No. 21-13340

IN THE UNITED STATES COURT OF
APPEALS FOR THE ELEVENTH CIRCUIT

BIDI VAPOR LLC,

Petitioner,

v.

U.S. FOOD AND DRUG ADMINISTRATION; JANET WOODCOCK, M.D., in her official capacity as Acting Commissioner of the FDA; and the U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Respondents.

On Petition for Review of a Final Marketing Denial Order Issued by the U.S. Food and Drug Administration Under the Federal Tobacco Control Act

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

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CERTIFICATE OF INTERESTED PERSONS AND CORPORATE DISCLOSURE STATEMENT

Pursuant to 11th Cir. R. 26.1-1 through 26.1-3, the undersigned counsel certifies that, in addition to those listed on the Certificates of Interested Persons and Corporate Disclosure Statements filed by Petitioner, Respondents, *Amici Curiae* 37 National and State Electronic Nicotine Delivery System Product Advocacy Associations, and *Amici Curiae* Dr. David B. Abrams, Clive D. Bates, and David T. Sweanor, J.D., to the best of my knowledge, the following persons and entities have an interest in the outcome of this case:

American Academy of Family Physicians, *amicus curiae*

American Academy of Pediatrics, *amicus curiae*

American Cancer Society Cancer Action Network, *amicus curiae*

American Heart Association, *amicus curiae*

American Lung Association, *amicus curiae*

American Medical Association, *amicus curiae*

Campaign for Tobacco-Free Kids, *amicus curiae*

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Medical Association of Georgia, *amicus curiae*

Parents Against Vaping e-cigarettes, *amicus curiae*

Truth Initiative, *amicus curiae*

Zuckerman Spaeder LLP, counsel for *amici curiae*

Pursuant to Fed. R. App. P. 26.1(a) and 11th Cir. R. 26.1-3, the undersigned counsel certifies that *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: December 22, 2021

/s/ Sara A. Lawson
Sara A. Lawson
Attorney for *Amici Curiae*

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Amici medical, public health, and community organizations submit this brief in support of Respondents U.S. Food and Drug Administration, Dr. Janet Woodcock, and the U.S. Department of Health and Human Services (collectively, "Respondents" or "FDA") and urge the Court to uphold the Final Marketing Denial Order ("MDO") issued to Petitioner Bidi Vapor LLC ("Petitioner" or "Bidi") because FDA's approach was consistent with the applicable statute, the MDO was not arbitrary and capricious, and FDA did not implement a legislative rule that was required to go through notice-and-comment rulemaking.

STATEMENT OF INTEREST OF *AMICI CURIAE*

Amici are the following state and 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, Campaign for Tobacco-Free Kids, Medical Association of Georgia, 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 help users 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.[1] Accordingly, *amici* have a direct and immediate interest in ensuring that Petitioner's highly-addictive and kid-appealing flavored disposable e-cigarettes 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 groups 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 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 now functions to protect the public health by taking off the market flavored e-cigarette products, like Petitioner's, that threaten the health and well-being of young people, with little evidence of any countervailing benefit to adult cigarette smokers.

STATEMENT OF COMPLIANCE WITH RULE 29(a)

Amici represent 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

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

counsel—contributed money that was intended to fund preparing or submitting this brief. This brief is filed with the consent of the parties.

STATEMENT OF THE ISSUES

1. Did FDA act consistently with the applicable statute by focusing its review of Petitioner's flavored e-cigarette applications on: (1) the risks of its products to non-tobacco users, including youth, and the (2) the potential benefits of those products to cigarette smokers?

2. Did FDA act reasonably in requiring Petitioner to provide robust and product-specific evidence that its flavored e-cigarettes more effectively help smokers stop smoking than tobacco-flavored e-cigarettes, given the overwhelming evidence of youth attraction to flavored e-cigarettes, particularly disposables, and the comparative absence of evidence that flavored e-cigarettes confer any benefit over tobacco-flavored products in helping cigarette smokers stop smoking?

3. Did FDA act reasonably in relying on its own experience, supported by other real-world data, showing that access and marketing restrictions are inherently insufficient to prevent youth usage of flavored e-cigarettes?

4. Was FDA's requirement for robust and product-specific evidence that flavored e-cigarettes more effectively help smokers stop smoking cigarettes than tobacco-flavored e-cigarettes required to go through notice-and-comment rulemaking given that the requirement was simply a clarification of the types of

evidence sufficient to satisfy the statutory standard and the agency had discretion to consider the individual facts in each application?

INTRODUCTION AND SUMMARY OF ARGUMENT

Petitioner is a manufacturer of flavored, disposable e-cigarettes, *see* Petitioner's Principal Brief (Nov. 19, 2021) ("Pet'r Br.), at 1, 14—the very type of e-cigarette product that is now most popular among youth. FDA denied Petitioner's application to market its youth-appealing e-cigarettes because the applications lacked sufficient evidence demonstrating that Petitioner's products—available in flavors like Dragonfruit Strawberry ("Bidi Stick – Regal") and Mango Apple Orange ("Bidi Stick – Tropic"), FDA-BIDIVAPOR-000036—provide a benefit in helping adult smokers to stop smoking cigarettes that would be sufficient to outweigh the known risks to youth. *See* FDA-BIDIVAPOR-000031.

I. FDA's review of Petitioner's products was entirely consistent with the Food, Drug and Cosmetic Act, as amended by the Family Smoking Prevention and Tobacco Control Act, Pub. L. 111-31, 123 Stat. 1776 et. seq. ("TCA") because the agency focused on the two issues Congress explicitly instructed it to address in evaluating whether a product meets the statutory standard for a marketing order: (1) the risks to non-tobacco users, including youth, and (2) the potential benefits to current tobacco users, particularly cigarette smokers.

II.A. In light of the mountain of evidence of youth attraction to flavored e-cigarettes, it was entirely reasonable for FDA to require Petitioner 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 its products vs. unflavored (i.e., tobacco-flavored) products in aiding smokers to stop smoking. It was not arbitrary and capricious for FDA to then issue an MDO once it determined that Petitioner failed to provide such evidence.

II.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, by their nature, are insufficient to prevent youth usage of these products, given their intense appeal to young people.

III. Contrary to Petitioner's argument, FDA's requirement that Petitioner submit rigorous studies showing that its flavored e-cigarettes help cigarette smokers stop smoking was not a legislative rule required to go through notice-and-comment rulemaking. Rather, it was a general policy statement that FDA was free to announce through adjudication; or, at most, it was an interpretive rule exempt from notice-and-comment requirements.

ARGUMENT

I. FDA's Focus on the Risks to Youth and Potential Benefits to Adult Smokers in Its Review of Petitioner's Applications Was Consistent with the TCA.

Petitioner argues (Pet'r Br. 35-39) that FDA violated the TCA because it denied Petitioner's Premarket Tobacco Product Applications ("PMTAs" or "applications") "based on nothing more than the mere absence of one, single-issue study," Pet'r Br. 38—namely a high-quality study showing that Petitioner's flavored products, as compared to tobacco-flavored products, help smokers to stop smoking cigarettes. This argument misapprehends both FDA's reasoning for issuing the MDO and the TCA.

FDA denied Petitioner's PMTAs because Petitioner did not provide robust and reliable evidence that its flavored and disposable e-cigarettes offer a benefit to adult cigarette smokers that is sufficient to overcome the known risks to youth from those products. *See, e.g.*, FDA-BIDIVAPOR-000075 ("All of your PMTAs lack sufficient evidence demonstrating that your flavored ENDS will provide a benefit to adult users that would be adequate to outweigh the risks to youth."). As such, FDA focused primarily on two issues: (1) the risks to non-tobacco users, including youth, and (2) the potential benefit to current tobacco users, particularly cigarette smokers. These are precisely the two issues Congress instructed FDA to consider in evaluating

whether a product is "appropriate for the protection of public health" ("APPH")—the standard for a marketing order under the TCA. The TCA provides that:

> [T]he finding as to whether the marketing of a tobacco product for which an application has been submitted is appropriate for the protection of the public health shall be determined with respect to the risks and benefits to the population as a whole…and tak[e] into account—
>
> (A) the increased or decreased likelihood that existing users of tobacco products will stop using such products; and
>
> (B) the increased or decreased likelihood that those who do not use tobacco products will start using such products.

21 U.S.C. § 387j(c)(4).

Evaluating these factors, FDA reasonably concluded that, because Petitioner's e-cigarette products are flavored, they constitute a substantial risk of youth tobacco initiation. It further found that Petitioner had not offered the kinds of reliable studies that would be sufficient to demonstrate that flavored products more effectively help smokers stop smoking than tobacco-flavored products and that this advantage outweighs the clear risk to young people. *See* discussion *infra* Section II.A. This analysis exactly tracks the TCA.

II. The MDO Was Not Arbitrary and Capricious.

In reviewing agency decisions under the Administrative Procedure Act, this Court has defined its task as "limited to determining 'whether the decision was based on a consideration of the relevant factors and whether there has been a clear error of

judgment." *Ryder Truck Lines, Inc. v. U.S.*, 716 F.2d 1369, 1378 (11th Cir. 1983) (quoting *Bowman Transportation, Inc. v. Arkansas-Best Freight System*, 419 U.S. 281 (1974)). "[A]s long as the 'agency policy is within the agency's delegated power and meets the test of reasonableness, a court may not upset it without usurping the agency's power." *Id.* (citation omitted.). The MDO issued to Petitioner plainly meets this standard.

A. Given the overwhelming evidence of youth attraction to flavored e-cigarettes, it was reasonable for FDA to require robust and product-specific evidence that flavored e-cigarettes help smokers to stop smoking more effectively than unflavored products.

As noted, in determining if an e-cigarette is APPH—the standard for a marketing order under the TCA—FDA must weigh two competing factors: (1) the likelihood that the product will help existing tobacco users, including cigarette smokers, to stop using tobacco products versus (2) the likelihood that the product will lead non-tobacco users, including youth, to begin using such products. *See* 21 U.S.C. § 387j(c)(4). Applying this to e-cigarettes, FDA found the evidence overwhelming that flavors appeal to youth more than tobacco-flavored products—and the evidence is even stronger with respect to disposable flavored e-cigarettes, the only type of product at issue in this litigation. Given this unequivocal evidence that flavors pose a greater risk of youth uptake compared to tobacco-flavored products, it was entirely reasonable for FDA to require "the strongest types of evidence" demonstrating that, compared to unflavored products, flavored products

like Petitioner's benefit smokers by helping them stop smoking cigarettes and to issue an MDO for failure to furnish such evidence. FDA-BIDIVAPOR-000064.

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." FDA-BIDIVAPOR-000066. 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." FDA-BIDIVAPOR-000066-67. 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." FDA-BIDIVAPOR-000067.

1. FDA found "robust and consistent" evidence that flavored e-cigarettes, like Petitioner's, are particularly attractive to youth.

As FDA explained in the TPL Review of Petitioner's PMTAs, 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." FDA-

BIDIVAPOR-000066-67.[2] Flavors, as FDA correctly found, are driving this youth vaping epidemic. *See* FDA-BIDIVAPOR-000067 ("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[s] 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." FDA-BIDIVAPOR-000068. In 2020, 84.7% of high school e-cigarette users reported using a flavored product. FDA-BIDIVAPOR-000067. And according to data from the FDA and National Institutes of Health's Population Assessment of Tobacco and Health ("PATH") Study,[3] over 93% of youth reported that their first e-cigarette product was flavored and 71% of current youth e-

[2] Since the time that FDA issued the challenged MDO, the 2021 NYTS 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, 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.* 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.

[3] *See FDA and NIH Study: Population Assessment of Tobacco and Health*, FDA, https://www.fda.gov/tobacco-products/research/fda-and-nih-study-population-assessment-tobacco-and-health (last updated Oct. 1, 2021).

cigarette users reported using e-cigarettes "because they come in flavors I like." FDA-BIDIVAPOR-000067. In denying a stay of an MDO in a similar case, the U.S. Court of Appeals for the Sixth Circuit found the special appeal of flavored e-cigarettes to youth to be "a matter of scientific consensus." *Breeze Smoke, LLC v. FDA*, 18 F. 4th 499, 508 (6th Cir. 2021).[4]

Petitioner's products are not only flavored, but disposable, making them even more appealing to young people. Indeed, use of disposable e-cigarettes by youth has surged in recent years. Between 2019 and 2020, "there was a ten-fold increase (from 2.4% to 26.5%) among high school current e-cigarette users" reporting using disposable products. FDA-BIDIVAPOR-000069. By 2021, disposables had become the most commonly used type of e-cigarette among youth, used by over half (55.8%) of youth e-cigarette users.[5]

Petitioner cites ***no data*** provided to FDA suggesting that youth are not using its products. And as FDA found, while youth preference for particular brands and types of e-cigarettes is fluid, FDA-BIDIVAPOR-000068, youth preference for flavors is not. Simply put, it has been consistently true that flavored e-cigarettes attract youth. *See* FDA-BIDIVAPOR-000069 ("[W]hen FDA changed its

[4] The Supreme Court denied a stay of the MDO on December 10, 2021. *Breeze Smoke, LLC v. FDA*, – S. Ct. –, No. 21A176, 2021 WL 5860294 (Dec. 10, 2021).

[5] Park-Lee et al., *supra* note 2, at 1387.

enforcement policy to prioritize pod-based flavored ENDS, which were most appealing to youth at the time, we subsequently observed a substantial rise in use of disposable flavored ENDS…underscoring the fundamental role of flavor in driving appeal."). Petitioner's flavored disposable products—which come in flavors like Dragonfruit Strawberry ("Bidi Stick – Regal"), Fresh Mango ("Bidi Stick – Gold"), and Mango Apple Orange ("Bidi Stick – Tropic"), FDA-BIDIVAPOR-000036—undeniably have the features that make e-cigarettes attractive to youth. As FDA observed, 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." FDA-BIDIVAPOR-000068.

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

Petitioner's products contain nicotine, which is "among the most addictive substances used by humans." *Nicopure Labs, LLC v. FDA*, 944 F.3d 267, 271 (D.C. Cir. 2019). In the 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." FDA-BIDIVAPOR-000069. FDA also found that the high prevalence of youth e-cigarette use was increasing nicotine dependence among young people. *Id.* According to the Surgeon General, adolescents are more likely to experience nicotine dependence at lower levels of exposure than adults and

can feel dependent after just minimal exposure and within a relatively short period of time. FDA-BIDIVAPOR-000419.[6] In 2019, as FDA noted, an estimated 30.4% of middle and high school e-cigarette users reported frequent use (i.e., use on more than 20 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, a strong indication of deep nicotine addiction. FDA-BIDIVAPOR-000069. Both frequent and daily use prevalence among high school students were even higher in both 2020[7] and 2021, with 43.6% of high school e-cigarette users reporting frequent use and 27.6% reporting daily use in 2021.[8] 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." FDA-BIDIVAPOR-000069. 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

[6] This report is part of the administrative record, *see* Administrative Record Index (Oct. 25, 2021) at 2, Doc. 5, but was not included in Petitioner's Corrected Appendix (Dec. 3, 2021). Full citation: OFFICE OF THE SURGEON GENERAL, U.S. DEP'T OF HEALTH & HUMAN SERVICES, PREVENTING TOBACCO USE AMONG YOUTH AND YOUNG ADULTS 24 (2012), https://www.ncbi.nlm.nih.gov/books/NBK99237/pdf/Bookshelf_NBK99237.pdf.

[7] 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.

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

pulmonary disease with increased ENDS use (i.e., daily use) relating to increased odds of disease." FDA-BIDIVAPOR-000070.

FDA also noted the data documenting a risk of progression from e-cigarettes to other tobacco products. In its TPL Review of Petitioner's products, FDA cited a "systematic review and meta-analysis that summarized nine prospective cohort studies" finding "significantly higher odds of smoking initiation . . . and past 30-day combusted cigarette use . . . among youth who had used ENDS as compared to youth who had not used ENDS." FDA-BIDIVAPOR-000069. A 2018 report by the National Academies of Sciences, Engineering, and Medicine found "substantial evidence that ENDS use increases [the] risk of ever using combusted tobacco cigarettes among youth and young adults." *Id.* 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. FDA-BIDIVAPOR-003378.[9] Thus, the threat of flavored e-cigarettes is not just to the health of youth today; it also is a threat to their future health by increasing the risk that they will progress to a lifetime of addiction to even more hazardous tobacco products.

[9] This study is part of the administrative record, *see* Administrative Record Index at 6, Doc. 48, but was not included in Petitioner's Corrected Appendix. Full citation: 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.

3. FDA acted reasonably in requiring robust evidence showing that Petitioner's flavored e-cigarettes help smokers stop smoking more effectively than unflavored products.

Precisely because the evidence showing that the youth appeal of flavors is so "robust and consistent," FDA-BIDIVAPOR-000068, it was entirely reasonable for FDA to require similarly "robust and reliable" evidence showing that flavored e-cigarettes are more effective in helping smokers to stop smoking than unflavored products, and that this benefit "is significant enough to overcome the risk to youth."[10] FDA-BIDIVAPOR-000072. Both the publicly available evidence, as well as the data submitted by Petitioner, fall woefully short.

"[I]n 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." FDA-BIDIVAPOR-000072. For example, a systematic review that examined consumer preference for various e-cigarette attributes found "inconclusive evidence" as to whether flavored e-cigarettes assisted cigarette

[10] *Amici* do not read the MDO or TPL Review as concluding that tobacco-flavored ENDS help smokers stop smoking; rather, these documents simply reflect the conclusion that a higher level of evidence of such a benefit is necessary for flavored products, given their intense appeal.

smokers in stopping smoking.[11] As FDA accurately concluded, "the literature does not establish that flavors differentially promote switching amongst ENDS users in general." FDA-BIDIVAPOR-000072. Thus, it was entirely reasonable for FDA to require Petitioner to demonstrate the effectiveness of its flavored products in helping smokers stop smoking through randomized controlled trials, longitudinal cohort studies, or other similarly rigorous studies.

Instead of doing rigorous scientific studies, Petitioner conducted two customer surveys that it claims show that its flavored products "significantly reduce cigarette use." Pet'r Br. 45; *see also* Pet'r Br. 20.[12] However, as FDA observed, such surveys 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 tobacco-flavored products. *See* FDA-BIDIVAPOR-000073 ("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."). In the TPL Review of Petitioner's products, FDA explained

[11] 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/.

[12] Petitioner submitted these studies as amendments to its PMTAs following the September 9, 2020 deadline. Pet'r Br. 20-21.

in detail why it is necessary to perform studies that "enable direct assessment of behavioral outcomes associated with actual product use over time," FDA-BIDIVAPOR-000073, which the surveys offered by Petitioner did not do. Petitioner presented no studies showing that users of their flavored products were more likely to stop smoking cigarettes than users of tobacco-flavored products. Only the kinds of rigorous studies required by FDA—measuring the extent to which smokers actually stop smoking cigarettes using flavored products vs. using tobacco-flavored products—can establish the link between flavors and smoking behavior. Thus, FDA did, in fact, consider the validity of the kinds of studies offered by Petitioner and reasonably concluded that they failed to establish such a link. 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. unflavored e-cigarettes in helping smokers to stop smoking was reasonable.

Petitioner contends that it actually did submit "the types of studies—RCTs/longitudinal cohort studies—the MDO claimed were missing." Pet'r Br. 45. However, none of these studies, which Petitioner submitted as part of a literature review, actually evaluated Petitioner's products. *See* Pet'r Br. 17. Moreover, the studies Petitioner cites do not appear to evaluate the comparative effectiveness of flavored vs. tobacco-flavored e-cigarettes in helping smokers to stop smoking. *See id.* ("A Randomized Trial of E-Cigarettes Versus Nicotine Replacement Therapy"

and "E-Cigarettes versus nicotine patches for perioperative smoking cessation: a pilot randomized trial."). FDA reasonably concluded that such general studies of e-cigarettes could not be sufficient to demonstrate that Petitioner's flavored products provide a comparative benefit over tobacco-flavored products in helping adult smokers to stop smoking cigarettes that would be sufficient to overcome the risks to youth from its flavored products.

In denying a motion for an emergency stay of a similar MDO, the Sixth Circuit recently held that FDA acted reasonably in "requiring [Petitioner] present more than literature reviews to justify its products' public health benefits." *Breeze Smoke*, 18 F.4th at 508. That is because, in contrast to the youth risks of flavored products, which "are understood as a matter of scientific consensus," *id.*, no such scientific consensus exists on whether flavors help cigarette smokers stop smoking to a greater degree than tobacco-flavored e-cigarettes. *See* FDA-BIDIVAPOR-000072 ("[T]he evidence regarding the role of flavors in promoting switching among adult smokers is far from conclusive."). Moreover, as FDA noted in the TPL Review, product-specific evidence showing that Petitioner's flavored e-cigarettes reduce users' cigarette smoking is necessary because 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]." FDA-BIDIVAPOR-000073. It was, therefore, entirely reasonable for FDA to require product-specific evidence to support such a claim.

Given the overwhelming evidence that flavored e-cigarettes have addicted millions of young people to nicotine and the relative absence of evidence that flavored e-cigarettes confer any advantage over tobacco-flavored products in helping people to stop smoking cigarettes, there was nothing arbitrary and capricious about FDA's requirement of scientifically-valid and product-specific studies to demonstrate that Petitioner's flavored products help cigarette smokers stop smoking so substantially as to outweigh their indisputable risks to youth.

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

Petitioner argues that FDA failed to consider its "underage prevention measures." Pet'r Br. 43-44. However, as is apparent from the TPL Review of Petitioner's products, 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 and other real-world data, reached the reasonable conclusion that such restrictions, by their nature, are insufficient to prevent youth usage of flavored and highly-addictive products that are so intensely appealing to young consumers. *See* FDA-BIDIVAPOR-000072 n.xix. While access and marketing restrictions are

important and indeed necessary, as FDA has emphasized time and again, *see* Pet'r Br. 43, they are not sufficient when it comes to flavored e-cigarettes.[13]

The core problem with flavored e-cigarettes is the product itself—namely 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[14] which "proposed to focus its enforcement priorities of flavored ENDS products on how the product was sold…." FDA, *Enforcement Priorities for Electronic Nicotine Delivery Systems (ENDS) and Other Deemed Products on the Market Without Premarket Authorization (Revised)**, at 21 (Apr. 2020) ("2020 Guidance").[15] However, in 2020, FDA—

[13] The specific measures proposed by Petitioner are certainly insufficient to prevent youth usage of its disposable flavored e-cigarettes. Petitioner does not itself sell directly to consumers, but sells only to retail stores and through an online delivery service (goPuff). Pet'r Br. 21-22. Thus, Petitioner's measures largely consist of informing retailers of the age-verification requirements of the law. *See id.* at 21-23. Moreover, adopting "single-word, non-characterizing product names (like Dawn and Summer)," avoiding advertising that makes its products resemble kid-friendly food or that use "youth appealing cartoons and graphics," and refraining from using social media influencers and young-looking models to promote its products, *id.*, accomplish little when the product itself has all the features that make it attractive to youth.

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

[15] https://www.fda.gov/media/133880/download. This document is part of the administrative record. *See* Administrative Record Index at 1, Doc. 2 ("FDA-BIDIVAPOR-000360-000411").

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 [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 TPL Review of Petitioner's products—is also supported by other data indicating that youth are able to obtain e-cigarettes with relative ease. According to the 2021 Monitoring the Future Survey, over half (54.6%) of 10th grade students reported that it was easy to get vaping devices.[16] Moreover, according to the 2020 NYTS, 22.2% of high school e-cigarette users report obtaining e-cigarettes from a gas station or convenience store in the past month and 17.5% from a vape shop.[17] Finally, as FDA found in its 2020 Guidance (at 28-29),[18] most youth e-cigarette users obtain e-cigarettes through social

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

[17] 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.

[18] FDA-BIDIVAPOR-000360.

sources, such as older friends or relatives—an avenue of access unlikely to be significantly affected by access restrictions.[19]

Given the shocking level of continued youth usage of flavored e-cigarettes, FDA can hardly be criticized for observing 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." FDA-BIDIVAPOR-000072 n.xix. It was entirely 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.

III. FDA's Requirement for Robust and Product-Specific Evidence That Flavored E-Cigarettes More Effectively Help Smokers Stop Smoking Cigarettes Than Tobacco-Flavored E-Cigarettes Was Not a Legislative Rule Subject to Notice-and-Comment Rulemaking.

According to Petitioner, FDA's requirement for robust and product-specific evidence demonstrating that flavored e-cigarettes confer an advantage over tobacco-flavored products in helping adults stop smoking (what Petitioner calls FDA's "Fatal Flaw approach") was a legislative rule that had to go through notice-and-comment

[19] Wang, *supra* note 17, at 5 (57.1% of high school e-cigarette users reported getting e-cigarettes from a friend).

rulemaking. Pet'r Br. 53.[20] This argument ignores the holdings in the very cases Petitioner cites, as well as long-standing Supreme Court precedents.

First, FDA's approach to the evidentiary requirements for flavored tobacco product PMTAs is a general policy statement—not a rule requiring notice and comment. In *Ryder Truck Lines, Inc. v. United States*, relied upon by Petitioner, this Court held that "whether a particular agency proceeding announces a rule or a general policy statement depends upon whether the agency action establishes 'a binding norm.'" 716 F.2d 1369, 1377 (11th Cir. 1983) (citation omitted). The Court continued, "[a]s long as the agency remains free to consider the individual facts in the various cases that arise, then the agency action in question has not established a binding norm." *Id.* Here, FDA has simply indicated the kinds of studies that could be sufficiently rigorous in showing that flavors are more effective than tobacco-flavored e-cigarettes in helping smokers stop smoking. Although FDA indicated that a randomized controlled trial or longitudinal cohort study would qualify, the

[20] Petitioner alternates between alleging that FDA's "Fatal Flaw approach" was a legislative rule and that specifically the "Fatal Flaw memorandum" was a legislative rule. *Compare* Pet'r Br. 34 ("[T]he Fatal Flaw approach…represents a legislative rule), *and* Pet'r Br. 53 ("The Fatal Flaw Approach Is A Rule…"), *with* Pet'r Br. 35 ("Even if the Fatal Flaw memorandum is not a rule…"), *and* Pet'r Br. 53 ("The MDO…is based on what amounts to a rule in the form of the Fatal Flaw memorandum…"). Because the Fatal Flaw memorandum was superseded, *see* Administrative Record Index at 8, *amici* focus on FDA's overall approach to Petitioner's PMTAs as delineated in the MDO, TPL Review, and other supporting materials.

agency left open the possibility that other types of studies, if equally robust and reliable, could demonstrate such a benefit. For example, the third criterion in FDA's "Review for Flavored ENDS PMTAs" form asks agency reviewers whether there is "[o]ther evidence in the PMTAs related to [the] potential benefit to adults." FDA-BIDIVAPOR-000054-55; *see also* FDA-BIDIVAPOR-000073 ("CTP will consider other types of evidence if it is sufficiently robust and reliable to demonstrate the impact of the new ENDS on adult switching or cigarette reduction."); FDA-BIDIVAPOR-000064 (The TPL Review provides that "other types of evidence could be adequate, and *will be evaluated on a case-by-case basis*.") (emphasis added). Even if an application did not include a randomized controlled trial or longitudinal cohort study, the agency remained "free to exercise its discretion" and authorize an application if the application contained other equally robust and reliable evidence demonstrating that the product helps adults to stop smoking cigarettes. *Ryder*, 716 F.2d at 1377. Moreover, even if such studies were undertaken by the applicant, FDA has discretion to decide that the particular studies did not show a comparative benefit to adult smokers from Petitioner's flavored products sufficient to outweigh the risks to youth from such products. Therefore, FDA's approach to flavored tobacco products did not create a binding norm and thus is not a rule under the Administrative Procedure Act.

Even if this Court finds that FDA's approach to flavored ENDS products is a rule, it is—at most—an interpretive rule because FDA simply clarified the types of evidence that are sufficient to satisfy the statutory APPH standard, as applied to highly-addictive, youth-friendly flavored e-cigarettes. *See Warshauer v. Solis*, 577 F.3d 1330, 1337 (11th Cir. 2009) ("[A]n administrative rule simply states what the administrative agency thinks the statute means….") (citation omitted). Interpretive rules are not required to go through notice-and-comment rulemaking. *Id.*

To determine whether a rule is legislative or interpretive, this Court in *Warshauer*, another case relied upon by Petitioner, laid out three factors, relying largely on precedents set by the D.C. Circuit. "First, it is relevant that the Secretary characterizes the rule as interpreting [the statute]." *Id.* at 1337-38. Here, FDA characterized its evidentiary requirement as an interpretation of the TCA, specifically section 910(c)(5) (21 U.S.C. § 387j(c)(5)). *See* FDA-BIDIVAPOR-000073 ("Consistent with section 910(c)(5), evidence generated using either an RCT design or longitudinal cohort study design is most likely to demonstrate such a benefit…."). "Second, the Secretary's interpretation is drawn directly from the plain language of the statute." *Warshauer*, 577 F.3d at 1338. Here, FDA's approach of requiring robust and reliable evidence is borne directly from the TCA, which provides that FDA "shall, when appropriate," decide applications "on the basis of well-controlled investigations, which may include 1 or more clinical

investigations…." 21 U.S.C. § 387j(c)(5)(A). Third, a rule is interpretive when "it only remind[s] affected parties of existing duties required by the plain language of the statute." *Warshauer*, 577 F.3d at 1338 (citation and quotations omitted). Here, by virtue of the statute, Petitioner was aware of its obligation to submit evidence of its products' impact on the "likelihood that existing users of tobacco products will stop using such products," 21 U.S.C. § 387j(c)(4)(A), and of FDA's authority to require, and make decisions on the "basis of well-controlled investigations." *See* 21 USC § 387j(c)(5)(A). FDA's expression of this requirement in the MDO and supporting materials "did not create any new law, right, duty, or have any effect independent of the statute." *Warshauer*, 577 F.3d at 1338. Rather, the TCA already required applicants to meet the public health standard, which necessarily involved presenting evidence as to the impact of the new products on existing tobacco users. In the MDO, FDA simply interpreted the plain language of the statute in determining the evidentiary requirements as they apply to Petitioner's flavored products. Therefore, FDA's approach to flavored ENDS is not a legislative rule.

Finally, in arguing that FDA was required to announce its approach to PMTAs for new flavored ENDS in notice-and-comment rulemaking, Petitioner disregards long-standing Supreme Court precedent that "make[s] plain that [an agency] is not precluded from announcing new principles in an adjudicative proceeding and that the choice between rulemaking and adjudication lies in the first instance within the

[agency's] discretion." *N.L.R.B. v. Bell Aerospace Co. Div. of Textron, Inc.*, 416 U.S. 267, 294 (1974); *see also N.L.R.B. v. Wyman-Gordon Co.*, 394 U.S. 759, 765 (1969) ("Adjudicated cases may and do, of course, serve as vehicles for the formulation of agency policies…."). It was well within FDA's discretion to choose how and where it would announce its policy on the types of evidence that PMTAs for flavored e-cigarette products must include. Thus, FDA's requirement for robust and product-specific evidence that Petitioner's flavored products are more effective than tobacco-flavored e-cigarettes in helping cigarette smokers stop smoking was not required to go through notice-and-comment rulemaking.

CONCLUSION

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

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Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

1. The foregoing brief complies with the word limits set forth in Fed. R. App. P. 29(a)(5) and Fed. R. App. P. 32(a)(7) because, excluding the parts of the document exempted by Fed. R. App. P. 32(f), the word count feature in Microsoft Word reports that this document contains 6,153 words.

2. The foregoing brief complies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the typestyle requirements of Fed. R. App. P. 32(a)(6) because this document has been prepared in a proportionally spaced typeface using Microsoft Word in Times New Roman, size 14 font.

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CERTIFICATE OF CONFERENCE

I hereby certify under Fed. R. App. P. 29(a)(2) that on December 16, 2021, I contacted counsel for the Petitioner and Respondents by electronic mail and that Petitioner and Respondents each consented to the filing of the brief of *amici curiae*.

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CERTIFICATE OF SERVICE

I hereby certify that on December 22, 2021, 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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