No. 22-1112

IN THE

Supreme Court of the United States

AVAIL VAPOR, LLC, *et al.*,

Petitioners,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION,

Respondent.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FOURTH CIRCUIT

REPLY BRIEF FOR PETITIONERS

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In a remarkable display of agency hubris, FDA ignores the requirement that it state "with 'ascertainable certainty' the standards with which the agency expects parties to conform," *ExxonMobil Pipeline Co. v. United States DOT*, 867 F.3d 564, 578-79 (5th Cir. 2017) (citing *Gen. Elec. Co. v. EPA*, 53 F.3d 1324, 1329 (D.C. Cir. 1995)). Instead, FDA argues that the Tobacco Control Act, when combined with an FDA Guidance, gave the ENDS industry adequate notice of the agency's longitudinal comparative efficacy study requirements for marketing authorization of non-tobacco-flavored ENDS, and that the entire industry simply failed to read those sources closely enough. That is the only way to understand FDA's argument given that the agency has denied 99 percent of the hundreds of thousands of applications filed for non-tobacco-flavored ENDS and has not granted a single such application.

For the reasons discussed below, FDA's "the entire industry got it wrong" argument and FDA's other arguments lack merit and this Court should grant the petition for writ of certiorari.

ARGUMENT

A. The Decision Below is Wrong.

FDA's denial of Petitioners' applications was arbitrary and capricious for two reasons: (1) FDA failed to put the public on notice that it would approve applications for non-tobacco-flavored ENDS only if the applications included data from randomized clinical trials, longitudinal cohort studies, or other studies conducted over time comparing the efficacy of the subject products to that of tobacco-flavored ENDS on adult smoking cessation; and (2) FDA

failed to evaluate Petitioners' proposed marketing and sales-access-restriction plans to limit youth use of their products. The circuit court's contrary conclusion is wrong, and FDA's efforts to defend it lack merit.

1. FDA argues (Opp. 7) that the TCA, when combined with its 2019 PMTA Guidance, put the public on notice of FDA's approval requirements for non-tobacco-flavored ENDS. In support of that argument, FDA points only to the fact that the TCA requires applicants to supply information that their product "presents less risk than other tobacco products" and that the 2019 Guidance recommended that an applicant "compare the health risks of its product to both products within the same category and subcategory, as well as products in different categories as appropriate." But "a party has fair notice" only "when, by reviewing the regulations and other public statements issued by the agency, it can identify with *ascertainable certainty* the standards with which the agency expects parties to conform." *Northstar Wireless, LLC v. FCC*, 38 F.4th 190, 216 (D.C. Cir. 2022) (emphasis added) (cleaned up). The quoted language from the TCA and 2019 Guidance can hardly be described as providing the industry with "fair notice" that FDA would consider approving applications for non-tobacco-flavored ENDS only if the applications included data from randomized clinical trials, longitudinal cohort studies, or other studies conducted over time comparing the efficacy of the products to that of tobacco-flavored ENDS on adult smoking cessation. *Christopher v. SmithKline Beecham Corp.*, 567 U.S. 142, 156 (2012). This highly specific longitudinal comparative efficacy requirement is far more particular than mere "comparative evidence" and the court below erred in concluding that "FDA told manufacturers about

the type and quality of evidence required to be included with their PMTAs." Pet. App 24a.

FDA ignores its *sub silentio* about-face on the types of studies that could provide persuasive data that an ENDS product (whether tobacco-flavored or non-tobacco-flavored) could help a smoker quit smoking. During its 2018 and 2019 public meetings, FDA specifically recommended that applicants include single-point-in-time studies on consumer perceptions and appeal of the subject products because such studies are "widely accepted" as predictors for initiation and cessation and would provide "useful information to FDA."[1] The 2019 Guidance similarly indicated that studies conducted at a single point in time (*e.g.*, cross-sectional studies, consumer perception studies) would provide persuasive data. CA.A260.[2] But when FDA later rejected Petitioners' applications, which included the single-point-in-time cross-sectional and

1. Petitioners' Petition for Certiorari contained an incorrect citation for FDA's presentation at its 2019 public meeting on page 7. The correct citation is Quida Holmes, MPH and Priscilla Callahan-Lyon, MD, *Premarket Tobacco Product Application Content Overview*, at 15, 18 (Oct. 28, 2019), https://perma.cc/B4CF-WLXH. *See also* Iilun Murphy, *Premarket Tobacco Product Application Content Overview*, at 13, 16 (Oct. 23, 2018), https://perma.cc/2JF4-J3ZR.

2. The 2019 Guidance stated: "Although randomized clinical trials could assess cessation behaviors of users of tobacco products, FDA believes this *would* also be true for observational studies (perception, actual use, or both) examining cessation behaviors." CA.A260 (emphasis added). In addition to perception studies, observational studies include, among other things, "cross-sectional" studies. *See* Federal Judicial Center, *Reference Manual on Scientific Evidence* 560 (3d ed. 2011) ("A third type of observational study is a cross-sectional study.").

consumer perception studies the agency had previously recommended, FDA took the new position that such studies are insufficient because they do not evaluate "behavior change over time." Pet. App. 82a.[3]

FDA concedes (Opp. 7) the 2019 Guidance told applicants that, "in general, FDA does not expect that applicants will need to conduct long-term studies to support an application." FDA implies that applicants should not have read that language to mean that perception

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3. FDA's new demand for longitudinal comparative efficacy evidence for non-tobacco-flavored ENDS was developed well *after* Petitioners submitted their applications in September 2020. In both its August 17, 2021 internal memorandum and its later TPL report supporting Petitioners' marketing denial order, FDA emphasized that:

> Our substantive review of PMTAs for ENDS and our completion of numerous scientific reviews *over the last 10 months* have deepened our understanding of the APPH evaluation with respect to behavior. *These reviews have clarified the position that the expectations for scientific evidence related to potential adult benefit can vary based on demonstrated risk to youth*. Although indirect evidence or bridged data from the literature may still be appropriate for many new products, including tobacco-flavored ENDS, robust and direct evidence demonstrating potential benefit has been needed when the known risks are high as with all flavored ENDS products. At the same time, *we have learned from experience that,* in the absence of strong direct evidence, we are unable to reach a conclusion that the benefit outweighs the clear risks to youth."

Compare CA.A81-82 (August 17, 2021 FDA internal memorandum; emphasis added), *with* Pet. App. 79a (TPL report).

and other single-point-in-time studies would be sufficient because the 2019 Guidance also told applicants that the agency wanted information on "long-term impact," and that such information could be "bridged" from already existing studies. (Opp. 7). But FDA does not explain how a suggestion for "long-term-impact" information "bridged" from other studies could have given applicants "fair warning" that consumer perception and other single-point-in time studies were *per se* inadequate, especially when the FDA's public meeting presentations and 2019 Guidance specifically recommended such studies.

Moreover, FDA, like the court below, wrongly limits its focus to only the 2019 Guidance, ignoring the multiple other instances—including during the 2018 and 2019 public meetings—when FDA encouraged applicants to conduct the very studies Petitioners submitted.

2. FDA asserts (Opp. 8) the court below correctly found no error in the agency's refusal to review Petitioners' plans to limit youth use of its products because FDA had found other applicants' "run-of-the-mill" plans were ineffective in preventing youth use. But as the Eleventh Circuit noted, FDA never provided specific details about other applicants' plans that the agency allegedly reviewed (let alone evidence showing that youth continued to use those applicants' products after those applicants implemented their plans). *See Bidi Vapor LLC v. FDA*, 47 F.4th 1191, 1204 (11th Cir. 2022) (stating it is "unclear from the record before this Court what marketing plans or sales access restrictions [FDA] considered before making the decision to ignore the plans proposed by these six [applicants]"); *see also* CA.A78 n.xix. So FDA's *ipse dixit* assertion that Petitioners' plans were no different than other applicants'

"run-of-the-mill" ineffective plans does not provide a reasoned explanation for the agency's decision. *See St. Vincent Randolph Hosp., Inc. v. Price*, 869 F.3d 510, 513 (7th Cir. 2017) (Easterbrook, J.) ("When the agency just asserts an *ipse dixit*, then the decision falls for the lack of a reason.").[4]

FDA also says (Opp. 8) the court below correctly determined that even if FDA erred in failing to review Petitioners' plans to limit youth access, such error was harmless. But as this Court recently noted, "where the agency has not considered all of the relevant factors, . . . the proper course, except in rare circumstances, is to remand to the agency for additional investigation or explanation." *Calcutt v. FDIC*, 143 S. Ct. 1317, 1320 (2023) (per curiam) (cleaned up). And such "rare circumstances" are limited to those "cases where there is not the slightest uncertainty as to the outcome of the agency's proceedings on remand." *Id.* Given FDA's previous representations regarding the importance of marketing plans and sales-access restrictions to its marketing authorization analysis,

4. Further, because FDA never reviewed Petitioner's marketing and sales-access-restriction plans and its sole contemporaneous justification was that it would be "inefficient" to do so at this stage of review, Pet. App. 78a-79a n.xix, FDA's contentions before the circuit court and this Court that, *based on their contents*, the plans would be ineffective amount to an impermissible *post hoc* rationalization in any event. *See Dep't of Homeland Security v. Regents of the Univ. of Cal.*, 140 S. Ct. 1891, 1908-10 (2020) ("Permitting agencies to invoke belated justifications . . . can upset the orderly functioning of the process of review, . . . forcing both litigants and the courts to chase a moving target. . . . An agency must defend its actions based on the reasons it gave when it acted") (cleaned up).

it cannot be said that FDA's refusal to consider Petitioners' marketing and sales-access-restriction plans "clearly had no bearing on the procedure used or the substance of decision reached." *United States Steel Corp. v. EPA*, 595 F.2d 207, 215 (5th Cir. 1979) (quoting *Braniff Airways v. CAB*, 379 F.2d 453, 466 (D.C. Cir. 1967)).

Because FDA did not provide specific details about other applicants' allegedly ineffective plans, the court below engaged in pure speculation in concluding that FDA would have found Petitioners' plans to be similarly ineffective. Speculation, however, cannot support a finding of harmless error. *Cf. United States v. Tilghman*, 134 F.3d 414, 420 (D.C. Cir. 1998). The circuit court's finding of harmless error was particularly speculative because, as both FDA and the outside public health experts supporting Petitioners have recognized, youth have little interest in the type of ENDS product at issue (e-liquids used in refillable tank systems). *See* CA.A10-11; Brief of *Amici Curiae* Public Health Experts in Support of Petitioners at 14 (noting "the use of refillable tanks has remained consistently low among youth" and "[y]outh rarely use refillable tank products as their usual device type").

FDA notes (Opp. 8) that before the ENDS application deadline it issued an Enforcement Guidance that stated, "focusing on how the product was sold would not appropriately address youth use" because "youth have continued to access" ENDS "even after voluntary action by some manufacturers." But that portion of the Enforcement Guidance addressed only cartridge-based products, not e-liquid/tank systems. *See* CA.A110 ("FDA determined that focusing on how the product was sold would not appropriately address youth use of the products

that are the most popular among youth – *i.e.*, flavored, cartridge-based products"); *see also Bidi Vapor*, 47 F.4th at 1205 ("The [Enforcement] Guidance did not state that existing marketing and sales-access-restriction plans were categorically ineffective for electronic nicotine-delivery systems other than flavored, cartridge-based products."); *Wages & White Lion Invs., LLC v. FDA*, 41 F.4th 427, 447 n.6 (5th Cir. 2022) (Jones, J., dissenting) ("The 2020 Guidance focuses almost exclusively on the continuing attractiveness to youth of closed-system ENDS products, and very little if at all on bottled e-liquids for use in open systems. To the extent FDA means to say that youth will migrate to any flavored ENDS products if other avenues are closed off, it provided no evidence of that migration toward petitioners' [bottled e-liquid] products during the periods in question."). Significantly, that same Enforcement Guidance outlined many measures FDA considered adequate to limit youth access for non-cartridge-based ENDS products, all of which were incorporated into Petitioners' marketing plan. *Compare* CA.A111 *with* CA.A39-40. Yet FDA, without bothering to even review Petitioners' marketing plan and sales-access restrictions, found them insufficient with no notice or warning of this changed position.[5]

5. It is also worth noting that, contrary to FDA's contention (Opp. 6) that the petition for certiorari in *Gripum, LLC v. FDA*, No. 22-708, 2023 WL 3440578 (May 15, 2023), raised "similar issues" to those presented by Petitioners here, in *Gripum*, the Seventh Circuit found that the petitioner had waived or forfeited any arguments based on FDA's failure to review any marketing plan. 47 F.4th 553, 558 n.1 (7th Cir. 2021).

B. There is a Circuit Split.

1. FDA wrongly asserts that the Fourth Circuit's decision does not conflict with the Eleventh Circuit's *Bidi Vapor* decision. (Opp. 12). Unlike the court below, the Eleventh Circuit held that FDA was not free to simply ignore an applicant's proposed marketing and sales-access-restriction plans based on FDA's purported "experience." *See Bidi Vapor*, 47 F.4th at 1204 ("Experience fails as a justification for ignoring the marketing and sales-access-restriction plans.").

FDA is just as wrong when it asserts (Opp. 12) that the Eleventh Circuit's finding of prejudice in *Bidi Vapor* hinged on the fact that the applicants in that case submitted "novel" marketing and sales-access-restriction plans. *Bidi Vapor* consolidated petitions for review from six applicants; and while two of those applicants submitted plans described as "novel," the court rejected FDA's harmless error argument as to all six applicants. *See Bidi Vapor*, 47 F.4th at 1205. In short, "novelty" had nothing to do with the *Bidi Vapor* decision, and any suggestion otherwise is just another example of FDA's *post hoc* rationalizations and a new post-submission requirement FDA added without notice to applicants.

2. FDA's back-of-the-hand dismissal (Opp. 11-12) of two Fifth Circuit motion panel decisions regarding FDA's rejection of applications for non-tobacco-flavored ENDS should not dissuade the Court from granting this petition for writ of certiorari. As Petitioners have noted (Pet. 32-33), at least six judges on the Fifth Circuit have already found that FDA violated the APA by changing the evidentiary standard for non-tobacco-flavored ENDS without giving proper notice to applicants, and an *en banc*

decision from the Fifth Circuit on the issue is pending. Even if this Court were to determine there is no current circuit split on this issue warranting a writ of certiorari, the Court should hold the petition in abeyance until the Fifth Circuit issues its *en banc* decision.

C. This Case Presents a Question of Great Importance.

FDA does not dispute that it is on a path to depriving smokers and current users of non-tobacco-flavored ENDS products of the ability to use or continue using those products to help them quit or prevent relapse back into smoking. FDA says (Opp. 13) that "Petitioners' disagreement with FDA's expert judgment" on whether adult smokers should have access to non-tobacco-flavored ENDS "does not warrant further review." As the above illustrates (and as the court below misapprehended), the thrust of this case is not about insufficient deference to FDA's expert judgment but rather about FDA's procedural corner-cutting to reach its desired outcome.

Nonetheless, Petitioners are not the only ones who disagree with FDA's exercise of its "expert judgment." Eight distinguished public health experts with extensive experience related to tobacco and ENDS products have filed an *amicus* brief in support of Petitioners in this case.[6]

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6. *See* Brief of *Amici Curiae* Public Health Experts in Support of Petitioners. Those experts include the Chair of the Department of Epidemiology at the New York University School of Global Public Health and a former Attorney General of the State of Iowa (who was one of the leaders in numerous states' landmark settlement with large tobacco companies to recover billions of dollars in healthcare costs associated with treating smoking-related illnesses). *Id.* at 1-3.

In urging the Court to grant review, those public health experts note, *inter alia*, that ENDS are much safer than cigarettes, *id.* at 5; ENDS are effective in helping adult smokers quit, *id.* at 8; ENDS are more effective than FDA-approved nicotine-replacement therapies (*e.g.*, gums and patches), *id.* at 8; most adult ENDS users use non-tobacco-flavored ENDS, *id.* at 10; youth ENDS use has declined by more than 50% since 2019, *id.* at 11-12; and "FDA regulatory practice that creates a *de facto* federal flavor ban" is "likely to have harmful unintended consequences of driving tobacco users towards cigarettes," *id.* at 21.

In short, public health experts agree that this case presents a question of great importance.

CONCLUSION

For these reasons and the reasons discussed in the petition for writ of certiorari, the Court should grant the petition.

Respectfully submitted,

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