with detailed instructions for the preparation and submission of PMTAs. Those instructions, which are discussed in more detail below, "are important to understand why every single [ENDS] manufacturer in the entire Nation behaved just as [Lotus] did." *Wages*, 2024 U.S. App. LEXIS 133, *7. And those instructions "are important to explain why FDA cannot now pretend that it gave the regulated community fair notice of the PMTA requirements." *Id.*

A. FDA's Public Meetings

At an October 2018 public meeting, FDA stated: "No specific studies are required for a PMTA; it may be possible to support a marketing order for an ENDS product without conducting new nonclinical or clinical studies given other data sources can support the

PMTA." Iilun Murphy, *Premarket Tobacco Product Application Content Overview*, at 26 (Oct. 23, 2018), https://perma.cc/2JF4-J3ZR.

FDA recommended that applicants "compare the new tobacco product to a representative sample of tobacco products on the market (*i.e.*, either grandfathered or with authorization)" and "[i]nclude justification for why using evidence or data from other products is appropriate." *Id.* at 11. In the area of human subject studies, FDA recommended including evidence from single-point-in-time studies on consumer perceptions and appeal of the subject product and noted that such studies were "widely accepted" as predictors for initiation and cessation. *Id.* at 13, 16. The presentation specified that "[p]roduct perceptions/intentions, including how consumers (especially youth) perceive, use, or intend to use the products is useful information to FDA." *Id.* at 16.

Nowhere in the presentation did FDA suggest that manufacturers of flavored ENDS products should conduct a switching study comparing the rates of reduction in use of combustible cigarettes by users of flavored ENDS products against those of users of tobacco-flavored ENDS products over time.[6]

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[6] The only reference to switching studies stated: "Switching studies: Participants could be directed to substitute an e-cigarette with similar nicotine delivery for usual brand cigarette." *Id.* at 20. Far from prescribing a required comparator product, FDA suggested instead that applicants provide a "[r]ationale for selection of comparator products (e.g., e-liquid nicotine concentrations, flavors, etc.)." *Id.*

In a slide titled "What is Appropriate for Protection of Public Health?," FDA described the evidence it required to find that a tobacco product meets the APPH standard for marketing authorization as follows:

> These are considerations that FDA has used in deciding whether a product is appropriate for the protection of public health:
>
> - Are the levels of [harmful and potentially harmful constituents] and other constituents of toxic concern in the new tobacco product similar or lower than levels of similar [tobacco products] or other appropriate comparator products currently on the US market?
> - Does the scientific evidence provided in the application support that the use of the [tobacco product] has a lower risk of disease for the individual than the use of other similar or appropriate comparator [tobacco products] on the market?
> - Will the marketing of the new [tobacco product] affect the likelihood of nonuser uptake, cessation rates, or other significant shifts in user demographics in a manner to

> decrease morbidity and mortality from tobacco product use?

Id. at 32.

At a similar public meeting a year later, FDA repeated many of these points, including its statements on switching studies and the three "considerations" for determining whether a tobacco product satisfies the APPH standard. Quida Holmes & Priscilla Callahan-Lyon, *Premarket Tobacco Product Applications Content Overview*, at 15, 18, 34 (Oct. 28, 2019), https://perma.cc/B4CF-WLXH.

B. FDA's PMTA Guidance

In June 2019, FDA published a guidance document on PMTAs for ENDS products. *See* CA.ER-139 ("PMTA Guidance").[7] In the Guidance, FDA stated: "Given the relatively new entrance of ENDS on the U.S. market . . . limited data may exist from scientific studies and analyses. . . . Nonetheless, in general, FDA does not expect that applicants will need to conduct long-term studies to support an application." CA.ER-153-54. FDA stated that "[a]lthough randomized clinical trials could address cessation behavior of users of tobacco products, FDA believes this would also be true for observational studies (perception, actual use, or both) examining cessation behaviors." CA.ER-179. A "cross-sectional" study is one type of observational study. *See* Federal

[7] "CA.ER" refers to Petitioner's Excerpts of Record filed with the court below.

Judicial Center, *Reference Manual on Scientific Evidence* 560 (3d ed. 2011).

The PMTA Guidance nowhere suggested that applicants should compare flavored ENDS against tobacco-flavored ENDS to determine whether more smokers reduced or eliminated their combustible cigarette use with the flavored ENDS product over time. The section of the Guidance that speaks to comparison studies focused on physiological health risks associated with the compared products and again emphasized that applicants could choose what they believed to be appropriate comparators and should justify their selections. CA.ER-154-55. FDA also specifically recommended that ENDS product manufacturers evaluate the risks of ENDS products in relation to the risks of combustible cigarettes. CA.ER-155. Similarly, the section that addressed cessation studies did not mention comparative cessation studies and specifically suggested that it would be appropriate to include information from peer-reviewed scientific journals on the likelihood of product use by nonusers, including youth. CA.ER-179.

The PMTA Guidance suggested that applicants "may propose specific restrictions on sale and distribution that can help support a showing that permitting the marketing of the product would be APPH." CA.ER-153. The Guidance recommended including a detailed marketing plan "to enable FDA to better understand the potential consumer demographic" and "better estimate the potential impact on public health." CA.ER-180. FDA promised to "weigh[] all of the potential benefits and risks from the information contained in the PMTA to make an

overall determination of whether the product should be authorized for marketing." CA.ER-153.

C. FDA's Proposed PMTA Rule

In September 2019, FDA issued a proposed rule governing PMTAs that reiterated that FDA did "not expect that long-term clinical studies (*i.e.*, those lasting approximately 6 months or longer) [would] need to be conducted for each PMTA." FDA, *Premarket Tobacco Product Applications and Recordkeeping Requirements, Proposed Rule*, 84 Fed. Reg. 50566, 50619 (Sept. 25, 2019). FDA confirmed that marketing plans would be "critical to FDA's determination of the likelihood of changes in tobacco product use behavior" and that the agency "will review the marketing plan to evaluate potential youth access to, and youth exposure to, the labeling, advertising, marketing, or promotion of, a new tobacco product." *Id.* at 50581.

Nowhere in the proposed PMTA rule did FDA require or even recommend that applicants seeking marketing authorization for flavored ENDS products conduct switching studies comparing the flavored ENDS products against tobacco-flavored ENDS products.

III. Lotus's PMTAs

Lotus submitted its PMTAs for various flavored bottled e-liquids to FDA by the September 2020 deadline. Lotus's bottled e-liquids are used with "open" ENDS—*i.e.*, devices with tanks, or reservoirs, that must be filled (and later re-filled) with e-liquid by the user. *See Wages*, 2024 U.S. App. LEXIS 133, *13-15 (discussing differences between "open" devices and

"closed" devices). Because open devices are harder to conceal and more complicated to operate than "closed" devices, they are not popular with youth ENDS users. *Id.* at *14-15; CA.FER-55.[8] Based on FDA's previous instructions, Lotus's PMTAs included, among other things, cross-sectional and other survey data, a comprehensive review of the scientific literature on ENDS products, and a detailed plan for limiting youth exposure and access to the products. CA.ER-194-229.

IV. FDA's *Sub Silentio* Changes to its Requirements for Flavored ENDS Products

Ten months after Lotus submitted its PMTAs, and without notice to anyone outside the agency, in July 2021, FDA issued an internal memorandum stating that, at the Acting Commissioner's urging, FDA would apply a new "standard for evidence" for PMTAs for flavored ENDS products. *See* CA.ER-61. This change deviated from FDA's original PMTA review plan and came just two weeks after the Acting Commissioner's testimony before Congress, during which she encountered substantial political pressure to deny all PMTAs for flavored ENDS products.[9]

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[8] "CA.FER" refers to Petitioner's Further Excerpts of Record filed with the court below.

[9] *See* Committee on Oversight and Accountability Democrats Press Release, *Subcommittee Hearing Offers Insight into Future of E-Cigarette Regulation* (June 23, 2021), https://perma.cc/74XV-8DR7.

Under the July 2021 memorandum, the Office of Science in FDA's Center for Tobacco Products ("CTP") was "tasked with developing a new plan to effectively manage the remaining non-tobacco flavored ENDS PMTAs" not already in substantive scientific review to enable FDA to take "final action on as many applications as possible by September 10, 2021." CA.ER-61. Under this new "standard for evidence," rather than review an entire PMTA and its contents in context, given the "large number of applications that remain[ed] to be reviewed by September 9, 2021,"[10] FDA would "conduct a Fatal Flaw review . . . a simple review in which the reviewer examines the submission to identify whether or not it contains the necessary type of studies." CA.ER-62. FDA decided the "fatal flaw" would be the absence of randomized controlled trials or longitudinal cohort studies demonstrating that an applicant's non-tobacco-flavored ENDS products provide a greater benefit to adult smokers in terms of promoting smoking cessation relative to tobacco-flavored ENDS products. *Id*. Any application lacking this evidence would "likely" be denied. *Id*.

Although FDA claims that this memorandum was later superseded, the "fatal flaw" analysis is substantially reflected in FDA's internal "scientific

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[10] FDA expected 6,800 product applications but received *6.5 million*, exceeding its anticipated volume "by orders of magnitude." FDA, *Deemed Product Review: A Conversation with the Office of Science* (June 11, 2021), https://perma.cc/Z65M-ZWMT.

review" forms. In these forms, FDA described the scope of its review as follows:

> This review determines whether the subject PMTAs contain evidence from a randomized controlled trial, longitudinal cohort study, and/or other evidence regarding the impact of the new ENDS on switching or cigarette reduction that could potentially demonstrate the benefit of their flavored ENDS over an appropriate comparator tobacco-flavored ENDS.

CA.ER-40.

On August 17, 2021, FDA issued another internal memorandum with a subject of "PMTA Review: Evidence to Demonstrate Benefit of Flavored ENDS to Adult Smokers." CA.ER-46. The August 17, 2021 memorandum purports to describe FDA's "findings with respect to the type of evidence that may support a finding that the marketing of a flavored ENDS is appropriate for the protection of public health." *Id*. The memorandum instructs that, based on FDA's "completion of numerous scientific reviews over the last 10 months," CA.ER-54—that is, *after* the PMTA submission deadline—product-specific evidence enabling a comparison between the applicant's new flavored ENDS product and an "appropriate comparator" tobacco-flavored ENDS product in terms of their impact on tobacco use behavior among adult smokers would be required. CA.ER-54-55. This evidence could be generated through either a randomized controlled trial or a longitudinal cohort study. CA.ER-55.

On August 25, 2021, the day before FDA issued its first marketing denial orders for flavored ENDS products, two FDA officials signed a three-sentence internal memorandum purportedly rescinding the August 17, 2021 memorandum. CA.ER-45. However, as discussed below, FDA incorporated substantial sections of the memorandum into its subsequent Technical Project Lead report on Lotus's applications and the reports for other applicants that also received denial orders for their flavored ENDS products.

As with the July 9, 2021 internal memorandum before it, FDA failed to contemporaneously disclose to applicants the conclusions it reached in its August 17, 2021 memorandum.

V. Lotus's Marketing Denial Orders and Technical Project Lead Report

On August 26, 2021, FDA revealed via a press release that marketing of flavored ENDS products would be authorized only if PMTAs included studies, such as a randomized controlled trial or longitudinal cohort study, showing that an applicant's flavored ENDS product was more effective at promoting switching or cessation of combustible cigarette use than a comparable tobacco-flavored ENDS product over time.[11] Only two weeks later, FDA announced

[11] FDA, Press Release, *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), https://perma.cc/8ZH8-SQ7F.

that it had issued marketing denial orders for more than 946,000 flavored ENDS products.[12]

On September 17, 2021, FDA issued a marketing denial order ("MDO") on Lotus's PMTAs on the ground that they did not satisfy the standard announced in the August 26 press release. App. 50-51. The MDO also noted that FDA did "not proceed to assess other aspects of these applications," such as Lotus's proposed marketing plan to limit youth exposure and access to the products. App. 51.

In its Technical Project Lead ("TPL") report supporting the MDO, FDA incorporated word-for-word much of its "rescinded" August 17, 2021 memorandum. *Compare* App. 59-89 *with* CA.ER-46-60. Thus, the TPL report disclaimed any notion that cross-sectional or other survey data could adequately address smoking cessation. App. 84. In further contrast to its earlier representations, FDA also concluded that "the general scientific literature, though informative for evaluation of some types of products, is not adequate to address this assessment because it does not provide product-specific information." App. 84.

VI. Proceeding Below

On October 14, 2021, Lotus timely petitioned the court below for review of the MDO pursuant to 21

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[12] FDA, Press Release, *FDA Makes Significant Progress in Science-Based Public Health Application for Review, Taking Action on Over 90% of More than 6.5 Million 'Deemed' New Tobacco Products Submitted* (Sept. 9, 2021), https://perma.cc/L9ZM-GFBW.

U.S.C. § 387*l*(a)(1)(B). Circuit courts review such petitions under the APA's "arbitrary and capricious" standard of review. *See* 21 U.S.C. § 387*l*(b).

Lotus argued that FDA's denial of its PMTAs was arbitrary and capricious because (1) FDA never told Lotus (or the public) that the agency would authorize a flavored ENDS product only if a randomized controlled trial, longitudinal cohort study, or some other study conducted "over time" showed the product was more effective than tobacco-flavored ENDS at getting smokers to reduce or quit smoking; (2) FDA had failed to take into account Lotus's reliance interests when the agency changed its policy on the types of studies that would be necessary to support a PMTA; and (3) FDA failed to consider Lotus's detailed plans to limit youth exposure and access to the products. The court below rejected the first two arguments; as to the third argument, the court found that any error in FDA's failure to consider Lotus's marketing and sales-access restriction plans was harmless. App. 24-40.

REASONS FOR GRANTING THE PETITION

I. The Decision Below Conflicts with Decisions by the Fifth Circuit (Sitting En Banc) and the Eleventh Circuit.

The Court should grant certiorari in this case because the decision below conflicts with the decisions of two other circuit courts: *Wages & White Lion Investments, LLC v. FDA*, 90 F.4th 357, 2024 U.S. App. LEXIS 133 (5th Cir. 2024) (en banc) and *Bidi Vapor LLC v. FDA*, 47 F.4th 1191 (11th Cir. 2022). In both cases, the circuit courts found that FDA's denials

of PMTAs for flavored ENDS were arbitrary and capricious.

In *Wages*, the Fifth Circuit found that FDA's denial of similar PMTAs for flavored bottled e-liquids was arbitrary and capricious because the agency had not given the ENDS industry fair warning that PMTAs for flavored ENDS would need to include studies comparing those products to tobacco-flavored ENDS, let alone randomized controlled trials, longitudinal cohort studies, or other studies conducted "over time." *See, e.g.*, *Wages*, 2024 U.S. App. LEXIS 133, *59 ("There is not a single sentence anywhere in the voluminous record before us that says: 'manufacturers should submit long-term scientific studies on the differences between their new flavored e-cigarette products and other [tobacco-flavored] e-cigarette products.'"); *id.* at *46-47 ("The problem of course is that FDA never gave petitioners fair notice that they needed to conduct long-term studies on their specific flavored products.").[13]

The Fifth Circuit also found that FDA's denial of the PMTAs was arbitrary and capricious because the agency failed to take into account that the industry had reasonably relied on FDA's previous public statements that the above-mentioned studies would not be required, and that other types of studies, such as cross-sectional studies, could support PMTAs. *See Wages*, 2024 U.S. App. LEXIS 133, *60 ("[W]hen the agency says: 'you need not submit long-term studies' and 'this is general guidance,' the regulated entity

[13] The Fifth Circuit referred to tobacco flavored ENDS as "unflavored" ENDS.

cannot have its application denied because it did not submit long-term studies."); *id.* at *61 (stating that the law "prohibits administrative agencies from saying one thing, pulling a surprise switcheroo, and ignoring the reasonable reliance interests engendered by its previous statements"); *id.* at *39 ("FDA ignored as irrelevant petitioners' cross-section studies without any acknowledgment that the agency previously invited them.").

Both the Fifth Circuit and the Eleventh Circuit found that FDA's denials of PMTAs for flavored ENDS were arbitrary and capricious because the agency did not bother to review the applicants' plans for limiting youth exposure and access to the products. *See Bidi*, 47 F.4th at 1203 ("Because the marketing and sales-access-restriction plans were relevant factors and addressed an important aspect of the problem, it was arbitrary and capricious for [FDA] not to consider them.") (cleaned up); *Wages*, 2024 U.S. App. LEXIS 133, *67 (stating that because FDA "repeatedly represented that the marketing plans were 'critical' and 'necessary' to a successful application," FDA "cannot now claim they were in fact always meaningless") (cleaned up). And both those courts rejected FDA's argument that any error in failing to review the plans was harmless. *Bidi*, 47 F.4th at 1205 ("Finally, ignoring the marketing and sales access restriction plans was not harmless error."); *Wages*, 2024 U.S. App. LEXIS 133, *72 ("[W]e agree with the

entirety of the Eleventh Circuit's analysis and its application of [the harmless error rule].").[14]

II. The Decision Below Conflicts with this Court's APA Principles Regarding Fair Warning, Reliance Interests, and Consideration of Important Aspects of the Relevant Problem.

The Court should also grant certiorari in this case because the decision below conflicts with this Court's well-settled principles regarding the fair warning agencies must provide to regulated entities—

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[14] In addition to the court below, five other circuits have denied petitions for review of FDA denials of PMTAs for flavored ENDS. *See Liquid Labs LLC v. FDA*, 52 F.4th 533 (3d Cir. 2022); *Gripum, LLC v. FDA*, 47 F.4th 553 (7th Cir. 2022); *Avail Vapor, LLC v. FDA*, 55 F.4th 409 (4th Cir. 2022), *cert denied*, 144 S. Ct. 277 (2023); *Magellan Technology, Inc. v. FDA*, 70 F.4th 622 (2d Cir. 2023), petition for certiorari filed (Jan. 22, 2024); *Prohibition Juice Co. v. FDA*, 45 F.4th 8 (D.C. Cir. 2022). But as the Fifth Circuit explained, "law is not a nose-counting exercise," and those other circuits misread FDA's 2019 Guidance. *Wages*, 2024 U.S. App. LEXIS 133, *61; *see also id.* at *64 ("Neither the D.C. Circuit nor any other court of appeals that has sided with FDA can point to a single word in the June 2019 Guidance (or any other guidance) that says existing data on [tobacco-flavored] e-cigarette use is categorically irrelevant to the public health benefits of flavored e-cigarettes."). Petitioner anticipates that, in addition to the instant petition and the already filed petition in *Magellan*, the Court will soon receive a petition for certiorari requesting review of a decision by the Third Circuit addressing a marketing denial order for menthol-flavored ENDS, *see Logic Tech. Dev. LLC v. FDA*, 84 F.4th 537 (3d Cir. 2023), mandate stayed pending petition for certiorari (Jan 4, 2024). FDA's deadline to file a petition for certiorari in *Wages* has also not yet expired.

particularly those with reliance interests in the agency's previous pronouncements—and an agency's obligation to consider all important aspects of the relevant problem.

A. With no warning to Petitioner, FDA adopted a comparative efficacy requirement for flavored ENDS.

An agency cannot pull the rug out from under a regulated party by imposing new requirements without notice after the party relied on the agency's prior representations. *See FCC v. Fox Television Stations, Inc.*, 556 U.S. 502, 515 (2009). A federal agency must give regulated entities "fair warning" of what the agency expects of them. *Christopher v. SmithKline Beecham Corp.*, 567 U.S. 142, 156 (2012). Anything less "would result in precisely the kind of 'unfair surprise' against which [this Court's] cases have long warned." *Id.* (collecting cases). Indeed, FDA concedes that it was required to give ENDS applicants fair warning of the agency's expectations for PMTAs. *See Wages*, 2024 U.S. App. LEXIS 133, *30-31 ("It is common ground between the parties that the fair notice doctrine applies.").

FDA violated the fair warning requirement by denying Lotus's PMTAs on the ground that Lotus did not satisfy FDA's comparative efficacy requirement for flavored ENDS—*i.e.*, because Lotus did not establish that its flavored ENDS had an added benefit relative to that of tobacco-flavored ENDS in facilitating smokers completely switching away from or significantly reducing their smoking. But FDA did not publicize this new comparative efficacy

requirement until *after* the agency began its *en masse* denial of PMTAs for flavored ENDS.

The court below found that FDA acted within its authority to adopt a comparative efficacy requirement because the FDCA requires the agency's evaluation of a new tobacco product to include "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." App. 25-26. In other words, the lower court found that FDA reasonably interpreted the FDCA as allowing the agency to impose the comparative efficacy requirement.

But even if FDA's new interpretation of the FDCA were a reasonable one, the APA still required FDA to give applicants "fair warning" of that interpretation. *SmithKline Beecham*, 567 U.S. at 156; *see also Gen. Elec. Co. v. EPA*, 53 F.3d 1324, 1329 (D.C. Cir. 1995) (holding that fair notice requires that regulated entities be able to identify with "ascertainable certainty" the standards with which an agency expects them to conform). The court below ignored this requirement, and did not, because it could not, point to any document or communication in which FDA timely advised the public about the agency's new interpretation of the FDCA.[15] For that reason alone, the decision below was incorrect.

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[15] Notably, in December 2022, an expert panel convened at the invitation of the FDA Commissioner to evaluate the Center for Tobacco Products criticized CTP for a lack of "adequate guidance and transparency regarding CTP's expectations" and a "lack of

FDA will argue that its actions were not arbitrary and capricious because agencies may interpret statutes through "adjudication." FDA's argument lacks merit. FDA formulated its new interpretation of the FDCA *before* it adjudicated any PMTAs for flavored ENDS and the agency did not apply that interpretation until it *later* adjudicated those PMTAs *en masse* by issuing marketing denial orders for flavored products. Therefore, under the APA, FDA's interpretation of the FDCA was a "rule making," not an "adjudication." *Compare* 5 U.S.C. § 551(4)-(5) (providing that a "rule" includes "the whole or a part of an agency statement of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy" and a "rule making" includes an "agency process for formulating . . . a rule") *with* 5 U.S.C. § 551(6)-(7) (stating that an "order" is "the whole or part of a final disposition . . . of an agency matter other than rulemaking" and that an "adjudication" is "the agency process for the formulation of an order").[16] And FDA

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clarity regarding review standards," concluding that applicants "will struggle to address the issues necessary to meet the APPH standard unless FDA clearly articulates its expectations." *See* Reagan-Udall Foundation for the FDA, *Operational Evaluation of Certain Components of FDA's Tobacco Program* (Dec. 2022), https://perma.cc/SVP9-DMJ4, at 11, 18, 20. The report found that "[a]s FDA's plans and approaches to tobacco regulation changed, such changes were not always announced and communicated clearly to external stakeholders *or even to staff*." *Id*. at 13 (emphasis added).

[16] FDA purported to rescind its August 17, 2021 internal memorandum, but still applied its new interpretation of the FDCA set forth therein when it adjudicated Lotus's PMTAs, as the nearly identical content of the TPL report illustrates.

must give the public advanced notice of new rules – either through notice and comment rule making (for substantive rules) or through guidance documents (for interpretive rules). *See* 5 U.S.C. § 553; 21 C.F.R. § 10.115(e); *see also R.J. Reynolds Vapor Co. v. FDA*, 65 F.4th 182, 193 (5th Cir. 2023) (concluding that FDA's comparative efficacy standard for flavored ENDS "bears all the hallmarks of a substantive rule") (cleaned up). FDA did neither here.

B. FDA failed to consider Petitioner's reliance interests when it changed its policy on the types of studies that would be required in a PMTA.

When an agency makes a "policy change," it must take into account "industry reliance on the [agency's] prior policy," *Encino Motorcars, LLC v. Navarro*, 579 U.S. 221, 222 (2016), and it "must consider the alternatives that are within the ambit of existing policy," *DHS v. Regents of the Univ. of Cal.*, 140 S. Ct. 1891, 1913 (2020) (cleaned up).

Here, FDA not only adopted a comparative efficacy requirement for flavored ENDS, the agency also "flip-flopped" on the types of studies that it required for PMTAs. *Wages*, 2024 U.S. App. LEXIS

Compare App. 59-89 *with* CA.ER-46-60. Because FDA applied the same interpretation to deny Lotus's PMTA, the "rescission" of the memorandum does not change the fact that the agency's new interpretation set forth in that memorandum was a "rule." *See Safari Club Int'l v. Zinke*, 878 F.3d 316, 332 (D.C. Cir. 2017) ("An agency may not escape the requirements of § 553 by labeling its rule an 'adjudication.'").

133, *38. Prior to the submission deadline, FDA repeatedly said that applicants would not need to conduct long-term studies to support an application. *See, e.g.*, CA.ER-154. And, prior to the submission deadline, FDA stated that single-point-in-time studies, such as observational studies (which include cross-sectional surveys) and consumer perception studies, could provide relevant data on initiation and cessation of tobacco product use. CA.ER-179.

But after the submission deadline, without notice to applicants, FDA decided that PMTAs for flavored ENDS would need a randomized controlled trial, longitudinal cohort study, or "other" study showing use of the specific products at issue "over time." App. 50-51. And after the submission deadline—and without notice—FDA decided that cross-sectional surveys and consumer surveys would be insufficient to support marketing authorization. App. 84.

Relying on FDA's pre-submission deadline statements, Lotus did not conduct any long-term studies, and instead submitted, among other things, cross-sectional and survey data and a comprehensive literature review. Even though FDA should have been aware that applicants like Lotus relied on FDA's previous representations regarding study requirements, FDA did not consider such reliance, let alone potential alternatives to simply denying PMTAs for lacking the newly required studies, such as announcing the new study requirements and allowing applicants a reasonable time to conduct new studies and amend their applications accordingly. FDA's

failures render its denial of Lotus's PMTAs arbitrary and capricious. *Regents*, 140 S. Ct. at 1913.

C. FDA ignored key aspects of Petitioner's PMTAs, including Petitioner's plans for limiting youth exposure and access to its products.

Agency action is arbitrary and capricious if the agency fails to "examine the relevant data and articulate a satisfactory explanation for its action," including when the agency "entirely fails to consider an important aspect of the problem." *Motor Vehicle Mfrs. Assn. of United States, Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983). Here, FDA failed to examine the relevant information in Lotus's applications, including Lotus's detailed plans to limit youth exposure and access to its e-liquid products.

FDA concedes that it did not bother to evaluate Lotus's marketing and sales-access restriction plans for the "sake of efficiency." App. 80-81 n.xix. Lotus's plans were designed to ensure that the company's products are attractive and available only to adults and not to youth. That FDA did not bother to evaluate those plans is striking because FDA *requires* applicants to include such plans in their PMTAs, *see* 21 C.F.R. § 1114.7(f), and the agency has repeatedly described the plans as "critical" and said that it *will* review such plans when evaluating PMTAs, *see, e.g.*, 84 Fed. Reg. at 50581.

The court below found that any error in failing to consider the plans was harmless because Lotus did not prove that those plans would have convinced FDA to authorize marketing of Lotus's products. App. 37-

40. But the lower court's finding of harmless error conflicts with this Court's opinion in *Calcutt v. FDIC*, 143 S. Ct. 1317 (2023) (per curiam). As this Court recognized in *Calcutt*, it is "well established" that "if the agency has not considered all of the relevant factors, the proper course, except in rare circumstances, is to remand to the agency for additional explanation or investigation." *Id.* at 1320 (cleaned up). Such "rare circumstances" do not include cases, such as this one, where an agency applies its discretion to "highly fact-specific" product applications. *Wages*, 2024 U.S. App. LEXIS 133, *71 (rejecting FDA's harmless error argument because "[t]his case is controlled by *Calcutt*"); *see also Bidi*, 47 F.4th at 1205 (rejecting FDA's harmless error argument).

III. This Case Presents a Question of Great Importance to the ENDS Industry, Former and Transitioning Smokers Who Use Flavored ENDS Products, and Cigarette Smokers Who Want to Quit Smoking.

It is not every day that FDA seeks to remove an entire class of products from the market. But that is exactly what FDA is attempting to do with respect to flavored ENDS. FDA has denied PMTAs for hundreds of thousands of flavored ENDS, and it has not authorized the marketing of a single flavored ENDS product. *Wages*, 2024 U.S. App. LEXIS 133, *21. In other words, FDA has implemented a "de facto ban on flavored e-cigarettes." *Id.* at *56 n.5. This de facto ban is not only devastating to the ENDS industry; it also poses a real risk to former and transitioning cigarette

smokers who use flavored ENDS products, as well as current cigarette smokers who want to quit smoking.

For at least four reasons, removing all flavored ENDS products from the market harms the interests of former cigarette smokers who have successfully used flavored ENDS products to quit, transitioning cigarette smokers who use those products now, and current cigarette smokers who want to quit smoking.

First, FDA has stated that, because they do not involve combustion, "ENDS are generally likely to have fewer and lower concentrations of harmful and potentially harmful constituents (HPHCs) than combustible cigarettes, and biomarker studies demonstrate significantly lower exposure to HPHCs among current exclusive ENDS users than current smokers." App. 77; *see also Breeze Smoke, LLC v. FDA*, 18 F.4th 499, 505 (6th Cir. 2021) (noting FDA's acknowledgment "that ENDS products may provide a beneficial alternative to combustible cigarettes because they deliver nicotine without also bombarding the user's lungs with the toxins found in cigarettes").

Second, nearly six percent of adults in the United States currently use ENDS products, whereas over eleven percent of adults in the United States currently smoke cigarettes. *See* CDC, *Early Release of Selected Estimates Based on Data from the 2022 National Health Interview Survey* (Apr. 23, 2023).[17]

[17] https://perma.cc/D25X-2ASE.

Third, an overwhelming majority of adult ENDS users use flavored ENDS. App. 68 (FDA stating that approximately 77% of adult ENDS users use flavored ENDS); CA.ER-97 (FDA stating that "the majority of adult [ENDS] users use [flavored ENDS]").

Fourth, among adult ENDS users, approximately 69.7% are former or current cigarette smokers, including 92.8% of users over 45 years old—the age group most susceptible to near-term adverse health impacts from smoking combustible cigarettes.[18]

In short, even though millions of adults who use ENDS as a less harmful alternative to cigarettes strongly prefer flavored ENDS, FDA is taking that option away from them. That fact alone warrants this Court's review.

CONCLUSION

For the forgoing reasons, this Court should grant the petition for certiorari.

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[18] CDC, *QuickStats: Percentage Distribution of Cigarette Smoking Status Among Current Adult E-Cigarette Users, by Age Group—National Health Interview Survey* (Mar. 10, 2023), https://perma.cc/TYR8-9KUV.

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