ORAL ARGUMENT SCHEDULED FOR APRIL 21, 2022

No. 21-1201
Consolidated with 21-1203, 21-1205, and 21-1207

IN THE UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA

PROHIBITION JUICE CO., et al.

Petitioners,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION,

Respondent.

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

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

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CERTIFICATE AS TO PARTIES, RULINGS, AND RELATED CASES

Pursuant to D.C. Cir. R. 28(a)(1), *amici curiae* Medical and Public Health Groups certify as follows:

A. Parties and *Amici*

Except for the following *amicus*, all parties, intervenors, and *amici* appearing in this Court are listed in the Briefs for Petitioners and Respondent:

Medical Society of the District of Columbia[1]

B. Rulings under Review

References to the rulings at issue appear in the Briefs for Petitioners and Respondent.

C. Related Cases

Related cases are listed in the Briefs for Petitioners and Respondent.

[1] The Medical Society of the District of Columbia joined this *amicus* brief after *Amici* Medical and Public Health Groups filed their Notice of Intention to Participate as *Amicus Curaie* (Feb. 4, 2022) and, therefore, were not listed on that filing.

DISCLOSURE STATEMENT

Pursuant to Fed. R. App. P. 26.1(a) and D.C. Cir. R. 26.1, *amici curiae* are all non-profit organizations committed to advancing the public health. No party to this filing has a parent corporation, and no publicly held corporation owns 10% or more of the stock of any of the parties to this filing.

Dated: February 11, 2022

/s/ Andrew N. Goldfarb
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GLOSSARY

CB	Cool Breeze
FDA	United States Food and Drug Administration
JSL	Jay Shore Liquids
PJ	Prohibition Juice

Amici medical, public health, and community organizations 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 Cool Breeze L.L.C., ECig Charleston L.L.C., Jay Shore Liquids L.L.C., and Prohibition Juice Co. because the orders were not arbitrary and capricious, FDA acted well within its statutory authority, the agency did not adopt a product standard requiring notice-and-comment rulemaking, and Petitioners' requested relief would harm public health. By issuing denial orders for Petitioners' flavored e-liquids, 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. This brief is filed with the consent of the parties.

STATEMENT OF INTEREST OF *AMICI CURIAE*

Amici are the following national and local 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, Medical Society of the District of Columbia, Parents Against Vaping e-cigarettes and Truth Initiative (collectively, "*amici*" or "medical and public health groups"). From physicians who counsel their

young patients and their parents about the hazards of tobacco use, to organizations with formal programs to urge users to quit, to 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 e-cigarettes and the e-liquids used in those products. 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 the marketing 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 well-being of young people without sufficient countervailing evidence of any benefit to adult cigarette smokers.

STATEMENT OF COMPLIANCE WITH RULE 29(a)

Amici represent that no party's counsel authored this brief, neither the parties nor their counsel contributed money 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 this brief.

INTRODUCTION AND SUMMARY OF ARGUMENT

Petitioners manufacture flavored "nicotine-containing e-liquids," Corrected Petitioners' Brief ("Petrs' Br.") (Jan. 11, 2022) at 10—a highly-addictive and harmful product that has 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. Charleston-FDA1-000054; Cool Breeze ("CB")-FDA1-000351; Jay Shore Liquids ("JSL")-FDA1-000040; Prohibition Juice ("PJ")-FDA1-000025.

I.A. 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, in the form of a randomized controlled trial,

longitudinal cohort study, or other similarly rigorous 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 marketing denial orders based on Petitioners' failure to provide such evidence.

I.B. It also was not arbitrary and capricious for FDA to conclude that youth access and marketing restrictions would be insufficient to reduce the risk of youth initiation of Petitioners' products given: (1) FDA's own experience with these types of restrictions; and (2) other real-world data showing that, with respect to flavored e-cigarettes, these restrictions are inherently inadequate to prevent youth usage of such products, given their intense appeal to young people.

I.C. 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 would be inadequate to protect the public health.

II. There is also no merit to Petitioners' argument that FDA lacks the statutory authority to require strong evidence that Petitioners' flavored products confer a greater benefit in helping cigarette smokers stop smoking than tobacco-

flavored products. Such a requirement is at the core of the statute's public health standard and does not improperly import the "safe and effective" standard for new drug approval under the Food, Drug and Cosmetic Act into premarket review of new tobacco products.

III. FDA's requirement of reliable evidence that Petitioners' flavored products confer a greater benefit in helping smokers stop smoking than tobacco-flavored products is not a product standard that is required to go through notice-and-comment rulemaking.

IV. Finally, Petitioners ask the Court to order FDA to allow their products to remain on the market while they conduct the required studies. Allowing Petitioners' highly-addictive flavored e-liquids to remain on the market for even one more day poses a significant risk to our children with no countervailing public health benefit. Therefore, Petitioners' requested relief, if granted, would harm public health.

ARGUMENT

I. The Marketing Denial Orders Were Not Arbitrary and Capricious.

A. Given the overwhelming evidence of youth attraction to flavored e-cigarettes, it was reasonable 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 if an e-cigarette is "appropriate for the protection of the public health"—the standard for a marketing order under the Tobacco Control Act—FDA must weigh two competing factors: (1) the likelihood that the product will help existing tobacco users stop using tobacco products, versus (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 device types—appeal to youth more than tobacco-flavored products. Charleston-FDA1-000125-28; CB-FDA1-000796-99; JSL-FDA1-000096-99; PJ-FDA1-000069-72. Given this unequivocal evidence, it was entirely reasonable for FDA to require Petitioners to submit "the strongest types of evidence" demonstrating that, compared to tobacco-flavored products, its flavored products benefit smokers by helping them to stop smoking cigarettes and to issue marketing denial orders based on their failure to furnish such evidence. Charleston-FDA1-000123; CB-FDA1-000794; JSL-FDA1-000094; PJ-FDA1-000067.

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." Charleston-FDA1-000125; CB-FDA1-000796; JSL-FDA1-000096; PJ-FDA1-000069. 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." Charleston-FDA1-000125; CB-FDA1-000796-97; JSL-FDA1-000096-97; PJ-FDA1-000069-70. 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." Charleston-FDA1-000125-26; CB-FDA1-000797; JSL-FDA1-000097; PJ-FDA1-000070.

1. FDA found "robust and consistent" evidence that flavored e-cigarettes, including open-system products, 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. Charleston-FDA1-000126; CB-FDA1-000797; JSL-FDA1-000097; PJ-

FDA1-000070. 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." Charleston-FDA1-000125-26; CB-FDA1-000796-97; JSL-FDA1-000096-97; PJ-FDA1-000069-70.[2]

Flavors are driving this youth vaping epidemic. *See* Charleston-FDA1-000126 ("The evidence shows that the availability of a broad range of flavors is one of the primary reasons for the popularity of [e-cigarettes] among youth."); CB-FDA1-000797 (same); JSL-FDA1-000097 (same); PJ-FDA1-000070 (same). "[T]he flavoring in tobacco products (including [e-cigarettes]) make them more palatable for novice youth and young adults, which can lead to initiation, more frequent and repeated use, and eventually established regular use." Charleston-FDA1-000127; CB-FDA1-000798; JSL-FDA1-000098; PJ-FDA1-000071. In

[2] Since the time FDA issued the challenged marketing denial orders, the 2021 National Youth Tobacco Survey data has 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. Even during the midst of the COVID-19 pandemic, over 2 million high school and middle school students reported current e-cigarette use. *Id.* at 1387. The Centers for Disease Control and Prevention has cautioned against comparing this data to previous survey years due to methodology changes, *id.*—a warning Petitioners disregard. Petrs' Br. 47. Whereas previous years' surveys were conducted entirely in-school, the 2021 survey included both in-school and at-home responses; students who completed surveys in school reported higher e-cigarette use, suggesting that rates may have been much higher had the survey been conducted entirely in schools as with previous surveys. Park-Lee, *supra* note 2, at 1387-89.

2020, 84.7% of high school e-cigarette users reported using a flavored product. Charleston-FDA1-000126; CB-FDA1-000797; JSL-FDA1-000097; PJ-FDA1-000070. And according to data from the federal government, 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." Charleston-FDA1-000126; CB-FDA1-000797-98; JSL-FDA1-000097-98; PJ-FDA1-000070-71. As the Sixth Circuit recently found in denying an emergency stay of a marketing denial order in a similar case, "[f]lavored [e-cigarette] products especially appeal to children." *Breeze Smoke, LLC v. FDA*, 18 F.4th 499, 505 (6th Cir. 2021).[3]

Despite the robust evidence establishing the youth appeal of flavored tobacco products, including e-liquids, Petitioners contend that "such concerns do not apply equally" to its products because they are bottled e-liquids intended for use with open-system devices." Petrs' Br. 47. Contrary to Petitioners' assertion, FDA's analysis and other real-world data show that flavored open-system products, which use e-liquids like those sold by Petitioners, pose a threat to youth. As FDA found, "the role of flavor is consistent" across different device types. Charleston-FDA1-000127; CB-FDA1-000798; JSL-FDA1-000098; PJ-FDA1-000071. Moreover,

[3] The Supreme Court denied a stay of the marketing denial order on December 10, 2021. *Breeze Smoke, LLC v. FDA*, 142 S. Ct. 638 (2021).

open-system products remain popular among youth. Smok and Suorin, for example, are open-system devices that are currently among the most popular e-cigarette devices used by youth.[4] Smok, for instance, is the preferred brand of nearly one in ten (9.6%) high school e-cigarette users and has surpassed JUUL in popularity.[5]

Petitioners misleadingly 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. 47. The 7.5% figure, which still translates to an estimated 120,000 high schoolers, refers to the percent of high school e-cigarette users who reported using "*Tanks or mod systems*" most often.[6] However, an additional 28.9% of high school e-cigarette users (roughly 480,000 students) reported using "Prefilled or refillable pods or cartridges," which include popular refillable open-system products like Smok and Suorin that can use Petitioners' e-liquids.[7] Thus, the true percentage of high school e-cigarette users who report using open-system products is necessarily far greater than the 7.5% figure Petitioners cite.

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[4] *See* Park-Lee et al., *supra* note 2, at 1388 tbl.

[5] *Id.*

[6] *Id.* (emphasis added).

[7] *Id.*

Petitioners also 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. 46. However, these 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 Petitioners' e-liquids. For reference, the Smok devices below weigh less than 0.2 pounds and measure roughly 3.7 inches tall, 1.2 inches wide, and 0.75 inches deep.[8]

Figure 1: Suorin Drop Rainbow Chrome open-system e-cigarette device.[9]

Figure 2: Smok Nord open-system e-cigarette devices.[10]

[8] *Nord Kit*, SMOK, https://www.smoktech.com/product/pod_mod/nord-kit (last visited Feb. 10, 2022).

[9] *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 Feb. 10, 2022).

[10] *Nord Kit*, *supra* note 8.

Petitioners also ignore the fact that e-cigarette use by young people was a serious problem before closed system cartridge-based products came to dominate the youth market beginning in 2017; indeed, youth e-cigarette prevalence reached 16% in 2015. *See* FDA, *Enforcement Priorities for Electronic Nicotine Delivery Systems (ENDS) and Other Deemed Products on the Market Without Premarket Authorization (Revised)*, at 11 (Apr. 2020) ("2020 Guidance").[11] More fundamentally, the salient point is not whether a particular kind or brand of flavored e-cigarette device or e-liquid is popular among youth at a specific point in time—youth preference for particular types and brands of e-cigarettes is "likely fluid and affected by the marketplace, that is, the options, especially flavors, that are available for consumers to choose from." Charleston-FDA1-000127 CB-FDA1-000799; JSL-FDA1-000099; PJ-FDA1-000072. Most critically, youth preference for flavors is *not* fluid. The "published literature" showing "the substantial appeal to youth of flavored [e-cigarettes]…is robust and consistent" and this youth preference for flavored products "is consistently demonstrated across large, national surveys and longitudinal cohort studies." Charleston-FDA1-000127; CB-FDA1-000798; JSL-FDA1-000098; PJ-FDA1-000071. It is undeniable that Petitioners' products have the central feature that make e-cigarettes attractive to youth.

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

2. As FDA found, flavored e-cigarettes, such as Petitioners', pose a direct threat of addiction and other health harms to young people.

Petitioners' e-liquids contain nicotine, Petrs' Br. 10, 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." Charleston-FDA1-000128; CB-FDA1-000799; JSL-FDA1-000099; PJ-FDA1-000072. FDA found that the high prevalence of youth e-cigarette use was increasing nicotine dependence among young people. Charleston-FDA1-000128; CB-FDA1-000799; JSL-FDA1-000099; PJ-FDA1-000072. In 2019, as FDA noted, 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. Charleston-FDA1-000128; CB-FDA1-000799; JSL-FDA1-000099; PJ-FDA1-000072. Frequent and daily use prevalence among high school students were even higher in both 2020[12] and 2021, with 43.6%

[12] Teresa W. Wang et al., *E-cigarette Use Among Middle and High School Students – United States, 2020*, 69 MORBIDITY & MORTALITY WKLY. REP. 1310, 1310 (2020), https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6937e1-H.pdf.

of high school e-cigarette users reporting frequent use and 27.6% reporting daily use in 2021.[13]

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." Charleston-FDA1-000128; CB-FDA1-000799; JSL-FDA1-000099; PJ-FDA1-000072. FDA cited other health harms from e-cigarettes as well, including "associations between [e-cigarette] use and self-reported history of asthma, chronic bronchitis, emphysema, or chronic obstructive pulmonary disease with increased [e-cigarette] use (i.e., daily use) relating to increased odds of disease." Charleston-FDA1-000129; CB-FDA1-000800; JSL-FDA1-000100; PJ-FDA1-000073.

FDA also noted the data documenting a risk of progression from e-cigarettes to other tobacco products. *See* Charleston-FDA1-000128-29; CB-FDA1-000800; JSL-FDA1-000099-100; PJ-FDA1-000072-73. 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 [e-cigarettes] as compared to youth who had not…." Charleston-FDA1-000128; CB-FDA1-000800; JSL-FDA1-000099-100; PJ-FDA1-000072-73. A 2018 report by the National Academies of Sciences, Engineering, and Medicine, cited in the technical project

[13] Park-Lee et al., *supra* note 2, at 1388 tbl.

lead reviews, found "substantial evidence that e-cigarette use increases [the] risk of ever using combusted tobacco cigarettes among youth and young adults." Charleston-FDA1-000128; CB-FDA1-000800; JSL-FDA1-000100; PJ-FDA1-000073. A nationally representative analysis also found that from 2013 to 2016, youth e-cigarette use was associated with more than four times the odds of trying combustible cigarettes and nearly three times the odds of current combustible cigarette use compared to youth with no prior tobacco use.[14] 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.

3. FDA acted reasonably in requiring robust evidence showing that flavored e-cigarettes 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," Charleston-FDA1-000127; CB-FDA1-000798; JSL-FDA1-000098; PJ-FDA1-000071, it was entirely reasonable for FDA to require similarly "robust and reliable" evidence showing that Petitioners' flavored e-cigarettes help smokers stop smoking more effectively than tobacco-flavored products, and that such a benefit be " substantial enough to overcome the significant

[14] Kaitlin M. Berry et al., *Association of Electronic Cigarette Use with Subsequent Initiation of Tobacco Cigarettes in US Youths*, 2 JAMA NETWORK OPEN 1, 7 (2019), https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2723425.

risk of youth uptake and use posed by the flavored [e-cigarette] product." Charleston-FDA1-000130; CB-FDA1-000801; JSL-FDA1-000101; PJ-FDA1-000074. Both the publicly available evidence of such benefits to adult smokers, as well as the data submitted by Petitioners, fall woefully short.

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." Charleston-FDA1-000131; CB-FDA1-000802-03; JSL-FDA1-000102; PJ-FDA1-000075. 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.[15] As FDA reasonably concluded, "the literature does not establish that flavors differentially promote switching amongst [e-cigarette] users in general." Charleston-FDA1-000131; CB-FDA1-000803; JSL-FDA1-000102-03; PJ-FDA1-000075-76. Thus, it was entirely reasonable for FDA to require Petitioners to demonstrate the effectiveness of their flavored products in helping smokers stop smoking through randomized controlled trials, longitudinal cohort studies, or other similarly rigorous studies.

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[15] 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/.

Instead of submitting any such studies, Petitioners offered customer surveys, Petrs' Br. 37, and randomized controlled trials containing "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 35-36. 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* Charleston-FDA1-000132 ("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."); CB-FDA1-000804 (same); JSL-FDA1-000103 (same); PJ-FDA1-000076 (same). 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," Charleston-FDA1-000132; CB-FDA1-000804; JSL-FDA1-000104; PJ-FDA1-000077, which the studies offered by Petitioner did not do. Thus, there was nothing arbitrary and capricious about the agency's approach.

4. FDA's requirement for product-specific evidence showing the comparative benefit of flavored vs. tobacco-flavored e-cigarettes in helping smokers to stop smoking was reasonable.

Contrary to Petitioners' claim (Petrs' Br. 44-48), 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. The Sixth Circuit rejected a similar argument in *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* Charleston-FDA1-000131; CB-FDA1-000802-03; JSL-FDA1-000102-03; PJ-FDA1-000075-76.

While Petitioners claim to have submitted randomized controlled trials as part of its literature review, Petrs' Br. 35-36; *supra* p.17, as well as "information on switching and cessation, [and] outcomes based on flavor type," *id.* at 37, there is no

indication 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]." Charleston-FDA1-000132; CB-FDA1-000804; JSL-FDA1-000104; PJ-FDA1-000077. It was thus reasonable for FDA to require product-specific evidence to support this claim.

B. FDA's determination that access and marketing restrictions are insufficient to reduce youth initiation of flavored products was not arbitrary and capricious.

Petitioners also 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. 40. As is apparent from the technical project lead reviews, FDA gave due consideration to the role of access and marketing restrictions on youth usage of e-cigarettes and, based on the agency's experience with those restrictions and other real-world data, reached the reasonable conclusion that they are, by their nature, insufficient to prevent youth usage of flavored and highly-addictive products that are so intensely appealing to young consumers. *See* Charleston-FDA1-000131 n.xix; CB-FDA1-000802 n.xix; JSL-FDA1-000102 n.xix; PJ-FDA1-000075 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. 40-42, FDA concluded they are not sufficient when it comes to flavored e-cigarettes.[16]

The core problem with flavored e-cigarettes is the product itself—in particular, its appeal to youth and its addictiveness—not simply youth access or the marketing of these products. FDA's experience confirms this. In March 2019, in response to the youth vaping epidemic, FDA issued Draft Guidance[17] which "proposed to focus its enforcement priorities of flavored [e-cigarettes] on how the product was sold…." 2020 Guidance at 21 (describing 2019 Draft Guidance). However, in 2020, FDA—armed with more data—announced in its Final Guidance that these access restrictions had been insufficient to protect youth from flavored e-cigarettes. "The reality," FDA found, "is that youth have continued access to these

[16] The specific measures proposed by Petitioners are certainly insufficient to prevent youth access to its flavored e-liquids. For example, Petitioner Cool Breeze claims that it has "rigorous age-gating…for entry to…its website." Petrs' Br. 40. However, simply by pressing "Enter," anyone under the age of 21 can access Cool Breeze's website and view e-liquids such as "Lemon Crunch" and "Strawberry Dream." *See* https://www.coolbreezevapor.com/e-liquid.html. Petitioners' other measures, such as using "dull less vibrant colors" and "refraining from using mascots," Petrs' Br. 40, also accomplish little given that their products have the central feature—flavors—that make them attractive to youth.

[17] FDA, *Modifications to Compliance Policy for Certain Deemed Tobacco Products; Draft Guidance for Industry; Availability*, 84 Fed. Reg. 9,345 (Mar. 14, 2019), https://www.govinfo.gov/content/pkg/FR-2019-03-14/pdf/2019-04765.pdf.

[e-cigarette] products in the face of legal prohibitions and even after voluntary actions by some manufacturers." *Id.* "[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.*

FDA's conclusion—in both its 2020 Guidance and the technical project lead reviews—is also supported by other data indicating that youth obtain e-cigarettes with relative ease. According to the 2021 Monitoring the Future Survey, 48.5% of 10th grade students reported that it would be easy to get e-liquids and 54.6% reported that it would be easy to get vaping devices.[18] As FDA recognized in its 2020 Guidance (at 28-29), most 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.[19]

Given the alarming level of continued youth usage of flavored e-cigarettes, FDA reasonably concluded that "we are not aware of access restrictions that, to date, have been successful in sufficiently decreasing the ability of youth to obtain and use

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[18] *Table 16: Trends in Availability of Drugs as Perceived by 10th Graders*, MONITORING THE FUTURE, http://monitoringthefuture.org/data/21data/table16.pdf.

[19] Teresa W. Wang et al., *Characteristics of e-Cigarette Use Behaviors Among US Youth, 2020*, 4 JAMA NETWORK OPEN 1, 5 (published online June 7, 2021), https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2780705 (57.1% of high school e-cigarette users reported getting e-cigarettes from a friend).

[e-cigarettes]." Charleston-FDA1-000131 n.xix; CB-FDA1-000802 n.xix; JSL-FDA1-000102 n.xix; PJ-FDA1-000075 n.xix. It was similarly reasonable for FDA to rely on its own experience—bolstered by other real-world data—to conclude that marketing and access restrictions are inherently insufficient to adequately reduce the risk of youth initiation of these flavored products that are so appealing to the young.

C. 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. 49-50. Petitioners also contend FDA could use its post-market authority "to restrict or even prohibit the further sale of [Petitioners' e-cigarettes] as necessary." *Id.* at 49. 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) (emphasis added). 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,[20] and can withdraw a marketing order or take other post-market action based on that information, cannot itself be 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 cannot be 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.

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 2017 to 2018) and catching FDA by surprise.[21] In the words of then-Commissioner

[20] *See* 21 C.F.R. §§ 1114.39 & 1114.41.

[21] *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-

Gottlieb, "[w]hat I did not predict was that, in 2018, youth use of e-cigarettes…would become an epidemic."[22] 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.

II. FDA's Requirement of Reliable Evidence that Petitioners' Flavored Products Confer a Greater Benefit in Helping Smokers to Stop Smoking than Tobacco-Flavored Products Is Well Within the Agency's Statutory Authority.

A. FDA's evidentiary requirement is at the core of the Tobacco Control Act's public health standard.

In addition to arguing that the marketing denial orders were arbitrary and capricious, Petitioners assert that FDA lacks any authority under Section 910 to impose a requirement that Petitioners' flavored products are more effective in helping smokers stop smoking than a comparable tobacco-flavored product. Petrs' Br. 50-55. Petitioners, however, ignore the relevant statutory language. As noted, under Section 910, whether the marketing of a new tobacco product is appropriate for the protection of the public health requires a determination of whether non-users

commissioner-scott-gottlieb-md-proposed-new-steps-protect-youth-preventing-access.

[22] *Id.*

of tobacco products "will start using such products" and whether "existing users of tobacco products will stop using such products." 21 U.S.C. § 387j(c)(4). FDA expressly made these determinations when it found overwhelming evidence that non-tobacco flavors drive youth initiation to a greater degree than tobacco-flavored products, and further required Petitioners to marshal robust evidence that Petitioners' flavored products produce a countervailing benefit in helping smokers stop smoking greater than whatever such benefit may be conferred by tobacco-flavored products.[23]

If flavored products yield no greater benefit than unflavored products in helping smokers stop smoking, but have the added problem of enticing children to begin using e-cigarettes, then there can be no net public health benefit from authorizing flavored products. Rather, the increased youth initiation from flavored products would be a clear public health detriment. Not only does Section 910 give FDA the authority to engage in such a risk-benefit assessment of flavored products vs. tobacco-flavored products, but that assessment is required by Section 910 because it is at the core of the public health standard.

[23] *Amici* do not read the marketing denial orders or technical project lead reviews as concluding that tobacco-flavored e-cigarettes help smokers stop smoking; rather these documents reflect the conclusion that a higher level of evidence of such a benefit is necessary for flavored products, given their intense appeal to youth.

B. FDA did not evaluate Petitioners' applications under the drug approval standard.

Contrary to Petitioners' suggestion (Petrs' Br. 52-53), FDA's approach does not import the standards for drug approval under the Food, Drug and Cosmetic Act into Section 910; the drug approval standard is entirely different from the standard in Section 910, and the issue here is whether FDA complied with the requirements of Section 910.

In contrast to Section 910, which requires FDA to decide whether a new product meets the public health standard considering "the risks and benefits to the population as a whole," drug approval requires FDA to decide whether the drug is safe and effective for its intended use, which under the agency's drug authorities requires a weighing of risks (safety) and a determination of whether the drug has the beneficial effect it is claimed to have under the conditions of use in its labeling (effectiveness). 21 U.S.C. § 355(d). The safe and effective standard needs to be met before a company can claim that its product has a therapeutic benefit, i.e., that it can be used in the "diagnosis, cure, mitigation, treatment, or prevention of disease." 21 U.S.C. § 321(g)(1)(B). But a premarket tobacco product application does not seek authorization to make such a claim and thus the drug standard has no relevance here. There is simply nothing in the marketing denial orders, technical project lead reviews, or any other supporting materials that suggests FDA evaluated Petitioners' applications under the drug standard. Petitioners applied to market its products as

tobacco products, and FDA properly denied authorization based on Petitioners' failure to satisfy Section 910's public health standard.

III. FDA's Requirement of Strong Evidence that Petitioners' Flavored Products Confer a Greater Benefit in Helping Smokers Stop Smoking than Tobacco-Flavored Products Is Not a Product Standard Requiring Notice-and-Comment Rulemaking.

According to Petitioner, FDA's requirement of strong evidence that flavored products help smokers stop smoking cigarettes more effectively than tobacco-flavored products is itself a product standard, requiring notice-and-comment rulemaking. Petrs' Br. 55-57. This argument simply misunderstands the nature of a product standard under the Tobacco Control Act.

Under Section 907 of the Tobacco Control Act, FDA has the authority to set product standards if the agency can demonstrate that they are appropriate for the protection of the public health, a required showing that parallels the showing companies generally must make to market new tobacco products under Section 910.[24] Section 907 makes clear that a product standard is necessarily a rule that restricts the manufacture of products with certain properties, whether those products are "new" products (first marketed after February 15, 2007) or not. That section

[24] *Compare* 21 U.S.C. § 387g(a)(3)(A) ("The Secretary may adopt tobacco product standards…if…appropriate for the protection of the public health"), *with* 21 U.S.C. § 387j(c)(2) ("The Secretary shall deny an application…if…there is a lack of showing that permitting such tobacco product to be marketed would be appropriate for the protection of the public health.").

itself establishes a product standard (the "Special Rule for Cigarettes") prohibiting flavors in cigarettes, providing that they "shall not contain, as a constituent (including a smoke constituent) or additive, an artificial or natural flavor (other than tobacco or menthol) or an herb or spice . . . that is a characterizing flavor of the tobacco product or tobacco smoke." 21 U.S.C. § 387g(a)(1)(A). Section 907 then grants FDA the authority to "adopt product standards in addition to" the cigarette "Special Rule" if shown to be appropriate for the protection of the public health. 21 U.S.C. § 387g(a)(3)(A). It provides that a product standard "shall, where appropriate for the protection of the public health, include provisions respecting the construction, components, ingredients, additives, constituents, including smoke constituents, and properties of the tobacco product." 21 U.S.C. § 387g(a)(4)(B); *see also U.S. Smokeless Tobacco Mfg. Co. LLC v. City of New York*, 708 F.3d 428, 433 (2d Cir. 2013) (In Section 907, Congress "banned the use of flavoring additives in cigarettes and authorized the FDA to prohibit the use of other ingredients in tobacco products if it deems them particularly harmful to the public health.").

In requiring particularly probative evidence of a benefit of non-tobacco-flavored products in helping cigarette smokers to stop smoking for purposes of a marketing order under Section 910, FDA has not prohibited the manufacture of e-cigarettes with such flavors, as a product standard would do; indeed, the agency has

set forth the kind of evidence that may be sufficient to market new, flavored products in the absence of a product standard prohibiting those flavors.[25]

Therefore, FDA's requirement of rigorous studies showing that specific flavored e-cigarette products help smokers stop smoking for purposes of product review under Section 910 has nothing to do with product standard rulemaking under Section 907.

IV. Petitioners' Requested Relief Would Harm Public Health.

Petitioners demand that, if the Court vacates the denial orders but determines that FDA acted within its statutory authority, "the Court should go one step further" and enjoin FDA from taking adverse action against Petitioners' applications for 18 months to allow them to conduct the studies necessary to secure approval. Petrs' Br. 58-62. The Court should reject this argument because such relief, if granted, would be profoundly contrary to public health.

As discussed, *supra* Section I.A., Petitioners' flavored products are highly attractive to youth; and Petitioners have offered insufficiently probative evidence that their products provide a countervailing public health benefit to justify allowing their continued marketing despite having failed the public health standard. Under

[25] Under Section 910, FDA is required to deny a marketing order if the tobacco product "is not shown to conform in all respects to a tobacco product standard in effect under section 387g [Section 907], and there is a lack of adequate information to justify the deviation from such standard." 21 U.S.C. § 387j(c)(2)(D).

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. *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 the FDA. *See generally, Am. Acad. of Pediatrics v. FDA*, 379 F. Supp. 3d 461, 468, 493 (D. Md. 2019) (noting that e-cigarette manufacturers have enjoyed "a holiday from meeting the obligations of the law"). Should the Court vacate the marketing denial orders, but recognize FDA's authority to require the kinds of studies necessary to show a benefit to adult smokers, any further relief to Petitioners allowing them to keep their products on the market during the requested 18-month period would effectively place the burden of Petitioners' continuing failure to meet the public health standard on the young people who have already suffered so much at the hands of flavored e-cigarette manufacturers. If granted, Petitioners' requested relief would have profound negative public health consequences and should 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 February 11, 2022, 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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