

July 19, 2018

Scott Gottlieb, M.D., Commissioner
Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. ID: FDA-2017-N-6565 Regulation of Flavors in Tobacco Products

Dear Commissioner Gottlieb:

Reason Foundation is grateful for the opportunity to submit this comment regarding the Food and Drug Administration's (FDA) Advance Notice of Proposed Rulemaking regarding the Regulation of flavored tobacco products.

Reason Foundation's nonpartisan public policy research promotes choice, competition and a dynamic market economy as the foundation for human dignity and progress.

Introduction

Flavored tobacco products have long been the subject of controversy particularly with regards to their potential appeal to youth. While all non-tobacco flavors in combustible cigarettes have been prohibited with the only exception being menthol, thousands of flavors proliferate among Electronic Nicotine Delivery Systems (ENDS) and smokeless tobacco products (STPs). There is strong support among some public health organizations for the development of a tobacco product standard which either prohibits or severely restricts the number and types of flavors in non-combustible tobacco products.

The reasoning for such a standard is that these flavors are inherently appealing to youth and could facilitate youth tobacco use, leading potentially nicotine addiction and or subsequent use of combustible tobacco products. If this hypothesis were correct, flavored ENDS and STPs could present a net public health harm rather than a net benefit. However, the available scientific evidence clearly demonstrates this hypothesis to be incorrect. Instead of presenting a net public health harm, flavored ENDS and STPs are on net beneficial to public health.

This comment will focus on the role flavors play in STPs, youth ENDS initiation and progression to combustible tobacco use, adult switching and cessation, toxicity, consumer surplus, marketing, and the dangers of deploying the precautionary principle. As it stands, there is no justification by way of scientific evidence for a tobacco product standard prohibiting or severely limiting the number of ENDS or STP flavors. Developing such a standard would be counterproductive, degrading the appeal and user experience of products which when used

exclusively in place of combustible cigarettes dramatically reduce the risks of tobacco-related disease.

Role of flavors in smokeless tobacco

When considering the regulation of flavors in STPs, the discussion must be placed in a context of low and falling youth use. According to data from the 2014 National Youth Tobacco Survey, 690,000 or 2.6 percent of middle and high school students reported using flavored smokeless tobacco.¹ Total high school STP use has declined, falling from 7.9 percent in 2011 to 5.5 percent in 2017. Middle school STP use also fell from 2.7 percent to 1.9 percent over the same period.² Regardless of flavor, STPs present limited and diminishing appeal to youth.

STP flavors are, however, popular among adult users. This should not be surprising as without processing or flavoring tobacco and nicotine is often bitter and unappealing. According to the 2013-2014 National Adult Tobacco Survey (NATS), the three most popular flavors among young adults were menthol/mint, fruit, and clove/spice.³

Cross-sectional data from Wave 1 (2013-2014) of the 2016 PATH Study found 48.7 percent of STP users reported using flavored products.⁴ A more recent study of 151 smokers, published in 2017, found the vast majority expressed a strong preference for mint flavored snus, regardless of their menthol smoking status.⁵

Flavors are clearly an important characteristic of STPs. They appeal to adult tobacco users and provide a satisfying user experience. This is crucial for understanding the role STPs can play in tobacco harm reduction.

Smokers who switch to STPs and adults who may have smoked combustible cigarettes were it not for STPs enjoy significant benefits in terms of reducing their potential for tobacco-related disease. As there is no combustion and no smoke is inhaled, STPs present substantially less risk than other tobacco products. In terms of assessing the risk of Swedish snus compared to

¹ Corey, Catherine G. "Flavored Tobacco Product Use Among Middle and High School Students — United States, 2014." Centers for Disease Control and Prevention. October 2, 2015 / 64(38);1066-1070. <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6438a2.htm#Tab>

² Wang, Teresa W. et al. "Tobacco Product Use Among Middle and High School Students — United States, 2011–2017." Centers for Disease Control and Prevention. June 8, 2018 / 67(22);629–633. <https://www.cdc.gov/mmwr/volumes/67/wr/mm6722a3.htm>

³ Bonhomme, M.G., E. Holder-Hayes, B.K. Ambrose, et al., "Flavoured Non-Cigarette Tobacco Product Use Among US Adults: 2013-2014," Tobacco Control, 25(Suppl 2):ii4-ii13, 2016. https://tobaccocontrol.bmj.com/content/tobaccocontrol/25/Suppl_2/ii4.full.pdf

⁴ Villanti, A.C., A.L. Johnson, B.K. Ambrose, et al., "Flavored Tobacco Product Use in Youth and Adults: Findings From the First Wave of the PATH Study (2013-2014)," American Journal of Preventive Medicine, 53(2):139-151, 2017. <https://www.ncbi.nlm.nih.gov/pubmed/28318902>

⁵ Schneller, Liane M. et al., "Strong preference for mint snus flavor among research participants," Addictive Behavior Reports, Vol. 6, December 2017, p. 55, <https://www.sciencedirect.com/science/article/pii/S2352853217300299>.

combustible cigarettes, estimates range from 90⁶ to 98 percent risk reduction for tobacco-related diseases.⁷

Snus has proved an effective smoking cessation tool over many years both in Scandinavia and the U.S. In 2008, a report on U.S. smokers using different quitting aids showed 73 percent who used snus succeeded in quitting, double the success rate for those using nicotine patches, gum or inhalers.⁸ Decades of epidemiological evidence from Sweden shows snus contributed both to the decreasing initiation of smoking and increasing smoking cessation. Snus has been shown beyond any reasonable doubt to be the single biggest contributory factor to Sweden's record-low smoking prevalence and the lowest level of tobacco-related mortality among European men.⁹

In countries where snus use is common, there is also precious little evidence that it encourages a transition to combustible tobacco use. A review of studies among adolescents in three Scandinavian countries showed that baseline snus use "was not a precursor to exclusive cigarette smoking; that is, tobacco initiation with snus or current snus use was not a predictor of future cigarette smoking."¹⁰ According to a 2007 report from the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR), "the Swedish data, with its prospective and long-term follow-up do not lend much support to the theory that smokeless tobacco (i.e. Swedish snus) is a gateway to future smoking." In the US, adult dual use of cigarettes and STPs is extremely low, ranging from <1 to 3 percent.

While every effort should be made to discourage youth use of STPs, it should be recognized that considerable success has already been achieved in this area. Considering the harm reduction potential of STPs, which has been well-documented with sound epidemiological data, FDA should avoid rules that will limit and degrade the appeal of STPs to smokers who may switch to these products or current users who may switch to combustible products if their preferred flavors are removed from the market.

⁶ Levy DT et al. "The relative risks of a low-nitrosamine smokeless tobacco product compared with smoking cigarettes." *Cancer Epidemiol Biomarkers Prev* 2004;13:2035-2042.

<https://www.ncbi.nlm.nih.gov/pubmed/15598758>

⁷ Rodu B, Godshall WT: "The scientific foundation for tobacco harm reduction," 2006-2011. *Harm Reduction Journal* 2011, 8:19, Open Access, at www.harmreductionjournal.com/content/8/1/19

⁸ Rodu B, Phillips CV. "Switching to smokeless tobacco as a smoking cessation method: evidence from the 2000 National Health Interview Survey." *Harm Reduction Journal*. May 23; 2008.

<https://www.ncbi.nlm.nih.gov/pubmed/18500993>

⁹ Ramstrom, Lars, Borland, Ron, Wikmans, Tom. "Patterns of Smoking and Snus Use in Sweden: Implications for Public Health." *International Journal of Environmental Research and Public Health*. November 9, 2016. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5129320/>

¹⁰ Environ International Corporation. "Tobacco Use Behaviors for Swedish Snus and US Smokeless Tobacco." May 2013.

<https://www.accessdata.fda.gov/Static/widgets/tobacco/MRTP/19%20appendix-6b-enviro-tub-report-2013.pdf>

Role of flavors in youth initiation of ENDS use

Much of the concern surrounding the appeal of ENDS flavors to youth is based on a 2016 analysis of the 2013-14 Population Assessment of Tobacco and Health (PATH) survey.¹¹ When asked why they used ENDS, 81 percent of teens who vaped in the past month answered 'yes' to the statement: "because they come in flavors I like." While these responses appear to lend credence to the argument that ENDS flavors are especially appealing to youth, they're actually of very limited value.

Firstly, it's an answer from adolescents who already use ENDS, not those who may be susceptible to ENDS. It would be highly eccentric for those who already use a product to say they did so because it came in flavors they 'didn't' like or to use a product whose flavor they did not enjoy. It's also not the only reason teens gave for vaping. According to the same survey, 79 percent of respondents said they use ENDS because "they might be less harmful to me than cigarettes," while 78 percent said they did so because "they might be less harmful to people around me than cigarettes." Even among those who cited flavors as important in their decision to use ENDS, 92 percent said harm reduction was a motivating factor.

Another piece of evidence offered in support of the view that ENDS flavors are appealing to youth is a study based on a national phone survey which found teens were more interested in trying ENDS offered by a friend if it were flavored like fruit, candy or menthol rather than tobacco or alcohol.¹² This study was in fact cited by the Robert Wood Johnson Foundation (RWJF) in their comment submission to FDA as a reason for developing a Proposed Rule requiring manufacturers to demonstrate that specific flavors help smokers quit or switch completely to ENDS and that the benefits outweigh any potential harms from youth initiation.¹³

What wasn't highlighted by the study's authors or the RWJF submission is the total percentage of teens who expressed an interest in trying ENDS of all flavors. Just 7.4 percent of those surveyed said they would be interested. Of the teens who had never used ENDS, just 1.7 percent expressed an interest and of those who had never smoked the number was 3.3 percent. Furthermore, 5.2 percent of the study's participants were current vapers and 3.6 percent current smokers. In fact, when we examine nonsmoking teens we find interest in ENDS flavors is

¹¹ Ambrose, Bridget K., et al. "Flavored Tobacco Product Use Among US Youth Aged 12-17 Years, 2013-2014." *Journal of the American Medical Association*. November 3, 2015.

<https://jamanetwork.com/journals/jama/fullarticle/2464690>

¹² Pepper, J K, Ribisl, K M, Brewer, N T. "Adolescents' interest in trying flavoured e-cigarettes." *Tobacco Control*. September 15, 2016.

http://tobaccocontrol.bmj.com/content/tobaccocontrol/25/Suppl_2/ii62.full.pdf

¹³ Robert Wood Johnson Foundation. "Comments from Richard Besser, MD, on Advanced Notice of Proposed Rulemaking on Regulation of Flavors in Tobacco Products." July 12, 2018.

<https://www.rwjf.org/en/library/articles-and-news/2018/07/comments-from-richard-besser-on-advanced-notice-of-proposed-rulemaking-on-regulation-of-flavors-in-tobacco-products.html>

negligible. A 2015 survey of nonsmoking teens aged 13-17, found interest levels in flavored ENDS of 0.4 out of a possible score of 10.¹⁴

Despite widespread media coverage to the contrary, ENDS of all kinds including ones with sweet flavors, are not especially appealing to young people with no history of tobacco or nicotine use. In fact, a study of the 2015 National Youth Tobacco Survey found just 0.3 percent of U.S. youth who had never smoked were frequent vapers.¹⁵ According to a 2015 study of 1941 high school students in Hawaii, the prevalence of ENDS use was 17.1 percent. However, only two percent reported daily ENDS use and the same percentage reported weekly use.¹⁶

Flavors can appeal to both adults and minors for a variety of reasons and it is extremely difficult to delineate what kinds of flavors will appeal to adults but not appeal to youth. But on the basis of the evidence, as it stands, the claim that ENDS flavors of the sweet or fruit varieties present an especially appealing proposition to youth is not borne out by the available data.

Most youth ENDS use is occasional and experimental. There is no empirical evidence that ENDS manufacturers produce flavors specifically designed to appeal to children. This should not be surprising as such a strategy would be unethical and a poor business strategy. There is little incentive for ENDS producers to risk the ire of parents and regulators by appealing to cash-poor teens when there is a lucrative market of 34 million adult smokers.

Developing a tobacco product standard requiring prior ENDS manufacturers to demonstrate that a specific flavor will both appeal to and assist smokers in switching to ENDS while presenting no appeal to youth would be both unrealistic and counterproductive.

The role of ENDS flavors in progression to combustible tobacco

Critics of ENDS as a harm reduction tool warn youth use of these products often can progress to combustible tobacco use and ENDS are the causal mechanism for such progression. This so-called “gateway” effect has elicited much comment due to several studies showing that teens who initiate ENDS use, later use combustible cigarettes.¹⁷ The gateway effect is a popular

¹⁴ Shiffman, Saul et al., “The impact of flavor descriptors on nonsmoking teens’ and adult smokers’ interest in electronic cigarettes.” *Nicotine and Tobacco Research* 17:10 (October 2015), pp. 1255-62. <http://www.ncbi.nlm.nih.gov/pubmed/25566782>.

¹⁵ Farsalinos, Konstantinos, Tomaselli, Venera, Polosa, Riccardo. “Frequency of Use and Smoking Status of U.S. Adolescent E-Cigarette Users in 2015.” *American Journal of Preventive Medicine*. June, 2018. <https://www.ncbi.nlm.nih.gov/pubmed/29631871>

¹⁶ Thomas A. Wills, Rebecca Knight, Rebecca J. Williams, et al, “Risk Factors for Exclusive E-Cigarette Use and Dual E-Cigarette Use and Tobacco Use in Adolescents,” *Pediatrics* 2015 135(1):e43-51. doi: 10.1542/peds.2014-0760.

¹⁷ Bold, Krysten W. “Trajectories of E-Cigarette and Conventional Cigarette Use Among Youth.” *Pediatrics*. December, 2017. <http://pediatrics.aappublications.org/content/pediatrics/141/1/e20171832.full.pdf>

concept and has long been an argument for the continued prohibition of illicit drugs such as marijuana.¹⁸

But just because someone tries a product, even one with addictive properties, does not mean the use of this product causes that person to try another, more harmful product. While youth ENDS use may be associated with later cigarette use in some adolescents, it is nearly impossible to discern a causal link.

A 2015 study on school students in Los Angeles found those who use e-cigarettes are 2.7 times more likely to report using conventional tobacco over the next year.¹⁹ But study's own authors concede they "cannot conclude that e-cigarette use directly leads to smoking." The ability to account for confounding factors in these studies is extremely limited. On the population level, we see no evidence of a gateway from ENDS use to combustible tobacco use despite the proliferation of thousands of ENDS flavors.

Seven years of data from the Centers for Disease Control and Prevention show a consistent trend of declining high school and middle school smoking rates whether adolescent vaping is up, down or flat. In 2017, the high school smoking fell to the lowest level on record - 7.6 percent - compared to 15.8 percent in 2011. As for ENDS use, after several years of substantial increases, there was a 30 percent decline in 2016. Current high school ENDS use was 11.7 percent in 2017, substantially down from its high point of 16 percent in 2015. Adolescent cigar, waterpipe, and pipe tobacco smoking have also declined. In fact, the rate of decline in adolescent smoking since 2010 is four times greater than it was between 1975 and 2010.²⁰

If ENDS did serve as a gateway to combustible tobacco use, we should see some of this effect filtering through in the population level data on high school smoking rates, but no such effect has been observed. Assessing the state of the evidence on adolescents and ENDS, Kozlowski and Warner conclude the available studies at best support the view "that a minority of the relatively small number of e-cigarette triers – who haven't also been experimenting with other tobacco products already – will go on to some experimentation with cigarettes."²¹

Considering the vast majority of adolescent ENDS users are current or former tobacco users, there is little reason to think ENDS flavors are especially appealing to teens with no history or

¹⁸ Morris, Julian. "The Gateway Effect of Marijuana." Reason Foundation. May 2018.

<https://reason.org/wp-content/uploads/2018/05/gateway-effect-of-marijuana.pdf>

¹⁹ Leventhal, Adam M et al. "Association of Electronic Cigarette Use With Initiation of Combustible Tobacco Product Smoking in Early Adolescence." Journal of the American Medical Association. August 13, 2015. <https://jamanetwork.com/journals/jama/fullarticle/2428954>

²⁰ Bates, Clive. "Trends in tobacco and nicotine use in the United States." The Counterfactual. April 2018. <https://www.clivebates.com/documents/USTrendsApril2018.pdf>

²¹ T. Kozlowski, Lynn et al. "Adolescents and e-cigarettes: Objects of concern may appear larger than they are." Drug and Alcohol Dependence 209-14. May 1, 2017. <http://www.sciencedirect.com/science/article/pii/S0376871617300236?showall%3Dt+rue%26via%3Dihub>

propensity toward tobacco use. Flavored or not, there is no evidence to date suggesting ENDS are a gateway to smoking in the real world.

ENDS flavors, switching, and smoking cessation

As of yet, the evidence on whether ENDS flavors assist adults switching from combustible to tobacco to ENDS is limited both in volume and quality. There is plenty of anecdotal evidence from thousands of individual ENDS users, which FDA acknowledges is important.²²

A systematic review of consumer preference for ENDS attributes including flavor, found the evidence to be inconclusive.²³ However, the review found that both young adults and adults more generally prefer sweet ENDS flavors. This runs counter to the view that sweet or other non-tobacco ENDS flavors are designed to and are especially appealing to youth.

A 2013 study of dedicated, long-term vapers showed flavors "appear to contribute to both perceived pleasure and the effort to reduce cigarette consumption or quit smoking." Published in the International Journal of Environmental Research and Public Health, the study found ENDS users typically preferred tobacco flavors when initially switching from cigarettes to ENDS. Longer term ex-smokers actually showed a preference for non-tobacco flavors. Respondents showed substantial heterogeneity of flavor preference, often switching between flavors, with former smokers switching more frequently than current smokers. Almost three-quarters of respondents said they liked a variety of flavor choices.

Almost 70 percent of the respondents said flavor variety was "very important" in their efforts to quit or reduce smoking and that removing flavor options would reduce the enjoyment of vaping. Nearly half said banning flavors would increase their cravings for cigarettes and 40 percent said it would lessen their chances of reducing or quitting smoking. The number of ENDS flavors regularly used was also independently associated with smoking abstinence.

Demand for varieties of flavors and nicotine strengths are reflected among ENDS users across the world. A 2016 analysis of European and South Korean ENDS users showed 16 percent of users opted for nicotine free e-liquids, 28 percent for tobacco flavors, 23 percent for fruits and 20 percent for botanicals.²⁴ In the U.S., a survey conducted by the Consumer Advocates for

²² Gottlieb, Scott. "Nicotine and the Role of Science in Regulation." Society for Research on Nicotine and Tobacco (SRNT). Baltimore, MD. February 23, 2018.

<https://www.fda.gov/NewsEvents/Speeches/ucm598073.htm>

²³ Zare, Samane, Nemat, Mehdi, Zheng, Yuqing. "A systematic review of consumer preference for e-cigarette attributes: Flavor, nicotine strength, and type." PLOS One. March 15, 2018.

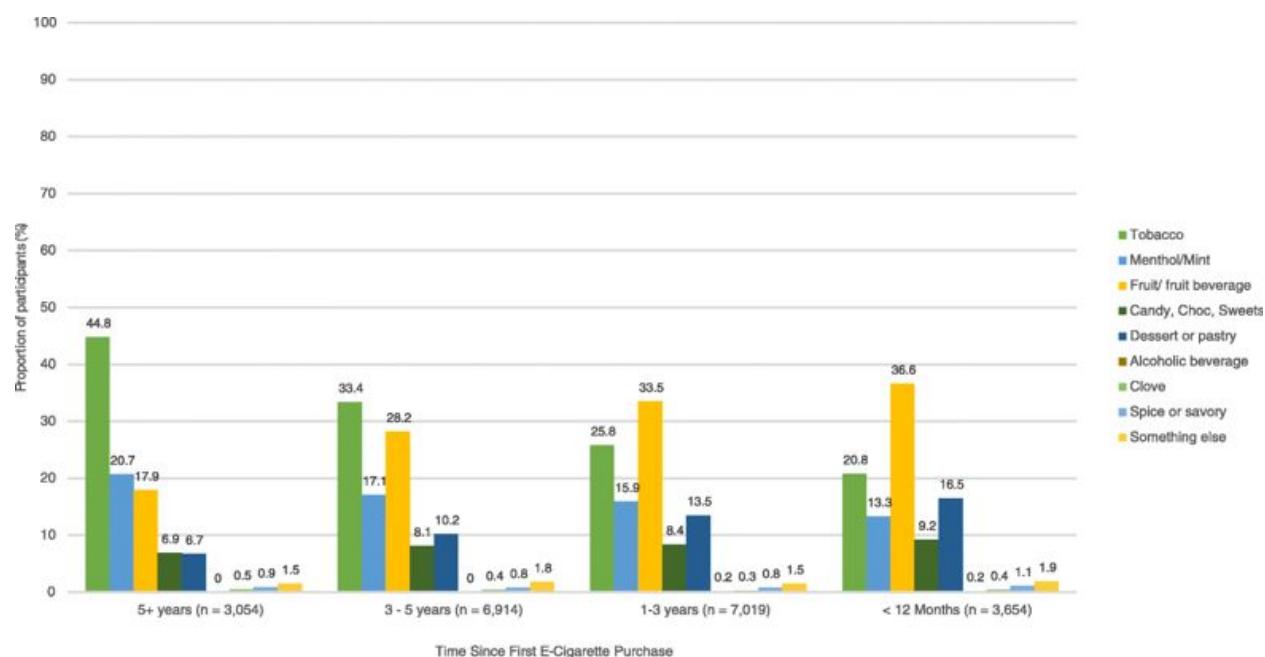
<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0194145>

²⁴ EY. "E-cigarettes: An emerging category." May, 2016.

<https://www.ey.com/Publication/vwLUAssets/E-cigarettes-an-emerging-category/%24FILE/EY-E-Cigarette-report.pdf>

Smoke-Free Alternatives Association in 2015 examined 27,343 adult ENDS users. More than seventy percent of those surveyed “credit[ed] interesting flavors with helping them quit.”²⁵

More recent analysis confirms these patterns, with long-term switchers initially preferring tobacco flavors and more recent switchers preferring fruit and dessert flavors. A study published in 2018 examined 20,836 adults in the U.S. who were using ENDS on a frequent basis, of whom 75.9 percent had completely switched from cigarettes to ENDS.²⁶ The study represents one of the largest academic surveys of adult vapers ever conducted. It found frequent ENDS users are now most likely to have started vaping with products flavored to taste like fruit or a fruit drink and are increasingly likely to have started vaping with dessert or pastry flavors.



Flavor of first e-cigarette purchased by time since first e-cigarette purchase: frequent e-cigarette users

“Between 2011 and 2016, the proportion of first e-cigarette purchases that were flavored to taste like a fruit had almost doubled, while tobacco-flavored first e-cigarette purchases had almost halved,” said the study’s authors. “These data suggest a transition in flavor preference at e-cigarette use initiation over time, from tobacco to non-tobacco flavors, which is consistent with

²⁵ Phillips, Carl V. “CASAA ecig survey results.” Consumer Advocates for Smoke-free Alternatives Association. January 4, 2016.

<https://casaa.org/wp-content/uploads/CASAA-Vaping-Survey-Results-CVP-post-4-January-2016.pdf>

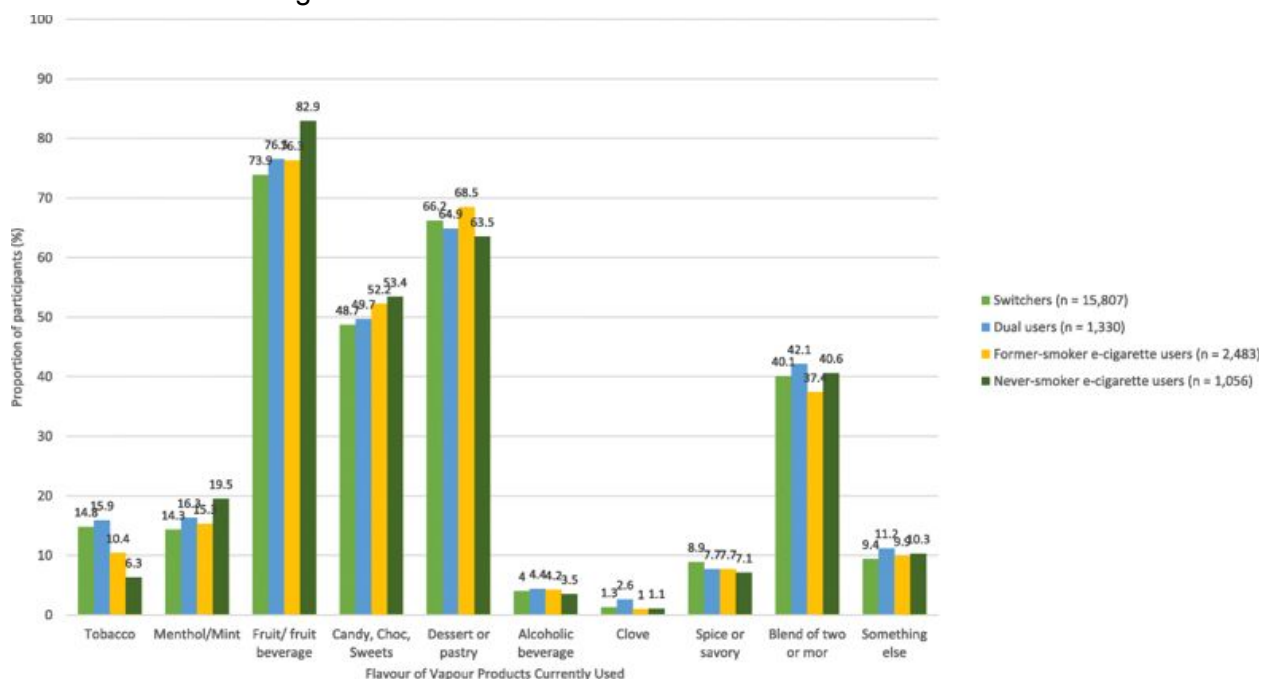
²⁶ Russell, Christopher et al. “Changing patterns of first e-cigarette flavor used and current flavors used by 20,836 adult frequent e-cigarette users in the USA.” Harm Reduction Journal. April 18, 2018.

<https://harmreductionjournal.biomedcentral.com/articles/10.1186/s12954-018-0238-6>

data from a US nationally representative survey that found both former-smoking exclusive e-cigarette users and dual users reported significantly higher rates of current use of a non-tobacco-flavor—72.5 and 72.9 percent, respectively—compared to initiation."

Current ENDS use was dominated by fruit/fruit beverage, dessert/pastry, and/or candy/chocolate/sweets flavors. The trend toward sweet flavors is demonstrated in the chart below, which shows that tobacco/menthol flavors, which were once the most popular first flavors for switchers and dual users, currently rank as the 5th and 6th most popular flavors.

According to the study's authors, restricting the availability of non-tobacco flavors could reduce adult smokers' interest in switching to ENDS and raises the possibility that current ENDS users could return to smoking.



E-cigarette/e-liquid flavors currently used by 20,676 US adult frequent e-cigarette users stratified by Tobacco Use Pathway (TUP) group

This is in concurrence with a recent study published in *Tobacco Control* which examined the possible impact of a ban on all flavored tobacco products, including e-cigarettes. The study concluded such a ban would "likely reduce the smoking/vaping rates, but the use of cigarettes would be higher than in the status quo."²⁷ Consumers of ENDS, not the manufacturers, are the primary drivers of the variety of flavors and nicotine strengths seen in the ENDS market.

²⁷ Buckell, John, Marti, Joachim, Sindelar, Jody L. "Should flavours be banned in cigarettes and e-cigarettes? Evidence on adult smokers and recent quitters from a discrete choice experiment." *Tobacco Control*. 28 May, 2018.

<http://tobaccocontrol.bmj.com/content/early/2018/05/28/tobaccocontrol-2017-054165>

The ENDS manufacturer Juul Labs has received a barrage of media criticism over the alleged popularity of their product among youth. Juul has been criticised both for the nicotine strength of their product and flavor varieties such as ‘fruit medley’ and ‘creme brulee.’ What hasn’t received so much attention is a study of 19,000 Juul users examining transitions in cigarette smoking associated with Juul use.

87 percent were current or former smokers when they first started using Juul and of those who were smoking when they first started, 64 percent were no longer smoking. More than three-quarters of respondents attributed their smoking cessation to Juul.²⁸ Furthermore, 56 percent of Juul users who were still smoking reported they had reduced their daily cigarette consumption by more than 50 percent.

Considering that dual use is often the first stage on the road to smoking cessation, these results are extremely encouraging. Just eight percent of respondents who were former smokers when they started using Juul relapsed to smoking. “In total, the number of smokers who quit after using Juul was 137 times the number of never-smokers who started smoking and 21 times the number of former smokers who relapsed,” writes Reason’s Jacob Sullum.²⁹ Even accounting for sampling bias, these results should be taken into account when assessing the possible impact of a tobacco product standard limiting ENDS flavor choice.

Since ENDS entered the market in a substantial way in 2010, adult smoking has decreased substantially and at an accelerated rate. After decades of consistent decline the adult smoking rate leveled off between 2006 and 2008 at 21 percent. Between 2011 and 2017, however, adult smoking rates fell from 19 percent to 13.9 percent, with many public health experts conceding ENDS played a significant role. The success of ENDS in reducing smoking rates cannot be attributed solely to the appeal of the delivery system or nicotine content, as many ENDS consumers use products without any nicotine.

The availability and variety of flavors is a contributory factor in increasing the appeal of ENDS relative to combustible cigarettes. These adult preferences must be taken into account when considering current patterns of use in terms of avoiding cigarette smoking relapse and the decision to switch to ENDS in the first place.

²⁸ Russell, Christopher, McKeganey, Haseen, Farhana. “Transitions in Cigarette Smoking Associated with Use of the JUUL Vaping Device Among 18,799 Adults in the United States.” Centre for Substance Use Research. June 28, 2018. <http://csures.com/wp-content/uploads/2018/07/Russell-et-al-2018-Smoking-Transitions-Among-Adult-JUUL-Users.pdf>

²⁹ Sullum, Jacob. “Survey of Juul Customers Shows Many Vapers Stop Smoking.” Reason.com. July 2, 2018. <http://reason.com/blog/2018/07/02/survey-of-juul-customers-suggests-many-v>

Toxicity

Concerns have been raised over potential differences in the toxicity of flavored ENDS products compared with non-flavored or tobacco flavored ENDS. These concerns should be considered within the wider context of the differential risks between a flavored ENDS product and a combustible cigarette. The presence of a hazardous agent in a flavored ENDS product does not mean the product presents an unacceptable level of risk. The dosage of harmful and potentially harmful chemicals is the central factor in assessing toxicological risk and this dosage must always be compared to the relevant alternative which is combustible cigarettes.

Studies attempting to analyze the toxicity of flavored ENDS products must reflect how consumers actually use the product in the real-world. It is the responsibility of ENDS manufacturers to ensure their products are as safe as possible. But completely removing non-tobacco flavor constituents from ENDS risks degrading the product to such an extent that many ENDS users may revert to smoking.³⁰

FDA is right to be concerned with the lack of widely recognized product standards among ENDS manufacturers, which can lead to mislabelling and confusion among consumers as to what it is they are purchasing. Efforts should be made both among industry actors and FDA to develop product standards which minimize ENDS users exposure to harmful or potentially harmful chemicals while ensuring the user experience is not degraded.

Consumer surplus

In FDA's ANPRM regarding the possible introduction of a product standard limiting levels of nicotine in combustible cigarettes, FDA asked: "How should potential consumer surplus or utility loss from the removal of nicotine in cigarettes be considered, given the availability of other sources of nicotine such as ENDS and the continued availability of combustible tobacco products?"

Although no such question is present in the ANPRM regarding flavored tobacco products, consumer surplus is an essential part of any analysis of developing a product standard which could limit or prohibit non-tobacco ENDS flavors. The necessity of such analysis cannot be overstated, particularly as the entire purpose of eliminating flavors in ENDS is to reduce consumer surplus in the hope of limiting the appeal to youth.

³⁰ Wade, Carrie L, Bates, Clive. "Think before you ban: The awkward case for e-cigarette flavor bans." R Street Institute No. 144. June, 2018.
<https://2o9ub0417chl2lg6m43em6psi2i-wpengine.netdna-ssl.com/wp-content/uploads/2018/06/144.pdf>

“The consumer’s surplus is the most crucial concept in the measurement of social benefits in any social cost-benefit calculation,” wrote the welfare economist E.J. Mishan.³¹ In the case of combustible cigarettes, much of the recent public health literature ignores consumer surplus, asserting that smoking is an involuntary disease that presents only costs to smokers with no commensurate benefit. While this view is hotly contested, it is not relevant in the case of flavored ENDS products.

There is no justification for supplanting the preferences of ENDS consumers for the preferences of those engaged in research or advocacy demanding stricter ENDS regulation when assessing the desirability of a tobacco product standard for ENDS flavors. Consumer surplus analysis is not new to FDA although it has been limited due to a backlash from anti-smoking campaigners.

In August 2011, FDA issued analysis measuring lost consumer surplus associated with graphic health warnings on cigarette packages. FDA concluded that lost consumer surplus offset 76-93 percent of the predicted health benefits.³² FDA has also estimated the impact of mandatory calorie counts, finding they would cost between \$2.2 billion and \$5.27 billion over 20 years in lost consumer surplus due to foregone consumption of energy-dense food.³³

Unlike combustible cigarettes, ENDS and STPs are harm reduction products. The success of these products lies in their ability to give consumers utility that other products such as nicotine replacement therapies cannot. This is one of the many reasons why ENDS are now the most popular smoking cessation aid in the U.S.³⁴

Recognizing the utility or pleasure consumers derive from ENDS and STPs is crucial in evaluating their value as harm reduction products. If all utility besides nicotine delivery is removed from these products, there will be less incentive for smokers to switch. As of yet, no one has argued, as they have in the case of combustible cigarettes, that consumer surplus should be ignored when analyzing the value of the ENDS. Consumers must be adequately informed of the both the risks and rewards of ENDS.

³¹ Lemieux, Pierre. “The war on consumer surplus.” Regulation, Cato Institute. Spring, 2017.

<https://object.cato.org/sites/cato.org/files/serials/files/regulation/2017/3/regulation-v40n1-4.pdf>

³² Norton, Edward, Smith, Jeffrey A., Levy, Helen. “Improving Cost-Benefit Analysis of Tobacco Regulation,” August 2011.

<https://www.psc.isr.umich.edu/research/project-detail/35956>

³³ Food Labeling: Nutrition Labeling of Standard Menu Items in Restaurants and Similar Retail Food Establishments Final Regulatory Impact Analysis,” Office of Regulations, Policy, and Social Sciences Center for Food Safety and Applied Nutrition. November, 2014.

<https://www.fda.gov/downloads/Food/IngredientsPackagingLabeling/LabelingNutrition/UCM423985.pdf>

³⁴ Rodu, Brad, Plurphanswat, Nantaporn. “Quit Methods Used by American Smokers, 2013–2014.” International Journal of Environmental Research and Public Health. October 4, 2017.

<http://www.mdpi.com/1660-4601/14/11/1403/htm>

But forbidding the option to consumer certain kinds of ENDS flavors, will clearly diminish consumer surplus for many if not most current ENDS users, which poses an existential threat to their success in reducing tobacco-related harms and would doubtless fail a credible cost-benefit analysis.

Marketing

FDA has raised concerns over the marketing of ENDS with so-called “kid-appealing” flavors.³⁵ Common flavors cited include bubblegum, cotton candy, and creme brulee. But as has already been discussed, fruit, dessert, and pastry flavors are extremely popular with current adult ENDS users.

The categorization of these flavors as ‘kid-friendly’ is not just fundamentally subjective but directly contradictory to the patterns of use we see among adult ENDS users. Marijuana and alcohol are far more prevalent among youth than ENDS products.³⁶ Yet there is no suggestion that the flavor of marijuana, beer or wine is designed to appeal to children or is the primary cause of youth use of these products. Youth use of adult products is determined by a number of factors such as curiosity, peer influence, and home environment.

Marketing of ENDS products is routinely demonized as one of the causes of youth use of these products. Yet there is little empirical evidence to suggest this is the case beyond associations of youth ENDS users recalling seeing ENDS marketing. The obvious flaw with such associations is that they only measure what an individual recalls not how much they actually saw and there is no establishment of a causal relationship.

It is true that young people are more susceptible to advertising, but it has also been recognized that by the age of 11 children quickly distinguish between regular programming and advertising and have “acquired the general capability to recognize commercial persuasion.”³⁷ It is certainly a laudable ambition that no advertising of adult products should appeal to children, but when the age of purchase for ENDS is 18 or 21 it is nearly impossible for marketers to produce material that appeals to a 21-year-old that won’t appeal to some 16-year-olds.

³⁵ Gottlieb, Scott. “Remarks by Commissioner of Food and Drug Administration— Protecting American Families: Comprehensive Approach to Nicotine and Tobacco” U.S. Food and Drug Administration, July 28, 2017. <https://www.fda.gov/NewsEvents/Speeches/ucm569024.htm>

³⁶ Johnston, Lloyd D et al. “Monitoring the Future Survey: National Survey Results on Drug Use.” The National Institute on Drug Abuse National Institutes of Health. January, 2018. http://www.monitoringthefuture.org/pubs/monographs/mtf-overview2017.pdf?mod=article_inline

³⁷ Robertson, Thomas, Rossiter, John R. “Children's Attributions of Intent in Television Commercials.” Advances in Consumer Research Volume 1. 1974. <http://www.acrwebsite.org/volumes/5658/volumes/v01/NA-01>

Marketing is vitally important for promoting ENDS use among smoking adults. Marketing imparts information to consumers and alerts them to the existence of new flavors and products which may facilitate their switch from smoking to ENDS. Because some children may be exposed to ENDS marketing is no case for draconian restrictions. Minors are forbidden from purchasing alcohol but frequently encounter alcohol advertising online, on television and on the radio. No one would suggest that alcohol advertising should be severely restricted because a minority who illicitly obtain alcohol have been exposed to alcohol marketing.

ENDS manufacturers are already severely impeded from informing consumers about the benefits of their products. Due to the Modified Risk Tobacco Application process, ENDS and STP manufacturers have to negotiate an expensive and complex regulatory hurdle just to communicate accurate and truthful information to their consumers. Not only is this damaging the potential of ENDS products to reduce tobacco-related harms but it may very well be unconstitutional. According to Jonathan H. Adler, professor of law at Case Western University School of Law, "Insofar as the federal Tobacco Act, and the FDA's implementing regulation, prohibit product makers and sellers from making factually true statements about their products, they likely violate the First Amendment."³⁸

The deleterious effects of ENDS advertising restrictions were documented in a 2018 study published in the National Bureau of Economic Research. The study was the first of its kind to provide causal evidence on whether ENDS advertising on television and in magazines encourages adult smokers to quit.

The authors concluded the answer was yes for TV advertising but no for magazine advertising. The results indicated that a policy banning TV advertising of ENDS would have reduced the number of smokers who quit in the recent past by approximately three percent, resulting in roughly 105,000 fewer quitters. The authors added that if FDA were not "considering regulations and mandates that would likely eliminate many e-cigarette producers during our sample period, e-cigarette ads might have reached the number of nicotine replacement therapy TV ads during that period. That would have increased the number of smokers who quit by around 10 percent, resulting in an additional 350,000 quitters."³⁹

Accurate advertising and marketing is also critical in correcting the widespread misperception around the relative risks of ENDS products. At present, consumers are grossly misinformed

³⁸ Adler, Jonathan H. "Why FDA regulations limiting e-cigarette marketing may cost lives and violate the Constitution." Reason.com. December 12, 2017.

<https://reason.com/volokh/2017/12/12/why-fda-regulations-limiting-e>

³⁹ Dhaval, M et al. "Does E-Cigarette Advertising Encourage Adult Smokers to Quit?." National Bureau of Economic Research. February, 2018.

<http://www.nber.org/papers/w24277>

about the risks of ENDS, which prevents switching and results in a suboptimal satisfaction of preferences.⁴⁰

The precautionary principle

Given the insubstantial evidence about the appeal of ENDS flavors to youth and how widespread such use actually is many public health groups are urging FDA to counter in advance any possible harms that may arise, such as nicotine addiction in adolescents, by developing an onerous product standard which would in effect prohibit the vast majority of the 7,000 non-tobacco ENDS flavors on the market.

This is in essence, an application of the precautionary principle. There are many definitions of the precautionary principle most of which are incredibly vague but this definition from the Wingspread Statement, a consensus document drafted and adopted by environmental activists and academics in January 1998, applies aptly to the case for restricting ENDS flavors: “When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically. In this context the proponent of an activity, rather than the public, should bear the burden of proof.”⁴¹

Cause and effect relationships both in terms of ENDS use and subsequent cigarette smoking and appeal of ENDS flavors to youth, have clearly not been fully established scientifically.

Harvard law professor and former administrator of the Office of Information and Regulatory Affairs in the Obama administration, Cass Sunstein highlights some of the major flaws of a precautionary approach in regulatory policy: “The precautionary principle, for all its rhetorical appeal, is deeply incoherent. It is of course true that we should take precautions against some speculative dangers. But there are always risks on both sides of a decision; inaction can bring danger, but so can action. Precautions, in other words, themselves create risks—and hence the principle bans what it simultaneously requires.”⁴²

Banning or restricting ENDS flavors when no scientific basis has been established to do so, creates the risk that current ENDS users may revert to smoking or that smokers who may have switched to ENDS continue to smoke. FDA must be cognizant not just of the risks of on ENDS

⁴⁰ Viscusi, Kip W. “Risk Beliefs and Preferences for E-cigarettes.” American Society of Health Economists and Massachusetts Institute of Technology. April 20, 2016.

https://www.mitpressjournals.org/doi/10.1162/AJHE_a_00042

⁴¹ “Wingspread Statement on the Precautionary Principle.” Science and Environmental Health Network, <http://www.sehn.org/wing.html>.

⁴² Sunstein, Cass R. “Throwing Precaution to the Wind: Why the ‘Safe’ Choice Can Be Dangerous.” Boston Globe. July 13, 2008.

http://archive.boston.com/bostonglobe/ideas/articles/2008/07/13/throwing_precaution_to_the_wind/

flavors but the risks of action. It is also striking to note that many of the advocates of precaution in ENDS regulation never apply the precautionary principle to the risk of action. Instead, they seek to further burden the ENDS market, which already faces substantial regulatory costs under FDA's Deeming Rule.

As University of Texas law professor Frank Cross observes, "The truly fatal flaw of the precautionary principle, ignored by almost all the commentators, is the unsupported presumption that an action aimed at public health protection cannot possibly have negative effects on public health."⁴³

The dangers of precaution are already prominent in FDA's own history of drug approvals. The delays in drug approvals caused by FDA's demand for drugs to be demonstrated as "safe and effective" poses major risks to public health, despite its seemingly innocuous nature. If a new medical treatment will save lives almost immediately once approved, then it is necessarily the case that the longer the approval process, the more people will die awaiting treatment.⁴⁴

Jonathan H. Adler points to the example of Misoprostol, which prevents gastric ulcers and was first approved in some nations in 1985. Misoprostol, however, was not approved in the U.S. until 1988 and was subjected to a nine and a half month review process. Had Misoprostol been approved more quickly, Adler estimates it could have saved between 8,000 to 15,000 lives. By attempting to ensure absolute safety and efficacy, FDA created risk by preventing the use of Misoprostol by patients suffering with gastric ulcers.⁴⁵

The precautionary principle is appealing to many and Sunstein has identified several cognitive biases that reinforce its appeal. These include loss aversion, the myth of a benevolent nature, the availability heuristic, probability neglect, and system neglect.⁴⁶

According to modelling by Levy et al, replacement of cigarettes by ENDS over a 10-year period yields 6.6 million fewer premature deaths with 86.7million fewer life years lost under their optimistic scenario. Under the model's pessimistic scenario, 1.6 million premature deaths are averted with 20.8 million fewer life years lost.⁴⁷ ENDS present an enormous opportunity for

⁴³ Cross, Frank B. "Paradoxical Perils of the Precautionary Principle." *Washington and Lee Law Review* 53, no. 3. 1996. <https://scholarlycommons.law.wlu.edu/cgi/viewcontent.cgi?article=1656&context=wlulr>

⁴⁴ Kazman, Sam. "Deadly Overcaution: FDA's Drug Approval Process." *Journal of Regulation and Social Costs*. September, 1990. <https://cei.org/content/deadly-overcaution-fdas-drug-approval-process>

⁴⁵ Adler, Jonathan H. "The Problems with Precaution: A Principal without Principle." *American Enterprise Institute*. May 25, 2011.

<http://www.aei.org/publication/the-problems-with-precaution-a-principle-without-principle/>

⁴⁶ Sunstein, Cass R.. "Beyond the Precautionary Principle." *John M. Olin Law and Economics Working Paper No. 149*. University of Chicago Law School. January, 2003.

https://papers.ssrn.com/sol3/papers.cfm?abstract_id=307098

⁴⁷ Levy et al. "Potential deaths averted in USA by replacing cigarettes with e-cigarettes." *Tobacco Control*. October 2, 2017.

tobacco harm reduction. Limiting their appeal or degrading their characteristics through prohibiting or requiring specific demonstration of individual flavors efficacy in aiding smoking cessation presents far greater risks than the disastrous experience of Misoprostol.

Conclusion

The available evidence on both flavored ENDS and STPs suggests they have little to no appeal for non-smoking adults or adolescents. There is, however, a substantial and growing literature on how and why these products appeal to smoking adults and their potential to help consumers switch from smoking to a reduced risk nicotine products.

A tobacco product standard which prohibits the vast majority of ENDS and STP flavors will not just degrade the value proposition of these products, it will stifle further innovation in the market for reduced risk nicotine products. Until more substantial and credible evidence emerges clearly demonstrating that these products produce a net public health harm, FDA should refrain from acting against flavored ENDS and STPs.

Sincerely,

Guy Bentley, Research Associate