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 OF ELECTRONIC NICOTINE DELIVERY SYSTEM TRADE ASSOCIATIONS AND SMALL BUSINESSES AS *AMICI CURIAE* IN SUPPORT OF RESPONDENTS

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GLOSSARY

APPH	Appropriate for the Protection of the Public Health
CDC	Centers for Disease Control
ENDS	Electronic Nicotine Delivery Systems
FDA	U.S. Food and Drug Administration
MDO	Marketing Denial Order
MGO	Marketing Granted Order
NAS	National Academies of Sciences
PMTA	Premarket Tobacco Product Application
TCA	Family Smoking Prevention and Tobacco Control Act
TPL	Technical Project Lead

INTERESTS OF *AMICI CURIAE*

Amici are national and state trade associations, as well as small businesses, who represent manufacturers, distributors, and retailers of Electronic Nicotine Delivery Systems ("ENDS") (commonly known as "e-cigarettes").[1] Millions of addicted smokers in the U.S. have used ENDS to transition away from more dangerous traditional cigarettes. Indeed, many of these companies were started by individuals who themselves relied on ENDS to successfully move on from their own smoking habits. *Amici* therefore share a common goal in advocating for a reasonably regulated marketplace that gives consumers access to less risky tobacco products.

Amici also have a substantial interest in this litigation. Over the past several years, they have watched with great alarm as the U.S. Food and Drug Administration ("FDA") has reached far beyond any reasonable interpretation of the Family Smoking Prevention and Tobacco Control Act ("TCA") and rejected premarket applications for virtually all non-tobacco flavored ENDS. What is worse, the majority of circuit courts considering challenges to FDA's denials have afforded FDA extreme deference in rubber-stamping a wholly unlawful regulatory scheme.

In this brief, *Amici* thus reflect on the adverse impact that FDA's approach has had on this industry and the addicted adult smokers it serves, and demonstrate that FDA's overall approach to reviewing premarket applications for non-tobacco flavored ENDS products, particularly in light of *Loper Bright Enters. v. Raimondo*, 144 S.Ct. 2244 (2024), has no basis in the TCA itself.

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[1] This brief was not authored in whole or in part by counsel for any of the parties; no party or party's counsel contributed money for preparing or submitting this brief; and no one other than *amici* and their counsel have contributed money for preparing or submitting this brief. *Amici* are listed in the attached appendix.

SUMMARY OF ARGUMENT

Congress granted FDA authority in the TCA to ensure addicted, adult cigarette smokers in this country have access to lower risk tobacco products to help them move away from more dangerous, combustible cigarettes. ENDS are now firmly recognized by the scientific community as a risk reduction tool for cigarette smokers.

Under the statute, ENDS manufacturers must submit to FDA premarket tobacco product applications ("PMTAs") to obtain marketing authorization for their products. FDA is required by the TCA's plain language to then evaluate all information and data submitted by a manufacturer when determining whether a given product is "appropriate for the protection of the public health" ("APPH"). Significantly, this is not a one-size-fits-all process; rather, it obligates FDA to weigh all evidence in each PMTA on a case-by-case basis.

By way of example, part of the APPH process involves ensuring ENDS do not appeal to minors. But any concerns about youth (under 21 years-old) use must be balanced against all other evidence contained in the PMTA warranting a grant of marketing authorization, such as underage marketing and access restrictions implemented by the manufacturer. Before FDA ever received a PMTA, Congress had already made a policy choice, in creating its first ever *population-level* health standard, that only through a complete review of a PMTA would FDA be able to fairly balance all of the evidence and account for all stakeholder interests involved. Congress did so by mandating that FDA consider, *inter alia*, both the "risks and benefits" of a tobacco product across the "population as a whole." 21 U.S.C. § 387j(c)(4).

Unfortunately, FDA has applied a generic, across-the-board scheme resulting in the denial of virtually all non-tobacco flavored (*e.g.*, mint and fruit) ENDS products, and in the process focusing its attention largely on underage use at the expense of adult smokers. FDA had initially read the TCA correctly – and consistently put forth that interpretation over the span of five years in guidance and other public statements – obligating the agency to conduct a full scientific review of an entire PMTA before making a marketing authorization decision. However, in an about-face, FDA adopted a new strategy following a deluge of PMTAs filed prior to a court-imposed deadline – what FDA described in an internal memo as the "fatal flaw" approach – expressly designed to quickly deny marketing authorization for as many non-tobacco flavored ENDS as possible. Agency staff were suddenly ordered to engage in a simple box-checking exercise and issue a marketing denial if the PMTA merely failed to contain a single study comparing the cessation benefits of the manufacturer's tobacco and non-tobacco flavored ENDS (what is referred to in this *amici* brief as the "comparative efficacy" study or test requirement).

Needless to say, FDA's interpretation – concluding it could base a marketing denial solely on the absence of one piece of evidence – does not accurately reflect Congressional intent. FDA's cookie-cutter approach to PMTA reviews clearly violates the plain language of the TCA. In Section 910, the statute lists numerous factors that are relevant to an APPH finding. Indeed, the population-level health standard itself incorporates the term "appropriate," which this Court has held is a broad and all-encompassing term requiring consideration of all relevant factors. And this reading is consistent with the statute's command that the "risks and

benefits" of a product be considered across the "population as a whole."

FDA argues in its merits brief that Section 910(c)(5)(B) authorizes it to reject a PMTA simply because it does not include a comparative efficacy study. FDA seriously misreads that provision. Rather, the "best" reading of Section 910(c)(5)(B), pursuant to this Court's recent decision in *Loper Bright Enters. v. Raimondo*, 144 S. Ct. 2244 (2024), is that the absence of such a study must still be weighed and balanced against all other information and data contained in a given PMTA, including those that favor a marketing granted order. That much is required by the statute's plain text, context, and structure.

The Questions Presented in the instant case do not directly implicate FDA's claimed authority to review PMTAs under the abbreviated comparative efficacy approach. Rather, this Court has been asked to resolve more discrete issues of fair notice and whether FDA arbitrarily and capriciously failed to consider Respondents' underage marketing and access restrictions. However, the fact that FDA never had, in the first instance, authority to rely solely on the absence of a comparative efficacy study to deny ENDS marketing authorization may generally inform this appeal. *Amici* therefore request this Court decide in favor of Respondents and affirm the judgment below.

ARGUMENT

I. Non-Tobacco Flavored ENDS Present Less Risk Than Cigarettes And Are Effective In Helping Transition Adult Smokers

It is now well-established ENDS pose far less health risk than traditional cigarettes. For instance, in 2018, the National Academies of Sciences ("NAS") completed a comprehensive review of over 800 research and scientific papers examining ENDS and their health impacts.[2] NAS found "**substantial evidence** that except for nicotine, under typical conditions of use, exposure to potentially toxic substances from e-cigarettes is significantly lower compared with combustible cigarettes."[3] This is because ENDS do not burn tobacco leaf or even contain tobacco, and there is no combustion or smoke. Rather, the aerosol produced by an ENDS is created by heating and vaporizing an e-liquid solution. Not surprisingly, NAS concluded the "evidence about harm reduction suggests that across a range of studies and outcomes, e-cigarettes pose less risk to an individual than combustible tobacco cigarettes."[4]

Most adult ENDS users in this country are also either current or former smokers, with many of these

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[2] National Academies of Sciences, *Public Health Consequences of E-Cigarettes* ("NAS"), NAT'L ACADEMIES PRESS, at Preface (2018), https://tinyurl.com/bde9fyw2.

[3] *Id.* at 18 (emphasis in original).

[4] *Id.* at 11. FDA agrees. 81 Fed. Reg. 28974, 29030 (May 10, 2016) (FDA concluding in rule applying the TCA to ENDS products that "completely switching from combusted cigarettes to [e-cigarettes] may reduce the risk of tobacco-related disease for individuals currently using combusted tobacco products, given the products' comparative placements on the continuum of nicotine-delivering products.").

individuals turning to ENDS to reduce or completely quit their smoking habits.[5] Recent studies validate these efforts, with a Cochrane Systematic Review being particularly instructive. A group of university researchers from the United States and around the world reviewed 88 completed studies, including randomized controlled trials and cross-over trials, which investigated whether ENDS help adults stop smoking.[6] Those studies represented 27,235 participants, of which 47 were randomized controlled trials ("RCTs"). The review concluded that "[p]eople are more likely to stop smoking for at least six months using nicotine e-cigarettes than using nicotine replacement therapy (7 studies, 2544 people), or e-cigarettes without nicotine (6 studies, 1613 people)." In addition, studies comparing nicotine e-cigarettes with behavioral or no support also showed

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[5] Ping Due, MD, Ph.D, et al., *Changes in E-Cigarette Use Behaviors and Dependance in Long-term E-Cigarette Users*, AM. J. PREV. MED. 2019:57(3):374-383, at 375; Yoonseo Mok, MPH, et al., *Associations between e-cigarette use and e-cigarette flavors with cigarette smoking quit attempts and quit success: Evidence from a US large, nationally representative 2018-2019 survey*, NICOTINE AND TOBACCO RESEARCH, at 5 (2022) ("Mok, et al."). According to the Centers for Disease Control ("CDC"), among adult ENDS users, approximately 69.7% are former or current cigarette smokers, including 92.8% of users over 45 years old – the age group most susceptible to near-term health impacts from smoking combustible cigarettes. CDC, *QuickStats: Percentage Distribution of Cigarette Smoking Status Among Current Adult E-Cigarette Users, by Age Group—National Health Interview Survey* (Mar. 10, 2023), https://perma.cc/TYR8-9KUV. FDA has calculated that approximately 77% of adult ENDS users use non-tobacco flavored (*i.e.*, flavored) ENDS. Pet. App. 188a.

[6] Nicola Lindson, et al., *Electronic cigarettes for smoking cessation*, Cochrane Database of Systematic Reviews 2024, Issue 1. Art. No.: CD010216, DOI: 10.1002/14651858.CD010216.pub8, https://tinyurl.com/s4jzw8wv.

higher quit rates in people using nicotine e-cigarettes (9 studies, 5024 people).[7]

The largest ENDS clinical trial in the U.S. to date also confirmed the role of these products in smoking cessation.[8] The 2023 study demonstrates that ENDS can be a viable means of quitting or reducing more harmful combustible cigarette use for adult smokers (21+). This study, significant because it supports the role that ENDS play in combustible cigarette reduction or quitting *in the real-world setting* (*i.e.*, without detailed instructions or additional cessation support), was conducted using 638 adult smokers across 11 U.S. cities over a span of four years. Previous studies showing ENDS can lead to cessation have been far more structured and included smokers wanting to quit. But

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[7] *Id.*; *see also*, *e.g.*, NAS, *supra* note 2, at 19 (finding "moderate evidence from randomized controlled trials that e-cigarettes with nicotine are more effective than e-cigarettes without nicotine for smoking cessation"); Mok, et al., *supra* note 5, at 14 (data from nationally representative survey "clearly indicat[ing] that those who use e-cigarettes more intensely (at least 20 of the past 30-days)…have…a higher odds of making a quit attempt and of succeeding in quitting cigarette smoking"); Karin A. Kasza, et al., *Associations between nicotine vaping uptake and cigarette smoking cessation vary by smokers' plans to quit: longitudinal findings from the International Tobacco Control Four Country Smoking and Vaping Surveys*, ADDICTION 2022;1-13, at 1-2, 7 (finding smokers "not planning to quit in the next 6 months who started vaping daily experienced a 32% cigarette quit rate compared with a 7% quit rate among their counterparts who did not take up vaping").

[8] Matthew J. Carpenter, et. al., *Effect of unguided e-cigarette provision on uptake, use, and smoking cessation among adults who smoke in the USA: A naturalistic, randomised, controlled clinical trial*, Lancet eClinical Medicine, 2023;63:102142, doi: 10.1016/j.eclinm.2023.102142; PMCID: 10518503, https://tinyurl.com/2ee6ttyc.

in this clinical trial, cessation and smoking reduction outcomes favored the ENDS group, even among smokers who expressed little interest in quitting at study outset. Smokers in the ENDS group showed declines in combustible cigarette dependence and increased motivation and confidence to quit smoking. Key to the study's findings is the fact that smokers spontaneously ceased smoking even when they had no intention of quitting. Importantly, these participants received no encouragement, motivation, or rewards for their smoking cessation efforts during the trial.[9]

The latest research also places into serious question the wisdom of preventing adult access to non-tobacco flavored ENDS which are increasingly recognized as a key factor in enhancing adult smokers' ability to quit combustible cigarettes for good. For example, the greater efficacy of flavored ENDS in supporting adult smokers quitting combustible cigarettes was explored in depth by Gades, *et al*. Experts at the University of Minnesota conducted an extensive literature review of research, including clinical studies, from 2007 to 2020.[10] Results from 104 of those studies suggested that access to a variety of non-tobacco flavors is likely to be associated with higher use levels and appeal for cigarette smokers, and that flavor variety "might facilitate complete substitution for cigarettes."[11] Accordingly, the researchers warned "[r]egulation of…flavors aimed at decreasing naïve uptake may

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[9] *Id.*

[10] Mari S. Gades BA, et al., *The Role of Nicotine and Flavor in the Abuse Potential and Appeal of Electronic Cigarettes for Adult Current and Former Cigarette and Electronic Cigarette Users: A Systematic Review*, NICOTINE AND TOBACCO RESEARCH 2022:1332-1343, at 1332.

[11] *Id.* at 1332, 1339.

inadvertently decrease uptake and complete switching among smokers, reducing the harm reduction potential of e-cigarettes. Evidence-based effects of regulating… flavors must be considered for the population as a whole, including smokers."[12]

II. FDA Received PMTAs Covering Millions Of Flavored ENDS Products, But Adopted An Across-The-Board Strategy Of Denying Marketing Authority For Virtually All Non-Tobacco Flavored ENDS

Congress enacted the TCA in 2009.[13] While the statute initially applied to only four listed tobacco products (*i.e.*, cigarettes, smokeless tobacco, roll-your-own tobacco, and cigarette tobacco), Congress authorized FDA to "deem" additional tobacco products as subject to the TCA via rulemaking.[14] In August 2016, FDA's

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[12] *Id.* at 1332; *see also*, *e.g.*, Robyn L. Landry, et al., *The role of flavors in vaping initiation and satisfaction among U.S. adults*, ADDICT. BEHAV. 2019 Dec;99:106077, at 14, https://tinyurl.com/24j47x8c (survey of over 1,000 adult vapors showing "[t]hose who used flavors, particularly mint/menthol and flavors other than tobacco flavor, had higher odds of reporting high satisfaction with vaping…than respondents who did not use flavored e-cigarettes."); Lin Li, Ph.D., et al., *How Does the Use of Flavored Nicotine Vaping Products Relate to Progression Toward Quitting Smoking? Findings From the 2016 and 2018 ITC 4CV Surveys*, NICOTINE AND TOBACCO RESEARCH 2021:1490-1497, at 1490-91, 1494 (survey of concurrent (or dual) users of cigarettes and ENDS finding that the greatest success in quitting occurred among adult smokers using sweet flavored ENDS (13.8%) relative to tobacco flavored ENDS (9.6%)).

[13] 21 U.S.C. § 387, *et seq.*

[14] 21 U.S.C. § 387a(b).

"Deeming Rule" went into effect, which applied the TCA to ENDS.[15]

At the time, tens of thousands of ENDS products were already on the market.[16] Under the Deeming Rule, these ENDS, and those introduced into the marketplace in the future, were immediately subject to numerous TCA provisions, including a requirement that manufacturers obtain premarket authorization from FDA before continuing to market and sell their products.[17] A manufacturer must submit a PMTA which entails a time-consuming and costly process (often totaling millions of dollars per product) of compiling extensive scientific, technical, and marketing data that FDA must review before granting or denying market authorization.[18]

To avoid a sudden, mass market exit of ENDS products, FDA adopted an enforcement policy which permitted existing ENDS to remain on the market for up to a year after a timely filed PMTA. Initially, the Deeming Rule set an August 8, 2018 PMTA filing deadline.[19] FDA said this balanced concerns regarding underage use and providing access to products adult smokers may be using to move away from more

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[15] 81 Fed. Reg. 28974 (May 10, 2016).

[16] *Vapor Tech. Ass'n v. FDA*, 977 F.3d 496, 498 (6th Cir. 2020).

[17] 21 U.S.C. § 387j. Under the TCA, ENDS are subject to the PMTA requirement because they are "new" tobacco products – *i.e.*, they were introduced into the marketplace after February 15, 2007 and therefore were not grandfathered from the PMTA process, as were more dangerous cigarettes that had been commercialized prior to that date. 21 U.S.C. § 387j(a).

[18] 21 U.S.C. § 387j(b)-(c).

[19] 81 Fed. Reg. at 28978.

dangerous cigarettes.[20] Over the ensuing years, FDA extended the PMTA deadline, finally landing on August 8, 2021.[21] But in response to a lawsuit filed by anti-vaping groups, a federal judge in Maryland eventually moved the due date back to September 9, 2020 and allowed products with timely filed applications to remain on the market for an additional year (or until September 2021) without the threat of enforcement.[22]

Although FDA anticipated it would receive less than 6,800 PMTAs,[23] applications covering *26 million products* were eventually submitted.[24] Mitch Zeller, then-Director of FDA's Center for Tobacco Products, admitted in February 2021 that these unexpectedly large numbers would present review "challenges" for FDA due to the

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[20] *Id.* at 28977-78.

[21] FDA, News Release: *FDA announces comprehensive regulatory plan to shift trajectory of tobacco-related disease, death* (July 27, 2017), https://tinyurl.com/vrubw8tz; FDA, *Modifications to Compliance Policy for Certain Deemed Tobacco Products* (March 2019), https://tinyurl.com/vr6ph8.

[22] Mem. Op. and Order, *Am. Academy of Pediatrics v. FDA* ("*AAP*"), 8:18-cv-00883-PWG (D. Md.) (Dkt. 127 & 182).

[23] *AAP*, Dkt. 120-1 at 15 (Declaration of Mitch Zeller, Director, FDA Center for Tobacco Products).

[24] FDA, *FDA Makes Determinations On More Than 99% of the 26 Million Tobacco Products For Which Applications Were Submitted* (March 15, 2023), https://tinyurl.com/3spczmy5. This figure includes PMTAs for 6.7 million products filed by September 9, 2020, applications for more than 18 million products received after that deadline, and PMTAs for another 1 million products covering e-liquids made with non-tobacco derived nicotine (or synthetic nicotine) that were filed by a May 14, 2022 PMTA deadline established by a new federal law (Consolidated Appropriations Act of 2022) passed in March 2022, which added such products to coverage under the TCA. *Id.*

"size, complexity and diversity" of the PMTAs.[25] Since mid-2021, while FDA has made determinations on 99% of these PMTAs,[26] it has issued Marketing Granted Orders ("MGOs") for only 34 ENDS products, only four of which were for non-tobacco flavored ENDS.[27] In contrast, FDA has issued Marketing Denial Orders ("MDOs") for over 1.2 million products, almost all of which were for non-tobacco flavored ENDS.[28] Just in its initial release of MDOs in August 2021, FDA denied applications *en masse* for about 55,000 non-tobacco flavored ENDS products.[29] And a few weeks later, FDA announced it had resolved applications for 6.5 million products subject to timely filed PMTAs, including MDOs issued for 946,000 non-tobacco flavored ENDS based on the "fatal flaw" approach.[30]

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[25] *Bidi Vapor LLC v. FDA* ("*Bidi*"), No. 21-13340 (11th Cir.) (Public Statement of Mitch Zeller) (Dkt. 40 at FDA-BIDIVAPOR-005261-62).

[26] *Supra* note 24.

[27] FDA, Premarket Tobacco Product Marketing Granted Orders, https://tinyurl.com/4dmxe4v3. On June 21, 2024, FDA granted marketing authorization for four menthol-flavored ENDS manufactured by NJOY. FDA, News Release: *FDA Authorizes Marketing of Four Menthol-Flavored E-Cigarette Products After Extensive Scientific Review* (June 21, 2024), https://tinyurl.com/yzy38mnm.

[28] *Supra* note 24. The remaining 25 million determinations constituted refusals to accept or file incomplete or otherwise non-compliant PMTAs based on an initial screening process. *Id*.

[29] FDA, News 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://tinyurl.com/n9c9rwu8.

[30] FDA, News Release: *FDA Makes Significant Progress in Science-Based Public Health Application Review, Taking Action on Over 90% of More Than 6.5 Million 'Deemed' New Tobacco*

III. The TCA's Clear Text, Context, And Structure Require FDA To Conduct A Full Scientific Review Of Each PMTA; FDA Cannot Shortcut That Process

Under this Court's decision in *Loper Bright*, the pertinent question is "Does the statute authorize the challenged agency action?"[31] And here, the answer is an emphatic "no." The "best" interpretation of the APPH standard is that FDA must consider, weigh, and balance *all* evidence contained in a PMTA before it determines whether to grant an ENDS product marketing authorization.[32] It cannot shortcut that process by limiting its review solely to a comparative efficacy study. Once FDA receives a complete PMTA, it must do more than a cursory evaluation; it must assess and balance the application's contents in its entirety.

The plain language of the TCA makes this clear. Section 910(c)(2) of the TCA explicitly provides that a PMTA shall only be denied if "*upon the basis of the information submitted* to [FDA]…and any other information before [FDA]" the product is not APPH.[33] Section 910(c) of the statute describes APPH in broad terms with respect to "the risks and benefits to the population *as a whole*," including "users and nonusers of the tobacco product."[34] In this context, Section 910(b) enumerates numerous forms of evidence that must be in any PMTA, including data on health risks,

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Products Submitted (Sept. 9, 2021), https://tinyurl.com/24kmkdnb.

[31] 144 S. Ct. at 2269.

[32] *Id.* at 2266 (holding that it is a court's independent duty to discern the "best" interpretation of statutory language).

[33] 21 U.S.C. § 387j(c)(2) (emphasis added).

[34] 21 U.S.C. § 387j(c)(4) (emphasis added).

ingredient and additive information, product design, manufacturing practices, product samples, labeling specimens, and any other information required by FDA.[35] Section 910(c) then obligates FDA to also evaluate whether an ENDS product will help people quit other tobacco products (*i.e.*, cessation) or compel them to start (*i.e.*, initiation).[36]

More specifically, when the TCA says FDA must consider the *whole* population, this necessarily includes not only adult smokers and underage non-smokers, as is the focus of FDA's comparative efficacy test, but also any other demographics that might be impacted by a particular ENDS product (*e.g.*, adult non-smokers, underage cigarette smokers, etc.). Indeed, the very notion of "public health" is broad and contemplates protecting the "community" as a whole, not just certain sub-populations.[37] And FDA must also gauge all other *risks and benefits* of a given product, including health factors, like the extent to which a product results in relatively less or more exposure to harmful constituents.[38] The statute also explicitly makes relevant the impact

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[35] 21 U.S.C. § 387j(b)(1).

[36] 21 U.S.C. § 387j(c)(4). As part of the APPH analysis, FDA must account for "(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."

[37] Merriam-Webster Dictionary, https://tinyurl.com/55p876pn ("the art and science dealing with the protection and improvement of community health"); American Heritage Dictionary, https://tinyurl.com/ywxdthby ("The science and practice of protecting and improving the health of a community").

[38] *See*, *e.g.*, 21 U.S.C. § 387g(a)(4) (defining APPH in context of tobacco control standards as including reduction or elimination of harmful constituents).

that restrictions on the sale or distribution of a product could have on the APPH determination.[39] These include constraints on access to a given product, as well as advertising and marketing limitations, aimed at reducing underage use (*e.g.*, only allowing face-to-face transactions in adult-only facilities).[40]

The all-inclusive nature of the APPH standard is further confirmed by other references to "APPH" in the TCA. This is evident, for example, in Section 907 where FDA is authorized to promulgate "tobacco product standards."[41] Such standards may govern everything from nicotine yields, the reduction or elimination of harmful constituents, characterizing flavors, and product design, to product testing protocols and sales restrictions.[42] In adopting a tobacco product standard, FDA must find that it is APPH.[43] But that finding is not limited to issues of comparative efficacy. Like the TCA's PMTA provision, Section 907(a)(3)(B)(i) separately provides that FDA must also consider "the risks and benefits to the population as a *whole*."[44]

Finally, all of these provisions comport with one of the underlying purposes of the statute – to boost harm reduction efforts. To be sure, Congress set out in the

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[39] 21 U.S.C. § 387j(c)(1)(B).

[40] *Id.* (referencing examples of restrictions identified in 21 U.S.C. § 387f(d)).

[41] 21 U.S.C. § 387g.

[42] 21 U.S.C. § 387g(a)(4).

[43] 21 U.S.C. § 387g(a)(3).

[44] 21 U.S.C. § 387g(a)(3)(B)(i); *see also* 21 U.S.C. § 387f(d) authorizing FDA to impose sales and distribution restrictions on a tobacco product if it would be APPH, taking into account, in addition to initiation and cessation, the "risks and benefits to the population as a whole."

TCA, in part, to protect underage consumers.[45] But it also requires FDA to "provide new and flexible enforcement authority to ensure that there is effective oversight of the tobacco industry's efforts to develop, introduce, and promote less harmful tobacco products."[46] FDA also must "continue to permit the sale of tobacco products to adults in conjunction with measures to ensure that they are not sold or accessible to underage purchasers."[47] In the TCA, Congress decided that these goals would be best achieved by broadly defining the APPH standard to include a weighing and balancing of numerous factors.[48]

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[45] 21 U.S.C. § 387 note (2) (Sec. 3. Purpose).

[46] *Id.* at note (4).

[47] *Id.* at note (7).

[48] We note that youth ENDS usage peaked in 2019, when 27.5% of high school students reported using ENDS within the last 30 days. Teresa W. Wang, et al., *Tobacco Product Use and Associated Factors Among Middle and High School Students – United States*, *2019*, 68 MMWR 1-22 (Dec. 6, 2019), https://www.cdc.gov/mmwr/volumes/68/ss/ss6812a1.htm. At the time, the federal minimum age for the purchase of ENDS products was only 18, meaning many high school seniors could legally purchase the products. The federal minimum age was increased to 21 in late 2019, and use of ENDS products by youth has steadily declined since, with only 7.8% of high school students reporting use in 2024. Eunice Park-Lee, et al., *Notes from the Field: E-Cigarette and Nicotine Pouch Use Among Middle and High School Students – United States*, *2024*, 73 MMWR 774-78 (Sept. 5, 2024), https://www.cdc.gov/mmwr/volumes/73/wr/mm7335a3.htm?_cid=mm7335a3_w. While 15.8% of high school students reported past 30-day use of combustible cigarettes in 2011, when ENDS were still novel, by 2023, that figure had declined to 1.9%. *See* A. Arrazola, *Tobacco product use among middle and high school students – United States, 2011 and 2012,* 62 MMWR (Nov. 15, 2023); 62(45): 893-897, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4585347/; J. Birdsey, et al., *Tobacco Product Use Among U.S.*

IV. FDA Consistently Interpreted The TCA As Requiring A Full Scientific Review Of All Information Contained In A PMTA

In *Loper Bright*, this Court also recognized that due respect to an agency's reading of a statute may be "especially warranted when [the agency] interpretation was issued roughly contemporaneously with enactment of the statute and remained consistent over time."[49] This has particular relevance here. Beginning in 2016 when the Deeming Rule was promulgated, FDA also interpreted the TCA as obligating FDA to consider all information and data contained in a PMTA before deciding whether to grant marketing authorization. Along with the Deeming Rule, FDA published draft guidance to assist ENDS manufacturers in preparing PMTAs, which included identifying information that must be submitted in an application and would be relevant to the APPH review.[50] Significantly, FDA stated it "will weigh *all* of the potential benefits and risks from the information contained in the PMTA to make an overall determination of whether the product

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Middle and High School Students – National Youth Tobacco Survey, 2023, 72 MMWR 1173-1182 (Nov. 3, 2023), http://dx.doi.org/10.15585/mmwr.mm7244a1.

[49] *Loper Bright*, 144 S. Ct. at 2258; *see also id.* at 2259 (citing *Skidmore v. Swift & Co.*, 323 U.S. 134, 140 (1944) (whether an agency's statutory interpretation deserves respect would "depend on the thoroughness evident in its consideration, the validity of its reasoning, *its consistency with earlier and later pronouncements*, and all those factors which give it power to persuade, if lacking power to control") (emphasis added).

[50] FDA, *Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems: Guidance for Industry (Draft Guidance)* (May 2016), at 1, https://tinyurl.com/mp3d462.

should be marketed."[51] FDA then confirmed this view three years later when it finalized the guidance. Again, FDA said it will "weigh[] *all* of the potential benefits and risks from information contained in the PMTA to make an overall" APPH determination.[52]

FDA consistently took this view over time. In a 2019 proposed PMTA rule, FDA described its comprehensive analysis under the APPH standard as involving the weighing and balancing of multiple factors:

> Finding that there is a showing that permitting the marketing of a new tobacco product would be APPH is a *complex determination* that must be made with respect to risks and benefits to the population as a whole….When determining whether the marketing of a particular new tobacco product would be APPH, FDA will evaluate the factors in light of available information regarding the existing tobacco product market, tobacco use behaviors, and the associated health risks at the time of review….Section 910(c) of the [TCA] requires FDA to consider *an array of potential risks and benefits* of the new tobacco product with respect to the population as a whole when determining whether permitting the marketing of a new product would be APPH….Because the APPH standard *requires a balancing of product-specific potential risks and benefits*, the factors that could help demonstrate that

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[51] *Id.* at 13 (emphasis added).

[52] FDA, *Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems: Guidance for Industry (Draft Guidance)* (June 2019), at 12 (emphasis added), https://tinyurl.com/2s33cz3h.

> the marketing of a particular new tobacco product would be APPH might not support the marketing of a different new tobacco product.[53]

Indeed, in the 2016 and 2019 versions of the PMTA guidance, FDA detailed, over the course of 50-plus pages each, numerous types of information and data it deemed relevant to APPH. Just a sampling includes information related to an ENDS product's aerosol constituents (*e.g.*, harmful and potentially harmful substances or "HPHCs"); toxicology (*e.g.*, cytotoxicity, genotoxicity, carcinogenicity, respiratory, reproductive, developmental); user topography (*e.g.*, puff duration, puff intensity, duration of use); abuse liability (*i.e.*, addictiveness potential); health risks compared to other tobacco products (*e.g.*, HPHC exposures); underage marketing and access restrictions; sales data; ingredients; design features; performance specifications; and manufacturing processes. FDA sought much of this information through, *inter alia*, extensive public literature reviews, *in vitro* and *in vivo* studies, consumer intention and perception surveys, observational studies, and marketing plans.[54] FDA did not overstate matters when, during 2018 and 2019 public informational meetings directed at ENDS manufacturers, it described the APPH analysis as being "multi-disciplinary."[55]

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[53] FDA, *Premarket Tobacco Product Applications and Recordkeeping Requirements* (Proposed Rule), 84 Fed. Reg. 50566, 50618 (Sept. 25, 2019) (emphasis added), https://tinyurl.com/4ajzm434.

[54] *See*, *e.g.*, *supra* note 50 at 10-46; *supra* note 52 at 19-50.

[55] FDA, Tobacco Product Application Review Public Meeting (Oct. 22, 2018), at 116, 119, https://tinyurl.com/yc6hm88c; FDA, Deemed Tobacco Product Applications: A Public Meeting (Oct. 28, 2019), at 114, 117-18, https://tinyurl.com/2vmbtxv3.

Even when adopting the final PMTA rule in October 2021, just after issuing the first MDOs, FDA continued to maintain that the APPH standard involves a "complex determination," 86 Fed. Reg. 55300, 55335 (Oct. 5, 2021), that FDA "considers many factors," *id.* at 55314, and that FDA does not make a "determination on one static set of requirements," *id*. at 55385. FDA further declined "to assign weight to different types of evidence," *id.,* emphasizing APPH "requires a balancing" of risks and benefits. *Id.* at 55384. FDA also refused "to create a series of criteria" that all products must meet for APPH, stated that an APPH "determination would involve consideration of many factors," and noted it "will be made with respect to…the population as a whole, rather than whether a product meets each item in a series of specific criteria." *Id.* at 55386. FDA committed to determining APPH on an "individualized" basis, the "risks and benefits of a specific tobacco product" and "based on *all* of the contents of the application." *Id.* at 55320, 55390 (emphasis added).

Tellingly, during the rulemaking, FDA also rejected a comment demanding that an APPH evaluation focus on population segments most likely to be affected by ENDS and "require applications to show a public health benefit for those specific groups." FDA concluded that APPH does not require applicants to show a public health benefit for specific population segments. *Id* at 55385. Further, in response to comments asking FDA to impose specific requirements on flavored tobacco products before issuing a marketing order, FDA again "declin[ed] to create a series of criteria that either all products or a specific subset of products must meet…to be considered APPH." *Id.* at 55386.

And all of this makes sense. FDA "has interpret[ed] the APPH standard in 910(c)(2)(A) to require a showing that permitting the marketing of a new tobacco product would likely have at least a *net benefit* to public health based upon the risks and benefits to the population as a whole."[56] In other words, the APPH standard is a relative concept and thus will always entail a weighing and balancing of all evidence in an individual PMTA – both for and against marketing authorization. Restricting PMTA review to just a comparative efficacy study is the very antithesis of FDA's longstanding views.

V. FDA Did A Sudden About-Face, Interpreted The TCA As Allowing It To Forgo Full Scientific Reviews And, Instead, Uniformly Denied Marketing Authorization For Virtually All Non-Tobacco Flavored ENDS Based On The Mere Absence Of One Type Of Specific Evidence

Unfortunately, FDA ultimately did not adhere to either the TCA nor its own interpretation of the APPH standard. Despite the statute's clear language, FDA proceeded to issue cookie-cutter MDOs for over one million non-tobacco flavored ENDS products without conducting a full scientific review of each PMTA. FDA has denied marketing authorization for virtually every non-tobacco flavored ENDS product for the same reason – because the PMTAs did not contain a single,

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[56] *Supra* note 53 at 50618 (emphasis added) (proposed PMTA rule); *see also* 86 Fed. Reg. at 55386 (final PMTA rule) (same); *infra* note 65 at 4 (sample Technical Project Lead (TPL) review) (requiring applicant to "show a *net population health benefit* necessary to determine that permitting the marketing of the new tobacco product is APPH.") (emphasis added).

highly-specific study designed to elicit a discrete data-point in which the cessation benefits of the applicant's non-tobacco flavored ENDS were compared to the applicant's tobacco-flavored products.[57]

Without warning, FDA informed applicants that absent this distinct evidence manufacturers could not demonstrate there would be an added benefit to smokers of using non-tobacco flavored ENDS sufficient to outweigh risks of such products to underage users, and thus the products were not APPH.[58] Significantly, the MDOs stated FDA did not proceed to assess any other part of the applications once it noted the absence of a comparative efficacy study – *i.e.*, FDA did not conduct a scientific review.[59]

In fact, FDA's assessment of the PMTAs consisted of nothing more than a literal box-checking exercise. For each application, FDA staff completed a check-list indicating the PMTA did not include a randomized controlled trial, longitudinal cohort study, or other similarly robust evidence evaluating the impact of the manufacturer's non-tobacco flavored ENDS on adult switching or cigarette reduction over time compared to a tobacco flavored ENDS.[60] As with the MDOs, these checklists indicated FDA would only move to a "full scientific review" if such evidence was present.[61]

And that is not all. The MDOs and checklists tracked an approach outlined by FDA in an internal

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[57] *See*, *e.g.*, *Bidi* Dkt. 40 at FDA-BIDIVAPOR-000031-33 (MDO example).

[58] *Id.*

[59] *Id.* at FDA-BIDIVAPOR-000032.

[60] *See*, *e.g.*, *id.* at FDA-BIDIVAPOR-000057-60 (checklist example).

[61] *Id.* at FDA-BIDIVAPOR-000059.

document distributed just a month before the first MDOs were issued. In a July 9, 2021 memo, FDA set forth what it called a "fatal flaw" review in which PMTAs for non-tobacco flavored products that did not contain a comparative efficacy study would likely be denied.[62] This "simple" review would be implemented in lieu of a full scientific review.[63] Importantly, the stated goal of the fatal flaw memo placed expediency over substance by allowing FDA to "manage" the large number of PMTAs and to "take final action on as many applications as possible by September 10, 2021," when the year-long grace period for timely filed PMTAs ended.[64] FDA kicked this process off by issuing MDOs for 55,000 products in one fell swoop.[65] So much for the APPH standard.

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[62] *Id.* at FDA-BIDIVAPOR-005226-27.

[63] *Id.* at FDA-BIDIVAPOR-005227.

[64] *Id.* at FDA-BIDIVAPOR-005226.

[65] *Supra* note 29. In ensuing litigation over the MDOs, FDA has argued the "fatal flaw" memo was "Superseded." *See*, *e.g.*, *Bidi* Dkt. 16 at 8 (certified administrative record index). Whether true or not, FDA clearly implemented an across-the-board, fatal flaw approach for non-tobacco flavored products in which an MDO would issue if a PMTA did not contain any study or other evidence going to a comparative efficacy test. *See R.J. Reynolds Vapor Co. v. FDA*, 65 F.4th 182, 193 n.9 (5th Cir. 2023) (noting the checklists followed the fatal flaw memorandum). Along with each MDO, FDA also issued a document titled "Technical Project Lead (TPL) Review of PMTAs" that sought to justify the fatal flaw and comparative efficacy approach. *See* FDA, Tobacco Products Marketing Orders: FDA Sample Decision Summary Document (Sept. 17, 2021), https://tinyurl.com/npn2x4ec. The TPLs, however, at no point reviewed all the evidence contained in a given PMTA aside from confirming whether a comparative efficacy analysis was conducted. *Id.* at 11, 13 (stating the scope of review was limited to confirming the absence of a comparative efficacy study). For example, despite conceding that the efficacy of a manufac-

VI. TCA Section 910(c)(5)(B) Governing The Use Of "Valid Scientific Evidence" Does Not Authorize FDA To Deny A PMTA Solely Because It Does Not Contain A Comparative Efficacy Study

In its merits brief, FDA argues that Section 910(c)(5)(B) authorizes it to make an APPH determination based solely on "valid scientific evidence" that is submitted in lieu of "well-controlled investigations" (*i.e.*, clinical trials).[66] FDA no doubt leans heavily on this alternative as it had repeatedly told applicants that long-term clinical trials would likely not be necessary.[67] In doing so, however, FDA places more weight on that provision than it can bear. Section 910(c)(5)(B) does not authorize FDA to reject a PMTA – and applications for over one million products – merely because they did not contain a single comparative efficacy study. FDA has it wrong.

First, FDA demands deferential review and, for support, cites to *Loper Bright* for the proposition that the term "appropriate" gives FDA significant "flexibility."[68] Yet FDA leaves out *Loper Bright's* further admonition that any discretion is constrained by "limits imposed by [the] term or phrase." Importantly, *Loper Bright* relies on *Michigan v. EPA*, 576 U.S. 743,

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turer's access and marketing restrictions aimed at reducing underage use could be "critical" to an APPH determination, FDA admitted that "for the sake of efficiency" it had "not evaluated any marketing plans submitted with these applications." *Id.* at 11 n.xix. *See Bidi Vapor LLC v. FDA*, 47 F.4th 1191, 1195 (11th Cir. 2022) (holding failure to consider marketing plans was arbitrary and capricious).

[66] FDA Br. 13, 18; *see* 21 U.S.C. § 387j(c)(5).

[67] Wages Br. at 13, 41.

[68] FDA Br. 16 (citing *Loper Bright*, 144 S. Ct. at 2263).

752 (2015), where the Court considered EPA's authority under the Clean Air Act ("CAA") to regulate power plants if "appropriate and necessary." In interpreting the meaning of "appropriate," the Court viewed the term in its "present context."[69] Stated differently, a term like "appropriate" must be read in light of any surrounding provisions and cannot be employed by an agency to claim implicitly delegated authority Congress did not give.

As discussed above, Section 910(c) of the TCA makes clear that the APPH standard is broad and that it encompasses a range of considerations well beyond a comparative efficacy test. In fact, this Court in *Michigan* described "appropriate" in the CAA as "the classic broad and all-encompassing term that naturally and traditionally includes consideration of all the relevant factors."[70] As such, Section 910(c)(5)(B) cannot be read as permitting FDA to *automatically* issue an MDO simply because a single study on one of many relevant factors was missing. While FDA is correct that it has discretion (or flexibility) in weighing and balancing all of those factors, it does not have authority to rely on only one factor to the complete exclusion of all others.

Second, this is the "best" reading of Section 910(c)(5)(B). That provision states "for purposes of [making a determination under] paragraph (2)(A)" that FDA "may authorize" that it be made based on "valid scientific evidence" (hardly a surprising notion given the subject

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[69] *Loper Bright*, 144 U.S. at 2263; *Michigan*, 576 U.S. at 752-53 (also stating that "[s]tatutory context reinforces" a court's interpretation); *see also Sossamon v. Texas*, 563 U.S. 277, 287 (2011) (holding the "word 'appropriate' is inherently context dependent").

[70] *Id*. at 752 (also noting the "capaciousness" of the term in holding that it would include "cost" considerations).

matter). But that does not mean, as FDA argues, the absence of a single study may, without more, also result in an across-the-board denial of marketing authorizations. Rather, paragraph (2)(A) provides, in turn, that a marketing decision be based on the APPH standard which, as we have already demonstrated, Congress intended to encapsulate all relevant information and data in a PMTA. In that context, Section 910(c)(5)(B) can only mean that if a PMTA is missing "valid scientific information" that FDA deems relevant to evaluating an ENDS product, such absence must still be weighed and balanced against other data favoring a marketing granted order (*e.g.*, evidence showing that minors are not using a product subject to a PMTA). Indeed, FDA's approach would completely read out of paragraph (2)(A) the all-encompassing term "appropriate," as well as the statute's command that a marketing decision be based on "the risks *and* benefits to the population as a whole."[71]

Third, FDA never explains how Section 910(c)(5)(B) can be better read as authorizing the agency to completely ignore all other relevant evidence in a PMTA. For instance, what if there is no evidence minors are using a manufacturer's product and the circumstances indicate that any future underage use is unlikely (*e.g.*, a PMTA submitted by a single vape shop located in a sparsely populated area that employs strict marketing and access restrictions, and only makes e-liquids "to order" for known, adult customers)? Surely, under

[71] Section 910(c)(5)(B) is also limited to "scientific" evidence. As such, that provision cannot be interpreted to mean that Congress somehow relied on that provision alone to implicitly give FDA authority to completely ignore all of the non-scientific information that Congress otherwise considered relevant to APPH, like marketing and access restrictions.

those circumstances, the scales would tip heavily in favor of granting market authorization, provided other evidence showed those e-liquids are being used by the adult customers to reduce or quit their smoking habits and such products are less risky than combustible cigarettes. But under the FDA's interpretation of the TCA, those factors would have never been considered and, in fact, would have been rendered totally irrelevant. FDA would have completely failed to ascertain whether there was a "net benefit." Accordingly, FDA's across-the-board MDOs simply cannot be reconciled with Section 910's APPH standard.

CONCLUSION

Based on the foregoing, *amici* ask that this Court affirm the judgment below.

Respectfully submitted,

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October 15, 2024

APPENDIX

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List of *Amici Curiae*

American Vape Company, LLC d/b/a Ludicrous Distro (TX)

American Vapor Manufacturers Association (AZ)

American Vapor Group d/b/a Red Star Vapor (AZ)

Bidi Vapor, LLC (FL)

Breeze Smoke, LLC (MI)

ECIG Charleston (SC)

Flavour Art North American (Canada)

FLV USA d/b/a Flavorah (WA)

Lead by Sales, LLC d/b/a White Cloud Cigarettes (FL)

Lotus Vaping Technologies, LLC (ID)

Magellan Technology, Inc. (NY)

Matrix Minds, LLC (TX)

NicQuid, LLC (OH)

Ohio Vapor Trade Association, Inc. (OH)

Pastel Cartel, LLC (TX)

Smoke-Free Alternatives Trade Association (DC)

SS Vape Brands (FL)

Streamline Vape/MH Global (CA)

SV3, LLC (CA)

Vape Element LLC d/b/a BLVK E-Liquid (CA)

Vertigo Vapor, Inc. d/b/a Baton Vapor (WA)

White Horse Vapor (RI)

YLSN Distribution LLC d/b/a Happy Distro (AZ)