Juul Labs, Inc. (JLI or the Company) previously submitted a redacted version of this comment to the U.S. Food and Drug Administration (FDA) for public disclosure in response to FDA's 2018 Advance Notice of Proposed Rulemaking on Tobacco Product Standard for Nicotine Level of Combusted Cigarettes, Docket No. FDA-2017-N-6189. JLI requested that the redacted information be withheld from public disclosure because, at the time, the information described ongoing studies and their results which had not yet been made public and, therefore, were not subject to public disclosure under federal law and FDA regulations. *See* 5 U.S.C. § 552(b)(4); 21 C.F.R. Part 20. Since then, these studies along with their results have been made public and, therefore, are no longer exempt from public discourse. As a result, JLI has decided to publish an unredacted version of the comment on its website.

JUUL LABS

THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION

July 16, 2018

By Courier
Dockets Management Staff (HFA–305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Advance Notice of Proposed Rulemaking: Tobacco Product Standard for Nicotine Level of Combusted Cigarettes; Docket No. FDA–2017–N–6189

To Whom It May Concern:

On March 16, 2018, FDA issued an advance notice of proposed rulemaking to obtain information for consideration in development of a tobacco product standard to set the maximum nicotine level for combusted cigarettes (hereinafter, the Nicotine Level ANPRM).[1] The Nicotine Level ANPRM states FDA is considering a standard to reduce the level of nicotine so combusted cigarettes are minimally addictive or nonaddictive, which would make it potentially easier for smokers to quit. It also notes that "[f]ormer smokers that choose to switch completely to a potentially less harmful nicotine delivery product (e.g., electronic nicotine delivery systems (ENDS)) to maintain their nicotine dose also would, to the extent that those products result in less harm, significantly reduce their risk of tobacco-related death and disease."[2]

JUUL Labs strongly supports this and other recent FDA statements acknowledging that a comprehensive approach to reducing the harms associated with tobacco product use should include efforts to encourage adult smokers to switch to potentially less harmful products, including ENDS.[3] We share FDA's vision of a future where combusted cigarettes

[1] 83 Fed. Reg. 11,818 (Mar. 16, 2018).

[2] *Id.* at 11,824.

[3] *See, e.g.*, FDA, *Advancing Medicinal Nicotine Replacement Therapies as New Drugs – A new step in FDA's comprehensive approach to tobacco and nicotine* (Nov. 29, 2017), https://blogs.fda.gov/fdavoice/index.php/tag/nrt/ ("[N]icotine is delivered through products posing a

would no longer create or sustain nicotine dependence, thereby making it harder for coming generations to become dependent in the first place. And, like FDA, we understand that in order to build this future, the Agency will need to consider taking steps to make combusted cigarettes less likely to create dependence, while also making it possible for current adult smokers to switch to potentially less harmful products, including ENDS.

To assure the development of sound policy in this area, we urge FDA to consider a range of scientific evidence, including emerging data regarding the individual and public health benefits of our ENDS product JUUL. We recently submitted other comments to FDA providing information regarding these potential benefits of JUUL, which are achieved through complete switching by adult cigarette smokers, along with potential health benefits for individual smokers who switch to JUUL.[4] We respectfully request that FDA fully consider those comments here, particularly as they bear on the likelihood that smokers would choose to switch completely from combusted tobacco products to JUUL or other ENDS if FDA were to proceed with the nicotine level standard under consideration.

In addition, if FDA moves forward with the standard, we urge the Agency to assure that its policies allow adult smokers to have full access to adequate alternatives such as ENDS, and to encourage innovation in the development of such products. As FDA has recognized, without access to adequate alternatives, adult smokers may turn to more harmful sources of nicotine such as illicit products, which would contravene the goals of a nicotine level standard and substantially minimize the public health benefits that could be gained.

The Tobacco Control Act requires that FDA consider (among other things) "information concerning the countervailing effects of the tobacco product standard on the health of adolescent tobacco users, adult tobacco users, or nontobacco users, such as the creation of a significant demand for contraband or other tobacco products that do not meet the requirements of [the Act] and the significance of such demand."[5]

In FDA's Draft Concept Paper on Illicit Trade in Tobacco Products after Implementation of an FDA Product Standard (Draft Concept Paper), the Agency recognized

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continuum of risk. This ranges from combusted cigarettes at one end, to nicotine replacement therapy (NRT) products . . . at the other."); Transcript of FDA Media Briefing on Pivotal Public Health Step to Explore Dramatically Reducing Smoking Rates by Lowering Nicotine in Combustible Cigarettes to Minimally or Non-Addictive Levels, Statements by Mitch Zeller (Mar. 15, 2018), https://www.fda.gov/downloads/NewsEvents/Newsroom/MediaTranscripts/UCM601541.pdf ("[C]ombustible cigarettes are far and away the deadliest way to deliver nicotine," and in "figuring out a way to transition people who are currently getting their nicotine from the deadliest and most harmful form . . . we absolutely have a responsibility to make it available in alternative and less harmful ways.").

[4] *See* JUUL Labs, Comment to Docket No. FDA-2017-6565 (ANPRM: Regulation of Flavors in Tobacco Products), Parts I and II (July 16, 2018) (attached).

[5] 21 U.S.C. § 387g(b)(2).

that a nicotine level standard would affect user experience, which, in turn, likely would create consumer demand for products that do not conform to the standard.[6] Moreover, FDA concluded that illicit trade could be a primary source of nonconforming tobacco products following issuance of such a product standard.[7] We agree with FDA that if consumers, however, "could use other tobacco products to achieve the 'experience' missing due to the product standard, there might be little interest in engaging in illegal behavior."[8] We also agree that if "consumers used a product standard such as a nicotine standard for cigarettes as an opportunity to quit the most harmful products, or tobacco products altogether, demand for illicit products would drop, especially over time."[9]

As discussed above, preliminary data demonstrate that JUUL products serve as a satisfying alternative to cigarettes and can facilitate complete displacement of cigarettes for adult smokers. In addition, as discussed above, complete switching from combusted cigarettes to e-cigarettes, such as JUUL products, would reduce users' exposure to numerous toxicants and carcinogens in a manner that would be consistent with a potential reduction in tobacco-related health risk.

As such, if FDA implements a nicotine product standard, it is imperative that the Agency take adequate measures to assure that adult smokers have access to ENDS that are viable alternatives to cigarettes, and that provide nicotine without the same risks and public health burdens.[10] Otherwise, implementation of the nicotine product standard would be unlikely to achieve the desired public health impacts. In particular, absent adequate access to satisfying ENDS and other lawful and less harmful nicotine products, smokers would be more likely to turn to nonconforming tobacco products, thereby driving the market for illicit trade.[11] The availability of and access to ENDS is a critical component of these considerations, and FDA should assure that its efforts to reduce the harm associated with tobacco products are "done in concert and not in isolation," in accordance

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[6] FDA, *Draft Concept Paper: Illicit Trade in Tobacco Products after Implementation of an FDA Product Standard*, 4 (Mar. 15, 2018), https://www.fda.gov/downloads/tobaccoproducts/newsevents/ucm601047.pdf.

[7] *Id.* at 3.

[8] *Id.* at 23.

[9] *Id.*

[10] *See, e.g.*, Action on Smoking and Health (ASH), *Fact Sheet: Use of E-Cigarettes (Vapourisers) Among Adults in Great Britain*, Figs. 2, 5, 6 & 15 (May 2017), http://ash.org.uk/information-and-resources/fact-sheets/use-of-e-cigarettes-among-adults-in-great-britain-2017/ (reporting that 60% of adult smokers in the U.K. have tried e-cigarettes and returned to smoking and that 90% of those relapsed smokers found that e-cigarettes they had tried or which were available to them were not as satisfying as a cigarette).

[11] *See Draft Concept Paper, supra* note 6, at 13-14 and 23.

with its commitment to do so under its Comprehensive Plan for Tobacco and Nicotine Regulation.[12]

Respectfully submitted,

for and on behalf of

Ashley Gould
Chief Administrative Officer
JUUL Labs, Inc.

[12] FDA, *News Release: FDA Announces Comprehensive Regulatory Plan to Shift Trajectory of Tobacco-Related Disease, Death*, (July 28, 2017), https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm568923.htm.

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July 16, 2018

By Courier
Dockets Management Staff (HFA–305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Advance Notice of Proposed Rulemaking: Regulation of Flavors in Tobacco Products; Docket No. FDA–2017–N–6565

To Whom It May Concern:

On March 21, 2018, FDA issued an advance notice of proposed rulemaking regarding the regulation of flavors of tobacco products (hereinafter, the Flavor ANPRM).[1] The Flavor ANPRM seeks "comments, data, research results, or other information about, among other things, how flavors attract youth to initiate tobacco product use and about whether and how certain flavors may help adult cigarette smokers reduce cigarette use and switch to potentially less harmful products," including electronic nicotine delivery systems (ENDS).

The Flavor ANPRM states that FDA "is seeking this information to inform regulatory actions FDA might take with respect to tobacco products with flavors," which may include, but are not limited to, tobacco product standards and restrictions on sale and distribution of tobacco products with flavors. The Flavor ANPRM further states that potential regulatory actions include a prohibition on flavors in tobacco products, beyond the statutory prohibition that already exists for characterizing flavors other than tobacco or menthol in cigarettes.[2]

JUUL Labs strongly supports FDA's efforts to help existing smokers reduce cigarette use, including through switching to potentially less harmful products, while also preventing

[1] 83 Fed. Reg. 12,294 (Mar. 21, 2018).

[2] *Id.* at 12,295, 12,299.

This submission contains trade secret and/or confidential information. This information is exempt from public disclosure under the Freedom of Information Act, 5 U.S.C. § 552(b)(4), and may not be disclosed without the prior written authorization of JUUL Labs, Inc. Such disclosure is prohibited by the Federal Trade Secrets Act, 18 U.S.C. § 1905, the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 331(j), and FDA regulations, 21 C.F.R. § 20.61(c). If FDA receives a request for this submission or for any information contained therein under the Freedom of Information Act and/or FDA regulations at 21 C.F.R. Part 20, and the agency determines that disclosure may be appropriate, the agency must comply with all provisions of 21 C.F.R. § 20.61(e), including by providing JUUL Labs with timely advance notice and a meaningful opportunity to object before making the disclosure, and a copy of any specific records the agency proposes to disclose.

youth initiation of tobacco products. To achieve both of those goals, it is fundamentally important for FDA—and the scientific and public health communities at large—to fully understand how flavors impact both adult switching behavior and youth initiation. We are actively engaged in research related to these topics, and believe our initial results provide promising preliminary evidence that flavors effectively help adult smokers switch, and stay switched, from cigarettes to our ENDS product JUUL, with a net positive impact on public health.

Although more research is needed, we believe the existing results demonstrate that an overly restrictive approach to flavors in ENDS, such as an across-the-board prohibition, would not serve public health. Instead, it would be a significant public health detriment because it would significantly undermine efforts to encourage switching by adults who are not yet ready, or have tried and failed, to quit use of tobacco products entirely.

We also believe there is inadequate scientific research to date to suggest that a highly restrictive approach to flavors will effectively reduce youth initiation of tobacco use, particularly with respect to ENDS. There is evidence that youth are interested in flavored ENDS, but there is also evidence that they are less interested than adult smokers. In addition, the reasons why any particular individual initiates tobacco use are complex and varied, and more research is needed to understand the specific role played by flavors.

As alternatives, we believe more effective public health measures by FDA would involve case-by-case evaluation of specific flavors in specific ENDS products (e.g., through review of product-specific applications), along with enforcement and other actions by FDA against illegal sales to minors and any marketing that blatantly targets children and adolescents. To the extent there are concerns about specific toxicants and impurities in ENDS flavor ingredients, we also support establishment of science-based purity standards for those ingredients.

I. SWITCHING FROM CIGARETTES TO ENDS HAS POTENTIAL BENEFITS FOR INDIVIDUAL SMOKERS AND THE PUBLIC HEALTH

FDA officials have recognized that "nicotine is delivered through products posing a continuum of risk. This ranges from combusted cigarettes at one end, to nicotine replacement therapy (NRT) products . . . at the other."[3] Indeed, as the Director of FDA's Center for Tobacco Products put it, "combustible cigarettes are far and away the deadliest

[3] FDA Voice, *Advancing Medicinal Nicotine Replacement Therapies as New Drugs – A new step in FDA's comprehensive approach to tobacco and nicotine* (Nov. 29, 2017), https://blogs.fda.gov/fdavoice/index.php/tag/nrt/.

way to deliver nicotine" and "we absolutely have a responsibility to make it available in alternative and less harmful ways."[4]

Along that continuum, FDA has further recognized that ENDS are likely to be significantly less harmful to individual users than combusted cigarettes,[5] such that cigarette smokers who switch completely to ENDS "would, to the extent that those products result in less harm, significantly reduce their risk of tobacco-related death and disease."[6]

Similarly, the National Academies of Sciences, Engineering, and Medicine (NASEM) has concluded, in relevant part, that "[t]here is conclusive evidence that completely substituting e-cigarettes for combustible tobacco cigarettes reduces users' exposure to numerous toxicants and carcinogens present in combustible tobacco cigarettes," and "[t]here is substantial evidence that completely switching from regular use of combustible tobacco cigarettes to e-cigarettes results in reduced short-term adverse health outcomes in several organs systems."[7] As such, NASEM has concluded that "e-cigarettes pose less risk to an individual than combustible tobacco cigarettes," and "complete switching from combustible tobacco cigarettes to e-cigarettes would be expected to reduce tobacco-related health risk."[8]

Lead authors for the NASEM report on e-cigarettes, Drs. Eaton and St. Helen, also published a follow-on Evidence to Practice article, which recommended that, "if a smoker's initial treatment has failed or not been tolerated, or if the smoker refuses to use approved medications and counseling and wishes to use e-cigarettes to aid quitting, *physicians should encourage the smoker to switch completely to e-cigarettes.* We agree with Public Health England that behavioral support should be provided to smokers who want to use

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[4] *Transcript of FDA Media Briefing on Pivotal Public Health Step to Explore Dramatically Reducing Smoking Rates by Lowering Nicotine in Combustible Cigarettes to Minimally or Non-Addictive Levels* (Mar. 15, 2018), https://www.fda.gov/downloads/NewsEvents/Newsroom/MediaTranscripts/UCM601541.pdf.

[5] 83 Fed. Reg. 11,818, at 11,836 (Mar. 16, 2018) [hereinafter Nicotine ANPRM] (citing Apelberg model, in which ENDS were assumed to have same risks as smokeless tobacco products).

[6] *Id.* at 11,824.

[7] The National Academies of Sciences, Engineering, and Medicine, Committee on the Review of Health Effects of Electronic Nicotine Delivery Systems, *Public Health Consequences of E-Cigarettes* 11 (2018), http://nationalacademies.org/hmd/Activities/PublicHealth/HealthEffectsofElectronicNicotineDeliverySystems.aspx.

[8] *See id.* at 11 and 490.

e-cigarettes to help them quit smoking, and that health professionals should receive education and training in use of e-cigarettes in quit attempts."[9]

The American Cancer Society has also offered clinical guidance stating smokers who will not use FDA-approved cessation medications should "switch to the least harmful form of tobacco product possible; switching to the exclusive use of e-cigarettes is preferable to continuing to smoke combustible products."[10]

This opportunity for reduction in harm to individual smokers could correspond to a significant public health benefit, although the benefit depends on several factors, including the extent to which current smokers are likely to completely switch to ENDS, use ENDS to quit tobacco products altogether, and/or dual use ENDS with cigarettes, as well as the extent to which non-smokers, including youth, initiate use of ENDS.

We share the same goals as FDA and our mission is to benefit public health by substantially reducing, if not eliminating, the most harmful effects of smoking, which come from smoking combusted products. To assure sound policy that is well understood by all stakeholders, we urge FDA to consider a range of scientific evidence related to the important public health questions raised by FDA policy regarding ENDS, including our own emerging and compelling data regarding the efficacy of JUUL in facilitating complete switching by adult smokers from cigarettes to ENDS, and the role of flavors in that process.

II. PRELIMINARY DATA SUPPORT THE INDIVIDUAL AND PUBLIC HEALTH BENEFITS OF JUUL

JUUL Labs is actively working to provide important data to answer many relevant public health questions raised by FDA policy regarding ENDS, including questions regarding initiation and usage patterns for JUUL. One large survey study was recently completed, and our current scientific research program includes several completed, ongoing, and planned studies on biomarkers, behavior, consumer preferences, environmental assessment of second-hand vapor and harmful and potentially harmful constituent (HPHC) levels. Methods of behavioral research include online surveys, panels, and daily diaries to collect retrospective and prospective data over short and long time periods. This research is focused on our products rather than the entire and varied category of ENDS, so it will provide information about risks and benefits that are unique to our products.

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[9] St. Helen, G. and Eaton, D., *Public Health Consequences of e-Cigarette Use*, 178 JAMA Internal Medicine, 984-86 (July 2018), https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2680315 (emphasis added).

[10] *See* American Cancer Society, *Position Statement on Electronic Cigarettes* (Feb. 2018), https://www.cancer.org/healthy/stay-away-from-tobacco/e-cigarette-position-statement.html.

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A. Toxicity and HPHC testing support the potential health benefits for individual smokers who switch to JUUL.

For all currently distributed JUULpod flavors, JUUL Labs has completed a three-part toxicity testing and evaluation program. The Company also has initiated preclinical toxicity assessments for other JUULpod flavors, which are part of its product portfolio and were distributed by the company on August 8, 2016. The results support a positive toxicological profile for adult smokers who cannot or will not quit smoking cigarettes.[11]

JUUL Labs is also conducting testing related to HPHC levels for cigarette smoke versus JUUL vapor. Preliminary testing, conducted at a third-party laboratory using validated methods, has been reported at two recent scientific meetings for nine selected JUULpod flavors.[12] HPHC emissions were also compared against three leading brands of combusted cigarettes and a laboratory reference cigarette. In that testing, expected constituents, such as nicotine, propylene glycol, and glycerol, were identified in JUUL e-liquid and vapor, along with anabasine (a nicotine analogue) and menthol (in certain flavors). Almost all other HPHCs were found to be below the level of quantification (BQL) or detection (ND) for JUUL. In comparison to reference cigarette emissions, dramatic reductions were seen in multiple categories of HPHCs for comparable analytes measured. The following summarizes these results:

Class of Analyte	Percent Reduction in Aerosol by Total Weight Per Smoking Machine Puff (JUUL vs. Reference Cigarette)		
	Tobacco Flavors of JUUL	Mint / Menthol Flavors of JUUL	Fruit and Dessert Flavors of JUUL
Tobacco Specific Nitrosamines (TSNAs)	>99% reduction	>99% reduction	>99% reduction
Carbonyls	>99% reduction	>99% reduction	>99% reduction
Poly Aromatic Amines (PAAs)	>99% reduction	>99% reduction	>99% reduction
Poly Aromatic Hydrocarbons (PAHs)	>99% reduction	>99% reduction	>99% reduction
Volatile Organic Compounds (VOCs)	>99% reduction	>99% reduction	>99% reduction
Metals	>88% reduction	>88% reduction	>90% reduction

[11] *See, e.g.*, Misra, M. *et al.*, *TSRC Abstract: Neutral Red Uptake (NRU) Cytotoxicity Analysis of Aerosol Generated From a Temperature-Regulated Nicotine-Salt Based ENDS Product* (forthcoming 2018); Wynne, C. *et al.*, *Acute Use of Nicotine Salt-based ENDS and Combusted Cigarettes* (Poster Presentation at Society for Research on Nicotine and Tobacco (SRNT) Conf. (Feb. 24, 2018) Baltimore, MD) (finding that, in adult smokers, exhaled carbon monoxide was not seen to increase when compared 15 minutes after use of JUUL vs. 5 minutes before use; in contrast exhaled carbon monoxide significantly increased post use of a combusted cigarette, and this difference in exposure was itself significant).

[12] Gilman, G. *et al.*, *Characterization of Temperature Regulation and HPHC Profile of a Nicotine-Salt Based ENDS Product*, (Poster Presentation at SRNT Conf. (Feb. 24, 2018) Baltimore, MD); Gilman, G. et al., *HPHC Analysis of Eight Flavors of a Temperature-Regulated Nicotine Salt-Based ENDS Product* (Poster Presentation at the 2018 Global Forum on Nicotine (June 14-16, 2018) Warsaw, Poland).

Of note, the overall HPHC profile of aerosol generated from JUULpod fruit flavors did not differ from aerosol generated from tobacco-flavored JUULpods.

In a separate study that has been submitted for presentation at an upcoming scientific conference, the cellular toxicity of aerosol generated from flavored JUULpods (Menthol, Mint, Cucumber), was compared to that of unflavored control, cigarette smoke, and positive SLS control. Among all of the different samples tested, no aerosol-mediated significant toxicity was observed at any of the concentrations tested for any of the JUUL aerosols. At the doses tested, EC50 for the e-cigarette aerosol and carrier control aerosol could not be calculated because cell viability was greater than 70% at all concentrations tested (0-300 μg/mL). In contrast, cigarette smoke showed an expected toxicity which increased with dose of aerosol, with a calculated EC50 of 59.46 μg/mL with $r^2 = 0.98$.[13]

Although these data are preliminary, they are informative and highlight the opportunity for significant reduction in exposure to toxicants of concern for individual smokers who switch to JUUL across a range of flavors, including fruit flavors. The Company is also conducting further tests to support this potential, and currently plans to submit a more complete data package and analysis to FDA as part of a premarket tobacco application (PMTA) submission.

B. Recent survey data support the potential public health benefits of JUUL, through helping smokers stop smoking cigarettes.

Preliminary results from a recently completed survey provide compelling evidence that the majority of JUUL users were smoking at the time of their first use of JUUL, and that most of those smokers had completely stopped or significantly reduced their smoking by the time of the survey. The Center for Substance Use Research (CSUR) conducted the survey, which was designed to describe changes in adults' smoking status between their first use of JUUL and the time of the survey, and the rate at which these adults have stopped smoking, reduced smoking, restarted smoking, or started smoking since they first used JUUL.[14]

The vast majority (90.2%) of survey respondents reported they had used nicotine through cigarettes or ENDS before their first use of JUUL,[15] and 74.5% were using nicotine through cigarettes or ENDS at the time of the first use. More specifically, 87.2% reported

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[13] Misra, *supra* note 11.

[14] CSUR, *Transitions in Cigarette Smoking Associated with Use of the JUUL Vaping Device Among 18,799 Adults in the United States* (2018), http://csures.com/wp-content/uploads/2018/07/Russell-et-al-2018-Smoking-Transitions-Among-Adult-JUUL-Users.pdf.

[15] The remainder comprised 6.9% of all participants who reported they had never smoked a cigarette or used an ENDS product, and 2.9% for whom prior nicotine status could not be determined.

they were either smoking cigarettes or had smoked cigarettes in the past when they used JUUL for the first time,[16] and 62.2% were smoking cigarettes every day or some days when they first used JUUL. These data suggest that the vast majority of adults who are using JUUL have a history of using nicotine, and most were smoking when they initiated use.

The survey's results also suggest that JUUL may help adult smokers stop smoking cigarettes. Of the 11,689 individuals who were smoking every day or some days when they first started using JUUL, 64.3% (n = 7,520) transitioned to "new former smokers"—they reported they had stopped smoking (no smoking in the past 30 days or now smoking not at all) at the time of the survey—whereas, 35.7% (n = 4,169) reported they were continuing to smoke (still smoking every day or some days). In other words, approximately two out of three JUUL users who were smoking when they first used JUUL reported they had stopped smoking cigarettes.

Even among those JUUL users who continued to smoke, the intensity with which they smoked decreased. Of the 2,228 individuals who were smoking an average of six or more cigarettes per day when they first used JUUL and are still smoking (which includes individuals who were smoking between 11 and 20 cigarettes per day when they first used JUUL and are still smoking), 50.6% reported smoking between 0 and 5 cigarettes per day at the time of the survey.

The survey findings also indicate that smoking re-initiation after first JUUL use by former smokers is uncommon. Of the 4,695 individuals who had smoked cigarettes in the past but were smoking not at all when they used JUUL for the first time, 92.4% (n = 4,336) were still former smokers (no smoking in the past 30 days or now smoking not at all) at the time of the survey. At this time, it is unclear how many former smokers would have re-initiated smoking if they were not able to use JUUL as a satisfying alternative to cigarettes.

Initiation of smoking by those who have never smoked before first JUUL use also appears to be uncommon. Individuals who had never smoked a cigarette—not even a puff—represented 12.7% (n=2,385) of all survey participants. Of those, 419 had smoked at least one cigarette by the time of the survey, which represents only 2.2% of all survey participants. Breaking down the group further, 50 were smoking on some days (0.3% of all survey participants) and 5 were smoking every day (0.03% of all survey participants).

While the findings of this survey are only preliminary, and more robust studies need to be completed to yield conclusory evidence, they suggest that the majority of adults who are using JUUL were smoking cigarettes when they started using the product, that the majority of these individuals are now former smokers or have decreased the intensity with

[16] About half of the 12.7% of respondents who reported they had never smoked a cigarette at the time of first use also reported they had never used an ENDS product at the time of first use. The 12.7% comprised 3.1% who were using an ENDS product containing nicotine, 0.6% who were using an ENDS product not containing nicotine, 2.1% who were former ENDS users, and 6.9% who had never used ENDS.

which they smoke cigarettes, and that initiation and re-initiation of cigarette smoking among JUUL users is uncommon.

III. FLAVORS HELP ADULT SMOKERS SWITCH TO ENDS, INCLUDING JUUL

The CSUR survey provides evidence that flavors play a significant role in initiating switching from cigarettes to ENDS. The great majority (78.5%) of all participants who transitioned to being new former smokers initiated use of JUUL with characterizing flavors other than tobacco, and 88.4% of these new former smokers were using these flavors at the time of the survey.[17]

Furthermore, smokers had different JUUL flavor preferences depending on whether they were smokers of tobacco flavored cigarette or smokers of menthol flavored cigarettes: 93.1% of new former smokers who were smoking menthol-flavored cigarettes initiated JUUL use with a non-tobacco flavor. Non-tobacco flavors were also important for new former smokers of tobacco-flavored cigarettes, as 68.8% them initiated JUUL use with these flavors.

Several different types of flavor journeys were seen for new former smokers. Those who were initial tobacco-flavor users were significantly more likely to be using only non-tobacco flavors at the time of the survey than initial non-tobacco flavor users were to be now only using tobacco flavors. This provides evidence that non-tobacco flavors are important for multiple types of journeys.

In order of frequency, these switching journeys were observed for new former smokers:

Initial JUUL Flavor Use	Current JUUL Flavor Use	Frequency of Switching Journey
Non-tobacco	Non-tobacco	68.1%
Tobacco	Tobacco	9.6%
Non-tobacco	Both	8.5%
Tobacco	Both	7.2%
Tobacco	Non-tobacco	4.7%
Non-tobacco	Tobacco	2.0%

These data suggest that availability of both tobacco and non-tobacco flavors are important for displacement of combusted cigarettes. This makes any FDA action that would eliminate the availability of non-tobacco flavors problematic.

[17] Data on file. The eight JUULpod flavors addressed by the survey comprise two tobacco flavors (Classic Tobacco and Virginia Tobacco) and six non-tobacco flavors (Classic Menthol, Cool Cucumber, Cool Mint, Crème Brulee, Fruit Medley, and Mango).

There is also support in the literature for the role of flavors in facilitating switching from cigarettes to ENDS.[18] For example, Farsalinos concluded that flavors "contribute to both perceived pleasure and the effort to reduce cigarette consumption or quit smoking."[19] The scientific community has also observed that flavored ENDS played an important role in switching when flavors were removed from combusted products. In particular, Ontario's ban on menthol cigarettes in 2017 led to "a considerable increase in use of flavored e-cigarettes,"[20] rather than switching to unflavored combusted cigarettes or other flavored combusted tobacco products.

The scientific literature further points to the appeal of flavors as a common reason for adult smokers to be interested in e-cigarettes, with a majority of adult smokers (both current and former) choosing non-tobacco flavors for regular use, consistent with the preliminary results of the CSUR research described above. Farsalinos found that adult smokers, particularly former smokers, move from tobacco-flavoring to non-tobacco flavoring over time. A majority of these same users said that taking away flavors would make ENDS less appealing as alternatives to cigarettes.[21]

Although the CSUR survey did not ask JUUL consumers about the impact of a potential ban on flavors, the survey showed the same pattern of most smokers using non-tobacco flavored JUUL as a significant part of their journey to becoming former smokers, with an increasing number of former smokers initiating ENDS usage with a non-tobacco flavor or transitioning to non-tobacco flavors over time. A recently published study of

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[18] FDA has itself acknowledged that "some flavors could help adult cigarette smokers switch to potentially less harmful tobacco products." FDA Website, *Menthol and Other Flavors in Tobacco Products* (last updated Mar. 29, 2018), https://www.fda.gov/syn/html/ucm2019416 (citing Barbeau, A.M. *et al.*, *Perceived Efficacy of E-Cigarettes Versus Nicotine Replacement Therapy Among Successful E-cigarette Users: A Qualitative Approach*, 8 Addiction Sci. & Clinical Practice 1 (2013); Farsalinos, K.E. *et al.*, *Impact of Flavour Variability on Electronic Cigarette Use Experience: An Internet Survey*, 10 Int. J, Environ. Res. Public Health 7272-82 (2013); Litt, M.D., *Cigarette Smoking and Electronic Cigarette Vaping Patterns as a Function of E-cigarette Flavourings*, 25 Tobacco Control ii67-ii72 (2016)).

[19] Farsalinos, *supra* note 18 at 7273.

[20] Chaiton, M *et al.*, *Association of Ontario's Ban on Menthol Cigarettes with Smoking Behavior 1 Month After Implementation*, JAMA Internal Med. (2018), https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2673373.

[21] Farsalinos, *supra* note 18 at 7273; *see also* Bucknell, J. *et al.*, *Should flavours be banned in cigarettes and e-cigarettes? Evidence on adult smokers and recent quitters from a discrete choice experiment*, Tobacco Control (published online May 28, 2018) ("A ban on flavoured e-cigarettes alone would likely increase the choice of cigarettes in smokers, arguably the more harmful way of obtaining nicotine, whereas a ban on menthol cigarettes alone would likely be more effective in reducing the choice of cigarettes. A ban on all flavours in both products would likely reduce the smoking/vaping rates, but the use of cigarettes would be higher than in the status quo."), https://tobaccocontrol.bmj.com/content/early/2018/05/28/tobaccocontrol-2017-054165.

ENDS users surveyed in the U.S. showed similar results with the authors cautioning against taking action on ENDS flavors.[22]

Similarly, a variety of ENDS flavors and the ability to rotate flavors may help prevent smokers from relapsing. Farsalinos gathered data from ENDS users who were former smokers and current smokers who had greatly reduced their smoking intensity. When surveyed, these ENDS users said that variability of flavors was "very important" in their effort to reduce or quit smoking. Nearly half of this group said that fewer flavors would increase their craving for cigarettes and almost 40% said that restricting flavors would make elimination or reduction of smoking less likely. Farsalinos also noted that nearly 70% of former smokers switched flavors on a daily basis or even more often, with users moving from tobacco-flavored products at the beginning of cessation to more fruit flavorings after about a year of ENDS use.[23]

We also see the importance of flavors and flavor variety in the context of NRT, where they are used to enhance appeal to adult smokers. Indeed, Nicorette does not offer a tobacco flavored product, and uses a variety of non-tobacco flavors to attract adult smokers, including "White Ice Mint," "Fruit Chill," "Cinnamon Surge," "Spearmint Burst," and "Mint."[24]

JUUL Labs is planning future research in this area, which will drill down on which user demographics favor certain flavors and provide a stronger understanding of whether any flavors might be particularly attractive to adult vs. non-adult users.

More work is needed to understand the relative risks and benefits of flavored ENDS with respect to youth and young adults in comparison to adult smokers. At least one study provides evidence that adult smokers have a stronger interest in ENDS flavors than non-smoking teens.[25] Before depriving millions of adult smokers of tools that may help them

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[22] Russell, C. *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*, 15 Harm Reduction J. 33 (June 2018), https://harmreductionjournal.biomedcentral.com/track/pdf/10.1186/s12954-018-0238-6 ("Restricting access to non-tobacco e-cigarette flavors may discourage smokers from attempting to switch to e-cigarettes.").

[23] Farsalinos, *supra* note 18 at 7273.

[24] Nicorette Website, https://www.nicorette.com/products/nicorette-gum.html (last visited July 5, 2018).

[25] Shiffman, S. *et al., The Impact of Flavor Descriptors on Nonsmoking Teens' and Adult Smokers' Interest in Electronic Cigarettes*, 17 Nicotine and Tobacco Research 1255-62 (2015) ("Nonsmoking teens' interest in e-cigarettes was very low (mean = 0.41 ± 0.14 [SE] on 0–10 scale). Adult smokers' interest (1.73 ± 0.10), while modest, was significantly higher overall ($p < .0001$) and for each flavor (most p values < .0001). Teen interest did not vary by flavor ($p = .75$), but adult interest did ($p < .0001$). Past-30-day adult e-cigarette users had the greatest interest in e-cigarettes, and their interest was most affected by flavor. Adults who never tried e-cigarettes had the lowest interest, yet still higher than nonsmoking teens' interest ($p < .0001$).").

quit smoking,[26] FDA should fully understand whether flavored ENDS actually pose risks to youth that cannot be mitigated by other regulatory alternatives discussed below.

IV. FDA CURRENTLY LACKS ADEQUATE INFORMATION TO CATEGORICALLY PROHIBIT OR RESTRICT ENDS FLAVORS

To regulate ENDS flavors by promulgating either a tobacco product standard or a restriction on tobacco product sale or distribution, FDA must rely on scientific evidence to determine that the action is appropriate for protection of the public health. Specifically, FDA must consider scientific evidence regarding (1) "the risks and benefits to the population as a whole, including users and nonusers of tobacco products"; (2) "the increased or decreased likelihood that existing users of tobacco products will stop using such products"; and (3) "the increased or decreased likelihood that those who do not use tobacco products will start using such products."[27] This is the same evidentiary standard that applies to a manufacturer seeking approval of a PMTA.[28]

FDA has itself acknowledged that the public health impacts of a prohibition or other categorical restriction on ENDS flavors are not yet fully understood.[29] We agree and set forth below some specific reasons why FDA does not yet have the evidence required to take these actions.

A. FDA should not seek to promulgate categorical restrictions until it has reliable information on the way ENDS flavors impact adult switching.

Because the literature on how ENDS flavors contribute to adult switching behavior is sparse and inconclusive, we are in the process of conducting several studies regarding the longer-term impact of JUUL use on former smokers' ability to avoid relapse. Research that takes complex variables like taste preferences among various subgroups into account is needed in order to make policies that will benefit public health. Given these complexities and the need for more data, we respectfully urge FDA to facilitate continued research regarding the role that flavors play in the use of ENDS by adult smokers, particularly with respect to helping adult smokers transition to less harmful products. In addition, we ask

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[26] Chen, J.C. *et al., Flavored E-Cigarette Use and Cigarette Smoking Reduction and Cessation—A Large National Study among Young Adult Smokers,* Substance Use & Misuse (published online 2018), https://doi.org/10.1080/10826084.2018.1455704 (based on PATH data) ("E-cigarette users with one (AOR = 2.5, $p < 0.001$) and multiple [non-tobacco/non-menthol] flavors (AOR = 3.0, $p < 0.001$) were more likely to have reduced or quit smoking over the past year compared to non-e-cigarette users.").

[27] 21 U.S.C. §§ 387f(d)(1), 387g(a)(3)(B).

[28] *Id.* § 387j(c)(2)(A) & (c)(4).

[29] *See generally* FDA, *Illicit Trade in Tobacco Products after Implementation of an FDA Product Standard* (Mar. 15, 2018), https://www.regulations.gov/document?D=FDA-2018-N-0529-0002.

that the Agency allow for adequate time for this body of research to be evaluated, and for consensus to emerge on its implications for public health.

B. FDA should not seek to promulgate categorical restrictions until it has reliable information on the way ENDS flavors impact youth initiation.

FDA has not gathered sufficient evidence to support a determination that categorical regulation of ENDS flavors is appropriate for the protection of public health. A key aspect of this determination is weighing the risks of youth ENDS initiation against the public health impact of converting adult smokers to ENDS. On several occasions, FDA has emphasized the importance of ENDS to transitioning adult smokers to a lower-risk source of nicotine but then expressed concern that the continued marketing of ENDS will "hook another generation of kids on nicotine."[30]

FDA has nonetheless acknowledged in the Flavor ANPRM and elsewhere that it does not yet have the evidence it needs to appropriately regulate ENDS and that the regulations should be based on the "net impact on the public health."[31] These statements acknowledge that FDA does not yet have the information on youth initiation needed to promulgate categorical restrictions on ENDS flavors.

JUUL Labs is committed to working with FDA to develop this information in a thoughtful and well-structured manner. To that end, the company is engaged with FDA to discuss the implementation of a study to better understand appeal, perception, and use patterns of JUUL and other ENDS products among youth.

C. Compelling evidence suggests that categorical regulation would result in a gray market for flavored products.

In order to set a product standard, FDA is also required to consider potential countervailing effects, including whether a product standard will create an illicit market.[32] Banning flavors is known to create a gray market. After Ontario's menthol cigarette ban, a

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[30] *See, e.g.*, Statement from FDA Commissioner Scott Gottlieb, M.D., *2017 National Youth Tobacco Survey results and ongoing FDA efforts to protect youth from the dangers of nicotine and tobacco products* (June 7, 2018), https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm610206.htm.

[31] *See, e.g.*, 83 Fed. Reg. at 12,299 (requesting public comment, specifically studies or information, regarding the role of flavor in initiation among youth and young adults); Remarks by Dr. Gottlieb on the Regulation of Nicotine (Oct. 19, 2017), https://www.fda.gov/NewsEvents/Speeches/ucm581314.htm ("On this issue, we see two sides – on the one hand, we need to know the role that flavors, including menthol, play in attracting youth to initiate tobacco use. On the other hand, we also need to know whether or not and how certain flavors may help adult cigarette smokers switch to potentially less harmful forms of nicotine delivery; for example, when flavors are used in non-combustible products such as electronic nicotine delivery systems. It's possible for flavors to do both harm and good, perhaps in different product types. FDA's responsibility is to determine how they compare to each other and to issue regulations based on their net impact on the public health.").

[32] 21 U.S.C. § 387g(b)(2).

significant proportion (14%) of menthol cigarette smokers turned to gray market (First Nations reservation sales) or illegal sales locally or through the Internet post-ban.[33] Researchers have also concluded that the U.S. ban on flavored cigarettes in 2009 likely caused consumers to migrate to other flavored tobacco products, including combusted products like flavored cigars.[34] Several law enforcement groups have already expressed their concerns about creation of an illicit market in public comments on the Nicotine ANPRM.[35]

If FDA chooses to restrict the use of menthol in combusted tobacco, in order to transition menthol smokers to potentially less harmful products, flavors should be continued to be allowed in alternative products as an "off-ramp," as was seen after menthol cigarettes were banned in Ontario.[36]

V. SEVERAL ALTERNATIVES TO CATEGORICAL REGULATION WOULD BETTER SERVE THE PUBLIC HEALTH

Rather than categorically limit flavors for ENDS, there are a variety of alternative options for FDA that are more likely to improve public health. These policy options include:

- ***Using Premarket Submissions and the Ingredient Listing Process to Evaluate Flavors on a Product-by-Product Basis***

FDA is already engaged in reviewing PMTAs and ingredient reports, which include information about flavors, and it will soon have a complete picture of how flavors are used in legally marketed tobacco products when the submission process is complete.

Using these processes to determine which ENDS flavors should remain on the market is desirable for several reasons: (1) FDA can and should evaluate the use of a particular flavor in a particular format with structured, granular manufacturer data regarding youth attractiveness and clinical study information; (2) ingredient reports enable the agency to look at whether particular flavors in products might make them more attractive to youth based on use patterns; and (3) FDA can build its scientific understanding of the public health impact of ENDS flavors, a relatively new tobacco product that has not been adequately studied.

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[33] Chaiton, *supra* note 20.

[34] Courtemanche, C. *et al.*, *Influence of the Flavored Cigarette Ban on Adolescent Tobacco Use*, 52 Am. J. Prev. Med. 139-146 (2017), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5401634/pdf/nihms842675.pdf.

[35] *See* Comment from California Statewide Law Enforcement Association, Comment from Anaheim Police Association, Comment from Maricopa County Sheriff's Office, and the Orange County Coalition of Police and Sheriffs, Docket No. FDA-2017-N-6189 (Nicotine ANPRM).

[36] Chaiton, *supra* note 20.

The ANPRM process in which FDA is currently engaged will no doubt offer some insights into flavors in tobacco products, but the level of scientific evidence needed to support a product standard or sales and distribution restriction is much more likely to be obtained through the premarket submission and ingredient reporting processes.

- ***Focusing resources on youth access and youth-oriented marketing***

Instead of potentially disrupting a market for products that are helping adult smokers switch, FDA could devote its limited resources to youth access prevention efforts, which are focused solely on keeping all tobacco products out of the hands of adolescents and teens.

FDA has already begun a crackdown on illegal sales of tobacco products to minors at the retail level.[37] JUUL Labs supports FDA's enforcement activities, particularly when they do not unfairly single out ENDS. Selling tobacco products to a person younger than 18 years of age violates 21 C.F.R. § 1140.14(b), as does the failure to check photographic identification for any person under the age of 27 who attempts to purchase tobacco products. Further, these violations cause the tobacco products to be "misbranded" under FDCA 903 (21 U.S.C. § 387c), meaning that the retailer has committed a prohibited act under the FDCA, potentially subjecting the individual to civil and criminal penalties. Rather than limiting adult options, FDA should continue to use its existing enforcement authorities as a key tool to prevent youth access.

FDA and the Federal Trade Commission have also recently initiated enforcement against companies that have marketed ENDS with packaging and advertising designed with cartoon characters or copying branding of childhood treats.[38] The agencies issued 13 warning letters to manufacturers, distributors, and retailers for selling e-liquids used in e-cigarettes with labeling and/or advertising that cause them to resemble kid-friendly food products, such as juice boxes, candy or cookies, some of them with cartoon-like imagery. These products were misbranded in violation of the FDCA because the labeling or

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[37] "FDA has conducted 908,280 inspections of retail establishments that sell tobacco products, issued 70,350 warning letters to retailers for violating the law and initiated about 17,000 civil money penalty cases. We have also issued more than 110 No-Tobacco-Sale Order Complaints, which can result in retailers being prohibited from even selling tobacco products for specified periods of time." FDA, Press Release: Statement from FDA Commissioner Scott Gottlieb, M.D., on new enforcement actions and a Youth Tobacco Prevention Plan to stop youth use of, and access to, JUUL and other e-cigarettes (Apr. 24, 2018), https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm605432.htm. *See also* FDA, List of All No Tobacco Sale Orders (NTSOs), https://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/ucm232109.htm#NTS0 (last visited July 5, 2018) (FDA has issued at least 40 NTSOs since January 2018).

[38] FDA, *Press Release: FDA, FTC take action against companies misleading kids with e-liquids that resemble children's juice boxes, candies and cookies* (May 1, 2018), https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm605507.htm.

advertising designed to imitate kid-friendly food is false or misleading. JUUL Labs does not engage in these practices and supports this enforcement.

FDA could also issue product standards or sales and distribution restrictions that would expressly prohibit this type of marketing to youth, rather than relying on the misbranding provisions of the FDCA, as amended by the TCA. If FDA determines that it would be appropriate for the protection of the public health, FDA could issue a rule under FDCA 906(d)(1) (21 U.S.C. § 387f(d)(1)) to restrict the naming, advertising and promotion of tobacco products using candy, kid-friendly food, or cartoon references and imagery. This would proactively put companies on notice of which advertising and promotion practices are prohibited and shift the burden to show that the products are misbranded during an enforcement action from FDA to the manufacturer or marketer. JUUL Labs supports such standards.

Because demand often shifts based on the availability of the supplier, FDA and industry must take a multi-faceted approach to preventing youth access. While FDA has recently enhanced its enforcement efforts to prevent sales to minors in the retail setting, as well as online, FDA and industry should take further action to understand and then shut off youth access to tobacco products. JUUL Labs is committed to working with FDA on this issue.

- ***Considering science-based purity standards for ENDS flavor ingredients***

In the Flavor ANPRM, FDA noted that flavors in some tobacco products have been found to contain or form toxic compounds.[39] The agency also expressed interest in learning more about toxicants and impurities in ENDS flavor ingredients. To address these issues, JUUL Labs would support FDA using its product standard authority to establish science-based purity standards for common ENDS flavor ingredients.

If standards are imposed, however, FDA should provide manufacturers with a process to easily modify their formulations to comply with the new requirements, for the benefit of public health.

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[39] 83 Fed. Reg. at 12,298.

JUUL LABS

JUUL Labs strongly supports FDA's efforts to examine the role of flavors and to help existing smokers reduce cigarette use, including through switching to potentially less harmful products. Preventing youth initiation of tobacco products is also our goal. We encourage FDA to allow the scientific evidence to further develop, including some of the research that JUUL is conducting, to fully understand how flavors can impact both adult switching behavior and youth initiation for the greatest net positive impact on public health.

Respectfully submitted,

for and on behalf of

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