August 20, 2021

Mr. Mitchell Zeller
Director, Center for Tobacco Products
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Sent by Email

RE: Recent international developments relevant to premarket review of Juul and other e-cigarettes

Dear Director Zeller:

With the court-mandated one-year deadline for FDA review of pending Premarket Tobacco Product Applications (PMTAs) for newly deemed tobacco products less than one month away, we write to highlight two recent international developments relevant to FDA's consideration of PMTAs for e-cigarettes:[1] (1) the ***World Health Organization Report on the Global Tobacco Epidemic 2021: Addressing New and Emerging Products*** **(WHO Report)**[2] and (2) **Canada's product standard for maximum nicotine concentration for vaping products (Canadian Nicotine Standard)**.[3] Both developments highlight the importance of ensuring that FDA decisions on PMTAs will protect the public, and particularly our youth, against highly addictive and flavored e-cigarettes.

The issuance of marketing orders for products that have demonstrated they are appealing and addictive to young people would be inconsistent with both the global public health consensus reflected in the WHO Report, that e-cigarettes pose a threat to the significant tobacco control progress over the last few decades, and the policy direction of the Canadian government in responding to youth usage of e-cigarettes in that country. These new developments underscore that, to this point, the U.S. has been an example to the world of how *not* to address the problem of youth vaping. With the approaching deadline, the FDA is at a crossroads on e-cigarette policy. It is critical that FDA make PMTA decisions consistent with the international community's efforts to stem nicotine addiction among young people.

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[1] This letter uses the terms "e-cigarettes," "ENDS," and "vaping products" synonymously.
[2] World Health Organization (WHO), WHO Report on the Global Tobacco Epidemic 2021: Addressing New and Emerging Products (2021), https://www.who.int/teams/health-promotion/tobacco-control/global-tobacco-report-2021.
[3] Nicotine Concentration in Vaping Products Regulations, SOR/2021-123, 1608 (Can.) (2021), https://www.gazette.gc.ca/rp-pr/p2/2021/2021-06-23/pdf/g2-15513.pdf [hereinafter Canadian Nicotine Standard].

I. WHO Report

The WHO has issued an annual report tracking global tobacco control progress since 2008, but the 2021 WHO Report is the first to include data specific to e-cigarettes. Its focus on e-cigarettes and other new and emerging products is based on the current state of the science and various regulatory documents implementing the Framework Convention on Tobacco Control, which serve as "markers of global sentiment capable of cutting through the commercially interested noise and tobacco industry obfuscation that surrounds such products."[4]

The WHO Report also reminds us that almost all major multinational tobacco companies have purchased shares in e-cigarette companies or developed their own brands.[5] With some industry evidence suggesting "there has been an increase in the total nicotine users (new users) over recent years," and consumers in the U.S., Canada, and Western Europe comprising the largest portion of the e-cigarette market,[6] this is relevant to FDA's review of e-cigarette PMTAs because it calls into question whether the harm reduction potential of these products is being—or is likely to be—realized. If the total nicotine user market simply expands, e-cigarettes present a threat to public health that may undermine global tobacco control progress. This is the conclusion of the WHO Report,[7] which summarizes the global scientific consensus on e-cigarettes as follows:[8]

- Using ENDS poses the risk of nicotine addiction, including among children and adolescents. Research findings show that ENDS users are more likely to become cigarette smokers, exposing them to the harmful effects of smoking.
- ENDS are harmful. For example, nicotine can have deleterious impacts on brain development, leading to long-term consequences for children and adolescents in particular.
- ENDS are marketed in thousands of flavors, which can increase the palatability of the product and make them particularly appealing to children and young adults. More specifically, flavors attract young people because they can mask the harshness of nicotine, make the inhalation of aerosols easier, and change the perceived risk associated with their use.
- ENDS are marketed and promoted by tobacco and e-cigarette companies, employing prior established tobacco industry tactics to target their products at young people.
- Evidence on the potential role for ENDS in smoking or tobacco cessation is still inconclusive.

The WHO Report also reveals the myriad of measures 111 countries have taken to either prohibit or regulate the sale of e-cigarettes.[9] Despite such measures, an estimated 19.9% of kids across the world have used ENDS, with current use estimated to be almost 9%.[10] The U.S. is one of the countries with the highest prevalence of youth e-cigarette ever-, current-, and daily-use,[11] and the WHO Report singles out the U.S. as having declared youth e-cigarette use an epidemic.

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[4] WHO, *supra* note 2, at 28.
[5] *Id.* at 32.
[6] *Id.*
[7] *Id.* at 40.
[8] *Id.* at 31; 34-38.
[9] *Id.* at 21; 98-103; 105-6.
[10] *Id.* at 38 (citing Sze Lin Yoong et al., *Prevalence of electronic nicotine delivery systems and electronic non-nicotine delivery systems in children and adolescents: a systematic review and meta-analysis*, LANCET PUB. HEALTH 1, 1 (2021), https://doi.org/10.1016/S2468-2667(21)00106-7, with corrected estimates of 17.2% and 7.8% respectively).
[11] Yoong et al., *supra* note 10, at 9.

Acknowledging the challenge and threat that the rapidly evolving e-cigarette marketplace poses to public health, the WHO Report emphasizes that while tobacco and e-cigarette companies "attempt to appear part of the solution to the tobacco epidemic," they are in fact the "instigators and perpetrators of the epidemic … target[ing] children and adolescents by using marketing strategies and thousands of flavours that make ENDS … appealing."[12] Thus, the WHO Report implores countries to "protect their populations, and in particular their children and adolescents," rather than "remain[ing] vulnerable to [industry] tactics … to expand their markets."[13] This is a clarion call to action that should be heeded by FDA as it evaluates whether individual e-cigarette products benefit the public health. Denying marketing orders to all non-tobacco flavored e-cigarettes is essential to protecting U.S. children and adolescents.

II. Canadian Nicotine Standard

Effective July 8, 2021, like the European Union standard,[14] no vaping product intended for retail sale in Canada may contain nicotine in a concentration that exceeds 20 mg/mL.[15] The Canadian Nicotine Standard was adopted because "[l]owering the maximum concentration of nicotine allowed in vaping products is expected to contribute to reducing the appeal of these products to youth, which would help address the rapid rise in youth vaping."[16][17]

Health Canada identified the availability of high-nicotine concentration e-cigarettes in the Canadian marketplace since 2018 as one of the key factors that contributed to the doubling of Canada's youth vaping rate from 2016-17 to 2018-19.[18] The Canadian Nicotine Standard described a new generation of vaping products introduced in 2018, characterized by high concentrations of nicotine salts,[19] which like the sharp increase in youth e-cigarette use in the U.S., coincided with the introduction of Juul and Juul-like products. Despite a potential levelling off of the Canadian youth e-cigarette use increase between 2019 and 2020,[20] Health Canada was "concerned that young persons are being exposed to vaping product-related harms, including those related to nicotine exposure, which can result in a dependence on nicotine and an increased risk of tobacco use and adverse health effects."[21] Additionally, a recent survey of Canadians aged 15 and older found that "[y]outh vapers [aged 15-19] were more likely (45%) to report using vaping products with nicotine concentration equal to or above 20 mg/mL or 2%, as compared to adults 25 years and over (33%)."[22] Thus, similar to what the WHO Report concluded, Health Canada concluded its "public health achievements in tobacco control are at risk of

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[12] WHO, *supra* note 2, at 109.
[13] *Id.*
[14] Council Directive 2014/40/EU, art. 20(3)(b), 2014 O.J. (L 127) 1, 26 (EU), https://ec.europa.eu/health/sites/default/files/tobacco/docs/dir_201440_en.pdf.
[15] Canadian Nicotine Standard, *supra* note 3, at 1609. Previously, regulations had prohibited vaping products with nicotine concentrations of 66 mg/mL or more. *Id.* at 1619.
[16] *Id.* at 1611.
[17] While our organizations have not collectively endorsed a specific maximum level that would be appropriate for the situation as it exists in the United States, FDA should recognize the global concern about products with high nicotine levels.
[18] Canadian Nicotine Standard, supra note 3, at 1612.
[19] *Id.* at 1620.
[20] *Id.* at 1616.
[21] *Id.* at 1617.
[22] *Id.* at 1621.

being eroded if young persons who experiment with vaping products develop a dependence on nicotine, particularly those who would not otherwise have tried smoking."[23]

Finally, one specific conclusion in the Canadian Nicotine Standard is particularly relevant to FDA's review of PMTAs for e-cigarettes: "Leaving high-nicotine-concentration products on the market, even only in certain flavours, is expected to continue to act as an inducement for youth to use these products."[24] This is sure to be the case in the U.S. if FDA maintains its permissive e-cigarette policies. It is time for the FDA to end its outlier status among similarly situated international regulators by denying marketing authorization to the highly addictive and flavored e-cigarettes that have led to the youth e-cigarette epidemic in the U.S.

Sincerely,

American Academy of Pediatrics

American Cancer Society Cancer Action Network

American Lung Association

Campaign for Tobacco-Free Kids

Truth Initiative

CC: Dr. Janet Woodcock, Acting FDA Commissioner

[23] *Id.* at 1617.
[24] *Id.* at 1626.