No. 21-71328

IN THE UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

LOTUS VAPING TECHNOLOGIES, LLC,

Petitioner,

v.

U.S. FOOD & DRUG ADMINISTRATION,

Respondent.

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

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

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DISCLOSURE STATEMENT

Pursuant to Fed. R. App. P. 26.1(a), *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: March 17, 2022

/s/ Jordan Raphael
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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 Order ("MDO") issued to Petitioner Lotus Vaping Technologies, LLC ("Petitioner"). By issuing an MDO for Petitioner's flavored e-liquids—which include flavors like Blue Raspberry, Custard Cream, and Fruit Punch, ER-7-8—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 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, California Medical Association, Campaign for Tobacco-Free Kids, Parents Against Vaping e-cigarettes and Truth Initiative. 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 electronic nicotine delivery system ("ENDS" or "e-cigarette") products and the e-liquids used in those products.[1] Accordingly, *amici* have a direct and immediate interest in ensuring that Petitioner's highly-addictive and youth-appealing flavored e-liquids not be permitted on the market, which can only be assured by upholding the MDO.

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 ("PMTAs" or "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 Petitioner's e-liquids, that threaten the health and well-being of young people without sufficient countervailing evidence of any benefit to adult cigarette smokers.

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

STATEMENT OF COMPLIANCE WITH RULE 29(a)

Amici affirm that no party's counsel authored this brief in whole or in part, 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

Petitioner manufactures and sells nicotine-containing flavored e-liquids, Petr's Br. 12—a highly-addictive and harmful product that has consistently been shown to appeal to youth. FDA denied Petitioner's application to market its flavored e-liquids because the application lacked sufficient evidence that Petitioner's 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 flavored products. ER-3.

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 Petitioner's e-liquids, used in open-system e-cigarettes—it was entirely reasonable for FDA to require Petitioner to submit, in support of its marketing application, robust, product-specific evidence of the benefit of its products compared to tobacco-flavored products in aiding smokers to stop

smoking. It was not arbitrary and capricious for FDA to issue an MDO based on Petitioner's 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 Petitioner's 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 Petitioner's assertion, the Federal Food, Drug and Cosmetic Act ("FFDCA"), as amended by the Family Smoking Prevention and Tobacco Control Act, Pub. L. 111-31, 123 Stat. 1776 ("TCA"), makes FDA's authority to require post-market surveillance and review of Petitioner's products immaterial to FDA's determination of whether a product satisfies the statutory standard for a marketing order. Reliance on such authority would also be inadequate to protect the public health.

II. There is no merit to Petitioner's argument that FDA lacks the statutory authority to require strong evidence that Petitioner's 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 TCA's public health standard and

does not improperly import the "safe and effective" standard for new drug approval under the FFDCA into premarket review of new tobacco products.

III. FDA was not required to use notice-and-comment rulemaking to require reliable evidence that Petitioner's flavored products confer a greater benefit than tobacco-flavored products in helping smokers stop smoking.

IV. Finally, after enjoying a lengthy period of time to market its products without the order required by statute, Petitioner now asks the Court to order FDA to allow its products to remain on the market for an additional period while it conducts the studies necessary to demonstrate a public health benefit from its flavored products. Allowing Petitioner's highly-addictive flavored e-liquids to remain on the market for even one more day poses a significant risk to children with no countervailing public health benefit. It also defies the TCA's requirement that a product may be marketed only after it has been shown to be appropriate for the protection of the public health. Petitioner's requested relief, if granted, would run counter to the TCA and harm public health.

ARGUMENT

I. The MDO Was Not Arbitrary and Capricious.

A. Given the overwhelming evidence of youth attraction to flavored e-cigarettes, it was reasonable for FDA to deny Petitioner's application for failure to provide robust evidence that its flavored e-liquids help smokers stop smoking more effectively than unflavored products.

In determining if the marketing of an e-cigarette is "appropriate for the protection of the public health"—the standard for a marketing order under the TCA—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 device types—appeal to youth more than tobacco-flavored products. ER-18-20. Given this unequivocal evidence, it was entirely reasonable for FDA to require Petitioner 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 an MDO based on Petitioner's failure to furnish such evidence. ER-15.

The impact of a product on youth initiation is particularly critical because, as FDA noted in its Technical Project Lead Review ("TPL Review") of Petitioner's 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." ER-17. 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." ER-17-18. 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." ER-18.

1. FDA found "robust and consistent" evidence demonstrating that flavored e-cigarettes, including open-system products, are particularly attractive to youth.

As FDA explained in its TPL Review, 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 ("NYTS"). *Id.* 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." ER-17-18.

Flavors are driving this youth vaping epidemic. *See* ER-18 ("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,

which can lead to initiation, more frequent and repeated use, and eventually established regular use." ER-19. In 2020, 84.7% of high school e-cigarette users reported using a flavored product. ER-18. 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." ER-18-19. As the Sixth Circuit recently found in denying an emergency stay of an MDO in a similar case, "[f]lavored ENDS products especially appeal to children." *Breeze Smoke, LLC v. FDA*, 18 F.4th 499, 505 (6th Cir. 2021).[2]

Despite the robust evidence establishing the youth appeal of flavored tobacco products, Petitioner contends that "such concerns do not apply equally" to its products because they are "bottled e-liquids intended for use with open system devices." Petr's Br. 42. Contrary to Petitioner's assertion, open-system ENDS products, which use flavored e-liquids like those sold by Petitioner, pose a threat to youth. As FDA found, "the role of flavor is consistent" across different device types. ER-19. Moreover, open-system products remain popular among youth. Smok and Suorin, for example, are open-system devices and are currently among the most

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

popular e-cigarette devices used by youth.[3] 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.[4]

Petitioner compares the 2020 and 2021 NYTS data—which the Centers for Disease Control and Prevention ("CDC") explicitly warned against because of methodology changes in 2021 that may have resulted in underreporting[5]—to argue that FDA relied on outdated data regarding youth vaping generally, and youth usage of open-system products specifically. Petr's Br. 42-43. But, even putting this methodological issue aside, the 2021 NYTS confirmed that the prevalence of youth vaping remains at unacceptably high levels. Even during the midst of the COVID-19 pandemic, over 2 million middle and high school students reported current e-cigarette use, according to the 2021 survey.[6]

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[3] *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, 1388 tbl (2021), https://www.cdc.gov/mmwr/volumes/70/wr/pdfs/mm7039a4-H.pdf.

[4] *Id.*

[5] 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. *Id.* at 1387-89.

[6] Park-Lee, *supra* note 3, at 1387.

Regarding youth usage of open-system products, Petitioner's reliance on the NYTS data is misleading by omission. For example, Petitioner claims that according to the 2021 NYTS, "only 7.5% [of high school e-cigarette users] reported using a tank system device compatible with bottled e-liquids." Petr's Br. 43. Petitioner, however, fails to mention that 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 Petitioner's e-liquids.[7] Thus, the actual percentage of high school e-cigarette users who report using open-system products is necessarily far greater than the 7.5% figure Petitioner cites.

Petitioner also points to a 2019 quote from then-FDA Commissioner Gottlieb to portray open-system devices as large and unwieldy—and therefore, having little youth appeal. Petr's Br. 42. 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

[7] Park-Lee, *supra* note 3, at 1388 tbl.

Petitioner's 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 ENDS device.[9]

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

Petitioner also ignores the fact that e-cigarette use by young people was a serious problem before closed-system cartridge-based products began to dominate the youth market in 2017; indeed, youth e-cigarette prevalence reached 16% in 2015. *See* ER-84. 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—FDA found that youth preference for particular types and

[8] *Nord Kit*, SMOK, https://www.smoktech.com/product/pod_mod/nord-kit (last visited Mar. 15, 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 Mar. 15, 2022).

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

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." ER-20. Rather, the critical fact is that youth preference for flavors is *not* fluid. The "published literature" showing "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." ER-19. It is undeniable that Petitioner's products have the central feature—flavors—that makes e-cigarettes attractive to youth.

2. As FDA found, flavored e-cigarette products, including Petitioner's flavored e-liquids, pose a direct threat of addiction and other health harms to young people.

The vast majority of Petitioner's e-liquids contain nicotine, ER-7-11, 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 TPL Review, 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." ER-20. FDA found that the high prevalence of youth e-cigarette use was increasing nicotine dependence among young people. *Id.* 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. *Id.* Frequent and daily use prevalence among high

school students were even higher in both 2020[11] and 2021, with 43.6% of high school e-cigarette users (roughly 750,000 students) reporting frequent use and 27.6% (roughly 470,000 students) reporting daily use in 2021.[12]

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." ER-20. 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 pulmonary disease with increased ENDS use (i.e., daily use) relating to increased odds of disease." ER-21.

FDA also noted the data documenting a risk of progression from e-cigarettes to other tobacco products. ER-20-21. In its TPL Review, FDA cited a "systematic review and meta-analysis that summarized nine prospective cohort studies" finding

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[11] 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.

[12] Park-Lee et al., *supra* note 3, at 1388 tbl. Petitioner's brief (at 43 n.5) incorrectly reports certain 2021 NYTS results, including the percent of high school e-cigarette users who reported daily use. Petitioner asserts that the "2021 NYTS results suggest that approximately 1.89% of all high school students (that is, 24.6% of the 7.6% who reported any use of ENDS products) engaged in daily use of any ENDS products." *Id.* However, the correct percentages reported by the 2021 NYTS are as follows: roughly 3.12% of all high school students reported using e-cigarettes every day (that is, 27.6% of the 11.3% who reported any use of ENDS products). Park-Lee, *supra* note 3, at 1338 tbl. In any event, as indicated above, an unacceptably high number of young people are showing signs of addiction to e-cigarette products.

"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…." *Id.* A 2018 report by the National Academies of Sciences, Engineering, and Medicine, cited in the TPL Review, found "substantial evidence that ENDS use increases [the] risk of ever using combusted tobacco cigarettes among youth and young adults." ER-21. 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 of progression 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," ER-19, it was entirely reasonable for FDA to require similarly "robust and reliable" evidence showing that Petitioner's flavored e-cigarettes help smokers stop smoking more effectively than tobacco-flavored products, and that such a benefit is "substantial enough to overcome the significant risk of youth uptake and use posed by the flavored ENDS product." ER-22-23. Both the publicly available evidence of such benefits to adult smokers, as well as the data submitted by Petitioner, 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 support strong conclusions—the evidence regarding the role of flavors in promoting switching among adult smokers is far from conclusive." ER-23. 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 concluded, "the literature does not establish that flavors differentially promote switching amongst ENDS users in general." ER-23-24. Thus, it was entirely reasonable for FDA to require Petitioner to demonstrate the effectiveness of its flavored products in helping smokers to stop smoking through randomized controlled trials, longitudinal cohort studies, or other similarly rigorous studies.

Instead of submitting any such studies, Petitioner offered a literature review and two cross-sectional surveys—one that it conducted and one conducted by a coalition of ENDS manufacturers. Petr's Br. 39. While Petitioner contends that the survey it conducted assessed "actual use" by its consumers, Petr's Br. 39, it simply asked respondents, at one point in time, to recall their "usage perceptions and

[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/.

habits." ER-215. As FDA concluded, cross-sectional surveys like those cited by Petitioner are necessarily insufficient to establish that users of Petitioner's flavored products are actually more likely to stop smoking cigarettes than users of tobacco-flavored products. ER-24. "[A]lthough participants can be asked to recall their past behavior, the single data collection does not enable reliable evaluation of behavior change over time." *Id.* The survey Petitioner conducted also suffers from the same flaw as the survey that the Sixth Circuit found "present[ed] methodological issues." *Breeze Smoke*, 18 F.4th at 506. As with the *Breeze Smoke* survey, Petitioner solicited responses from customers "by request in…retail stores," which suggests "biased respondents." *Id.*; *cf.* ER-224 (Petitioner "conducted its own survey in its customer retail locations….").

In short, Petitioner presented no reliable studies showing that users of its flavored products were more likely to stop smoking cigarettes than users of tobacco-flavored products. In its TPL Review, 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," ER-24, 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 Petitioner's claim (Petr's Br. 41-44), the MDO was not arbitrary and capricious because it 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 Petitioner's products. The Sixth Circuit rejected a similar argument in *Breeze Smoke.* 18 F.4th at 508 (concluding that FDA acted lawfully in "considering literature that supported the thesis that flavored ENDS products pose special health risks to children[, while] requiring [Petitioner] present more than literature reviews to justify its products' public health benefits").

FDA 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.* 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. ER-23-24. FDA further concluded that product-specific evidence is necessary because the effectiveness of a product 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]." ER-25. It was thus appropriate 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 reasonable.

Petitioner also argues that FDA failed to consider its marketing plan. Petr's Br. 34-39. As is apparent from the TPL Review, FDA gave due consideration to the role of access and marketing restrictions on youth usage of e-cigarettes. Based on the agency's experience with those restrictions and other real-world data, it reasonably concluded that such restrictions are, by their nature, insufficient to prevent youth usage of flavored and highly-addictive products that are so intensely appealing to young consumers. *See* ER-23 n.xix. While access and marketing restrictions are important and indeed necessary to support a PMTA, as FDA has emphasized time and again, *see* Petr's Br. 36, they are not sufficient when it comes to flavored e-cigarettes.

The specific measures proposed by Petitioner are plainly insufficient to prevent youth access to its flavored e-liquids. For example, Petitioner's claim of limited youth access because its "marketing plan called for its products to be only sold in age-gated vape and specialty tobacco shops and through age-gated online sales, and not in general retail or convenience stores," Petr's Br. 34, ignores the fact that more youth report buying e-cigarettes from vape or tobacco shops (22.2%) than

from gas stations or convenience stores (17.7%), according to the 2021 NYTS.[14] A 2019 study also found that in California, e-cigarette sales to minors violations are significantly higher in tobacco and vape shops than in any other type of retailer, with 44.7% selling to underage buyers.[15]

Apart from Petitioner's specific measures, 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[16] which "proposed to focus its enforcement priorities of flavored ENDS products on how the product was sold…." ER-94 (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 [e-cigarette] products in the face of legal prohibitions and even after

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[14] Andrea S. Gentzke et al., *Tobacco Product Use and Associated Factors Among Middle and High School Students – National Youth Tobacco Survey, United States, 2021*, 71 MORBIDITY & MORTALITY WKLY. REP. 1, 23 tbl.7 (2022), https://www.cdc.gov/mmwr/volumes/71/ss/pdfs/ss7105a1-H.pdf.

[15] April Roeseler et al., *Assessment of Underage Sales Violations in Tobacco Stores and Vape Shops*, 173 JAMA PEDIATRICS 795, 796 (2019), https://jamanetwork.com/journals/jamapediatrics/fullarticle/2735684.

[16] 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.

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.* Petitioner cites the provision in its marketing plan that requires retailers to abide by the existing legal requirements for age verification, Petr's Br. 35, but it is precisely those legal requirements that FDA has previously determined, based on its experience, are insufficient in protecting against youth usage of flavored products. ER-117 ("FDA believes that age verification alone is not sufficient to address this issue, given…that youth use of ENDS products continues to increase.").

FDA's conclusion—in both its 2020 Guidance and TPL Review—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.[17] As FDA recognized in its 2020 Guidance (ER-118, ER-119), many 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.

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

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 ENDS." ER-23 n.xix. It was similarly appropriate 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 Petitioner's products is immaterial to the determination of whether those products are appropriate for the protection of the public health.

Petitioner asserts that the MDO was 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 "labeling, advertising, marketing, promotional materials, and marketing plans that were not previously submitted." Petr's Br. 45. Petitioner also contends that FDA could use its post-market authority "to later revoke or suspend a marketing order should it determine that [Petitioner's] products are no longer appropriate for the protection of the public health." *Id.* Contrary to Petitioner's argument, not only does the TCA 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 FFDCA 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 has the burden of showing that its new products are 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,[18] and can withdraw a marketing order or take other post-market action based on that information, cannot itself be a basis for granting 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 may 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

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

to 2018) and catching FDA by surprise.[19] 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."[20] 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, and the patterns of addiction may be difficult to reverse. 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 Petitioner's 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 TCA's public health standard.

In addition to arguing that the MDO was arbitrary and capricious, Petitioner asserts that FDA lacks any authority under Section 910 to impose a requirement that Petitioner's flavored products are more effective in helping smokers stop smoking than a comparable tobacco-flavored product. Petr's Br. 45-52. Petitioner's

[19] *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.

[20] *Id.*

argument ignores the relevant statutory language. As previously 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 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 Petitioner to marshal robust evidence that its flavored products produce a countervailing benefit in helping smokers stop smoking greater than whatever such benefit may be conferred by tobacco-flavored products.[21]

If flavored products yield no greater benefit than unflavored products in helping smokers stop smoking, but have the serious added harm of enticing children to begin using ENDS, 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 vs. tobacco-

[21] *Amici* do not read the MDO or TPL Review as concluding that tobacco-flavored ENDS 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.

flavored products, that assessment is required by Section 910 because it is at the core of the public health standard.

B. FDA did not evaluate Petitioner's application under the drug approval standard.

Contrary to Petitioner's suggestion (Petr's Br. 47-48), FDA's approach does not import the standards for drug approval under the FFDCA into Section 910; the drug approval standard is entirely different from the standard in Section 910, and the issue here is whether FDA applied the requirements of Section 910 in evaluating Petitioner's application.

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," 21 U.S.C. § 387j(c)(4), drug approval in section 505 of the FFDCA requires FDA to decide whether the drug is safe and effective for its intended use. In addition to requiring a demonstration of effectiveness, the agency's drug authorities require a demonstration of safety, which involves weighing a drug's risks against its benefits. *See* 21 U.S.C. § 355(b)(1)(A).

While Petitioner is correct that products "marketed with [tobacco] cessation claims," such as nicotine replacement therapies, must meet the "safe and effective" drug standard (Petr's Br. 47 & n.7), that standard has no application to tobacco products which do not make such therapeutic claims and are inherently unsafe. Petitioner applied to market its products as tobacco products and do not claim that

they can be used in the "diagnosis, cure, mitigation, treatment, or prevention of disease." 21 U.S.C. § 321(g)(1)(B). Thus, Petitioner's application was properly assessed under Section 910's new tobacco product authorization standards and there is nothing in the MDO or TPL review that suggests otherwise.

III. FDA's Requirement of Strong Evidence that Petitioner's 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. Petr's Br. 50-52. This argument simply misunderstands the nature of a product standard under the TCA.

Under Section 907 of the FFDCA, 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.[22] Section 907 makes clear that a product standard is necessarily a rule that restricts the

[22] *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.").

manufacture of products with certain properties, whether those products are "new" products (first marketed after February 15, 2007) or not. That section 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.").

By 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. Rather, 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.

Petitioner is relegated to asserting that, although the MDO is not "identical in form" to a product standard prohibiting flavored e-cigarettes, FDA could achieve the same result by denying a marketing order to products even if the products assisted 1,000 adult smokers with quitting cigarettes "for every one non-tobacco-user who initiates use with the product." Petr's Br. 51. Of course, if FDA issued an MDO even though the rigorous studies it is requiring showed that an ENDS product's flavors were 1,000 times more likely to cause adult smokers to stop smoking cigarettes than to cause young people to initiate use, such an agency action itself would be subject to challenge as inconsistent with the public health standard in Section 910. That such a fanciful hypothetical can be imagined does not convert the MDO at issue here into a product standard.

IV. Petitioner's Requested Relief Would Be Contrary to the TCA and Harm Public Health.

Petitioner demands that, if the Court vacates the MDO but determines that FDA acted within its statutory authority, "the Court should go one step further" and enjoin FDA from taking adverse action against Petitioner's PMTA while Petitioner conducts the studies necessary to secure approval. Petr's Br. 52-56. The Court

should reject this argument because such relief, if granted, would be contrary to the TCA and profoundly harmful to public health.

As discussed *supra* Section I.A., Petitioner's flavored products are highly attractive to youth, and Petitioner has not offered evidence sufficient to show that its products provide a countervailing public health benefit to justify allowing their continued marketing. Under the TCA, 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, Petitioner's products have been on the market only through the enforcement forbearance of FDA. *See generally*, *Am. Academy 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 MDO, but recognize FDA's authority to require the kinds of studies necessary to show a benefit to adult smokers, any further relief to Petitioner allowing it to keep its products on the market while it conducts the required studies would turn the TCA on its head by allowing Petitioner to market its products despite having failed to satisfy the statutory public health standard, a showing the TCA requires applicants to demonstrate *before* marketing a tobacco

product. 21 U.S.C. § 387j(c)(2)(A). Further relief would also effectively place the burden of Petitioner's 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, Petitioner's requested relief would run counter to the TCA 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 MDO.

Dated: March 17, 2022

Respectfully submitted,

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UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

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I hereby certify that, pursuant to Fed. R. App. P. 29(a)(2), on March 7, 2022, I contacted counsel for both the Petitioner and the Respondent by electronic mail seeking consent to file the subject Brief of Amici Curiae and that counsel for both Petitioner and Respondent provided their consent on March 7, 2022.

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I hereby certify that on this 17th day of March, 2022, a true and correct copy of the foregoing was filed with the Clerk of the United States Court of Appeals for the Ninth Circuit via the Court's CM/ECF system, which will send notice of such filing to all counsel who are registered CM/ECF users.

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