



January 24, 2023

The Honorable Xavier Becerra  
Secretary, U.S. Department of Health and Human Services  
200 Independence Avenue, S.W.  
Washington, D.C. 20201

Dr. Robert Califf, M.D.  
Commissioner, U.S. Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993

RE: Opposition to Citizen Petition filed by American Vapor Manufacturers requesting enforcement discretion regarding certain synthetic nicotine products, Docket No. FDA-2022-P-1211

Dear Secretary Becerra and Commissioner Califf:

Our organizations write to urge denial of the Citizen Petition filed by the American Vapor Manufacturers (AVM) requesting the U.S. Food and Drug Administration (FDA) to exercise enforcement discretion for certain open-system synthetic nicotine e-liquid products. The actions requested by AVM,<sup>1</sup> if granted, would leave thousands of unauthorized e-cigarettes,<sup>2</sup> most of

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<sup>1</sup> Petitioner AVM requests that: “(1) FDA should exercise enforcement discretion and allow manufacturers of synthetic nicotine e-liquids used in open-system ENDS devices who submitted timely PMTAs that meet FDA’s criteria for application acceptance . . . and filing . . . to keep those products on the market for their adult (21+) customers following the end of the ‘transition period’ on July 13, 2022. Specifically, [they] request that the CTP Office of Compliance and Enforcement (‘OCE’) permit the continued marketing and sale of such synthetic nicotine e-liquids to adults for the duration of the Agency’s full scientific review (i.e., until FDA reaches a final marketing authorization determination) of their respective applications. [And] (2) . . . the FDA CTP Office of Science (‘OS’) allow manufacturers of these products to continue to submit additional data and amend their applications, as the time provided (60 days between March 15, 2022 and May 14, 2022) was simply insufficient to prepare all of the product-specific data FDA requires PMTAs contain including, in some cases, long-term (6 months+) clinical or longitudinal evidence.” Pet. 2.

<sup>2</sup> We use the terms e-cigarettes, ENDS, and e-liquids interchangeably. Additionally, in its most recent update regarding review of PMTAs for synthetic nicotine products, FDA stated it had accepted over 1,600 applications, with the vast majority being for e-cigarette or e-liquid products. CTP News, *FDA Completes*

which are flavored,<sup>3</sup> on the market for an undetermined amount of time while their applications are pending review by FDA—an outcome that is unlawful and harmful to public health. Accordingly, FDA should deny the AVM Citizen Petition without further delay.

### **I. The Exercise of Enforcement Discretion Requested by the Citizen Petition is Inconsistent with Federal Law.**

The synthetic nicotine provisions enacted as part of H.R. 2471, the Consolidated Appropriations Act, 2022,<sup>4</sup> mandated that FDA apply the premarket review requirements of the Family Smoking Prevention and Tobacco Control Act (TCA) to synthetic nicotine products. H.R. 2471 created a “transition period” for products already on the market, which allowed certain products to remain on the market, free of possible FDA enforcement, for 120 days after enactment (until July 13, 2022), if they submitted a Premarket Tobacco Product Application (PMTA) within 60 days of enactment.<sup>5</sup> The transition period for products for which no application was submitted or that received a marketing denial order (MDO) or refuse-to-file letter for a tobacco-derived version of the product expired on May 14, 2022.<sup>6</sup> The statutory language is clear that, at the end of these transition periods, manufacturers who continue to market their products without premarket orders, including those with pending applications, are violating the law.<sup>7</sup> Therefore, under H.R. 2471, no unauthorized synthetic nicotine product, including those that are the subject of the Citizen Petition, may continue to be marketed after July 13, 2022.

Despite the clear letter of the law and FDA’s acknowledgement that no marketing orders have been granted for any synthetic nicotine products,<sup>8</sup> the market remains replete with unauthorized synthetic products, including a dizzying array of flavored e-cigarettes popular among

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*Initial Review of 95% of Non-Tobacco Nicotine Product Applications; Agency Has Issued Over 60 Warning Letters to Manufacturers, Including for Products with a Submitted Application and Negative Action* (Oct. 14, 2022), <https://www.fda.gov/tobacco-products/ctp-newsroom/fda-completes-initial-review-95-non-tobacco-nicotine-product-applications-agency-has-issued-over-60>.

<sup>3</sup> We use the term flavored to mean non-tobacco flavors, including, but not limited to, candy, fruit, and menthol flavors.

<sup>4</sup> Pub. L. No. 117-103, Division P, Title I, Subtitle B, 136 Stat. 49, 789-90 (2022).

<sup>5</sup> *Id.* § 111(d)(2)(B) and (d)(3), 136 Stat. 789-90.

<sup>6</sup> *Id.* § 111(d)(2)(A) and (C), 136 Stat. 789-90.

<sup>7</sup> *Id.* § 111(d)(3), 136 Stat. 790.

<sup>8</sup> <https://www.fda.gov/tobacco-products/products-ingredients-components/regulation-and-enforcement-non-tobacco-nicotine-ntn-products> (last updated Nov. 14, 2022) (“Currently, no [non-tobacco nicotine] products have received marketing authorizations.”).

young people.<sup>9</sup> This situation, which is highly reminiscent of what has occurred with tobacco-derived nicotine e-cigarettes,<sup>10</sup> is precisely what Congress sought to avoid in enacting H.R. 2471.

H.R. 2471 was enacted against a backdrop of repeated Congressional expressions of dissatisfaction with the lack of FDA enforcement of the TCA’s premarket review requirement against tobacco-derived nicotine e-cigarettes. After years of delay and inaction under the guise of FDA enforcement discretion, Congress enacted H.R. 2471’s synthetic nicotine provisions to ensure removal from the market of synthetic nicotine products that lacked premarket orders as of July 13, 2022—the end of the transition period. As explained in our September 22, 2022 letter to FDA’s Center for Tobacco Products (CTP) Director, Dr. Brian King, H.R. 2471 was enacted to impose a limit on the exercise of FDA’s enforcement discretion allowing the continued illegal marketing of synthetic nicotine e-cigarettes.

Here not only does Petitioner seek to keep an entire category of e-cigarette products on the market for an undetermined period until FDA reaches a final decision on their PMTAs, but it requests that manufacturers be allowed to submit additional data and PMTA amendments for an undetermined period while the products remain on the market. If granted, these requests would amount to a de facto exemption for these products from the requirement of a marketing order under H.R. 2471.

In the context of tobacco-derived nicotine e-cigarettes, a similar indefinite “holiday from meeting the obligations of the law” was found beyond FDA’s authority in *American Academy of Pediatrics v. FDA*, 379 F.Supp.3d 461, 493 (D. Md. 2019), *appeal dismissed sub nom. In re Cigar Ass’n of Am.*, 812 F.App’x 128 (4th Cir. 2020) (“AAP”), a lawsuit brought by many of the groups joining in these comments. In *AAP*, the U.S. District Court for the District of Maryland recognized that “an agency may decide whether to exercise its enforcement discretion as to one or more discrete violations, in light of the circumstances surrounding a particular violation and considering other responsibilities and resources that the agency has at that time . . .” “[b]ut this bears no relation to a decision to hold in abeyance enforcement of mandatory provisions of a statute that Congress viewed as integral to address public health dangers . . . .” 379 F.Supp.3d at 493. Thus, the court vacated an FDA Guidance that granted an “across-the-board suspension of the Tobacco Control Act’s premarket approval process” to tobacco-derived e-cigarette products for a period of at least four years and allowed companies to keep their products on the market until FDA issued decisions on their PMTAs. *Id.* at 492. In enacting H.R. 2471, Congress intended to prevent FDA from repeating this mistake for synthetic nicotine e-cigarette products—i.e., allowing them to remain on the market for an indefinite period, including while FDA considers their PMTAs. Yet, that is exactly the outcome that the AVM Citizen Petition seeks and a reason for why it should be denied.

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<sup>9</sup> See e.g., Campaign for Tobacco-Free Kids, *One Year After Deadline for FDA Action, Flavored E-cigarettes Remain Widely Available and America’s Kids Remain at Risk* (Sep. 9, 2022), [https://www.tobaccofreekids.org/press-releases/2022\\_09\\_09\\_fda-deadline](https://www.tobaccofreekids.org/press-releases/2022_09_09_fda-deadline); Chris Kirkham et al., *New ‘candy’ e-cigs catch fire after U.S. regulators stamp out Juul’s flavors*, Reuters (Aug. 16, 2022), <https://www.reuters.com/business/healthcare-pharmaceuticals/new-candy-e-cigs-catch-fire-after-us-regulators-stamp-out-juuls-flavors-2022-08-16/>.

<sup>10</sup> *Id.*; see also Nicholas Florko & Elissa Welle, *The FDA stands by as the vaping industry flouts its orders*, Stat (Aug. 24, 2022), <https://www.statnews.com/2022/08/24/the-fda-stands-by-as-the-vaping-industry-flouts-its-orders/>.

Petitioner asserts that H.R. 2471 gave manufacturers of synthetic products inadequate time to generate the studies and data necessary to support their PMTAs prior to expiration of the statutory transition period on July 13, 2022. However, these companies can take as long as they need to do the studies necessary to demonstrate that their products meet the public health standard of the TCA, i.e., that they are “appropriate for the protection of the public health.” The issue, however, is whether their products should be allowed to remain on the market for an indefinite period even though they have not yet met the statutory standard. In H.R. 2471, Congress answered this question decisively, making it clear that, after July 13, 2022, no synthetic nicotine e-cigarette has the legal right to be marketed without FDA authorization and all such products should be removed from the market.

## **II. The AVM Citizen Petition Should Be Denied Because Its Requests Would Harm Public Health.**

Petitioner is wrong that an exercise of enforcement discretion by FDA for manufacturers of open-system synthetic nicotine e-cigarette is consistent with promoting the public health. As FDA repeatedly has found in issuing MDOs for flavored tobacco-derived e-cigarette products, while the evidence is clear that e-cigarettes pose a serious health risk to young people due in large part to youth-appealing flavors, there is limited evidence that e-cigarettes—let alone flavored e-cigarettes—help adult smokers to stop smoking.

### *A. E-cigarettes have fueled a resurgence of unacceptably high rates of youth tobacco use.*

E-cigarettes have been the most commonly used tobacco product among youth since 2014,<sup>11</sup> and “[t]oday, more youth initiate tobacco use with e-cigarettes than all other tobacco products combined.”<sup>12</sup> The dramatic and rapid increase in youth e-cigarette use from 2017 to 2018 in particular led to its declaration as an epidemic by the FDA and U.S. Surgeon General in 2018.<sup>13</sup> That historic one-year increase was followed by another alarming increase in 2019,<sup>14</sup> and despite recent declines, rates of e-cigarette use by young people remain unacceptably high. In 2022, over 2.5 million youth, including 14.1% of U.S. high schoolers were current e-cigarette users.<sup>15</sup>

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<sup>11</sup> Rachel Boykan et al., *Flavored E-Cigarettes and Adolescent Health* at 3 (July 19, 2022), <https://www.massgeneral.org/children/news/flavored-e-cigarettes-and-adolescent-health>.

<sup>12</sup> *Id.* at 2.

<sup>13</sup> FDA, *Statement from FDA Commissioner Scott Gottlieb, M.D., on new steps to address epidemic of youth e-cigarette use* (Sep. 11, 2018), <https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-new-steps-address-epidemic-youth-e-cigarette-use>; Office of the Surgeon General, *Surgeon General’s Advisory on E-Cigarette Use Among Youth* (Dec. 18, 2018), <https://e-cigarettes.surgeongeneral.gov/documents/surgeon-generals-advisory-on-e-cigarette-use-among-youth-2018.pdf>.

<sup>14</sup> Boykan et al., *supra* note 11, at 3.

<sup>15</sup> Maria Cooper et al., *E-Cigarette Use Among Middle and High School Students—United States, 2022*, MMWR, 71(40): 1283-1285 (Oct. 7, 2022), <https://www.cdc.gov/mmwr/volumes/71/wr/pdfs/mm7140a3-H.pdf>.

Youth e-cigarette use is especially concerning because, as described by FDA, “the majority of tobacco use begins before adulthood . . . . In fact, 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.”<sup>16</sup> The 2022 National Youth Tobacco Survey (NYTS) data reveal that youth are not only using e-cigarettes, but they are using them frequently, a sign of nicotine dependence: 46% of high school e-cigarette users reported vaping on 20 or more days per month, and 30.1% reported vaping daily; in total, 700,000 middle and high school students are vaping every single day.<sup>17</sup>

The FDA also has found that among youth who use e-cigarettes, “there is a risk of progression to other tobacco products of generally greater health risk.” There also is a “positive association[ ] between ENDS use among those who never smoked and some health outcomes,” such as asthma, chronic bronchitis, emphysema, and chronic obstructive pulmonary disease.<sup>18</sup> Finally, youth and young adult e-cigarette users are also finding it difficult to quit e-cigarettes. According to the Truth Longitudinal Cohort survey, in 2019, more than half of young current e-cigarette users (15-24 years old) intended to quit using e-cigarettes but only one-third (33.3%) made a quit attempt in the past year.<sup>19</sup> And unfortunately, unsuccessful adolescent quit attempts for e-cigarettes are nearly two times higher than for combustible cigarettes (4.12% vs. 2.23%).<sup>20</sup> Thus, there is no question that youth e-cigarette use continues to present a challenge to reducing population-level tobacco use.

#### *B. Flavors drive the youth vaping crisis.*

According to the FDA, “[t]he evidence shows that the availability of a broad range of flavors is one of the primary reasons for the popularity of ENDS among youth. The majority of youth who use ENDS report using a flavored ENDS product, and the use of flavored ENDS has increased over time.”<sup>21</sup> The 2022 NYTS found that 85% of youth e-cigarette users use flavored products.<sup>22</sup> Among youth users of flavored e-cigarettes, the most commonly used flavor types were fruit (69.1%), candy/desserts/other sweets (38.3%), mint (29.4%) and menthol (26.6%).<sup>23</sup>

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<sup>16</sup> FDA, Sample Decision Summary Document at 5, <https://www.fda.gov/media/152504/download> (“Sample Decision”).

<sup>17</sup> Cooper et al., *supra* note 15, at 1284 tbl.

<sup>18</sup> Sample Decision, *supra* note 16, at 8-9.

<sup>19</sup> Alison F. Cuccia et al., *Quitting e-cigarettes: Quit attempts and quit intentions among youth and young adults*, *Prev. Med. Rep.*, 21:101287 (Jan. 5, 2021), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7808959/pdf/main.pdf>.

<sup>20</sup> Richard Miech et al., *Failed Attempts to Quit Combustible Cigarettes and e-Cigarettes Among US Adolescents*, *J. Am. Med. Assoc.*, 327(12): 1179-1181 (Mar. 22/29, 2022), <https://jamanetwork.com/journals/jama/fullarticle/2790303>.

<sup>21</sup> Sample Decision, *supra* note 16, at 6.

<sup>22</sup> Cooper et al., *supra* note 15, at 1284 tbl.

<sup>23</sup> *Id.*

Youth perceive flavored tobacco products as more appealing, better tasting, and less harmful than non-flavored tobacco products, which facilitates product initiation and progression to regular use.<sup>24</sup> The appeal of flavors is also consistent across e-cigarette device types.<sup>25</sup> In 2020, for example, “the majority of high school and middle school current e-cigarette users reported use of non-tobacco-flavored products (82.9%) and flavored use was favored among both users of closed (87%) and open (76%) ENDS.”<sup>26</sup> The FDA has also noted that “preference for device types and popularity of certain styles is likely fluid and affected by the marketplace, that is, the options, especially flavors, that are available for consumers to choose from.”<sup>27</sup>

*C. Like closed-system e-cigarettes, open-system products pose a threat to youth.*

Relying on FDA’s 2020 Enforcement Priorities Guidance, which drew some distinctions between different e-cigarette types,<sup>28</sup> Petitioner suggests that open-system products do not pose a threat to youth and contrasts such products to various closed-system e-cigarettes like Juul and Puff Bar.<sup>29</sup> However, Petitioner’s argument ignores the agency’s own analysis of the impacts of that Guidance, and its conclusions regarding the consistent role of flavors across e-cigarette device types, as outlined in FDA’s Sample Decision Summary for flavored products:

Some evidence [regarding the fluidity of device type preference and popularity in response to marketplace availability] was observed in the trends both leading up to, and coinciding with, the shifting marketplace following the 2020 Enforcement Priorities Guidance. In particular, the enormous rise in youth ENDS use from 2017-2019 coincided with the ascendance of JUUL (and copy-cat devices) in the marketplace, suggesting a relationship between the availability of JUUL as an option, and the sudden popularity of pod-based devices. Then, as noted earlier, when FDA changed its 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--a ten-fold increase (from 2.4% to 26.5%) among high school current e-cigarette users. *This trend illustrates that the removal of one flavored product option prompted youth to migrate to another ENDS type that offered the desired flavor options, underscoring the fundamental role of flavor in driving appeal.*<sup>30</sup>

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<sup>24</sup> Li-Ling Huang et al., *Impact of non-menthol flavours in tobacco products on perceptions and use among youth, young adults and adults: a systematic review*, *Tob. Control*, 26(6): 709-719 (Nov. 21, 2016), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5661267/pdf/tobaccocontrol-2016-053196.pdf>; Jessica K. Pepper et al., *Adolescents’ interest in trying flavoured e-cigarettes*, *Tob. Control*, 25(2): ii62-ii66 (Nov. 17, 2016), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5125087/pdf/nihms829318.pdf>.

<sup>25</sup> Sample Decision, *supra* note 16, at 7.

<sup>26</sup> *Id.* (citations omitted).

<sup>27</sup> *Id.*

<sup>28</sup> FDA, *Enforcement Priorities for Electronic Nicotine Delivery Systems (ENDS) and Other Deemed Products on the Market Without Premarket Authorization (Revised)* (Apr. 2020), <https://www.fda.gov/media/133880/download> (“2020 Guidance”).

<sup>29</sup> Pet. 7-10.

<sup>30</sup> Sample Decision, *supra* note 16, at 7-8 (emphasis added).

Because the role of flavors in driving youth usage is consistent across types of devices, FDA has consistently rejected industry arguments to treat open-system products differently and has issued MDOs for flavored open-system products which have been upheld by five federal circuit courts. *See Avail Vapor, LLC v. FDA*, 55 F.4th 409, 427 (4th Cir. 2022); *Liquid Labs LLC v. FDA*, 52 F.4th 533, 544-45 (3d Cir. 2022); *Gripum, LLC v. FDA*, 47 F.4th 553, 560 (7th Cir. 2022); *Prohibition Juice Co. v. FDA*, 45 F.4th 8, 26 (D.C. Cir. 2022); *Wages and White Lion Investments, LLC v. FDA*, 41 F.4th 427, 437-38 (5th Cir. 2022).

Moreover, open-system products remain popular among youth. SMOK and Suorin, for example, are open-system devices and are currently among the most popular e-cigarette devices used by youth.<sup>31</sup> SMOK, for instance, was the third most commonly reported brand among youth e-cigarette users in 2022.<sup>32</sup> Petitioner also portrays open-system devices as larger in size than their closed-system counterparts and therefore not as attractive to youth.<sup>33</sup> However, as shown below, many of the open-system devices on the market today are small and easy-to-conceal. 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.<sup>34</sup>



Figure 1: Suorin Drop Rainbow Chrome ENDS device.<sup>35</sup>



Figure 2: SMOK Nord open-system open-system ENDS devices.<sup>36</sup>

<sup>31</sup> Cooper et al., *supra* note 15, at 1284 tbl.

<sup>32</sup> *Id.*

<sup>33</sup> Pet. 9-10.

<sup>34</sup> SMOK, *Nord Kit*, [https://www.smoktech.com/product/pod\\_mod/nord-kit](https://www.smoktech.com/product/pod_mod/nord-kit) (last visited Jan. 6, 2022).

<sup>35</sup> Suorin USA, *Suorin Drop Rainbow Chrome – Pod System Device with Cartridge Kit*, <https://www.suorinusa.com/collections/suorin-drop/products/suorin-drop-rainbow-chrome> (last visited Jan. 6, 2022).

<sup>36</sup> SMOK, *supra* note 34.

But the issue 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. Rather, as FDA has stated, it is that “[t]he published literature is sufficient to demonstrate the substantial appeal to youth of flavored ENDS, because it is robust and consistent.”<sup>37</sup> Thus, if FDA were to exercise enforcement discretion to benefit flavored open-system products in particular, there is every reason to expect that youth would gravitate to those products.

Petitioner also suggests that open-system products are less accessible to youth because they “are available for purchase at age-restricted retail locations (*e.g.* vape shops) . . . but not in convenience stores and gas stations.”<sup>38</sup> The facts do not support this assertion. More youth report buying e-cigarettes from supposedly age-restricted vape or tobacco shops (22.2%) than from gas stations or convenience stores (17.7%), according to the 2021 NYTS.<sup>39</sup> 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.<sup>40</sup>

*D. Youth access and advertising restrictions are not sufficient to overcome the risks of e-cigarettes to youth.*

Petitioner limits their enforcement discretion request to those open-system manufacturers that, among other things, “have taken steps to ensure that their products will not contribute to illegal underage use,” demonstrate to FDA that they will “prohibit access by and sales to underage (under 21) consumers for brick-and-mortar stores and/or retail websites [and, w]ill only market to adults (21+) and not rely on any youth-friendly advertising.”<sup>41</sup>

Contrary to Petitioner’s claim, these measures are unlikely to significantly reduce youth access to or use of e-cigarettes. Despite federal laws prohibiting sales to youth<sup>42</sup> and prioritized enforcement by FDA against “ENDS products for which the manufacturer has failed to take (or is failing to take) adequate measures to prevent minors’ access . . . [and] ENDS products targeted to, or whose marketing is likely to promote use by, minors,”<sup>43</sup> youth continue to obtain e-cigarettes with relative ease. According to the 2022 Monitoring the Future Survey, 50.8% of 10<sup>th</sup> grade students reported that it would be easy to get e-liquids and 51.9% reported that it would be easy to

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<sup>37</sup> Sample Decision, *supra* note 16, at 7.

<sup>38</sup> Pet. 9.

<sup>39</sup> Andrea S. Gentzke et al., *Tobacco Product Use and Associated Factors Among Middle and High School Students – National Youth Tobacco Survey, United States, 2021*, MMWR 71(5): 1-29 (Mar. 11, 2022), <https://www.cdc.gov/mmwr/volumes/71/ss/pdfs/ss7105a1-H.pdf>.

<sup>40</sup> April Roeseler et al., *Assessment of Underage Sales Violations in Tobacco Stores and Vape Shops*, JAMA Pediatrics 173(8): 795-796 (June 24, 2019), <https://jamanetwork.com/journals/jamapediatrics/fullarticle/2735684>.

<sup>41</sup> Pet. 2.

<sup>42</sup> 21 U.S.C. § 387f(d)(5); 21 C.F.R. § 1140.10.

<sup>43</sup> 2020 Guidance, *supra* note 28, at 10-11.

get vaping devices.<sup>44</sup> As FDA recognized in its 2020 Enforcement Priorities Guidance, 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.<sup>45</sup>

With respect to flavored e-cigarettes, Petitioner’s proposals are particularly unlikely to be effective because, as FDA repeatedly has found, 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. And as recognized by the United States Court of Appeals for the Fifth Circuit in *Wages & White Lion Investments, LLC v. FDA*, “part of the reason Congress passed the TCA is *because* marketing restrictions simply were not working.” 41 F.4th at 440 (emphasis in original). The Court also noted that FDA has already explained that neither age-gated sales nor “traditional marketing schemes” work to reduce youth consumption and that “absent a ‘novel or materially different’ scheme, appeal [of flavored e-cigarettes] would continue.” *Id.* at 441-42. The FDA’s experience confirms this. In March 2019, in response to the youth vaping epidemic, FDA issued draft guidance<sup>46</sup> that proposed to focus its enforcement priorities of flavored ENDS products on how the product was sold. 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 voluntary actions by some manufacturers.”<sup>47</sup> In addition to the Fifth Circuit, other federal circuit courts have upheld MDOs for flavored products despite various traditional access and marketing restrictions proposed by the companies to reduce youth usage. *See Avail Vapor*, 55 F.4th at 426-427 (4th Cir. 2022); *Liquid Labs*, 52 F.4th at 544 (3d Cir. 2022); *Prohibition Juice*, 45 F.4th at 24-25 (D.C Cir. 2022).

*E. According to leading U.S. public health authorities, there is not sufficient evidence to recommend e-cigarettes for smoking cessation.*

The Citizen Petition drastically overstates the evidence regarding the effectiveness of e-cigarettes in helping people who smoke quit.<sup>48</sup> Public health authorities in the U.S., including the CDC, the Surgeon General, the U.S. Preventive Services Task Force and the National Academies of Sciences, Engineering, and Medicine (NASEM) have all concluded that there is not enough evidence to recommend any e-cigarettes for tobacco cessation, nor has the FDA’s Center for Drug Evaluation and Research ever found an e-cigarette to be safe and effective in helping smokers quit.<sup>49</sup> A 2018 report from NASEM concluded that, “[o]verall, there is limited evidence that e-

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<sup>44</sup> Monitoring the Future, *Table 16: Trends in Availability of Drugs as Perceived by 10th Graders* (2022), <https://monitoringthefuture.org/wp-content/uploads/2022/12/mtf2022table16.pdf>.

<sup>45</sup> 2020 Guidance, *supra* note 28, at 46.

<sup>46</sup> 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>.

<sup>47</sup> 2020 Guidance, *supra* note 28, at 21.

<sup>48</sup> Pet. 3-6.

<sup>49</sup> HHS, Office of the Surgeon General, *Smoking Cessation: A Report of the Surgeon General* (2020), <https://www.hhs.gov/sites/default/files/2020-cessation-sgr-full-report.pdf>; United States Preventive Services Task Force, *Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant*

cigarettes may be effective aids to promote smoking cessation.”<sup>50</sup> The 2020 Surgeon General’s Report on Smoking Cessation concluded that, “there is presently inadequate evidence to conclude that e-cigarettes, in general, increase smoking cessation.”<sup>51</sup> The Surgeon General’s Report also cautioned that because e-cigarettes are not a single product, but “a continually changing and heterogeneous group of products” that “are used in a variety of ways,” it is difficult to make broad generalizations about the efficacy of e-cigarettes for cigarette smoking cessation based on one study, or any one product. In a court brief from 2019, the FDA itself stated that, “the claim that vaping helps smokers quit in meaningful numbers remains unproven.”<sup>52</sup>

The research presented by Petitioner also has serious limitations. For instance, the New England Journal of Medicine study<sup>53</sup> cited in the Citizen Petition found that certain e-cigarettes may help individuals to stop smoking, but the study’s findings and implications, especially in the U.S., are limited because the study did not speak to the efficacy of e-cigarettes in a non-clinical setting. The patients in this study were enrolled in a clinical stop smoking program and received weekly face-to-face counseling support from local health care providers. The authors state that “further trials are needed to determine whether our results are generalizable outside the UK services.” In addition, the study was not generalizable to all people who smoke, focusing on those with an intention to stop smoking.

Further, while the Petition relies extensively on the Cochrane Review (the “Review”) regarding the role of e-cigarettes in quitting smoking, the Review found that e-cigarettes can “probably” help people stop smoking for at least six months, but also acknowledged that the evidence remains limited given that their findings are restricted by the small number of studies included in their meta-analyses.<sup>54</sup> Out of the fifty studies captured by the October 2020 Review, only four were rated with low risk of bias, meaning the Review relied on just four studies to reach its main conclusions. Critically important, the Review notes “we need more, reliable evidence to

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*Persons, Final Recommendation Statement*, (2021), <https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/tobacco-use-in-adults-and-pregnant-women-counseling-and-interventions>; NASEM, *Public Health Consequences of E-Cigarettes* (2018), <http://nationalacademies.org/hmd/Reports/2018/public-health-consequences-of-e-cigarettes.aspx>; Brian A. King et al., *Awareness and Ever Use of Electronic Cigarettes Among U.S. Adults, 2010-2011*, *Nicotine & Tobacco Research*, 15(9): 1623-1627 (2013), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4570561/>; see also Brian A. King et al., *Trends in Awareness and Use of Electronic Cigarettes among U.S. Adults, 2010-2013*, *Nicotine & Tobacco Research* 17(2): 219-227 (2015), <https://pubmed.ncbi.nlm.nih.gov/25239961/>.

<sup>50</sup> NASEM, *supra* note 49.

<sup>51</sup> HHS, Office of the Surgeon General, *supra* note 49.

<sup>52</sup> Government’s Opposition to the Motions for Stay Pending Appeal and Consent to the Motion to Expedite Review, Doc. No. 46, at 14 (filed Dec. 31, 2019), *In re Cigar Ass’n of Am.*, 812 F.App’x 128 (4th Cir. 2020).

<sup>53</sup> Peter Hajek et al., *A Randomized Control Trial of E-Cigarettes versus Nicotine Replacement Therapy*, *The New England Journal of Medicine* 380: 629-637 (2019), <https://www.nejm.org/doi/full/10.1056/nejmoa1808779>.

<sup>54</sup> Jamie Hartmann-Boyce et al., *Electronic cigarettes for smoking cessation*, *Cochrane Database of Systematic Reviews* (Sep. 14, 2021), <https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD010216.pub6/full>.

be confident about the effects of e-cigarettes, particularly the effects of newer types of e-cigarettes that have better nicotine delivery.”

An updated release of the Review was published in November 2022.<sup>55</sup> The findings from the updated Review remain inconsistent with those of other leading public health authorities and continue to suffer from important limitations. For example, the studies do not speak to the efficacy of e-cigarettes in general in helping those who smoke to stop smoking. With a wide variation in e-cigarette product availability, it is impossible to make sweeping generalizations about their effectiveness in helping smokers to stop smoking across e-cigarette product types. In addition, the studies do not speak to the efficacy of e-cigarettes used on their own. Four out of the six studies that define the Review’s main conclusions examined the effectiveness of e-cigarettes combined with another intervention, such as counseling or other behavioral support, making it impossible to determine if e-cigarettes would be effective in helping smokers to quit smoking if not used in combination with additional support. Further, the results are not generalizable to all smokers because the studies were conducted with specific smoker populations, such as those who are motivated to quit and seek help to do so.

As indicated in the Citizen Petition, some studies suggest that if used under certain conditions, some types of e-cigarettes may help smokers successfully stop smoking. For example, daily or frequent e-cigarette use has been found to be associated with increased smoking cessation,<sup>56</sup> as has use of e-cigarettes combined with behavioral support, or when used as a part of a clinical program.<sup>57</sup> These studies, however, do not reflect how e-cigarettes are used in the real world, where a notable percentage of e-cigarette users do not use e-cigarettes daily and most e-cigarette users are not using e-cigarettes as part of a clinical intervention or combined with other cessation support. Instead, many e-cigarette users report using both e-cigarettes and conventional cigarettes, which raise additional concerns beyond the potential health effects of e-cigarettes alone. According to the 2019 National Health Interview Survey, 36.9% of adult e-cigarette users are also current cigarette smokers (dual users).<sup>58</sup> While there is little available data on what happens with dual users over time, analysis of data from the government’s PATH survey found that nearly 9 out

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<sup>55</sup> Jamie Hartmann-Boyce et al., *Electronic cigarettes for smoking cessation*, Cochrane Database of Systematic Reviews (Nov. 17, 2022), <https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD010216.pub7/full>.

<sup>56</sup> Máirtín S. McDermott et al, *The effectiveness of using e-cigarettes for quitting smoking compared to other cessation methods among adults in the United Kingdom*, *Addiction* 116(10): 2825-2836 (2021), <https://pubmed.ncbi.nlm.nih.gov/33751671/>; Richard J. Wang et al., *E-Cigarette Use and Adult Cigarette Smoking Cessation: A Meta-Analysis*, *American Journal of Public Health* 111(2): 230-246 (2021), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7811087/>.

<sup>57</sup> Hartmann-Boyce et al., *supra* notes 54 & 55; Natalie Walker et al., *Nicotine patches used in combination with e-cigarettes (with and without nicotine) for smoking cessation: a pragmatic, randomised trial*, *The Lancet Respiratory Medicine* 8(1): 54-64 (2020), <https://pubmed.ncbi.nlm.nih.gov/31515173/>.

<sup>58</sup> Monica E. Cornelius et al., *Tobacco Product Use Among Adults — United States, 2019*, *MMWR* 69(46):1736-1742 (Nov. 20, 2020), <https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6946a4-H.pdf>.

of 10 early dual users were still smoking cigarettes at follow-up.<sup>59</sup> Research also has found that dual use of e-cigarettes and cigarettes can reduce a smoker’s chance of quitting cigarettes compared to not using e-cigarettes at all.<sup>60</sup>

Finally, approximately six months before Congress passed H.R. 2471, FDA determined that for flavored e-cigarettes to be deemed “appropriate for the protection of the public health” (APPH) under the TCA, “applicant[s] must show that the benefit to adults switching from or reducing cigarettes outweighs the risk to youth.”<sup>61</sup> To date, no tobacco-derived flavored e-cigarette has demonstrated to FDA that its potential benefit to adults who smoke outweighs the known and substantial risk to youth. It is highly unlikely that any of the products that are the subject of the Citizen Petition could meet the statutory APPH standard to justify continued marketing. Thus, the only outcome in conformance with the law and sufficient to protect the public’s health is for FDA to immediately deny the Citizen Petition.

The TCA’s premarket review requirement places the burden on e-cigarette manufacturers to meet the statutory public health standard *before* its products may be marketed. Any further relief to e-cigarette manufacturers allowing them to illegally keep their products on the market would effectively place the burden of their continuing failure to meet the standard on the young people who have already suffered so seriously at their hands. These companies have already enjoyed the benefit of a years-long regulatory “holiday,” and that must come to an end. The Citizen Petition should be denied and FDA should proceed to take all necessary enforcement actions to remove from the market all e-cigarettes without marketing orders, including all synthetic nicotine products.

Sincerely,

American Academy of Pediatrics

American Cancer Society Cancer Action Network

American Heart Association

American Lung Association

Campaign for Tobacco-Free Kids

Parents Against Vaping e-cigarettes

Truth Initiative

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<sup>59</sup> Blair Coleman et al., *Transitions in electronic cigarette use among adults in the Population Assessment of Tobacco and Health (PATH) Study, Waves 1 and 2 (2013-2015)*, Tobacco Control 28(1): 50-59 (2019), <https://pubmed.ncbi.nlm.nih.gov/29695458/>.

<sup>60</sup> *Id.*

<sup>61</sup> Sample Decision, *supra* note 16, at 3. Petitioner characterizes FDA’s approach to reviewing tobacco-derived flavored e-cigarettes as “unlawful,” Pet. 12, but MDOs for flavored e-cigarettes issued by FDA under that approach have now been upheld by five U.S. Courts of Appeals: *Wages & White Lions*, 41 F.4th 427 (5th Cir. 2022); *Prohibition Juice*, 45 F.4th 8 (D.C. Cir. 2022); *Gripum*, 47 F.4th 553 (7th Cir. 2022); *Liquid Labs*, 52 F.4th 533 (3d Cir. 2022); *Avail Vapor*, 55 F.4th 409 (4th Cir. 2022). *Contra Bidi Vapor v. FDA*, 47 F.4th 1191 (11th Cir. 2022).