Nos. 21-9577 and 21-9578

IN THE UNITED STATES COURT OF APPEALS
FOR THE TENTH CIRCUIT

ELECTRIC CLOUDS, INC.
Petitioner,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION,
Respondent.

CLOUD 9 VAPOR PRODUCTS, L.L.C.
Petitioner,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION,
Respondent.

On Petition for Review of a Marketing Denial Order Issued
by the United States Food and Drug Administration

BRIEF OF *AMICI CURIAE* MEDICAL, PUBLIC HEALTH, AND COMMUNITY GROUPS IN SUPPORT OF RESPONDENT

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

Statutes

Regulations

Other Authorities

GLOSSARY

ENDS	Electronic nicotine delivery system
FDA	United States Food and Drug Administration

Amici medical, public health, and community groups submit this brief in support of Respondent United States Food and Drug Administration ("FDA") and urge the Court to uphold the marketing denial orders issued to Petitioners Electric Clouds, Inc. and Cloud 9 Vapor Products, L.L.C. By denying authorization to Petitioners' flavored e-liquids—available in flavors such as Candy Man, Caramel Apple, Mango Melon Madness, and Sugar Cookie, Cloud9-FDA1-44-45—FDA has acted to protect public health by removing from the market flavored products that have fueled an epidemic of youth usage of highly addictive and harmful e-cigarettes, with no demonstrated countervailing benefit in helping adult smokers to stop smoking cigarettes. All parties have consented to the filing of this brief.

STATEMENT OF INTEREST OF *AMICI CURIAE*[1]

Amici are the following national and state medical, public health, and community organizations: American Academy of Family Physicians, American Academy of Pediatrics, American Cancer Society Cancer Action Network, American Heart Association, American Lung Association, American Medical Association, Campaign for Tobacco-Free Kids, Colorado Medical Society, Parents Against Vaping e-cigarettes, and Truth Initiative. *Amici* include physicians who

[1] Pursuant to Fed. R. App. P. 29(a)(4)(E), *amici* affirm that no party's counsel authored this brief in whole or in part, neither the parties nor their counsel contributed money that was intended to fund preparing or submitting this brief, and no person—other than *amici*, their members, or their counsel—contributed money that was intended to fund preparing or submitting the brief.

counsel their young patients and their parents about the hazards of tobacco use, organizations with formal programs to urge users to quit, and groups representing parents and families struggling to free young people from nicotine addiction. Each of these organizations works on a daily basis to reduce the devastating health harms of tobacco products, including electronic nicotine delivery system ("ENDS" or "e-cigarette") products and the e-liquids used in those products.[2] Accordingly, *amici* have a direct and immediate interest in ensuring that Petitioners' highly addictive and youth-appealing flavored e-liquids not be permitted on the market, which can only be assured by upholding FDA's denial orders.

Amici also have a special interest in this case because many of the *amici* were plaintiffs in *American Academy of Pediatrics v. FDA*, in which they obtained a federal court order: (1) establishing new deadlines for the required submission of premarket tobacco product applications for e-cigarette products, and (2) limiting the time period that e-cigarettes may remain on the market without the required premarket orders. 379 F. Supp. 3d 461 (D. Md. 2019); 399 F. Supp. 3d 479 (D. Md. 2019), *appeal dismissed sub nom. In re Cigar Ass'n of Am.*, 812 F. App'x 128 (4th Cir. 2020). *Amici* therefore have a strong interest in ensuring that the premarket review process functions to protect the public health by removing from the market flavored e-cigarette products, like Petitioners' e-liquids, that threaten the health and

[2] This brief uses the terms "e-cigarette" and "ENDS" interchangeably.

well-being of young people without sufficient countervailing evidence of any benefit to adults who smoke cigarettes.

INTRODUCTION AND SUMMARY OF ARGUMENT

Petitioners manufacture flavored "nicotine-containing e-liquids," Petrs' Br. 9, highly addictive and harmful products that have consistently been shown to appeal to youth. FDA denied Petitioners' applications to market their flavored e-liquids because the applications lacked sufficient evidence that Petitioners' flavored products are more effective than unflavored (i.e., tobacco-flavored) products in helping adult smokers stop smoking cigarettes, so as to outweigh the known risks to youth posed by these products. ElectricClouds-FDA1-3935; Cloud9-FDA1-40.

In light of the mountain of evidence of youth attraction to flavored e-cigarettes, and the addictiveness and health harms to young people from those products—including products, like Petitioners' e-liquids, used in open-system e-cigarettes—it was entirely reasonable for FDA to require Petitioners to submit robust, product-specific evidence of the benefit of their products compared to tobacco-flavored products in aiding smokers to stop smoking. It was not arbitrary and capricious for FDA to issue denial orders based on Petitioners' failure to provide such evidence.

It also was not arbitrary and capricious for FDA to conclude that Petitioners' youth access and marketing restrictions would be insufficient to reduce the risk of

youth initiation of Petitioners' products. FDA's experience, along with other real-world data, clearly demonstrate that, when it comes to flavored e-cigarettes, these types of restrictions are inadequate to reduce youth access, given flavored products' overwhelming appeal to young people.

Moreover, contrary to Petitioners' assertion, the Food, Drug and Cosmetic Act, as amended by the Family Smoking Prevention and Tobacco Control Act, Pub. L. 111-31, 123 Stat. 1776 ("Tobacco Control Act") makes FDA's authority to require post-market surveillance and review of Petitioners' products immaterial to FDA's determination of whether a product satisfies the statutory standard for a marketing order. Reliance on such post-market surveillance and action also would be inadequate to protect the public health.

Finally, after enjoying a lengthy period of time to market their products without the order required by statute, Petitioners now ask the Court to order FDA to allow their products to remain on the market for an additional period while they conduct studies in an effort to demonstrate that their flavored products provide a public health benefit.

Petitioners' request is contrary to law and if accepted would be detrimental to public health. The requested relief defies the Tobacco Control Act's requirement that a product may be marketed only *after* it has been shown to be appropriate for the protection of the public health, not while a company assembles the evidence

necessary to make that showing. Moreover, allowing Petitioners' highly addictive flavored e-liquids to remain on the market for even one more day poses a significant risk to children.

ARGUMENT

I. Given the Overwhelming Evidence of Youth Attraction to Flavored E-Cigarettes, Including Open-System Products, It Was Not Arbitrary and Capricious for FDA to Deny Petitioners' Applications for Failure to Provide Robust Evidence That Their Flavored E-Liquids Help Smokers Stop Smoking More Effectively Than Unflavored Products.

In determining whether the marketing of an e-cigarette meets the statute's "appropriate for the protection of the public health" standard, FDA must weigh two factors: (1) the likelihood that the product will help existing tobacco users stop using tobacco products, and (2) the likelihood that the product will lead non-tobacco users, including youth, to begin using such products. 21 U.S.C. § 387j(c)(4). Applying this framework to e-cigarettes, FDA found the evidence overwhelming that flavors—across all types of e-cigarette products—appeal to youth more than tobacco-flavored products. ElectricClouds-FDA1-11080; Cloud9-FDA1-108. Given this unequivocal finding, it was entirely reasonable, and certainly not arbitrary and capricious, for FDA to require Petitioners to submit "the strongest types of evidence" demonstrating that their flavored products, as compared to tobacco-flavored products, benefit smokers by helping them to stop smoking cigarettes. ElectricClouds-FDA1-11076; Cloud9-FDA1-104. And when Petitioners failed to

furnish such evidence, FDA correctly issued marketing denial orders. As the U.S. Court of Appeals for the Fourth Circuit held in a similar case involving a marketing denial order for flavored e-liquids, "FDA could not allow young adults to perceive e-cigarettes as another Baby Ruth or Milky Way, only to find themselves in the grip of a surreptitious nicotine addiction. This was hardly arbitrary." *Avail Vapor, LLC v. FDA*, 55 F.4th 409, 428 (4th Cir. 2022).

The impact of a product on youth initiation is particularly critical because, as FDA noted in its technical project lead reviews of Petitioners' products, "use of tobacco products, no matter what type, is almost always started and established during adolescence when the developing brain is most vulnerable to nicotine addiction." ElectricClouds-FDA1-11078; Cloud9-FDA1-106-07. Whereas "almost 90 percent of adult daily smokers started smoking by the age of 18 . . . youth and young adults who reach the age of 26 without ever starting to use cigarettes will most likely never become a daily smoker." ElectricClouds-FDA1-11078-79; Cloud9-FDA1-107. As FDA reasonably concluded, "[b]ecause of the lifelong implications of nicotine dependence that can be established in youth, preventing tobacco use initiation in young people is a central priority for protecting population health." ElectricClouds-FDA1-11079; Cloud9-FDA1-107.

A. FDA correctly concluded that there is "robust and consistent" evidence demonstrating that Petitioners' flavored e-liquids are particularly attractive to youth.

As FDA explained in its technical project lead reviews, e-cigarettes are the most popular tobacco product among youth, with more than 3.6 million young people reporting current use in 2020, according to the National Youth Tobacco Survey. ElectricClouds-FDA1-11079; Cloud9-FDA1-107. Nearly one in five (19.6%) U.S. high school students were current e-cigarette users in 2020—about the same level as in 2018 when the U.S. Surgeon General first declared youth e-cigarette use an "epidemic." ElectricClouds-FDA1-11078-79; Cloud9-FDA1-106-07.[3]

As FDA found, flavors are driving these high rates of youth e-cigarette use. *See* ElectricClouds-FDA1-11079; Cloud9-FDA1-107 ("The evidence shows that the availability of a broad range of flavors is one of the primary reasons for the popularity of ENDS among youth."). "[T]he flavoring in tobacco products (including ENDS) make them more palatable for novice youth and young adults,

[3] Since FDA issued the challenged denial orders, the 2021 and 2022 National Youth Tobacco Survey data have become available. *See* 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 MORBIDITY & MORTALITY WKLY. REP. 1387 (2021), https://www.cdc.gov/mmwr/volumes/70/wr/pdfs/mm7039a4-H.pdf; Maria Cooper et al., *Notes from the Field: E-cigarette Use Among Middle and High School Students, 2022*, 71 MORBIDITY & MORTALITY WKLY. REP. 1283 (2022), https://www.cdc.gov/mmwr/volumes/71/wr/pdfs/mm7140a3-H.pdf. Youth e-cigarette use remains unacceptably high, with over 2.5 million youth, including 14.1% of high schoolers, reporting current e-cigarette use in 2022. *Id.* at 1284 tbl.

which can lead to initiation, more frequent and repeated use, and eventually established regular use." ElectricClouds-FDA1-11079; Cloud9-FDA1-107. In 2020, according to the National Youth Tobacco Survey, 84.7% of high school e-cigarette users reported using a flavored product. ElectricClouds-FDA1-11079; Cloud9-FDA1-1070. And according to data from the FDA and National Institutes of Health's Population Assessment of Tobacco and Health Study, over 93% of youth users reported that their first e-cigarette product was flavored and 71% of current youth e-cigarette users reported using e-cigarettes "because they come in flavors I like." ElectricClouds-FDA1-11079-80; Cloud9-FDA1-107-08. As the U.S. Court of Appeals for the D.C. Circuit found in upholding several denial orders for flavored e-liquids, "[f]lavored tobacco products lie at the heart of the problem. A vast body of scientific evidence shows that flavors encourage youth to try e-cigarettes, and together with the nicotine, keep them coming back." *Prohibition Juice Co. v. FDA*, 45 F.4th 8, 11 (D.C. Cir. 2022); *see also Breeze Smoke, LLC v. FDA*, 18 F.4th 499, 505 (6th Cir. 2021) ("Flavored ENDS products especially appeal to children.").

Nevertheless, Petitioners contend that FDA failed to "account for the markedly reduced actual youth appeal of e-liquids for open-tank systems . . . compared to cartridge or disposable products . . . ." Petrs' Br. 44-45. This argument is without merit. First, the record shows that FDA considered the youth appeal of various device types and reasonably concluded that flavors—regardless of device

type—are what drives youth usage. ElectricClouds-FDA1-11080-81; Cloud9-FDA1-108-09. Second, the evidence shows that open-system products are in fact popular among youth.

FDA found that, "across . . . different device types, the role of flavor is consistent." ElectricClouds-FDA1-11080; Cloud9-FDA1-108. The "published literature" demonstrating "the substantial appeal to youth of flavored ENDS . . . is robust and consistent" and this youth preference for flavored products "is consistently demonstrated across large, national surveys and longitudinal cohort studies." ElectricClouds-FDA1-11080; Cloud9-FDA1-108. In contrast, FDA found that youth preference for particular device types and brands is "likely fluid and affected by the marketplace, that is, the options, especially flavors that are available for consumers to choose from." ElectricClouds-FDA1-11081; Cloud9-FDA1-109. Courts have consistently rejected the argument that "FDA ignored a material distinction between open and closed systems." *Prohibition Juice*, 45 F.4th at 26; *see also Avail Vapor*, 55 F.4th at 427; *Gripum, LLC v. FDA*, 47 F.4th 553, 560 (7th Cir. 2022); *Liquid Labs v. FDA*, 52 F.4th 533, 545 (3d Cir. 2022).

The role of flavors in driving youth e-cigarette use—regardless of device type—is perhaps most vividly demonstrated by what occurred after FDA, in 2020, changed its enforcement priorities to prioritize enforcement against flavored cartridge-based e-cigarettes (other than menthol), which at the time were the most

popular products among youth. *See* FDA, *Enforcement Priorities for Electronic Nicotine Delivery Systems (ENDS) and Other Deemed Products on the Market Without Premarket Authorization (Revised)* at 3 (Apr. 2020) ("2020 Guidance").[4] Following this prioritization of enforcement against cartridge-based e-cigarettes, the rates of high school use of disposables, which were available in flavors but were not prioritized for enforcement purposes, increased ten-fold. ElectricClouds-FDA1-11081; Cloud9-FDA1-109. As FDA noted, this youth migration to alternative device types for which flavors were available "underscor[es] the fundamental role of flavor in driving appeal." ElectricClouds-FDA1-11081; Cloud9-FDA1-109.

In an attempt to distinguish open-system products from other device types, Petitioners point to a 2019 quote from then-FDA Commissioner Gottlieb to portray open-system devices as large and unwieldy—and therefore, having little youth-appeal. Petrs' Br. 44. However, open-system products have evolved dramatically, and many current iterations bear little resemblance to the products Commissioner Gottlieb called "big open-tank contraptions." *Id.* For example, the sleek, easy-to-conceal Smok and Suorin devices pictured below can be used to consume

[4] https://www.fda.gov/media/133880/download.

Petitioners' e-liquids. For reference, the Smok devices below weigh less than 1.6 ounces and measure roughly 3.7 inches tall, 1.2 inches wide, and 0.75 inches deep.[5]

Suorin Drop Rainbow Chrome open-system e-cigarette device.[6]

Smok Nord open-system e-cigarette devices.[7]

Petitioners also ignore the fact that e-cigarette use by young people was a serious problem before cartridge-based products began to dominate the youth market in 2017 (and certainly before the rise in popularity of disposables among youth). In 2015, youth e-cigarette prevalence reached 16%. *See* 2020 Guidance 11. Flavor, and not the delivery system, is the consistent factor in driving youth use.

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[5] *Nord Kit*, SMOK, https://www.smoktech.com/product/pod_mod/nord-kit (last visited May 5, 2023).

[6] *Suorin Drop Rainbow Chrome – Pod System Device with Cartridge Kit*, SUORIN USA, https://www.suorinusa.com/collections/suorin-drop/products/suorin-drop-rainbow-chrome (last visited May 5, 2023).

[7] *Nord Kit*, *supra* note 5.

Moreover, the fact is that open-system products remain popular among youth. Smok and Suorin, for example, are open-system devices and are currently among the most popular e-cigarette devices used by youth.[8] In 2022, one in seven (14.3%) high school e-cigarette users reported using a Smok brand in the past month.[9]

Finally, in asserting that youth use of open-system products has dropped in recent years, Petitioners falsely claim that according to the 2021 National Youth Tobacco Survey, "only 7.5% of [high school e-cigarette users] reported using an open system device—and thus bottled e-liquids." Petrs' Br. 45. However, Petitioners fail to mention that an additional 28.9% of high school e-cigarette users (480,000 students) reported using "Prefilled or refillable pods or cartridges," which include popular refillable open-system products like Smok and Suorin which are compatible with Petitioners' e-liquids.[10] Thus, the true percentage of youth e-cigarette users who report using open-system products is far greater than the 7.5% figure Petitioners cite—and even that understated 7.5% figure translates to ***120,000*** high school students.[11]

[8] *See* Cooper et al., *supra* note 3, at 1284 tbl.

[9] *Id.*

[10] Park-Lee et al., *supra* note 3, at 1388 tbl.

[11] *Id.*

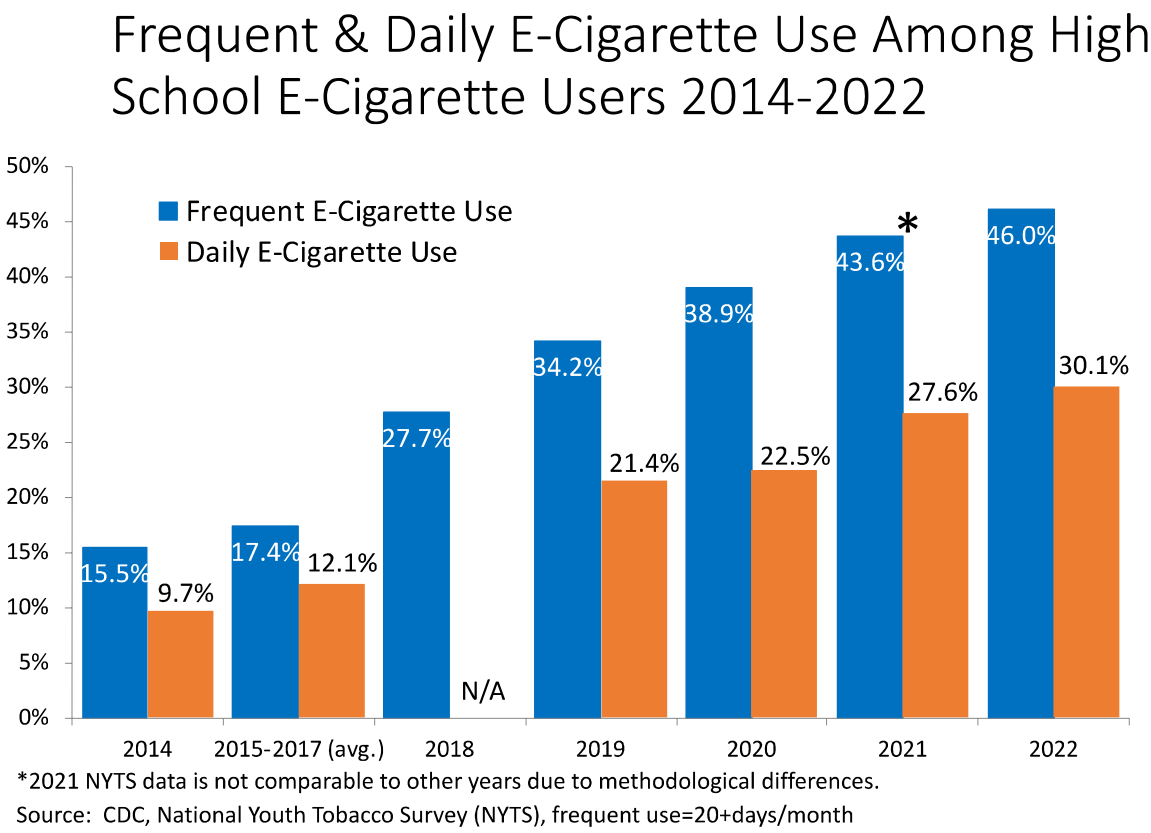
It is undisputed that Petitioners' products have the central feature—flavors—that makes e-cigarettes attractive to youth. It was therefore entirely reasonable for FDA to conclude that Petitioners' flavored e-liquids appeal to youth.

B. As FDA found, Petitioners' flavored e-liquids pose a direct threat of addiction and other health harms to young people.

Petitioners' e-liquids contain nicotine, Petrs' Br. 9, which is "among the most addictive substances used by humans." *Nicopure Labs, LLC v. FDA*, 944 F.3d 267, 270 (D.C. Cir. 2019). In its technical project lead reviews, FDA noted the factors making "[y]outh and young adult brains . . . more vulnerable to nicotine's effect than the adult brain due to ongoing neural development." ElectricClouds-FDA1-11081; Cloud9-FDA1-109. FDA found that the high prevalence of youth e-cigarette use was increasing nicotine dependence among young people. ElectricClouds-FDA1-11081; Cloud9-FDA1-109. FDA noted that in 2019, an estimated 30.4% of middle and high school e-cigarette users reported frequent use (i.e., use on 20 or more of the previous 30 days), and even more alarming, 2l.4% of high school users and 8.8% of middle school users reported *daily* use. ElectricClouds-FDA1-11081; Cloud9-FDA1-109. As shown in Chart 1 below, frequent and daily use prevalence among high school students has continued to rise, demonstrating that the level of addiction among high school e-cigarette users is also rising. In 2022, 46% of high school e-

cigarette users (980,00 students) reported frequent use and 30.1% (640,000 students) reported daily use, a strong sign of nicotine addiction.[12]

Chart 1



In addition to the risk of addiction, FDA found that youth exposure to nicotine "can induce short and long-term deficits in attention, learning, and memory." ElectricClouds-FDA1-11081; Cloud9-FDA1-109. FDA cited other health harms from e-cigarettes as well, including "associations between ENDS use and self-reported history of asthma, chronic bronchitis, emphysema, or chronic obstructive

[12] Cooper et al., *supra* note 3, at 1284 tbl.

pulmonary disease with increased ENDS use (i.e., daily use) relating to increased odds of disease." ElectricClouds-FDA1-11082; Cloud9-FDA1-110.

FDA also noted the data documenting a risk of progression from e-cigarettes to other tobacco products. *See* ElectricClouds-FDA1-11081-82; Cloud9-FDA1-110. In its technical project lead reviews, FDA cited a "systematic review and meta-analysis that summarized nine prospective cohort studies" finding "significantly higher odds of smoking initiation . . . and past 30-day combusted cigarette use . . . among youth who had used ENDs as compared to youth who had not . . . ." ElectricClouds-FDA1-11081-82; Cloud9-FDA1-110. A 2018 report by the National Academies of Sciences, Engineering, and Medicine, cited in the technical project lead reviews, found "substantial evidence that e-cigarette use increases [the] risk of ever using combusted tobacco cigarettes among youth and young adults." ElectricClouds-FDA1-11082; Cloud9-FDA1-110. Thus, the threat of flavored e-cigarettes is not just a short-term health threat; it also is a threat to a young person's future health by increasing the risk that they will progress to a lifetime of addiction to even more hazardous tobacco products.

C. FDA acted reasonably in requiring robust evidence showing that Petitioners' flavored e-liquids help smokers stop smoking more effectively than tobacco-flavored products.

Precisely because the evidence that flavored tobacco products appeal to youth is so "robust and consistent," ElectricClouds-FDA1-11080; Cloud9-FDA1-108, it

was entirely reasonable for FDA to require similarly "robust and reliable" evidence showing that Petitioners' flavored e-liquids help smokers stop smoking more effectively than tobacco-flavored products, and that such a benefit be "substantial enough to overcome the significant risk of youth uptake and use posed by the flavored ENDS product." ElectricClouds-FDA1-11084; Cloud9-FDA1-112. The available evidence falls far short of making such a showing.

FDA found that, "in contrast to the evidence related to youth initiation—which shows clear and consistent patterns of real-world use that supports strong conclusions—the evidence regarding the role of flavors in promoting switching among adult smokers is far from conclusive." ElectricClouds-FDA1-11084; Cloud9-FDA1-112-13. For example, a systematic review that examined consumer preference for various e-cigarette attributes found "inconclusive evidence" as to whether flavored e-cigarettes assisted smokers to stop smoking.[13] As FDA reasonably concluded, "the literature does not establish that flavors differentially promote switching amongst ENDS users in general." ElectricClouds-FDA1-11084-85; Cloud9-FDA1-113. Thus, it was entirely reasonable for FDA to require Petitioners to demonstrate the effectiveness of their flavored products in helping

[13] Samane Zare et al., *A systematic review of consumer preference for e-cigarette attributes: Flavor, nicotine strength, and type*, 13 PLoS ONE 1, 12 (2018), https://pubmed.ncbi.nlm.nih.gov/29543907/.

smokers stop smoking through randomized controlled trials, longitudinal cohort studies, or other similarly rigorous studies.

Instead of submitting any such studies, Petitioners offered customer surveys, Petrs' Br. 34, and "studies that included data on use measures and evidence of user behavior such as 'liking' and 'intent to use' for tobacco-flavored and other flavored e-liquids." *Id.* at 32-33. These studies are necessarily insufficient to demonstrate that Petitioners' flavored products better enable cigarette smokers to stop smoking than tobacco-flavored products. As FDA noted, such studies measure only users' beliefs about their experience with flavored products; they prove nothing about whether the use of flavors actually affects smoking behavior when compared to unflavored products. *See* ElectricClouds-FDA1-11085; Cloud9-FDA1-114 ("Consumer perception studies (surveys or experiments) typically assess outcomes believed to be precursors to behavior, such as preferences or intentions related to new products, but are not designed to directly assess actual product use behavior."). Petitioners presented no studies showing that users of their flavored products were more likely to stop smoking cigarettes than users of tobacco-flavored products. In its technical project lead reviews, FDA explained in detail why it is necessary to perform studies that "enable direct assessment of behavioral outcomes associated with actual product use over time," ElectricClouds-FDA1-11085; Cloud9-FDA1-

114, which the studies offered by Petitioners did not do. There was nothing arbitrary or capricious about the agency's approach.

Petitioners' studies also failed to compare their flavored e-liquids with tobacco-flavored e-cigarettes in terms of their ability to help smokers stop smoking. *See* Petrs' Br. 33. Contrary to Petitioners' assertion, requiring a comparison between flavored and tobacco-flavored products in terms of their effectiveness in helping smokers stop smoking certainly was not arbitrary and capricious. *See id.* The Tobacco Control Act "expressly asks for evidence concerning whether an applicant's 'tobacco product presents less risk than other tobacco products . . . .'" *Prohibition Juice*, 45 F.4th at 23 (quoting 21 U.S.C. § 387j(b)(1)(A)). Given that, as FDA found, "tobacco-flavored ENDS may offer the same type of public health benefit as flavored ENDS, i.e., increased switching and/or significant reduction in smoking, but do not pose the same degree of risk of youth uptake," ElectricClouds9-FDA1-11076; Cloud9-FDA1-104, such a comparison is reasonable and precisely the "judgment . . . the [Tobacco Control Act] envisioned the FDA could make." *Avail Vapor*, 55 F.4th at 421; *see also Liquid Labs*, 52 F.4th at 542 ("We also join our sister circuits in concluding that the FDA permissibly required a comparison of a

manufacturer's flavored products with tobacco-flavored ENDS' products in their ability to assist adult smokers to quit or switch.") (cleaned up).[14]

D. FDA's requirement for product-specific evidence showing the comparative benefit of flavored versus tobacco-flavored products in helping smokers to stop smoking was reasonable.

Contrary to Petitioners' claim (Petrs' Br. 42-46), the marketing denial orders were not arbitrary and capricious because they relied on general evidence of the impact of flavors on youth e-cigarette use, while requiring product-specific evidence to assess any benefits to smokers from use of Petitioners' products. Courts have consistently rejected this very argument. *See, e.g.*, *Prohibition Juice*, 45 F.4th at 22 (rejecting argument that "FDA imposed an evidentiary 'double standard' by using literature reviews to as evidence for flavored products' risks but eschewing literature

[14] Petitioners also argue that this comparative analysis requirement created an unfair surprise. Petrs' Br. 25-29, 25-26 n.4. As the D.C. Circuit concluded, "[t]his argument is far off base." *Prohibition Juice*, 45 F.4th at 23. Both the Tobacco Control Act (21 U.S.C. § 387j(b)(1)(A)), and FDA's 2019 Premarket Tobacco Product Applications for Electronic Nicotine Delivery System Guidance (ElectricClouds-FDA2-4411), which recommended that applicants compare their products to products in the same category or subcategory, "are clear about comparative analysis." *Liquid Labs*, 52 F.4th at 542-53. "Because the 2019 Guidance gave fair notice of the analysis the agency would perform and the purpose of those comparisons, we hold the agency did not create unfair surprise by focusing on comparisons between otherwise similar flavored and nonflavored products." *Prohibition Juice*, 45 F.4th at 24. Quoting *Prohibition Juice*, the Third Circuit similarly held that "FDA did not apply unannounced or changed standards . . . ." *Liquid Labs*, 52 F.4th at 542-53. Thus, Petitioners are wrong in claiming that the *Liquid Labs* decision does not address the "unfair surprise" argument they advance here. *See* Petrs' Br. 25-26 n.4.

reviews as evidence of their benefits."); *Avail Vapor*, 55 F.4th at 421 ("FDA did not use an 'evidentiary double standard' when reviewing petitioners' applications."); *Breeze Smoke*, 18 F.4th at 508 (concluding that FDA acted reasonably in "requiring [Petitioner] present more than literature reviews to justify its products' public health benefits").

FDA reasonably relied on general scientific literature to show the special appeal of flavored e-cigarettes to youth because, in the Sixth Circuit's words, "those risks are understood as a matter of scientific consensus." *Id.* There is no dispute that Petitioners' products have the primary characteristic—flavors—that attracts young people to e-cigarettes. In contrast, FDA found that no scientific consensus exists on whether flavors help cigarette smokers stop smoking to a greater degree than tobacco-flavored e-cigarettes. *See* ElectricClouds-FDA1-11084-85; Cloud9-FDA1-112-13. As the D.C. Circuit held, FDA "reasonably drew differing conclusions from evidence of differing strength." *Prohibition Juice*, 45 F.4th at 22.

While Petitioners claim that they submitted longitudinal studies as part of their literature reviews, Petrs' Br. 32-33, as well as "information on switching and cessation, [and] outcomes based on flavor type," *id.* at 37, even Petitioners do not claim that these studies actually evaluated *Petitioners'* products. This is a fatal omission because, as FDA noted, a product's effectiveness in "promoting switching among smokers arises from a combination of its product features—including labeled

characteristics like flavor and nicotine concentration—as well as the sensory and subjective experience of use (taste, throat hit, nicotine delivery), and can also be influenced by how the device itself looks and feels to the use[r]." ElectricClouds-FDA1-11086; Cloud9-FDA1-113. It was thus reasonable for FDA to require product-specific evidence to support Petitioners' claim that their products help people stop smoking cigarettes.

II. FDA's Determination That Access and Marketing Restrictions Are Insufficient to Reduce Youth Initiation of Flavored Products Was Reasonable.

Petitioners argue that FDA failed to consider their "youth prevention and traceability and marketing plans," which they allege "provided evidence to support that Petitioners' products currently do not, and would not in the future, induce youth initiation." Petrs' Br. 36. As is apparent from the technical project lead reviews, FDA gave due consideration to the role of access and marketing restrictions, like those proposed by Petitioners. *See* ElectricClouds-FDA1-11084 n.xix; Cloud9-FDA1-112 n.xix. Based on the agency's experience with those restrictions, FDA reasonably concluded that they are insufficient to prevent youth usage of flavored and highly addictive products that are so intensely appealing to young consumers. *See* ElectricClouds-FDA1-11084 n.xix; Cloud9-FDA1-112 n.xix.

While access and marketing restrictions are important and indeed *necessary* to support a premarket tobacco product application, as FDA has emphasized time

and again, *see* Petrs' Br. 38-39, Petitioners' proposed measures, such as requiring age-verification prior to entering a store or completing an online sale, and eschewing advertising that includes youth-appealing imagery, mirror those that FDA previously found were *insufficient* to curb youth usage of flavored e-cigarettes. *See* 2020 Guidance 6-8, 21.

In March 2019, in response to the youth vaping epidemic, FDA issued a Draft Guidance ("2019 Draft Guidance"),[15] which "proposed to focus its enforcement priorities of flavored ENDS products on how the product was sold . . . ." 2020 Guidance 21 (describing 2019 Draft Guidance). For example, FDA stated that it would prioritize enforcement against products "sold in locations that minors are able to enter at any time," "sold online without independent, third-party age- and identity-verification services," and whose "[l]abeling and/or advertising . . . has included . . . cartoons" and other youth-appealing imagery. 2019 Draft Guidance 13-15. These are all measures that Petitioners propose here. *See* Petrs' Br. 36-37.

In 2020, FDA announced in its Final Guidance that these access and marketing restrictions had been insufficient to protect youth from flavored e-cigarettes. "The reality," FDA found, "is that youth have continued access to these

[15] FDA, *Modifications to Compliance Policy for Certain Deemed Tobacco Products; Guidance for Industry; Draft Guidance* (Mar. 2019), https://tobacco.ucsf.edu/sites/g/files/tkssra4661/f/wysiwyg/Draft%20guidance%20-%20modifications%20to%20compliance%20policy%20-%20March%202019.pdf.

[e-cigarette] products in the face of legal prohibitions and even after voluntary actions by some manufacturers." 2020 Guidance 21. "[A]fter considering . . . comments, the public health threats, and the new evidence . . . FDA determined that focusing on how the product was sold would not appropriately address youth use of the products that are most popular among youth . . . ." *Id.* Petitioners here fail to explain why access and marketing restrictions that FDA previously found insufficient to curb youth access to flavored e-cigarettes would be effective as to its youth-appealing flavored e-liquids. Other courts have upheld marketing denial orders against similar company arguments. *See*, *e.g.*, *Prohibition Juice*, 45 F.4th at 17 ("The measures [applicants] highlight in their marketing plans are not materially different from those the FDA had previously found insufficient to stem the surge in youth e-cigarette use."); *Liquid Labs*, 52 F.4th at 544 (Applicant "has not explained how the approaches in its plan differ from ones previously found insufficient . . ."); *Avail Vapor*, 55 F.4th at 418 (Applicant's "marketing plan included only garden variety restrictions that the FDA had previously found wholly inadequate in preventing youth use").

FDA's conclusion regarding the inadequacy of Petitioners' proposed measures is also supported by other data indicating that youth obtain e-cigarettes with relative ease. According to the 2022 Monitoring the Future Survey, over half of 10th grade students reported that it would be easy to get vaping devices (51.9%)

and nicotine-containing e-liquids (50.8%).[16] As FDA explained in its 2020 Guidance (at 28-29), the majority of youth e-cigarette users obtain e-cigarettes through social sources, such as older friends or relatives—an avenue of access unlikely to be significantly affected by youth access restrictions.

Given FDA's experience with restrictions like the ones Petitioners proposed, the ease with which youth report obtaining e-cigarettes, and the alarming level of continued youth usage of flavored e-cigarettes, FDA reasonably concluded that Petitioners' access and marketing restrictions are insufficient to adequately reduce the risk of youth initiation of Petitioners' flavored products that are so appealing to the young.

III. FDA's Authority to Require Post-Market Surveillance and Review of Petitioners' Products Is Immaterial to the Determination of Whether Those Products Are Appropriate for the Protection of the Public Health.

Petitioners assert that the denial orders were also arbitrary and capricious because FDA "failed to consider other approaches" to address youth initiation, such as by exercising its authority to require post-market reporting and review of post-market "labeling, advertising, marketing, promotional materials, and marketing plans that were not previously submitted." Petrs' Br. 46-47. Petitioners also contend FDA could use its post-market authority "to restrict or even prohibit the further sale

[16] *Table 16: Trends in Availability of Drugs as Perceived by 10th Graders*, MONITORING THE FUTURE (2022), https://monitoringthefuture.org/wp-content/uploads/2022/12/mtf2022table16.pdf.

of [Petitioners' products] as necessary." *Id.* at 47. Contrary to Petitioners' argument, not only does the Tobacco Control Act make the availability of such post-market FDA action immaterial to the statutory public health determination; reliance on post-market surveillance and action would be inadequate to protect the public health.

Section 910 of the Tobacco Control Act requires FDA to deny a premarket application if "there is a lack of a showing that permitting such tobacco product to be marketed would be appropriate for the protection of the public health." 21 U.S.C. § 387j(c)(2)(A). By its plain terms, an applicant's new products must be appropriate for the protection of the public health *before* they can be marketed. The fact that FDA may exercise its authority to require extensive post-market information from a successful applicant, *see* 21 C.F.R. §§ 1114.39, 1114.41, and can withdraw a marketing order or take other post-market action based on that information, is not a reason to grant a marketing order for a product that is not appropriate for the protection of the public health based on premarket information. Thus, as important as FDA's post-market authority is to protect the public health, the exercise of that authority is not a factor that FDA is required to consider in determining, in the first place, if a product is appropriate for the protection of the public health. As the D.C. Circuit held, "FDA was not required to consider alternative regulatory approaches before denying the manufacturers' applications for premarket approval." *Prohibition Juice*, 45 F.4th at 26.

Moreover, the nation's experience with the public health consequences of flavored e-cigarettes demonstrates that the availability of post-market surveillance may not be sufficient to protect the public health in the absence of rigorous premarket review. Largely because of flavors, youth use of e-cigarettes quickly reached epidemic levels, increasing an astounding 78% in a single year (from 2.1 million youth in 2017 to 3.6 million in 2018) and catching FDA by surprise.[17] In the words of then-Commissioner Gottlieb, "[w]hat I did not predict was that, in 2018, youth use of e-cigarettes . . . would become an epidemic."[18] The lesson here is that by the time FDA determines that a new tobacco product has become a threat, substantial harm may already have occurred. To sufficiently protect public health, the availability of post-market surveillance is not an adequate substitute for the rigorous premarket review mandated by Section 910.

IV. Petitioners' Requested Relief Would Be Contrary to the Tobacco Control Act and Harm Public Health.

In addition to requesting that the Court vacate the marketing denial orders, Petitioners further urge the Court to enjoin FDA from "taking any further adverse

[17] *See* Press Release, FDA, *Statement from FDA Commissioner Scott Gottlieb, M.D. on proposed new steps to protect youth by preventing access to flavored tobacco products and banning menthol in cigarettes* (Nov. 15, 2018), https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-proposed-new-steps-protect-youth-preventing-access.

[18] *Id.*

action" on Petitioners' premarket tobacco product applications for 18 months "to allow time for further studies and supplementation." Petrs' Br. 48. Such relief would be contrary to the Tobacco Control Act and harmful to public health.

As discussed *supra* Part I, Petitioners' flavored products are highly attractive to youth, and Petitioners have failed to offer evidence sufficient to show that their products provide a countervailing public health benefit to justify allowing their continued marketing. Under the Tobacco Control Act, manufacturers may only market their tobacco products if they have first demonstrated that their products are appropriate for the protection of the public health; they have no inherent right to market their products without having met that standard. *See* 21 U.S.C. § 387j(c)(2)(A). Indeed, because they have no marketing order, Petitioners' products have been on the market only through the enforcement forbearance of FDA. *See generally*, *Am. Acad. of Pediatrics*, 379 F. Supp. 3d at 468, 493 (D. Md. 2019) (noting that e-cigarette manufacturers lacking a marketing order have enjoyed "a holiday from meeting the obligations of the law").

Should the Court vacate the denial orders, any further relief to Petitioners allowing them to keep their products on the market while they conduct the required studies would turn the Tobacco Control Act on its head by allowing Petitioners to continue to market their products despite having failed to satisfy the statutory public health standard, a showing the statute requires applicants to make *before* marketing

a tobacco product. 21 U.S.C. § 387j(c)(2)(A). Further relief would also effectively place the burden of Petitioners' continuing failure to meet the public health standard on the young people who have already suffered so seriously at the hands of flavored e-cigarette manufacturers, rather than on the companies that have enjoyed the benefit of a years-long regulatory "holiday." If granted, Petitioners' requested relief would run counter to the Tobacco Control Act and have profoundly negative public health consequences. It should therefore be denied by this Court.

CONCLUSION

For these reasons, and those presented by the government, *amici* urge the Court to uphold the marketing denial orders.

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on May 17, 2023, I filed the foregoing via the CM/ECF system, which will send a Notification of Electronic Filing to all counsel of record.

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