No. 23-1038

In the

Supreme Court of the United States

FOOD AND DRUG ADMINISTRATION,
Petitioner,

v.

WAGES AND WHITE LION INVESTMENTS, L.L.C., DBA TRITON DISTRIBUTION, ET AL.,
Respondents.

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

BRIEF FOR RESPONDENTS

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QUESTION PRESENTED

Respondents sell nicotine-containing bottled "e-liquids" used in electronic nicotine delivery systems ("ENDS"). Respondents began selling their e-liquids, including in flavors other than tobacco, years before FDA adopted a rule giving itself regulatory authority over ENDS. By a court-ordered deadline, Respondents filed applications with FDA so they could keep their products on the market and remain in business. But while the applications were pending, and with no notice to applicants, FDA decided (1) it would not grant marketing authorization for a flavored ENDS product without a product-specific longitudinal comparative efficacy study showing that the product was more effective than tobacco-flavored ENDS in helping adult smokers quit smoking; and (2) "for the sake of efficiency," the agency would not review applicants' plans to prevent youth from using their products even though FDA had previously said such plans were "critical" to the applications. Based on those decisions, FDA denied Respondents' applications. The en banc Fifth Circuit found FDA's denial orders arbitrary and capricious because FDA (1) changed its position on the authorization requirements without fair notice or consideration of Respondents' reliance interests, and (2) committed prejudicial error by refusing to consider Respondents' plans to prevent underage access and use.

The Court granted certiorari on the following question:

Whether the court of appeals erred in setting aside FDA's denial orders as arbitrary and capricious.

CORPORATE DISCLOSURE STATEMENT

Pursuant to Supreme Court Rule 29.6, the undersigned counsel of record certifies that neither Respondent Wages and White Lion Investments, L.L.C. (d/b/a Triton Distribution) nor Vapetasia, L.L.C. has a parent corporation and no publicly held company owns 10 percent or more of the stock of either Respondent. 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 (respondent below) is the Food and Drug Administration ("FDA"). Respondents (petitioners below) are Wages and White Lion Investments, L.L.C. (d/b/a Triton Distribution) ("Triton") and Vapetasia, L.L.C. ("Vapetasia").

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Pertinent statutory provisions are reproduced in the appendix to Petitioner's brief. Pet. App. 338a-352a. Additional pertinent statutory provisions are reproduced in the appendix to Respondents' brief.

STATEMENT

Respondents sell nicotine-containing liquids for use in electronic nicotine delivery systems, which are a less harmful alternative to traditional cigarettes and do not involve burning tobacco or inhaling smoke. Following extensive FDA guidance, Respondents filed premarket applications for their flavored products[1] by a court-ordered deadline that included the types of evidence FDA recommended, including evidence that their products had lower levels of harmful constituents than cigarettes and other tobacco products, extensive scientific literature concluding that allowing cigarette smokers to access products like Respondents' would lead to an overall decrease in disease and death from tobacco product use, and detailed plans and restrictions to keep Respondents' products out of the hands of youth.

But ten months later, FDA secretly changed its requirements for flavored products. Despite having never mentioned needing different studies for flavored products than tobacco-flavored products, FDA decided it would only authorize flavored products if they were more effective than tobacco-flavored products at helping smokers quit or reduce their use of cigarettes.

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[1] Consistent with FDA's practice in its brief, Respondents refer to non-tobacco-flavored products herein as "flavored."

And, contrary to FDA's previous statements, applications would have to show this through a randomized controlled trial, longitudinal cohort study, or some "other evidence" comparing the applicant's flavored product to a tobacco-flavored product over time. FDA then denied applications for more than a million flavored products for failing to meet these new requirements, including those of Respondents, while ignoring other contents of the applications.

FDA failed to provide the public with fair notice of its new application requirements or even that it had changed its original requirements. FDA also failed to consider applicants' reliance interests when it changed the requirements and its underlying positions regarding the role of device types in attracting youth.

Moreover, FDA's new requirements constitute a substantive rule imposed without notice and comment in violation of the Administrative Procedure Act ("APA"), not the result of evolving standards adopted through case-by-case adjudication.

And FDA's admitted error in ignoring the remainder of Respondents' applications, including their marketing plans, was prejudicial, not harmless. To hold otherwise would be to hold Respondents to an unreasonable evidentiary burden and vitiate the requirement that agencies engage in reasoned decisionmaking.

The en banc Fifth Circuit found FDA's actions arbitrary and capricious. This Court should affirm that judgment.

A. The Tobacco Control Act

In 2009, Congress enacted the Family Smoking Prevention and Tobacco Control Act ("TCA" or "Act") to grant FDA authority over tobacco products. Pub. L. No 111-31, Div. A, 123 Stat. 1776. The Act's findings reflect Congress's concerns about the risks of disease and death (in medical parlance, the "morbidity and mortality") presented by combustible cigarettes. Congress found that combustible cigarettes "cause cancer, heart disease, and other serious adverse health effects" and that tobacco use leads to over 400,000 deaths annually. § 2(2), (13), 123 Stat. 1777. Congress also found that "approximately 8,600,000 Americans have chronic illness related to smoking." § 2(13), 123 Stat. 1777. Through the Act, Congress gave FDA a "mandate to . . . reduce the risk of harm," § 2(44) 123 Stat. 1780-81, and, to that end, "encourage the development of innovative products," 21 U.S.C. § 387r(b)(1).

The TCA requires premarket authorization for any tobacco products that were not marketed as of February 15, 2007. *See* 21 U.S.C. § 387j. To obtain authorization, an applicant must show that the marketing of its tobacco product is "appropriate for the protection of the public health." 21 U.S.C. § 387j(c)(2)(A). Whether marketing a specific product is "appropriate for the protection of the public health" is determined "with respect to the risks and benefits of the population as a whole, including users and nonusers of the tobacco product," and taking into account both "(A) the increased or decreased likelihood that existing users of tobacco products will stop using such products; and (B) the increased or decreased

likelihood that those who do not use tobacco products will start using such products." 21 U.S.C. § 387j(c)(4).

B. Electronic Nicotine Delivery Systems

Electronic nicotine delivery systems, or ENDS, also known as electronic cigarettes, heat a solution containing nicotine, flavorings, and other ingredients (called "e-liquid") into an aerosol that the user inhales. Unlike traditional cigarettes, ENDS do not contain any tobacco leaf, do not rely on combustion, and do not generate smoke.

FDA considers that "ENDS are generally likely to have fewer and lower concentrations of harmful and potentially harmful constituents" than cigarettes and "biomarker studies demonstrate significantly lower exposure to [those harmful constituents] among current exclusive ENDS users than current smokers." Pet. App. 197a-198a. Thus, "smokers who switch completely to ENDS will have reduced toxic exposures and this likely leads to less risk of tobacco-related diseases."[2] And, while the nicotine found in ENDS is not harmless, FDA has emphasized that "the nicotine in cigarettes is *not* directly responsible for the cancer, lung disease, and heart disease that kill hundreds of thousands of Americans each year. . . . [Rather], it's the other chemical compounds in tobacco, and in the smoke created by setting tobacco on fire, that directly and primarily cause the illness and death."[3] As FDA

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[2] FDA, *Technical Project Lead (TPL) Review of PMTAs* at 6 (May 12, 2022), https://perma.cc/7BGZ-DUEH.

[3] FDA Commissioner Scott Gottlieb, Protecting American Families: Comprehensive Approach to Nicotine and Tobacco (June 28, 2017), https://tinyurl.com/4zjcmvjb (emphasis added).

has explained, "If you could take every adult smoker . . . and fully switch them to e-cigarettes, that would have a substantial public health impact."[4]

ENDS can be grouped into three categories: (1) prefilled, cartridge-based ENDS; (2) disposable ENDS; and (3) refillable, or "open-system" ENDS. Because cartridge-based and disposable ENDS are not refillable, they are referred to as "closed-system" products.

This case deals with Respondents' bottled e-liquids, which are sold for use in open-system ENDS. Although this case does not deal with cartridge-based or disposable ENDS, the differences between the three categories are important when determining whether FDA's denials of Respondents' premarket applications were arbitrary and capricious.

1. Cartridge-Based ENDS

Cartridge-based ENDS use a replaceable cartridge pre-filled with e-liquid. Once all the e-liquid in a cartridge is used, the user can replace the cartridge with a new cartridge. The following photo is an example of a cartridge-based ENDS with four cartridges and a USB charger from a CDC publication[5]:

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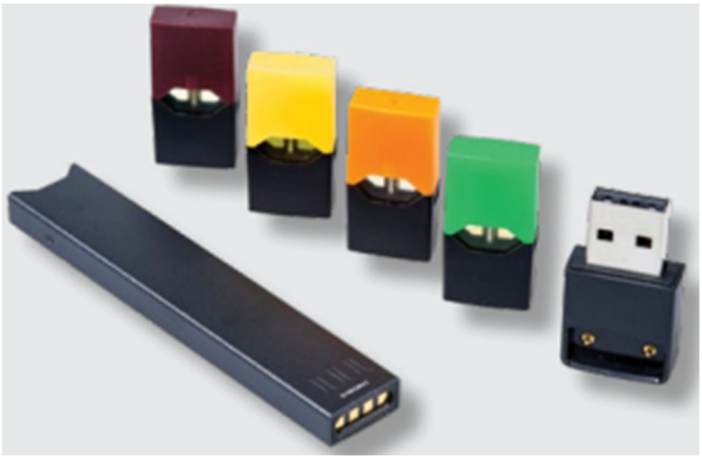
[4] CSPAN, *FDA Commissioner on E-Cigarettes and Public Health Concerns*, at 10:25 (Sept. 25, 2018), https://tinyurl.com/mujce8hr.

[5] CDC, Visual Dictionary for E-Cigarettes and Vaping Products, 12, https://perma.cc/ZE6S-J75L.



FDA says that cartridge-based products may have high nicotine content and have "intuitive and convenient features that facilitate ease of use," as well as "design features" that make them "popular with young people," including "a relatively small size that allows for easy concealability." J.A.155-56. According to FDA, this concealability "may allow youth to use" cartridge-based ENDS "in circumstances where use of tobacco products is prohibited, such as at school." *Id.*

2. Disposable ENDS

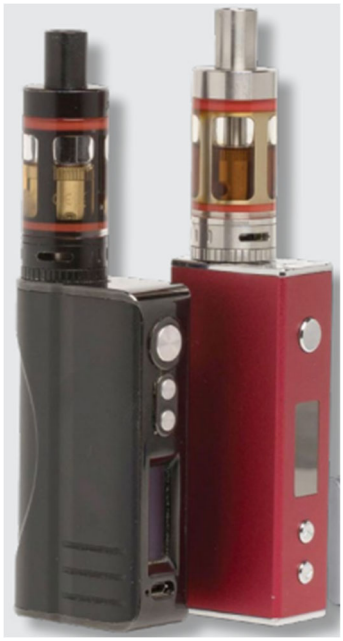
Disposable ENDS come pre-filled with e-liquid and are intended to be thrown away once that e-liquid is completely used; the user does not refill the device. Disposable ENDS are typically similar in size to cartridge-based ENDS. The photo below, taken from FDA's website,[6] shows two examples:

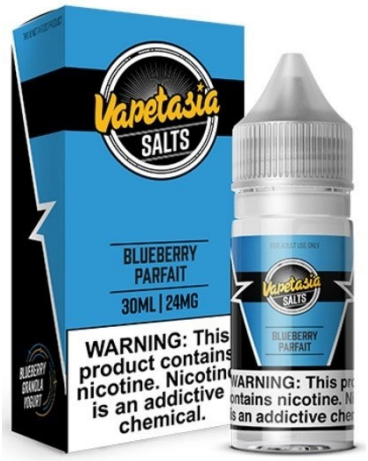
[6] FDA, E-Cigarettes, Vapes, and other Electronic Nicotine Delivery Systems (ENDS), https://tinyurl.com/5n73hv2p.

3. Open-System ENDS

Open-system ENDS do not come pre-filled with e-liquid or use pre-filled cartridges. Instead, the devices have an open tank. Users of open-system ENDS purchase bottles of e-liquid, typically manufactured by a different company than the manufacturer of the device, and then fill the tank with that e-liquid. The photo on the left below, also from CDC's Visual Dictionary,[7] shows two examples of open-system ENDS devices; the photo on the right shows one of the bottled e-liquids at issue in this case.

[7] *Supra* n.5 at 10.





Unlike cartridge-based and disposable ENDS, which are widely sold in convenience stores, open-system ENDS devices and bottled e-liquids are sold primarily in specialty "vape shops" that often do not sell traditional tobacco products. *See* C. Berg, et al., *Vape Shop Owners/Managers' Opinions About FDA Regulation of E-Cigarettes*, 23 Nicotine and Tobacco Research 535, 536 (2021). According to tobacco researchers, a "substantial proportion of vape shops are small businesses or single-store owners" and many vape shop workers used vaping to quit smoking and want to help other smokers quit. *Id*. at 536-37.

C. FDA's Shifting Deadline for Premarket Applications

The TCA defined the term "tobacco product" broadly to encompass "any product made *or derived*

from tobacco that is intended for human consumption, including any component, part, or accessory of a tobacco product." 21 U.S.C. § 321(rr)(1) (2010) (emphasis added).[8] But the TCA's requirements originally applied only to certain traditional tobacco products. *See* 21 U.S.C. § 387a(b). However, in 2016, FDA finalized a rule that "deemed" ENDS to be subject to the Act. 81 Fed. Reg. 28974 (May 10, 2016) (codified at 21 C.F.R. § 1143.1). These "deemed" products include the bottled e-liquid products at issue here.

Once FDA "deemed" ENDS to be tobacco products, they became subject to the Act's premarket authorization requirement. *See* 21 U.S.C. § 387j. And because no ENDS had premarket authorization, they were immediately "deemed to be adulterated" under the Act. 21 U.S.C. § 387b(6)(A). Selling adulterated tobacco products in interstate commerce is punishable by substantial civil penalties and/or criminal prosecution that can result in up to one year in prison. *See* 21 U.S.C. §§ 331(a), 333(a)(1), 333(f)(9).

Because millions of ENDS products, including Respondents' bottled e-liquids, were already marketed when FDA "deemed" them tobacco products in 2016, FDA adopted a deferred enforcement policy for those products whereby they could continue to be sold so long as their manufacturers submitted premarket applications for them by a specified deadline. *See* 81

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[8] Congress later expanded the definition of "tobacco product" to include all products "containing nicotine derived from any source." 21 U.S.C. § 321(rr)(1) (2022). This amendment is not relevant here.

Fed. Reg. at 28977-78, 29009-15. FDA's deferred enforcement policy was sensible because, unlike its typical practice, the agency had not even proposed, much less finalized, regulations for premarket applications.

After a change in administrations, in 2017, FDA delayed the application deadline under its deferred enforcement policy for four years from 2018 to 2022. Anti-vaping groups then brought litigation challenging the delay. *See Vapor Technology Ass'n v. FDA*, 977 F.3d 496, 497-502 (6th Cir. 2020) (summarizing district court litigation). Based on FDA's representation that such a deadline was feasible, the district court ordered FDA to advance the application deadline to May 2020, which was ultimately extended to September 9, 2020, due to COVID-19. *Id.* at 499-500; *Am. Acad. of Pediatrics v. FDA*, 399 F. Supp. 3d 479, 481 (D. Md. 2019).

D. FDA's Sub-Regulatory Guidance and Proposed Rule on Application Requirements

Although FDA's "deeming rule" subjected ENDS to the TCA's premarket authorization requirement, the rule did not explain how manufacturers of new tobacco products could satisfy that requirement. So, before the September 2020 deadline for applications, FDA publicized its expectations for the contents of applications in public informational meetings, a guidance document, and a proposed rule.

For example, FDA said it expected an application—called a premarket tobacco product

application, or "PMTA"—to include information on whether the proposed product has similar or lower levels of harmful or potentially harmful constituents ("HPHCs") than comparator tobacco products. *See, e.g.*, FDA Presentation from 2018 Public Meeting on PMTAs ("2018 FDA Presentation") at 32 ("Are the levels of HPHCs and other constituents of toxic concern in the new tobacco product similar or lower than levels in similar [tobacco products] or other appropriate comparator tobacco products currently on the U.S. market?").[9] And in one of its public meetings, FDA noted that a successful applicant had compared the HPHC levels for its new tobacco products (IQOS tobacco-flavored and menthol-flavored "heat sticks") to those of traditional cigarettes. *See* FDA Presentation from 2019 Public Meeting on PMTAs ("2019 FDA Presentation") at 40, 43.[10]

As another example, FDA said it expected applicants to include information on whether the proposed product would help reduce the overall adverse health effects from tobacco products by transitioning current tobacco users to less harmful tobacco products. *See, e.g.*, 2018 FDA Presentation at 32 ("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?"); 2019 FDA Presentation at 34

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[9] Available at https://perma.cc/MLR4-JUD6.

[10] Available at https://perma.cc/VGG5-VS5S. FDA apparently did not require this applicant to show that its menthol-flavored heat sticks were more effective than tobacco-flavored heat sticks in helping smokers quit smoking.

(same); PMTA Guidance (Jun. 2019), J.A.53 (recommending "an overall qualitative assessment of whether the product will have a positive impact on the health of the population as a whole by accounting for potential reductions in disease risk (as compared to other tobacco products) and the potential for current tobacco users to switch to the new tobacco product").

And as another example, FDA said it expected applications to include sales-and-marketing restriction plans designed to keep the proposed product out of the hands of underage users. *See, e.g.*, Premarket Tobacco Product Applications and Recordkeeping Requirements, 84 Fed. Reg. 50566, 50581 (proposed Sept. 25, 2019) (stating that FDA would "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"). In fact, FDA said that these plans would be "critical" to its evaluation of an application. *Id.*

FDA knew that a majority of adult ENDS users use flavored products.[11] But FDA did not say—in its public informational meetings, guidance document, or proposed rule—that it expected applications for flavored ENDS to include data showing that the product is more effective than a tobacco-flavored ENDS in helping smokers quit or reduce their use of cigarettes, let alone that FDA expected such data to

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[11] *See* FDA, Advance Notice of Proposed Rulemaking, Regulation of Flavors in Tobacco Products, 83 Fed. Reg. 12294, 12297 (Mar. 21, 2018) (noting study data that 63.2% of adult ENDS users reported using flavored ENDS); *accord* J.A.171-72.

come from a randomized controlled trial, longitudinal cohort study, or some other type of study conducted "over time." Rather, FDA said 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 given other data sources can support the PMTA." 2018 FDA Presentation at 26; 2019 FDA Presentation at 30. And FDA said those "other data sources" could include "peer-reviewed literature," "[l]iterature reviews," and "surveys." 2018 FDA Presentation at 18, 28, 29; 2019 FDA Presentation at 30, 31; *see also* PMTA Guidance, J.A.81 (stating that "[p]ublished literature" could help show that the use of a proposed ENDS could promote "switching behavior [and] cessation").

E. FDA's 2020 Enforcement Guidance

Less than 10 months before the September 2020 deadline to submit premarket applications, FDA published a guidance document (the "Enforcement Guidance") modifying its enforcement priorities for ENDS under its deferred enforcement policy. *See* J.A.126.[12] According to the Enforcement Guidance, FDA's top enforcement priority was now "[f]lavored, cartridge-based ENDS products (except for tobacco- or menthol-flavored ENDS products)." J.A.145.

FDA's decision to prioritize enforcement against flavored, cartridge-based ENDS was likely driven by the popularity of JUUL products among

[12] FDA revised the Enforcement Guidance in April 2020 due to the extension of the application deadline to September 9, 2020.

underage consumers. A paper published two months before the Enforcement Guidance was released, co-authored by officials from FDA and CDC, and cited in the Enforcement Guidance, noted:

> Most youth who were current e-cigarette users reported JUUL as their usual e-cigarette brand in 2019. . . . This mirrors trends in retail sales data showing that JUUL has held the majority of the market share of U.S. e-cigarette sales since December 2017.[13]

The Enforcement Guidance explained that FDA was prioritizing enforcement against flavored, cartridge-based ENDS because these products had "design features" that make the "products so popular with young people," including "small size," "easy concealability," ability to "use immediately after purchase," and "prefilled cartridges, which are convenient because they do not require filling prior to use and are easy to dispose of and replace." J.A.155-58. The Guidance also noted that "particularly easy-to-use products, such as cartridge-based products, may have lower barriers to initiation." J.A.157. FDA excluded from the "cartridge-based ENDS products" definition, and thus the top "priority" category for enforcement, "self-contained, disposable" ENDS

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[13] K. Cullen, et al., *E-Cigarette Use Among Youth in the United States, 2019*, 322 JAMA 2095 (2019) (cited in 2020 Enforcement Guidance at 12, n.31, J.A.149); *see also* J.A.155-56 (stating "the leading brand is a cartridge-based product that commands approximately 70 percent of the market").

products, even though these products share these same characteristics. J.A.143.

The Enforcement Guidance stated that FDA's other enforcement priorities were all "other ENDS products for which the manufacturer has failed to take (or is failing to take) adequate measures to prevent minors' access," and any "ENDS products targeted to, or whose marketing is likely to promote use by, minors." J.A.145. Importantly, the Enforcement Guidance repeatedly emphasized that "[t]his policy should have minimal impact on small manufacturers (e.g., vape shops) that primarily sell non-cartridge-based ENDS products, unless they market to youth or fail to take adequate measures to prevent youth access." J.A.160-61, 172-73; *see also* J.A.220.

The Enforcement Guidance also recommended several sales-access restrictions (so-called "adequate measures") that manufacturers of open-system ENDS and bottled e-liquids could adopt to prevent minors' access to their products and highlighted marketing strategies that such manufacturers would best avoid to prevent youth interest in and use of their products. *See* J.A.167-69 (sales-access restrictions); J.A.174-77 (marketing strategies).

F. Respondents' Applications

Respondents submitted their applications by the September 2020 deadline. Respondents' applications included data and information in line with the expectations FDA had set forth in its public

meetings, PMTA Guidance, proposed PMTA rule, and Enforcement Guidance.[14]

For example, Respondents' PMTAs included product-specific data showing their flavored bottled e-liquids had lower levels of HPHCs than combustible cigarettes.[15] This data also showed that Respondents' products had lower levels of HPHCs than the IQOS tobacco- and menthol-flavored "heat sticks" that had already received FDA marketing authorization. *See, e.g.* J.A.324; *see also* 330-31, 354, 414, 421, 444.

As another example, Respondents' applications included evidence showing that ENDS help reduce the overall adverse health effects from tobacco products by transitioning current tobacco users to less harmful tobacco products. Specifically, Respondents submitted a comprehensive scientific literature review showing that "consistent use of ENDS is associated with increased likelihood of cessation of combustible products and if not cessation, the reduction in overall consumption of cigarettes per day." J.A.328; *see also* J.A.418 (noting that the literature review showed "[t]here is strong population and randomized control trial (RCT) evidence suggesting that ENDS are effective for cessation of combustible cigarettes").[16]

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[14] *See, e.g.*, J.A.303, 310-11, 319, 322, 325, 327, 327 n.9, 375-93, 400, 409, 412, 415, 416 n.2, 445, 446, 447 n.15, 470, 640.

[15] *See* J.A.305, 312, 324, 330-32, 354, 394-95, 402, 413, 414, 421, 422, 444.

[16] *See also* J.A.303, 305, 307, 308, 310-11, 329-30, 370, 375, 392, 394, 396-97, 400-01, 406, 415-17, 420, 422, 446-48, 463-65, 470, 472-74 (references to scientific literature).

And as another example, Respondents' applications included sales-and-marketing restriction plans designed to keep their e-liquids out of the hands of underage users. Respondents' proposed plans were in line with those FDA recommended to bottled e-liquid manufacturers in the agency's Enforcement Guidance. *See, e.g.*, J.A.177 (Enforcement Guidance recommendation that bottled e-liquid manufacturers not market their products "through paid social media influencers"); J.A.316-17, 407 (applications stating the products would not be promoted by "influencers, bloggers, or brand ambassadors on social media, radio, or television"); J.A.177 (Enforcement Guidance recommendation that bottled e-liquid manufacturers not market their products using "minors or people who portray minors"); J.A.345, 435 (applications stating that Respondents would ensure that all models "are, and appear to be, at least 35 years old"); J.A.177 (Enforcement Guidance recommendation that bottled e-liquid manufacturers not market their products "with youth-appealing cartoon or animated characters"); J.A.344, 434 (applications stating the products would not be marketed using "material [that] includes childish images, cartoons, characters, mascots, or childish or juvenile designs that might appeal to youth"); J.A. 167-68 (Enforcement Guidance recommendation that manufacturers ensure retailers take steps to prevent youth purchases); J.A.345, 435-36 (applications stating Respondents would ensure that minors are not allowed to enter retail establishments that sell their products).

G. FDA's Undisclosed Decision to Change the Requirements for Flavored ENDS

By the September 9, 2020 deadline, FDA received applications for approximately 6.5 million products, exceeding its anticipated volume of applications "by several orders of magnitude."[17] FDA described the task of reviewing these applications by September 10, 2021—the court-ordered end of the enforcement discretion period for ENDS lacking marketing authorization—as "unprecedented."[18]

In January 2021, under a new presidential administration, FDA's leadership changed. On July 9, 2021, FDA issued an internal memorandum proposing a revised review process following the Acting FDA Commissioner's direction that the agency "develop[] a new plan" to "take final action on as many applications as possible by September 10, 2021." J.A.242. Procedurally, rather than review an entire application, 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." J.A.243. Substantively, the "fatal flaw" would be the absence of randomized controlled trials or longitudinal cohort studies demonstrating that an applicant's flavored ENDS

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[17] Transcript, FDA, *Deemed Product Review: A Conversation with the Office of Science*, at 8, 19 (June 11, 2021), https://perma.cc/3GSQ-WZRS.

[18] 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://bit.ly/33Av9oz.

product provides a greater benefit to adult smokers in terms of promoting smoking cessation relative to a comparator tobacco-flavored ENDS product. *Id*. Any application lacking this evidence would "likely receive a [denial order]." *Id*. FDA never disclosed the July 9, 2021 memorandum.

On August 17, 2021, FDA prepared an 11-page, single-spaced internal memorandum, J.A.245-80, memorializing its determination that applicants for flavored ENDS would have to meet "a high burden" for marketing authorization, J.A.246. Specifically, applicants would have to provide evidence that their "flavored products have an added benefit relative to that of tobacco-flavored ENDS in facilitating smokers completely switching away from or significantly reducing their smoking" to offset the alleged attractiveness of flavored products to youth. J.A.248. Based on its "completion of numerous scientific reviews over the last 10 months," J.A.266, FDA concluded that such evidence would "most likely" need to be "product specific" and in the form of a "randomized controlled trial" or a "longitudinal cohort study," J.A.246-47. Such studies would need to track participants over time and enable a comparison between the applicant's flavored ENDS product and an "appropriate comparator" tobacco-flavored ENDS product in terms of their impact on adult smoking behavior. J.A.267-69.

The August 17, 2021 memorandum stated that assessing the risk that youth will be attracted to and use a specific ENDS product "includes evaluating the appropriateness of the proposed marketing plan." J.A.265. But, echoing the earlier "Fatal Flaw"

memorandum, FDA said that "for the sake of efficiency, the evaluation of the marketing plans in applications will not occur at this stage of review." *Id.* n.xxii. According to FDA, none of the marketing plans included in the applications that it had already reviewed "would decrease appeal to youth to a degree significant enough to address and counter-balance the substantial concerns" about "youth use," and the agency was "not aware of access restrictions that, to date, have been successful in sufficiently decreasing the ability of youth to obtain and use ENDS." *Id.* However, FDA did not identify the marketing plans that it had already reviewed or the products for which it had determined marketing or access restriction measures had been unsuccessful.

Although the August 17, 2021 Memorandum made a few brief references to the PMTA Guidance,[19] the Memorandum did not focus on that Guidance. To the contrary, the Memorandum cited 65 publications other than the PMTA Guidance as "References." *See* J.A.271-80.

FDA did not contemporaneously disclose to applicants the August 17, 2021 memorandum or the new longitudinal comparative efficacy requirement. Instead, on August 25, 2021—the day before FDA announced its first *en masse* denials of applications for flavored ENDS—FDA "rescinded" the August 17, 2021 memorandum in a three-sentence "Memorandum to File." J.A.281. FDA did not say what, if any, "process" replaced the one set forth in the August 17, 2021 Memorandum.

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[19] *See* J.A.263-64, 269.

H. FDA's Denial of Respondents' Applications

On August 26, 2021, FDA announced its new longitudinal comparative efficacy requirement for the first time via a 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://bit.ly/2YsYmzd.

Less than a week later, Respondent Triton submitted a letter advising FDA that it intended to conduct additional behavioral studies on adult smoking cessation to supplement its applications. J.A.642-43. However, on September 14, 2021, FDA issued a denial order to Triton in which FDA stated it had not reviewed the letter because it was "received near the completion of scientific review." Pet. App. 166a, 176a. FDA similarly denied Vapetasia's applications. Pet. App. 278a-284a.[20]

FDA denied Respondents' applications because they did not present evidence sufficient to show that their products "will provide a benefit to adult users that would be adequate to outweigh the risks to

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[20] FDA denied applications for some 946,000 flavored ENDS on the same grounds in only two weeks. Pet. App. 19a, Indeed, the only applicant to have received a marketing order for its flavored ENDS, NJOY, only did so because it was allowed to submit amendments in December 2022—over two years *after* the deadline and over a year after Respondents received their denial orders—that included results from the longitudinal comparative efficacy studies FDA now demands. FDA, *TPL Review of PMTAs* 20-21, 66 (Jun. 21, 2024); https://perma.cc/BK26-RYF5; FDA, *TPL Review of PMTAs* 71 (Jun. 21, 2024), https://perma.cc/6ZF2-2FQN ("NJOY TPL").

youth." *See, e.g.*, Pet. App. 167a. The denial orders explained that this "evidence could have been provided using a randomized controlled trial and/or longitudinal cohort study that demonstrated the benefit of your flavored ends [sic] over an appropriate comparator tobacco-flavored ends [sic]," or "other evidence" that "reliably and robustly evaluated the impact of the new flavored vs. Tobacco-flavored [sic] products on adult smokers' switching or cigarette reduction over time." Pet. App. 167a-168a. FDA also explained that because this "key evidence" was "absent," the agency "did not proceed to assess other aspects of the applications" (*e.g.*, the proposed marketing and sales-access-restriction plans). Pet. App. 168a.

Each of FDA's denial orders was based on an internal document titled "Technical Project Lead ("TPL") Review." *See, e.g.*, Pet. App. 177a. Although the TPL reviews were not word-for-word copies of FDA's August 17, 2021 Memorandum, the TPL reviews were substantively the same as the Memorandum, using much of the same language and references. For example, the TPL reviews repeated the footnote about declining to review the applicants' proposed marketing and sales access restriction plans "for the sake of efficiency." *Compare, e.g.*, Pet. App. 200a-201a n.xix *with* J.A.265 n.xxii. As another example, with one exception, the 66 publications listed in the "References" section of the TPL reviews were the same 66 publications listed in the "References" section of the Memorandum. *Compare*, *e.g.*, Pet. App. 216a-225a *with* J.A.271-80.

Despite FDA's claim that the July 9, 2021 memorandum was superseded, FDA's "fatal flaw" analysis is substantially reflected in the internal "scientific review" forms the agency used to review Respondents' applications. J.A. 615-38. The review forms were "check the box" in nature and only inquire into whether the application contains a randomized controlled trial, longitudinal cohort study, or "other evidence" comparing the flavored products against tobacco-flavored products in terms of switching or cigarette reduction:

Presence of Evidence for Flavored ENDS Products

Criterion A	Present		Absent
Randomized Controlled Trial (RCT) on new product use and smoking behavior	☐		☒
Instructions: To select "Present", all of the following boxes must be checked "Yes":	**Yes**	**No**	**N/A**[2]
Was the RCT conducted using new products?	☐	☐	☒
Does the RCT include a tobacco-flavored arm and a flavored product arm[3]?	☐	☐	☒
Do the outcomes include users' ENDS and smoking behavior to assess switching and/or cigarette reduction (e.g., measures of cigarettes per day, smoking cessation, ENDS use)?	☐	☐	☒
Comment(s): N/A			

Criterion B	Present		Absent
Longitudinal Cohort Study (LCS) on new product use and smoking behavior	☐		☒
Instructions: To select "Present", all of the following boxes must be checked "Yes":	**Yes**	**No**	**N/A**[2]
Was the LCS conducted and does it include users of new products who are followed over time?	☐	☐	☒
Was use of tobacco-flavored products and other flavored products assessed[3]?	☐	☐	☒
Do outcomes include users' ENDS and smoking behavior to assess switching and/or cigarette reduction (e.g., measures of cigarettes per day, smoking cessation, ENDS use)?	☐	☐	☒
Comment(s): N/A			

[2] Not applicable, because no such study was present.
[3] Check "yes" if at least one non-tobacco flavored product is compared to a tobacco-flavored product.

Criterion C
Other evidence in the PTMA(s) related to potential benefit to adults
None

J.A.617-20.

I. FDA's Final PMTA Rule

FDA published its final PMTA rule just weeks after FDA issued nearly identical denial orders to Respondents and hundreds of other applicants. FDA, Premarket Tobacco Product Applications and Recordkeeping Requirements, Final Rule, 86 Fed. Reg. 55300 (Oct. 4, 2021) ("Final Rule"). The Final Rule confirms FDA's pledge to make individualized determinations "based on all of the contents of the application" and not on "one static set of requirements" or "series of criteria that either all products or a specific subset of products must meet." *Id*. at 55320, 55385-86, 55390.

J. Procedural History

Unable to sell its e-liquids without the threat of civil or criminal penalties and threatened with the imminent closure of its business, J.A.644, Triton sought an emergency stay of its denial orders from the Fifth Circuit. A unanimous motions panel granted the motion. Pet. App. 144a-165a. After a divided merits panel denied Respondents' petitions for review, *id.* at 99a-144a, the court ordered rehearing *en banc*, *id*. at 334a.

The en banc court held that FDA violated "[f]our well-established and longstanding principles of

administrative law independently." *Id.* at 21a. First, FDA failed to provide applicants "fair notice" of the agency's new requirements. *Id.* at 26a-41a. Second, FDA "failed to acknowledge its multiple changes in position" between its pre-application deadline guidance and its denial orders. *Id.* at 41a-48a. Third, FDA "change[d] its position" and then faulted Respondents for "relying in good faith" on the prior position. *Id.* at 48a-51a. Finally, FDA "invent[ed] post hoc justifications" for failing to "read the marketing plans it previously said were critical" when it claimed "the mere existence of flavor was sufficient to justify denial." *Id.* at 21a-26a.

SUMMARY OF ARGUMENT

The Fifth Circuit correctly held FDA's denial orders were arbitrary and capricious.

A. Basic administrative law principles require that agencies (1) provide the public with fair notice of regulatory requirements, including changes to those requirements; and (2) consider the public's reliance interests when changing those requirements. FDA violated those principles when it denied Respondents' applications to continue to market their bottled e-liquids.

Prior to the application deadline, FDA told the public that applications should focus on whether the proposed products had lower levels of harmful constituents than traditional tobacco products and whether the proposed products would lead to an overall decrease in adverse health effects by transitioning smokers to less harmful products. FDA also told the public that an applicant's plans to keep

the proposed products out of the hands of youth would be "critical" to the agency's evaluation of applications.

Respondents' applications included data and information in line with FDA's publicly stated expectations. But ten months after the application deadline FDA decided it would only authorize flavored ENDS if they were more effective than tobacco-flavored ENDS at helping smokers quit or reduce their use of cigarettes. FDA also decided that this showing would have to be made through a randomized controlled trial, longitudinal cohort study, or some "other evidence" comparing the applicant's flavored ENDS to tobacco-flavored ENDS over time. And FDA decided it would ignore applicants' plans to keep their products out of the hands of youth.

B. Despite FDA's claim to the contrary, the agency's new requirements did not evolve through case-by-case adjudication. Instead, FDA adopted the new requirements through a substantive rule—an internal memorandum that was not tied to any particular application and that the agency only later applied when adjudicating applications. FDA violated the APA by failing to follow the APA's notice-and-comment process when it adopted this substantive rule. And, even if FDA's new rule was "interpretive" rather than substantive, the Food, Drug, and Cosmetic Act ("FDCA") and FDA regulations required the agency to give the public advance notice of the rule.

C. FDA's admitted error in failing to consider Respondents' marketing and sales-access restriction plans was prejudicial, not harmless. Because FDA never identified the specific measures it

had previously considered and rejected when reviewing other applications, the Court has no way of determining whether there were material differences between those plans and Respondents' plans. Accepting FDA's bald assertion that non-record, undisclosed evidence shows harmless error would require Respondents to meet an "unreasonable evidentiary burden" and vitiate the requirement that agencies engage in reasoned decisionmaking.

Moreover, when FDA recently authorized a menthol-flavored ENDS, it found that the applicant's proposed marketing restrictions, which were no more restrictive than Respondents' proposed restrictions, were "robust" and may limit youth exposure to the applicant's products. Therefore, FDA cannot claim that its failure to review Respondents' marketing plans was harmless.

ARGUMENT

A. FDA Changed its Standard for Marketing Authorization Without Fair Notice, Adequate Explanation, or Consideration of Reliance Interests

Without notice, FDA abandoned the explanation of the statutory standard for marketing authorization it provided before the application deadline and foisted onto manufacturers a secret requirement that flavored ENDS be more effective than tobacco-flavored ENDS in promoting smoking cessation. Before the deadline, FDA told applicants that they were free to choose and justify comparator products and said nothing about comparing flavored products to tobacco-flavored products. Ten months

after the deadline, and overwhelmed with applications for millions of products, FDA secretly adopted a new requirement for evidence that flavored products better promote switching than tobacco-flavored products over time and then denied Respondents' applications on that basis. FDA engaged in quintessential arbitrary agency action.

Due process and principles of administrative law require that an agency "provide regulated parties fair warning" of the conduct the agency "prohibits or requires" and agencies cannot "unfair[ly] surprise" a party by penalizing it for "good-faith reliance" on the agency's prior positions. *Christopher v. SmithKline Beecham Corp.*, 567 U.S. 142, 156-57 (2012). Nor may an agency impose new requirements without notice after a regulated party has relied on the agency's prior representations. *See FCC v. Fox Television Stations, Inc.*, 556 U.S. 502, 515 (2009) ("An agency may not, for example, depart from a prior policy *sub silentio*."); *see also United States v. Nixon*, 418 U.S. 683, 696 (1974); *Rollins Env't Servs. (NJ), Inc. v. EPA*, 937 F.2d 649, 654 n.1, 655 (D.C. Cir. 1991) (Edwards, J., concurring in part and dissenting in part). Lower courts have interpreted "fair warning" to require that agencies communicate with "ascertainable certainty" the agency's interpretation or standard with which regulated parties must conform. *ExxonMobil Pipeline Co. v. United States DOT*, 867 F.3d 564, 578 (5th Cir. 2017); *Gen. Elec. Co. v. EPA*, 53 F.3d 1324, 1328-29 (D.C. Cir. 1995); *see also Martin v. OSHRC*, 499 U.S. 144, 158 (1991) (noting that lack of a pre-enforcement warning of interpretation of statute adopted in administrative adjudication raises questions about "the adequacy of notice to regulated parties"). Lower

courts have also concluded that the "dismissal of an application . . . is a sufficiently grave sanction to trigger this duty to provide clear notice." *Satellite Broadcasting Co. v. FCC*, 824 F.2d 1, 3 (D.C. Cir. 1987).

A "searching and careful" review of the record, *March v. Or. Nat. Res. Council*, 490 U.S. 360, 378 (1989), shows that FDA violated these basic principles of administrative law in at least three distinct ways: (1) FDA secretly imposed a new longitudinal comparative efficacy evidence requirement after the fact; (2) FDA changed its requirements, including the types of evidence it would consider, without explanation; and (3) FDA failed to consider Respondents' reliance interests.

1. FDA Secretly Imposed a New Requirement After the Fact.

FDA does not dispute that prior to the agency's August 26, 2021 press release, it made no public suggestion of any need to compare flavored and tobacco-flavored ENDS products in terms of their effectiveness at supporting smoking cessation over time. Yet such longitudinal comparative efficacy evidence became the *sine qua non* for applications after FDA developed its July 9, 2021 "fatal flaw" memorandum and August 17, 2021 memorandum; the July 9, 2021 memorandum labeled the longitudinal comparative efficacy study requirement a "standard for evidence," and observed that "any application lacking this evidence will likely receive a marketing denial order." J.A.242-43. The Fifth Circuit properly labeled FDA's actions a "regulatory switcheroo." Pet. App. 4a.

1. Before the September 9, 2020 deadline, FDA made no mention of any requirement to use flavor as a determining factor to compare one ENDS product against another with regard to switching and cessation of combustible cigarette use. Instead, FDA emphasized that in determining whether any ENDS product met the statutory standard, FDA would focus on (i) whether the constituents were less harmful than other tobacco products; (ii) whether the product presented a lower risk of disease than other tobacco products; and (iii) whether marketing the product would lead to an overall decrease in morbidity and mortality from tobacco product use.[21]

Indeed, FDA never recommended or required a *single* study that differed for flavored ENDS products than for tobacco-flavored ENDS products at all.[22] Rather, FDA repeatedly told applicants, including in public meetings and guidance,[23] that they could freely

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[21] 2018 FDA Presentation at 32.

[22] FDA attempts to minimize this fact by observing that "[m]ost of [the Guidance] concerned e-cigarettes generally, rather than flavored products in particular." Pet. Br. at 18.

[23] While FDA emphasizes that the slide deck at the public meeting stated that the presentation "does not represent Agency position or policy," Pet. Br. at 25, this observation only begs the question of whether applicants could possibly rely on *anything* the agency said about the required contents of applications, particularly when FDA advertised the purpose of the meetings as being "to improve public understanding . . . on the policies and processes for the submission and review of [PMTAs]." FDA, Tobacco Product Application Overview – A Public Meeting (Oct. 22, 2018), https://bit.ly/3FhPxJi. FDA itself relies on its own PMTA Guidance before this Court even though it contains a similar disclaimer, J.A.5, and specifically directed applicants to rely on the agency's "published guidance" and "webinars."

select the tobacco products against which they elected to compare their products and need merely provide a justification or rationale for their selection.[24,25] Indeed, shortly before the application deadline, FDA expressly told another applicant that the agency did "not have specific requirements for evaluating comparator products in studies."[26] And, in the section of its PMTA Guidance focused specifically on flavored products, FDA said nothing about comparing them to tobacco-flavored products. J.A.87-88.

However, ten months after Respondents filed their applications, FDA issued its internal memoranda requiring "evidence that can demonstrate whether an applicant's new non-tobacco-flavored product(s) will provide an incremental benefit to adult smokers relative to the applicant's tobacco-flavored product(s)." J.A.243. In contrast to FDA's previous statements disclaiming the need for any particular type of study, *see*, *e.g.*, J.A.28, 67, 84 Fed. Reg. at

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J.A.179-80. In any event, the D.C. Circuit has rejected any contention that such boilerplate disclaimers control the legal effect of agency statements. *See Appalachian Power Co. v. EPA*, 208 F.3d 1015, 1022-23 (D.C. Cir. 2000).

[24] 2018 FDA Presentation at 11, 20.

[25] If FDA recommended Respondents to compare their e-liquids against any particular tobacco product, it was the combustible cigarette, 2018 FDA Presentation at 11, and Respondents did just that.

[26] FDA Letter to Bidi Vapor LLC dated May 8, 2020, Corrected Appendix —Volume II, p. 28 of 147, FDA-BIDIVAPOR-005277, Bidi Vapor LLC v. FDA, No. 21-13340 (11th Cir. Dec. 3, 2021).

50619, or any particular comparator product, 2018 FDA Presentation at 11, 2019 FDA Presentation at 13, J.A.30-31, FDA's August 26, 2021 press release stated that FDA now required the studies it originally stated it did not need, Pet. App. 154a. Cribbing language from its July 9, 2021 memorandum, FDA stated that the required comparative efficacy evidence "would likely be in the form of a randomized controlled trial or longitudinal cohort study, although the agency does not foreclose the possibility that other types of evidence could be adequate if sufficiently robust and reliable and performed over time." *Id.* FDA provided no other indication of what could constitute sufficient "other" evidence.

Consistent with FDA's previous explanation of the statutory standard, Respondents' applications contained "voluminous, robust scientific studies" that showed "[ENDS] induce adults to switch from smoking (and thus save lives)." Pet. App. 32a. The applications referenced "peer-reviewed scientific studies involving unflavored products to draw inferences about flavored products (including at least one study that reviewed randomized controlled trials and longitudinal cohort studies to show the net public health benefits of [ENDS])." *Id.* at 17a. But FDA engaged in a check-the-box review, and finding neither of the two now-required longitudinal comparative efficacy studies or other evidence pitting Respondents' flavored e-liquids against tobacco-flavored ENDS in terms of switching efficacy over time, denied the applications because they "did not show *flavored* e-cigarettes promote more switching than *unflavored* ones." *Id.* at 32a.

Before applications were due, FDA assured manufacturers that no specific studies—including randomized controlled trials—were required, *see*, *e.g.*, J.A.27-30, 2018 FDA Presentation at 26, 2019 FDA Presentation at 30, and said its evaluation would focus on the products' harm profile and whether their marketing would decrease overall morbidity and mortality from tobacco product use, 2018 FDA Presentation at 32; 2019 FDA Presentation at 34. But FDA denied Respondents' applications based on entirely different criteria: that they lacked evidence that Respondents' flavored products were more effective in promoting switching than tobacco-flavored products over time. For this reason alone, FDA's denial orders are arbitrary and capricious and must be set aside.

2. FDA claims that the Fifth Circuit erroneously "concluded that the FDA had an affirmative obligation to issue specific guidance that gave applicants 'fair notice' of how it would evaluate flavored products," and that such an obligation is inconsistent with both the TCA and the APA. Pet. Br. at 25-27. FDA overstates the Fifth Circuit's actual holding. The Fifth Circuit did not mandate that FDA, in a vacuum, explain how the agency would evaluate flavored ENDS; rather, the Fifth Circuit merely concluded, as due process requires, that to the extent FDA *did* issue such guidance, the agency not change the requirements set forth therein without consideration of applicants' reasonable reliance interests, proper notice to applicants, and a reasonable opportunity for applicants to conform to the changed requirements. Pet. App. 45a-48a.

FDA also claims that the Fifth Circuit impinges on FDA's prerogative to "develop a regulatory standard" through adjudication. Pet. Br. at 27. However, as FDA's wholesale importation of significant sections of its "rescinded" August 17, 2021 memorandum into the nearly identical TPL reviews issued to Respondents and hundreds of other denied applicants reflects, FDA's imposition of the longitudinal comparative efficacy standard was not a product of "case-by-case evolution." *SEC v. Chenery Corp.*, 332 U.S. 194, 202-03 (1947). Rather, as explained *infra* at pages 47-49, FDA's longitudinal comparative efficacy standard bears all the hallmarks of a substantive rule imposed without notice and comment.

The Fifth Circuit traced the fair notice requirement to a line of circuit court cases dating back more than 55 years. *See* Pet. App. 26a-31a (citing, *inter alia*, *Radio Athens, Inc. v. FCC*, 401 F.2d 398, 404 (D.C. Cir. 1968) ("[I]ndustry is . . . entitled to expect rules defining the required content of applications that are reasonably comprehensible to men acting in good faith. . . . When the sanction is as drastic as dismissal . . . , elementary fairness compels clarity in the notice of the material required as a condition for consideration.")). FDA claims that the Due Process Clause "does not apply when a private party approaches the government to seek a benefit to which it lacks an established entitlement." Pet. Br. at 27. To the extent FDA means to claim that the fair notice requirement does not apply at all, it was "undisputed" below "that the fair notice doctrine applies," Pet. App. 29a, and so FDA has forfeited any argument to the contrary. *OBB Personenverkehr AG v.*

Sachs, 577 U.S. 27, 37 (2015); *see also Cutter v. Wilkinson*, 544 U.S. 709, 718 n.7 (2005) ("[W]e are a court of review, not of first view."). And, regardless of whether the fair notice obligation is rooted in the Due Process Clause itself or simply long-established circuit court precedent, the "requirement has now been thoroughly incorporated into administrative law." *Gen. Elec.*, 53 F.3d at 1329 (cleaned up).[27] And, as the Fifth Circuit noted, this line of cases includes denials of license applications that, if anything, would result in less severe consequences to the applicants than the denial orders that would "unquestionably put [Respondents] out of business." Pet. App. 28a-29a (citing, *inter alia*, *Satellite Broadcasting*, 824 F.2d at 3). Elementary fairness required that FDA, once it had explained the required contents of an application, not impose new and different requirements *sub silentio* and then deny the applications based on those new requirements without affording applicants an opportunity to satisfy them. Yet, in denying Respondents' applications because they lacked specific longitudinal comparative efficacy evidence, that is exactly what FDA did here.

3. Trying to minimize its about-face, FDA dances around its new requirement by suggesting the denial orders resulted from Respondents' purported failure to meet their burden of "showing" that

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[27] It goes without saying that no constitutional basis is required to find agency action arbitrary or capricious under 5 U.S.C. § 706. Indeed, this Court has never cited the Due Process Clause in an APA case as the basis for the rule that agencies must account for affected parties' "serious reliance interests" engendered by existing agency policy before changing that policy. *FCC v. Fox Television Stations,* 556 U.S. at 515.

marketing their e-liquids would be appropriate for the protection of the public health. Pet. Br. at 18. FDA's position elides the fact that Respondents only "failed" to meet their evidentiary burden because FDA belatedly (and secretly) required Respondents to show their flavored e-liquids were more effective at promoting smoking cessation than tobacco-flavored ENDS—the substantive component of FDA's new requirements.

FDA also references its prior statements about "bridging," Pet. Br. at 23, which is "inferring the effects of one product from studies about other products." But, again, FDA ignores that it *never* told applicants that they needed to compare their flavored products to tobacco-flavored products in terms of their efficacy at promoting switching from combustible cigarettes. Quite the opposite, FDA told applicants that they were free to select a comparator product of their choosing and simply had to justify that selection. 2018 FDA Presentation at 11; 2019 FDA Presentation at 13; J.A.30-31. For this reason, Respondents compared their flavored ENDS not only to combustible cigarettes, but also to a heat-not-burn product, IQOS, that FDA had previously authorized. *See, e.g.*, J.A.324, 414.

FDA also argues that its PMTA Guidance "made clear that FDA regarded flavored products as materially different from, rather than similar to, unflavored products." Pet. Br. at 24. But the two-paragraph section to which FDA cites says nothing about comparing flavored ENDS to tobacco-flavored ENDS, much less with respect to switching or smoking cessation. J.A.87-88.

4. FDA claims that the Fifth Circuit misinterpreted the record by concluding that the agency, without warning, required applicants to submit a randomized controlled trial or longitudinal cohort study. Pet. Br. 20-22. But, as the Fifth Circuit observed, while FDA did include a "single sentence regarding 'other' scientific evidence" of benefits in its "check-the-box" scientific review forms, "FDA made clear it could be persuaded by 'other evidence' '*only* if it reliably and robustly evaluated the impact of the new flavored vs. Tobacco flavored products on adult smokers' switching or cigarette reduction *over time*." Pet. App. 36a.[28] And, "[i]f 'reliably and robustly' evaluating impact 'over time' . . . means something else [other than a requirement for direct observations and controlled scientific studies], petitioners (and the courts) are left simply to imagine what the agency might have had in mind." Pet. App. 37a. Here, as before the court below, "FDA . . . do[es] not say what 'other evidence' [Respondents] might have supplied to win approval." *Id.*

[28] The circuit courts that have ruled in favor of FDA have consistently overlooked or downplayed the fact that any "other evidence" must still be of comparative efficacy in promoting smoking cessation between a flavored and tobacco-flavored product over time, and instead oversimplified the issue by framing it as one of a failure to provide "robust" and "reliable" evidence or "valid scientific evidence." *See*, *e.g.*, *Prohibition Juice Co. v. FDA*, 45 F.4th 8, 21-23 (D.C. Cir. 2022); *Lotus Vaping Techs., LLC v. FDA*, 73 F.4th 657, 672-73 (9th Cir. 2023), pet. for cert. pending, No. 23-871 (filed Feb. 9, 2024).

5. FDA also claims that it found Respondents' literature review "inadequate" to support their applications for their flavored e-liquids. Pet. Br. at 20. However, the literature review was inadequate solely because, as FDA admits in the very same paragraph of its brief, "the literature does not establish that flavors differentially promote switching amongst [e-cigarette] users." *Id*. In other words, Respondents' evidence was "inadequate" only because FDA now required a showing—through a randomized controlled trial, longitudinal cohort study, or some unspecified "other evidence"—that Respondents' flavored e-liquids "differentially promote switching" in smokers when compared to tobacco-flavored ENDS.[29]

6. FDA likewise argues that Respondents' evidence "did not support Respondents' scientific claims" that the benefits of their flavored e-liquids outweighed the risks. Pet. Br. at 20. However, FDA reached this conclusion only because, contrary to its promises in the PMTA Guidance to weigh all evidence in the applications, FDA assigned a set "risk" value to all flavored ENDS products ten months after the submission deadline and then refused to consider any countervailing evidence of benefits besides longitudinal comparative efficacy evidence. As the Fifth Circuit found, "it is flatly untrue that [Respondents'] 'other evidence' was 'None,'" notwithstanding FDA's check-the-box form. Pet. App.

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[29] It thus "blinks reality," *Egbert v. Boule*, 596 U.S. 482, 520 (2022) (Sotomayor, J., dissenting), to conclude that FDA does not now require that "robust and reliable" evidence "take the form of new studies or specific kinds of studies," as FDA claims, Pet. Br. at 23, 25.

at 38a. Respondents' applications included what FDA had said could be sufficient to address smokers' cessation behavior—surveys, "published studies and articles, as well as subject matter databases, related to topic areas identified in FDA's PMTA Guidance." *Id.* FDA just ignored this evidence because it was not the type of product-specific longitudinal comparative efficacy study evidence that, months after the fact, FDA decided it would now require. *See* Pet. App. 168a ("The review concluded that key evidence demonstrating [appropriate for the protection of the public health] is absent. Therefore, scientific review did not proceed to assess other aspects of the applications."), 228a (same), 280a (same and rejecting cross-sectional survey because "it does not evaluate the specific products in the application(s) or evaluate product switching or cigarette reduction resulting from use of these products over time").

Because this evidentiary requirement was never referenced, much less explained, in any of FDA's pre-submission deadline communications to applicants, Respondents lacked fair warning that FDA would require such evidence and the denial orders were arbitrary and capricious.[30]

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[30] Moreover, to the extent that FDA claims that its denials were premised on a conclusion that "[R]espondents' evidence did not sufficiently support the claims in their applications that 'flavors are crucial to getting adults smokers to make the switch and stay away from combustible cigarettes,'" Pet. Br. at 19-20, 24, FDA's argument amounts to an impermissible *post hoc* rationalization. *DHS v. Regents of the Univ. of Cal.*, 591 U.S. 1, 23 (2020). FDA's scientific review forms, TPL reviews, and denial orders make no reference to these claims by Respondents.

2. FDA Changed the Types of Evidence It Would Consider Without Explanation.

Comparing FDA's statements regarding the evidence it would accept before the application deadline and after the July 9, 2021 "fatal flaw" memorandum underscores that the denial orders result from FDA's belatedly moving the regulatory goalposts without explanation.

1. To lawfully change its position on evidentiary requirements, FDA must have, at minimum, acknowledged the change, offered a "reasoned explanation" for "disregarding facts and circumstances that underlay or were engendered by the prior policy," and offered applicants a reasonable opportunity to conduct the newly required, product-specific studies and update their applications accordingly. *Encino Motorcars, LLC v. Navarro*, 579 U.S. 211, 221-22 (2016) (internal citations omitted). Nothing in FDA's internal memoranda, the TPL reviews, or the denial orders suggests that FDA considered applicants' reliance on FDA's prior statements, let alone determined their significance or attempted to weigh them against competing policy concerns. Nor is there any evidence that FDA considered other, less disruptive alternatives, such as allowing applicants an opportunity to conduct the required studies and amend their applications before the agency commenced substantive scientific review.[31]

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[31] FDA has historically allowed extensive amendment of applications after their submission and before substantive scientific review. *See*, *e.g.*, FDA, Technical Project Lead (TPL) Review of PMTA, PM0000491, PM0000492, 11-14 (Dec. 4, 2018),

Cf. Regents, 591 U.S. at 30 ("[W]hen an agency rescinds a prior policy its reasoned analysis must consider the alternatives that are within the ambit of the existing policy.") (cleaned up). Instead, when Triton advised FDA that it intended to conduct the newly announced studies, the agency ignored this notice and issued the denial order anyway.

2. FDA changed its evidentiary requirements in multiple respects. Before the deadline, FDA stated that no new clinical studies would necessarily be required and recommended single point-in-time consumer surveys on perception and intent to use the subject products while disclaiming a need for randomized clinical trials. 2018 FDA Presentation at 13, 16, 26; 2019 FDA Presentation at 30; J.A.28, 81-82. Then, based on its "completion of numerous scientific reviews over the last 10 months" (i.e., *after* the deadline) FDA rejected such studies as insufficiently reliable. Pet. App. 201a, 204a. FDA concluded that studies conducted "over time" in the form of a randomized controlled trial or longitudinal cohort study would "most likely" be needed, Pet. App. 181a & n.vi, and denied Respondents' applications for failing to contain such evidence.

Similarly, before the deadline, FDA repeatedly represented that it did not expect long-term clinical studies would be needed, *see*, *e.g.*, J.A.28, 67, 84 Fed. Reg. at 50619; afterward, as the Fifth Circuit motions panel found, FDA "at the very least created a strong

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https://tinyurl.com/2p83ymvb (thirteen amendments); *see also* 21 C.F.R. § 1114.9.

presumption that such evidence is required." Pet. App. 159a.

Before the deadline, FDA also promised to "weigh[]*all* of the potential benefits and risks from the information contained in the [application] to make an overall determination" on marketing authorization. J.A.27 (emphasis added). FDA's denial orders, however, stated that the agency "did not proceed to assess other aspects of the applications" beyond whether they contained longitudinal comparative efficacy evidence. Pet. App. 168a, 280a.

Black-letter administrative law "demand[s] that [an agency] display awareness that it is changing position," *FCC v. Fox Television Stations,* 556 U.S. at 515; *accord Encino Motorcars*, 579 U.S. at 222. As the foregoing illustrates, FDA's claim that it never changed position is not only counterfactual, but also a tacit admission that the agency both failed to acknowledge its change in position and to provide a reasoned explanation for the change.

3. FDA Failed to Consider Respondents' Reliance Interests.

FDA's changed position created unfair surprise and failed to consider Respondents' reliance interests.

1. "When an agency changes course . . . it must be cognizant that longstanding policies may have engendered serious reliance interests that must be taken into account." *Regents*, 591 U.S. at 30 (quoting *Encino Motorcars*, 579 U.S. at 221-22). Because FDA was "not writing on a blank slate," but had provided applicants extensive instructions about what to include in their submissions, the agency was

"required to assess whether there were reliance interests, determine whether they were significant, and weigh any such interests against competing policy concerns." *Id*. at 33. There is no evidence that FDA did any of the foregoing.

2. FDA violated this basic administrative law principle by changing its application requirements after Respondents had already submitted their applications. Respondents' reliance interests were particularly critical here because they were provided no opportunity to amend their applications to meet FDA's new requirements (even through Triton specifically sought to do so). J.A.642-43. Additionally, FDA's deferred enforcement policy had allowed Respondents to continue selling their e-liquids while their applications were pending, but the denial orders required them to immediately cease sales. Pet. App. 167a. Respondents were threatened with substantial civil and even criminal penalties for selling "adulterated" tobacco products if they failed to comply. *See* 21 U.S.C. §§ 387b(6)(A), 331(a), 333(a)(1), 333(f)(9). The consequence of FDA's failure to consider Respondents' reliance interests was thus nothing less than the immediate closure of Respondents' businesses. J.A.644.

3. Respondents' reliance on FDA's pre-deadline statements and guidance, which contradicted what FDA later stated in its denial orders and supporting TPL reviews, was reasonable. FDA now claims that the Fifth Circuit "defer[red]" to Respondents' "incorrect but purportedly reasonable interpretation" of agency guidance. Pet. Br. at 29. But the court below did not conclude that Respondents'

interpretation of FDA's statements was either "correct" or "incorrect"; instead, it found that "FDA flip flopped" when it denied Respondents' "applications because they did not provide data from 'a randomized controlled trial and/or longitudinal cohort study' or other comparably robust evidence" to show that their "flavored [e-liquids] promote more switching [from cigarettes] than unflavored [ENDS]." Pet. App. 32a. To the extent FDA claims that it "has not changed its actual policy here," Pet. Br. at 30, it violates the principle that when an agency "wishes to use [its own] interpretation to cut off a party's right, it must give full notice of its interpretation." *Satellite Broadcasting*, 824 F.2d at 4; *accord Salzer v. FCC*, 778 F.2d 869, 875 (D.C. Cir. 1985) ("The quid pro quo for stringent acceptability criteria is explicit notice of all application requirements. . . . [An agency] cannot reasonably expect applications to be letter-perfect when . . . its instructions for those applications are incomplete, ambiguous or improperly promulgated."). The salient point is that FDA's guidance failed to provide *any notice at all* that FDA would require longitudinal comparative efficacy evidence for flavored products. *See* Pet. App. 18a ("FDA said nothing to acknowledge that its new requirement for scientific studies conflicted with its previous guidance.").

4. FDA cites to *Loper Bright Enterprises v. Raimondo*, 144 S. Ct. 2244, 2261 (2024), for the proposition that "the APA requires reviewing courts to 'determine the best reading of the law 'by applying their own judgment.'" But *Loper Bright* is inapposite. The Fifth Circuit only held that if a regulated party reasonably interprets an agency's guidance, and the

agency then turns around and rejects the party's application based on a different—indeed, a wholly opposite—interpretation of the guidance, then the regulated party has been deprived of fair notice and is entitled to an opportunity to submit evidence that satisfies the newly clarified standard. These facts do not implicate *Loper Bright*.

4. FDA Also Changed Position as to Device Type Without Explanation.

As part of its "switcheroo," FDA also changed its position regarding the importance of device type in attracting youth without explanation. Before the application deadline, FDA recognized a "material distinction," Pet. App. 46a, between the different types of ENDS products, acknowledging in its Enforcement Guidance that youth "overwhelmingly prefer" cartridge-based devices and stressing the characteristics, such as small size, concealability, high nicotine content, and ease of use for the uninitiated, that such products share with disposable ENDS devices, but not bottled e-liquids, J.A.155-57.

FDA discarded these distinctions (and ignored the many characteristics cartridge-based and disposable devices share) in its August 2021 memorandum and TPL reviews. There, FDA did not differentiate flavored bottled e-liquids from cartridge-based or disposable ENDS when it came to youth initiation, but instead concluded that "across . . . different device types, the role of flavor is consistent." Pet. App. 191a. To support its conclusion that flavors drive youth initiation, FDA pointed out that after its Enforcement Guidance banned flavored cartridge-based products, a ten-fold increase occurred in high

school-aged youth using flavored *disposable* ENDS. Pet. App. 192a. But actual youth usage data failed to support FDA's new stance; from 2020 to 2021, as flavored cartridge-based ENDS were removed from the market, the percentage of high school-aged ENDS users using devices compatible with flavored bottled e-liquids like Respondents' actually *decreased* from 14.8% to 7.5% even as overall youth ENDS use fell dramatically.[32] This trend suggested that it was device features common to both cartridge-based and disposable devices, as opposed to flavors, that drove youth usage.

FDA's actions thus reflect two failings. *First*, FDA failed to acknowledge the change between its previous position—as reflected in the Enforcement Guidance—of distinguishing between device types (and considering closed-system ENDS devices with characteristics appealing to uninitiated youth differently than open-system e-liquids) and FDA's new position that "across . . . different device types, the role of flavor is consistent." *See Encino Motorcars*, 579 U.S at 221-22. *Second*, given the inconsistency between the actual data around youth usage and FDA's actions, the agency failed to "reasonably explain[]" why it abandoned its previous position. *FCC v. Prometheus Radio Project*, 592 U.S. 414, 423 (2021); *accord Encino Motorcars*, 579 U.S. at 222 (requiring

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[32] *Compare* Teresa W. Wang, et al., E-cigarette Use Among Middle and High School Students — United States, 2020, 69 MMWR 1310-12 (Sept. 18, 2020), https://perma.cc/MFP5-MB45, *with* Eunice Park-Lee, et al., Notes from the Field: E-Cigarette Use Among Middle and High School Students — National Youth Tobacco Survey, United States, 2021, 70 MMWR 1387, 1387-88 (Oct. 1, 2021), https://bit.ly/2ZSLenl.

agencies to provide a "reasoned explanation" for "disregarding facts and circumstances").

B. FDA Failed to Follow Notice and Comment Requirements

FDA's new requirement for longitudinal comparative efficacy evidence also constituted a rule adopted and enforced in violation of the APA's and FDCA's notice and comment requirements. The standard adopted in the August 17, 2021 memorandum and reflected in the TPL reviews issued to Respondents and hundreds of other applicants was a "rule" because it was "an agency statement of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy." 5 U.S.C. § 551(4). FDA's August 17, 2021 memorandum reflected many of the features of a preamble in a notice of proposed rulemaking. *See* 1 C.F.R. § 18.12 (stating that proposed rules "shall" include "a preamble which will inform the reader . . . of the basis and purpose for the rule"). The memorandum included nearly 11 single-spaced pages of analysis to support the new longitudinal comparative efficacy requirement, including 24 footnotes and 66 endnotes in a "References" section listing 66 publications, nearly all of which were articles from medical or scientific journals. J.A.245-80. And, although FDA purportedly "rescinded" the August 17, 2021 memorandum the day before it released its first wave of denial orders for failing to meet the new standard, the TPL reviews for each denial were substantively the same as the memorandum.

An agency "may not escape [the notice-and-comment] requirements of [5 U.S.C. §] 553 by labeling its rule an 'adjudication.'" *Safari Club Int'l v. Zinke*, 878 F.3d 316, 332 (D.C. Cir. 2017); *see also Nat'l Ass'n of Home Builders v. U.S. Army Corp of Eng'rs*, 417 F.3d 1272, 1285 (D.C. Cir. 1985) ("It is of course the [agency's] decision whether to proceed by rule or adjudication, but 'rules is rules,' no matter their gloss.") (cleaned up). And even though the APA does not require notice and comment for "interpretive rules," 5 U.S.C. § 553(b)(4)(A), to the extent the new longitudinal comparative efficacy requirement fits that definition, both the FDCA and FDA's own regulations required the agency to provide advance notice of such a rule. *See* 21 U.S.C. § 371(h)(1)(C)(i); 21 C.F.R. § 10.115(c)(1), (g).

As the Fifth Circuit found in a parallel case, it is "not a close call" that the "heightened" longitudinal comparative efficacy standard is a rule and not a mere "statement of policy" under 5 U.S.C. § 553(b)(4)(A). *See R.J. Reynolds Vapor Co. v. FDA*, 65 F.4th 182, 193-94 (5th Cir. 2023). The standard, as set forth in the August 17, 2021 memorandum and subsequent TPL reviews "appears on its face to be binding" and was "applied by [FDA] in a way that indicates it is binding." *Id.* (citing, *inter alia*, *Syncor Int'l Corp. v. Shalala*, 127 F.3d 90, 94 (D.C. Cir. 1997)). The new evidentiary standard requires that applications contain "the necessary type of studies," J.A.243, and has served as the basis for denial orders for over one million flavored ENDS products. The standard also "took away FDA reviewers' former discretion to consider individual PMTAs solely on their merits and

instead requires a cursory, box-checking review." *R.J. Reynolds Vapor Co.*, 65 F.4th at 193-94.[33]

FDA's failure to comply with the APA's notice and comment requirements for its new longitudinal comparative efficacy requirement provides an independent reason to affirm the Fifth Circuit's judgment. *See Thigpen v. Roberts*, 468 U.S. 27, 30 (1984) ("[W]e may affirm on any ground that the law and the record permit and that will not expand the relief granted below.").

C. FDA Committed Prejudicial Error When it Failed to Evaluate Respondents' Marketing Plans

FDA understandably concedes that it violated the APA when it failed to evaluate Respondents' plans to limit youth use of their products. Pet. Br. 36. After all, the TCA requires FDA's evaluation of applications to take into account "the increased or decreased likelihood that those who do not use tobacco products will start using such products." 21 U.S.C. § 387j(c)(4)(B). And FDA is on record as saying that the "information" in an applicant's marketing plan is "critical," "necessary," and "directly relevant" to its determination, including as to the "likelihood that

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[33] Further, FDA's new requirement, which allowed for the "*en masse*" denial of applications for flavored ENDS, Pet. App. 18a, amounted to a de facto new tobacco product standard FDA imposed without complying with the TCA's notice and comment requirements. *See* 21 U.S.C. § 387g(c), (d). Under the TCA, "tobacco product standards" regulate tobacco product "properties" and Congress restricted characterizing flavors in cigarettes under this provision. *See* 21 U.S.C. § 387g(a)(1)(A), 387(g)(4)(B)(i).

youth will use the tobacco product." 84 Fed. Reg. at 50581, 86 Fed. Reg. at 55324. But FDA failed to review the applications for any evidence beyond whether they contained the randomized controlled trials, longitudinal cohort studies, or "other evidence" pitting the subject flavored e-liquids against tobacco-flavored ENDS that FDA now demanded—that is, one "static set of requirements" that FDA specifically disclaimed in its Final Rule. 86 Fed. Reg. at 55385.

FDA's concession (Pet. Br. at 31, 36) that overlooking the marketing and sales-access restrictions plans was error underscores the agency's changed position. FDA's issuance of the denial orders without even considering, *inter alia*, whether any youth *actually use* Respondents' e-liquids or evidence that two-thirds of Respondents' customers are over the age of 35, Pet. App. 18a, "entirely failed to consider an important aspect of the problem." *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983).

FDA claims that its error was "harmless" because Respondents' marketing plans "replicat[ed] measures that the agency has considered and rejected" when reviewing other applications. Pet. Br. at 35.[34] But FDA has never identified those other applications or the specific restrictions proposed

[34] Indeed, to the extent that FDA now claims it requires "novel" marketing restrictions to potentially authorize a flavored ENDS product, Pet. Br. at 38, 41, that requirement, in addition to being a change in FDA's pre-application deadline position, is also an impermissible post hoc rationalization. *Burlington Truck Lines, Inc. v. United States*, 371 U.S. 156, 168 (1962). Nothing in either the denial orders or TPL reviews required "novel" restrictions.

therein. FDA also claims that Respondents' marketing plans were similar to those FDA identified as ineffective in its Enforcement Guidance. But the Enforcement Guidance suggested only that certain restrictions on the sale of *cartridge-based* products were ineffective; it did not say those restrictions would be ineffective if applied to bottled e-liquids. Indeed, the Enforcement Guidance identified specific "adequate measures" to prevent youth access that Respondents adopted, including age- and identity-verification restrictions. *See Bidi Vapor LLC v. FDA*, 47 F.4th 1191, 1198 (11th Cir. 2022).

FDA also claims that the actions it took after it denied Respondents' applications show that its error in ignoring Respondents' marketing plans was harmless. But FDA's most recent action—granting marketing authorization for flavored ENDS with marketing plans similar to Respondents' plans—confirms that FDA's error was, in fact, prejudicial.

1. The *Shinseki*/*Calcutt* Framework for Determining Whether Agency Error Is Prejudicial.

The APA directs courts to determine whether an agency error was prejudicial to a party challenging an agency action. *See* 5 U.S.C. § 706 ("In making the forgoing determinations [*e.g.*, whether to set aside an agency action because it is arbitrary and capricious], the court shall review the whole record or those parts of it cited by a party, and due account shall be taken of the rule of prejudicial error."). Section 706's "reference to 'prejudicial error' is intended to 'sum up in succinct fashion the 'harmless error' rule applied by the courts in the review of lower court decisions as well

as of administrative bodies.'" *Shinseki v. Sanders*, 556 U.S. 396, 406 (2009) (quoting Dept. of Justice, Attorney General's Manual on the Administrative Procedure Act 110 (1947)) (cleaned up)).

When "determining whether an error is harmless," courts must use a "case-specific application of judgment, based upon examination of the record," rather than "mandatory presumptions and rigid rules." *Shinseki*, 556 U.S. at 407. And courts should avoid imposing "an unreasonable evidentiary burden" or an "evidentiary barrier so high that it could never be surmounted." *Id.* at 408-09 (cleaned up).

When the agency decision at issue was "discretionary" and "highly fact specific and contextual," and the agency's error was a failure to "consider[] all relevant factors" when it made that decision, "the proper course, except in rare circumstances, is to remand to the agency for additional investigation or explanation." *Calcutt v. FDIC*, 598 U.S. 623, 628-30 (2023) (per curiam) (cleaned up). The reviewing court "is not generally empowered to conduct a *de novo* inquiry into the matter being reviewed and to reach its own conclusions based on such an inquiry." *Id.* at 629 (cleaned up). That is because the reviewing court "must judge the propriety of agency action solely on the grounds invoked by the agency." *Id.* at 624 (cleaned up).

2. FDA Did Not Identify the Other PMTA Marketing Restriction Measures to Which It Alludes in Its TPL Reviews.

In its TPL reviews on Respondents' applications, FDA acknowledged that the assessment of the "risk" that a significant number of youth will use a particular ENDS product "includes evaluating the appropriateness of the proposed marketing plan" for that product. *See, e.g.*, Pet. App. 200a; Pet. App. 308a. But in a footnote, FDA said it declined to evaluate Respondents' marketing plans "for the sake of efficiency." *See*, *e.g.*, Pet. App. 200a-201a, n.xix; Pet. App. 308a-309a, n.xix.

FDA explained that no review of Respondents' marketing plans was necessary because "to date, none of the ENDS PMTAs that FDA has evaluated have proposed advertising and promotion restrictions that would decrease appeal to youth to a degree significant enough to address and counter-balance the substantial concerns" about "youth use." *See*, *e.g.*, Pet. App. 200a-201a, n.xix; Pet. App. 308a-309a, n.xix. FDA also said it was "not aware of access restrictions that, to date, have been successful in sufficiently decreasing the ability of youth to obtain and use ENDS." *See*, *e.g.*, Pet. App. 200a-201a, n.xix; Pet. App. 308a-309a, n.xix.

But as Chief Judge Pryor observed in *Bidi Vapor*, "the footnote explaining that [FDA] did not consider the marketing plans because of [the agency's] experience was included in every Technical Project Lead report, as it appears in every report given to the six [petitioners in *Bidi Vapor*] and appears in the

sample report provided on [FDA's] website," 47 F.4th at 1203-04. Therefore "it is unclear which applications [FDA] evaluated before making the decision not to consider any marketing or sales-access-restriction plans or which marketing and sales-access proposals were included in the applications allegedly evaluated." *Id*. at 1204.[35]

FDA now argues that "any error in its decision not to evaluate Respondents' marketing plans was harmless" because Respondents have failed "to show any material difference between the measures proposed in [their] plan[s] and others that FDA has reviewed and rejected." Pet. Br. at 31-32. But because the TPL reviews offered no details about the marketing plans FDA allegedly "reviewed and rejected" before ignoring Respondents' plans, the Court has no way of determining whether there were material differences between the previously rejected plans and Respondents' plans. For that reason alone, the Court should reject FDA's harmless error argument.

Indeed, FDA cites no authority for the proposition that a court can accept an agency's bald assertion that non-record, undisclosed evidence shows an agency's error was harmless. To accept such an assertion would render the harmless error rule a dead letter, as it would require the party claiming prejudice

[35] The various petitioners in *Bidi Vapor* sought marketing authorization for both bottled e-liquids and disposable ENDS. 47 F.4th at 1200.

to meet "an unreasonable evidentiary burden." *Shinseki*, 556 U.S. at 408.

Moreover, to allow FDA to claim harmless error based on its alleged reliance on undisclosed information would stand the APA on its head. The APA requires agencies to engage in "reasoned decisionmaking." *Regents*, 591 U.S. at 16 (quoting *Michigan v. EPA*, 576 U.S. 743, 750 (2015)). And an agency "decision falls for the lack of a reason" if "the agency just asserts an ipse dixit," *St. Vincent Randolph Hosp., Inc. v. Price*, 869 F.3d 510, 513 (7th Cir. 2017) (Easterbrook, J.). Allowing an agency to avoid remand simply by claiming that the outcome would be the same would grant agencies *carte blanche* to ignore procedural safeguards and then insulate their decisions from meaningful judicial review. As the Fifth Circuit recognized, "an administrative agency cannot avoid judicial review by gaming the APA's remand rules." Pet. App. 59a-60a n.7.

FDA's authorities, *Little Sisters of the Poor Saints Peter & Paul Home v. Pennsylvania*, 591 U.S. 657 (2020), and *Department of Commerce v. New York*, 588 U.S. 752 (2019), do not dictate a different result. The discussion regarding harmless error in both cases was dicta, since the Court found the procedural requirements had been satisfied, and neither case involved a highly fact-dependent discretionary determination that required the agency to weigh multiple factors, as in *Calcutt* and here. *See Little Sisters of the Poor*, 591 U.S. at 683-84, *Dep't of Comm.*, 588 U.S. at 779-80. Also, as the *Bidi Vapor* court noted, the petitioner in *Prohibition Juice* made "concessions of harmless error . . . at oral argument."

47 F.4th at 1208; *see also Prohibition Juice*, 45 F.4th at 35-36 (Katsas, J., concurring) ("In joining the court's opinion, I do not understand it to foreclose the possibility of our finding prejudicial error in other cases where manufacturers press the prejudice point more forcefully."). Respondents have never made such concessions.

3. FDA's Enforcement Guidance Does Not Support FDA's Harmless Error Argument.

FDA also claims its Enforcement Guidance "explained that marketing and sales access restrictions had proved insufficient to address e-cigarette use among youth." Pet. Br. at 33-34.

But as Chief Judge Pryor explained in *Bidi Vapor*, "the 2020 Guidance *did not* express a determination by [FDA] that marketing and sales-access-restriction plans for flavored [ENDS] are categorically ineffective." 47 F.4th at 1208 (emphasis added). Rather, the Enforcement Guidance said only that some such "measures were insufficient to curb youth use of flavored, *cartridge-based products* based on their nature and popularity." *Id.* (emphasis added). As for "other kinds of [ENDS], including . . . flavored [bottled e-liquid] products, . . . the 2020 Guidance stated that [FDA] intended to consider the companies' marketing and sales-access-restriction plans." *Id.* The Enforcement Guidance does not support FDA's claim that the agency found sales and marketing restrictions were ineffective at preventing youth use of bottled e-liquids in general (let alone Respondents' bottled e-liquids specifically).

4. FDA's Recent Authorization of Flavored ENDS Refutes the Agency's Harmless Error Argument.

FDA discusses at length its October 2022 written analysis of why another applicant's proposed marketing plan was insufficient to prevent youth access. *See* FDA Br. at 34-35. It is unclear why FDA includes that summary in its brief. This Court has never held that an agency can satisfy the requirement to reasonably explain a decision issued to one regulated party by pointing to a later decision issued to a different regulated party. To the contrary, "[i]t is well established that an agency's action must be upheld, if at all, on the basis articulated by the agency itself." *Motor Vehicle Mfrs. Ass'n*, 463 U.S. at 50.

FDA also refers to its June 2024 authorization of NJOY's menthol-flavored ENDS products. *See* Pet. Br. at 47. That authorization flatly refutes FDA's harmless error argument in the case *sub judice*.

One basis for FDA's authorization of the NJOY menthol ENDS was the agency's determination that NJOY's proposed marketing restriction plans were "robust" and "may help further limit youth exposure to the new products." *See* FDA, NJOY TPL at 61.[36] FDA highlighted NJOY's promises to avoid "social media promotions" and to use only "models over the age of 45." *Id.*

But Respondents' proposed marketing plans included provisions similar to NJOY's. *See*, *e.g.*, J.A.353-54 (stating Triton does not "endorse or permit use of youthful looking models" or "utilize social media

[36] *Supra* n.20; available at https://perma.cc/6ZF2-2FQN.

influencers"); J.A.407 (stating Vapetasia e-liquids would not be promoted "by influencers . . . on social media, radio or television"). If anything, Respondents' proposed plans were more "robust" than NJOY's. *Compare* J.A.316-18, 341-54, 406-09 (Respondents' proposed plans) *with* NJOY TPL at 33-34 (NJOY's proposed plan). So, FDA cannot be heard to say its decision to ignore Respondents' proposed marketing plans was harmless because the agency would have found those plans were insufficient to limit youth access.

CONCLUSION

The Court should affirm the judgment below.

Respectfully submitted,

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APPENDIX

TABLE OF APPENDICES

APPENDIX — RELEVANT STATUTORY AND REGULATORY PROVISIONS

1. 5 U.S.C. § 551 provides:

Definitions

For the purpose of this subchapter [5 USCS §§ 551 et seq.]—

* * * * *

(4) "rule" means 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 or describing the organization, procedure, or practice requirements of an agency and includes the approval or prescription for the future of rates, wages, corporate or financial structures or reorganizations thereof, prices, facilities, appliances, services or allowances therefor or of valuations, costs, or accounting, or practices bearing on any of the foregoing;

(5) "rule making" means agency process for formulating, amending, or repealing a rule;

* * * * *

Appendix

2. 5 U.S.C. § 553 provides:

Rule making

* * * * *

(b) General notice of proposed rule making shall be published in the Federal Register, unless persons subject thereto are named and either personally served or otherwise have actual notice thereof in accordance with law. The notice shall include—

(1) a statement of the time, place, and nature of public rule making proceedings;

(2) reference to the legal authority under which the rule is proposed;

(3) either the terms or substance of the proposed rule or a description of the subjects and issues involved; and

(4) the Internet address of a summary of not more than 100 words in length of the proposed rule, in plain language, that shall be posted on the Internet website under section 206(d) of the E-Government Act of 2002 (44 U.S.C. § 3501 note) (commonly known as regulations.gov).

Except when notice or hearing is required by statute, this subsection does not apply—

(A) to interpretative rules, general statements of policy, or rules of agency organization, procedure, or practice; or

(B) when the agency for good cause finds (and incorporates the finding and a brief statement of reasons therefor in the rules issued) that notice and public procedure thereon are impracticable, unnecessary, or contrary to the public interest.

(c) After notice required by this section, the agency shall give interested persons an opportunity to participate in the rule making through submission of written data, views, or arguments with or without opportunity for oral presentation. After consideration of the relevant matter presented, the agency shall incorporate in the rules adopted a concise general statement of their basis and purpose. When rules are required by statute to be made on the record after opportunity for an agency hearing, sections 556 and 557 of this title [5 USCS §§ 556 and 557] apply instead of this subsection.

(d) The required publication or service of a substantive rule shall be made not less than 30 days before its effective date, except—

(1) a substantive rule which grants or recognizes an exemption or relieves a restriction;

(2) interpretative rules and statements of policy; or

(3) as otherwise provided by the agency for good cause found and published with the rule.

(e) Each agency shall give an interested person the right to petition for the issuance, amendment, or repeal of a rule.

Appendix

3. 21 U.S.C. § 371 provides:

Regulations and hearings

* * * * *

(h) Guidance documents.

(1)

(A) The Secretary shall develop guidance documents with public participation and ensure that information identifying the existence of such documents and the documents themselves are made available to the public both in written form and, as feasible, through electronic means. Such documents shall not create or confer any rights for or on any person, although they present the views of the Secretary on matters under the jurisdiction of the Food and Drug Administration.

(B) Although guidance documents shall not be binding on the Secretary, the Secretary shall ensure that employees of the Food and Drug Administration do not deviate from such guidances without appropriate justification and supervisory concurrence. The Secretary shall provide training to employees in how to develop and use guidance documents and shall monitor the development and issuance of such documents.

(C)

(i) For guidance documents that set forth initial interpretations of a statute or regulation, changes in interpretation or policy that are of more than a minor nature, complex scientific issues, or highly controversial issues, the Secretary shall ensure public participation prior to implementation of guidance documents, unless the Secretary determines that such prior public participation is not feasible or appropriate. In such cases, the Secretary shall provide for public comment upon implementation and take such comment into account.

* * * * *

4. 21 C.F.R. § 10.115 provides:

Good guidance practices.

* * * * *

(b) What is a guidance document?

(1) Guidance documents are documents prepared for FDA staff, applicants/sponsors, and the public that describe the agency's interpretation of or policy on a regulatory issue.

(2) Guidance documents include, but are not limited to, documents that relate to: The design, production, labeling, promotion, manufacturing, and testing of regulated products; the processing, content, and evaluation or approval of submissions; and inspection and enforcement policies.

(3) Guidance documents do not include: Documents relating to internal FDA procedures, agency reports, general information documents provided to consumers or health professionals, speeches, journal articles and editorials, media interviews, press materials, warning letters, memoranda of understanding, or other communications directed to individual persons or firms.

(c) What other terms have a special meaning?

(1) "Level 1 guidance documents" include guidance documents that:

(i) Set forth initial interpretations of statutory or regulatory requirements;

(ii) Set forth changes in interpretation or policy that are of more than a minor nature;

(iii) Include complex scientific issues; or

(iv) Cover highly controversial issues.

(2) "Level 2 guidance documents" are guidance documents that set forth existing practices or minor changes in interpretation or policy. Level 2 guidance documents include all guidance documents that are not classified as Level 1.

(3) "You" refers to all affected parties outside of FDA.

(d) Are you or FDA required to follow a guidance document?

(1) No. Guidance documents do not establish legally enforceable rights or responsibilities. They do not legally bind the public or FDA.

(2) You may choose to use an approach other than the one set forth in a guidance document. However, your alternative approach must comply with the relevant statutes and regulations. FDA is willing to discuss an alternative approach with you to ensure that it complies with the relevant statutes and regulations.

(3) Although guidance documents do not legally bind FDA, they represent the agency's current thinking. Therefore, FDA employees may depart from guidance documents only with appropriate justification and supervisory concurrence.

(e) Can FDA use means other than a guidance document to communicate new agency policy or a new regulatory approach to a broad public audience? The agency may not use documents or other means of communication that are excluded from the definition of guidance document to informally communicate new or different regulatory expectations to a broad public audience for the first time. These GGP's must be followed whenever regulatory expectations that are not readily apparent from the statute or regulations are first communicated to a broad public audience.

* * * * *

(g) What are FDA's procedures for developing and issuing guidance documents?

(1) FDA's procedures for the development and issuance of Level 1 guidance documents are as follows:

(i) Before FDA prepares a draft of a Level 1 guidance document, FDA can seek or accept early input from individuals or groups outside the agency. For example, FDA can do this by participating in or holding public meetings and workshops.

(ii) After FDA prepares a draft of a Level 1 guidance document, FDA will:

(A) Publish a notice in the FEDERAL REGISTER announcing that the draft guidance document is available;

(B) Post the draft guidance document on the Internet and make it available in hard copy; and

(C) Invite your comment on the draft guidance document. Paragraph (h) of this section tells you how to submit your comments.

(iii) After FDA prepares a draft of a Level 1 guidance document, FDA also can:

(A) Hold public meetings or workshops; or

(B) Present the draft guidance document to an advisory committee for review.

(iv) After providing an opportunity for public comment on a Level 1 guidance document, FDA will:

(A) Review any comments received and prepare the final version of the guidance document that incorporates suggested changes, when appropriate;

(B) Publish a notice in the FEDERAL REGISTER announcing that the guidance document is available;

(C) Post the guidance document on the Internet and make it available in hard copy; and

(D) Implement the guidance document.

(v) After providing an opportunity for comment, FDA may decide that it should issue another draft of the guidance document. In this case, FDA will follow the steps in paragraphs (g)(1)(ii), (g)(1)(iii), and (g)(1)(iv) of this section.

(2) FDA will not seek your comment before it implements a Level 1 guidance document if the agency determines that prior public participation is not feasible or appropriate.

(3) FDA will use the following procedures for developing and issuing Level 1 guidance documents under the circumstances described in paragraph (g)(2) of this section:

(i) After FDA prepares a guidance document, FDA will:

(A) Publish a notice in the FEDERAL REGISTER announcing that the guidance document is available;

(B) Post the guidance document on the Internet and make it available in hard copy;

(C) Immediately implement the guidance document; and

(D) Invite your comment when it issues or publishes the guidance document. Paragraph (h) of this section tells you how to submit your comments.

(ii) If FDA receives comments on the guidance document, FDA will review those comments and revise the guidance document when appropriate.

(4) FDA will use the following procedures for developing and issuing Level 2 guidance documents:

(i) After it prepares a guidance document, FDA will:

(A) Post the guidance document on the Internet and make it available in hard copy;

(B) Immediately implement the guidance document, unless FDA indicates otherwise when the document is made available; and

(C) Invite your comment on the Level 2 guidance document. Paragraph (h) of this section tells you how to submit your comments.