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Via Electronic Submission

July 19, 2018

Scott Gottlieb, MD
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, Maryland 20993

Subject: Regulation of Flavors in Tobacco Products – (Docket No. FDA-2017-N-6565)

Dear Dr. Gottlieb:

The American Association for Cancer Research (AACR) and the American Society of Clinical Oncology (ASCO) appreciate the opportunity to provide input on the U.S. Food and Drug Administration's (FDA's) advanced notice of proposed rulemaking on the regulation of flavors in tobacco products. The AACR and ASCO are the preeminent scientific organizations for cancer researchers and physicians. The AACR, which has 40,000 members, is the world's oldest and largest professional organization dedicated to preventing and curing cancer through research, education, communication, and collaboration. ASCO represents nearly 45,000 oncology professionals who care for people living with cancer. Through research, education, and promotion of the highest-quality patient care, ASCO members are committed to ensuring that evidence-based practice for the prevention, diagnosis, and treatment of cancer are available to all Americans. Our organizations are engaged in promoting the reduction and ultimate elimination of tobacco products and exposure to environmental tobacco smoke to prevent cancer and improve public health.

The AACR and ASCO welcome the opportunity to provide comments and data on how flavors attract youth to initiate tobacco product use and whether and how certain flavors may help adult cigarette smokers reduce cigarette use and



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switch to potentially less harmful products. The AACR and ASCO support the agency's plan to regulate the use of flavors in tobacco products. It is our organizations' goal to ensure that e-cigarette flavorings appeal to current smokers who desire to quit but do not attract the youth and young adult populations. The AACR and ASCO recommend that flavorings designed for these products undergo FDA review to determine their safety for inhalation, appropriateness for current smokers seeking to quit using tobacco products, and that the product is not designed to attract nor is marketed to children. It is our understanding that the latter may require a collaboration between the FDA and FTC.

In 2009, the Tobacco Control Act gave the FDA authority to prohibit cigarettes from containing characterizing flavors other than tobacco or menthol. The statute also authorized the Agency to issue additional product standards, including to address flavors in tobacco products and preserved FDA's ability to act with respect to menthol.¹ After the ban on cigarette flavors, researchers estimate a 6 percent reduction in adolescent tobacco use occurred.² We suggest additional research on how flavors affect all aspects of ENDS use across the continuum of ages. The Centers for Disease Control and Prevention (CDC) notes that preventing tobacco use among youth is critical to ending the tobacco epidemic in the United States. According to the CDC, tobacco use is started and established primarily during adolescence, and nearly 9 out of 10 cigarette smokers first tried smoking by age 18. The CDC further notes in the Youth and Tobacco Use Fact Sheet that flavorings in tobacco products can make them more appealing to youth.³ Recent research suggests that appealing flavors are a primary reason for experimentation among youth and young

¹ Federal Food, Drug, and Cosmetic Act. Subchapter IX – Tobacco Products. 21 U.S.C. Section 907(a)(1)(A). <https://www.gpo.gov/fdsys/pkg/USCODE-2016-title21/html/USCODE-2016-title21-chap9-subchapIX-sec387.htm>

² Courtemanche, C.J., M.K. Palmer, and M.F. Pesko, "Influence of the Flavored Cigarette Ban on Adolescent Tobacco Use," *American Journal of Preventive Medicine*, 52(5):e139-e146, 2017.

³ Youth and Tobacco Use Fact Sheet, CDC. https://www.cdc.gov/tobacco/data_statistics/fact_sheets/youth_data/tobacco_use/index.htm



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adults.⁴ Further, in addition to the potential risks of future combustible tobacco smoking there remains great concern about the exposure to potentially toxic substances contained in ENDS emissions which include vaporized flavorants with unknown health implications when inhaled into the respiratory tract.

Nicotine is the primary addictive component of tobacco, and the 2014 Surgeon General's Report concluded that nicotine activates multiple biologic pathways through which smoking increases risk for disease. Nicotine adversely affects maternal and fetal health during pregnancy, and exposure to nicotine during fetal development has lasting postnatal adverse consequences.⁵ Moreover, evidence suggests that nicotine exposure during adolescence may have lasting adverse consequences on the developing brain.⁶

Tobacco cessation can substantially reduce or eliminate the adverse effects of using tobacco and is one of the most impactful interventions that can be readily supported by oncology providers to reduce cancer risk and improve outcomes in cancer patients. The AACR and ASCO have recognized the importance of continual support for tobacco control across the continuum of risk and issued a policy statement acknowledging that some experts believe that the availability of flavored ENDS may encourage adult smokers to switch from combustible products to ENDS. The National Academies of Sciences, Engineering, and Medicine reported in the 2018 *Public Health Consequences of E-Cigarettes*⁷ review that using e-cigarettes may help adults who smoke

⁴ Kong G, Morean ME, Cavallo DA, Camenga DR, Krishnan-Sarin S. Reasons for Electronic Cigarette Experimentation and Discontinuation Among Adolescents and Young Adults. *Nicotine & Tobacco Research*. 2015;17(7):847–854. doi: 10.1093/ntr/ntu257

⁵ Jennifer E. Bruin, Hertz C. Gerstein, Alison C. Holloway. *Toxicological Sciences*, Volume 116, Issue 2, 1 August 2010, Pages 364–374, <https://doi.org/10.1093/toxsci/kfq103>.

⁶ US Department of Health and Human Services: The Health Consequences of Smoking: 50 Years of Progress—A Report of the Surgeon General. Atlanta, GA, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014

⁷ National Academies of Sciences, Engineering, and Medicine. 2018. *Public Health Consequences of E-Cigarettes*. Washington, DC: The National Academies Press. <https://doi.org/10.17226/24952>.



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combustible tobacco cigarettes quit smoking, but more research is needed.

The NASEM committee also noted that e-cigarette use among youth increases the risk of initiating smoking combustible tobacco cigarettes. Additionally, in this same report the committee found that while e-cigarettes are not without health risks, they are likely to be less harmful than combustible tobacco cigarettes, but the long-term health effects of e-cigarettes are unknown. However, it is also important to note that the “generally recognized as safe” (GRAS) designation for many of the flavors used applies only to ingested food. Therefore, flavors may contain toxic compounds or result in toxicity when heated or burned.⁸ The GRAS status for the use of flavors in food does not deem the use of these flavors in e-cigarettes nor gives the regulatory authority to allow the use of these flavors in tobacco products. Thus, it is important that new research is funded and conducted to examine these important issues.

Finally, in the absence of strong evidence to support the use of electronic cigarettes as therapy for smoking cessation, AACR and ASCO encourage continued research investment to clarify the potential benefits and harms of electronic cigarettes and the patterns of use with flavored tobacco products. There is one research study that shows that smokers who have had unsuccessful attempts to quit smoking reported an unanticipated disinterest in continuing use of combustible cigarettes after initiating e-cigarettes. The role of flavors here suggests that some e-cigarette users intentionally choose sweet flavors to make the transition away from combustible cigarettes.⁹ However, there is a need to balance the appealing characteristic of flavors, particularly in e-cigarettes, with the potential for negative public health outcomes.

We recommend that all tobacco users have access to evidence-based tobacco cessation therapies and counseling. Tobacco use poses a huge burden to our society, including increase in cancer incidence and deaths. We believe it is part of the oncology community’s responsibility as health care professionals and

⁸ National Academies of Sciences, Engineering, and Medicine. 2018. *Public Health Consequences of E-Cigarettes*. Washington, DC: The National Academies Press. <https://doi.org/10.17226/24952>.

⁹ Simmons, Vani Nath et al. “E-Cigarette Use in Adults: A Qualitative Study of Users’ Perceptions and Future Use Intentions.” *Addiction research & theory* 24.4 (2016): 313–321. *PMC*. Web. 25 May 2018.



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cancer researchers to explore and address the devastating consequences of tobacco use and continue to educate and help patients with cancer quit.¹⁰

We appreciate the opportunity to provide these comments on the regulation and role of flavors in tobacco products. These comments are based on the evaluation of the extant literature on tobacco treatment by the AACR's Tobacco and Cancer Subcommittee (roster attached), ASCO's Tobacco Cessation and Control Subcommittee (roster attached). If we can provide any additional information or assistance to the FDA, please do not hesitate to contact Nicole Boschi, PhD, AACR Senior Science Policy Analyst, at (215) 446-7275 or nicole.boschi@aacr.org or Shimere Williams Sherwood, PhD, ASCO Associate Director, Research and Science Policy at (571) 483-1672 or Shimere.Sherwood@asco.org.

Sincerely,

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