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The Honorable Robert F. Kennedy Jr.
Secretary
Department of Health and Human Services
200 Independence Ave SW
Washington, DC 20201

The Honorable Marty Makary, M.D.
Commissioner
U.S. Food and Drug Administration
Department of Health and Human Services
10903 New Hampshire Ave
Silver Spring, MD 20993

Submitted electronically via regulations.gov

RE: Flavored Electronic Nicotine Delivery Systems (ENDS) Premarket Applications- Considerations Related to Youth Risk; Draft Guidance for Industry; Availability

Dear Commissioner Makary,

On behalf of the American Academy of Family Physicians (AAFP), which represents 124,500 family physicians and medical students across the country, we appreciate the opportunity to comment on the draft [guidance](#) published in the [Federal Register](#) on March 11, 2026, regarding Flavored Electronic Nicotine Delivery Systems (ENDS) Premarket Applications- Considerations Related to Youth Risk. The draft document outlines FDA's recommendations regarding evidentiary considerations for premarket tobacco product applications (PMTAs) for flavored ENDS submitted under section 910 of the Federal Food, Drug, and Cosmetic Act.

On behalf of family physicians who routinely care for patients with smoking and tobacco-related chronic diseases, **the AAFP continues to raise concern to the FDA on the youth harms of all ENDS use and extends cautious support for the proposed establishment of a robust evidentiary framework for PMTAs for flavored ENDS products.** Tobacco product use remains the leading cause of preventable death in the United States, claiming more than 490,000 lives each year and leaving over 16 million individuals currently living with a smoking-related illness, including cancer, heart disease, stroke, chronic lung disease, type 2 diabetes, and reproductive health conditions.ⁱⁱⁱ Family physicians witness this continuum of harm firsthand, often caring for patients who begin smoking or vaping in adolescence and later present with chronic, progressive disease that requires lifelong management.

Health impacts of flavored ENDS

The alarming rise in youth ENDS use, which has been consistently shown to lead to traditional cigarette initiation, is creating a new generation of individuals addicted to

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nicotine. Although youth vaping rates declined modestly following the U.S. Surgeon General's 2018 declaration of an epidemic, millions of adolescents continue to use e-cigarettes, drawn by fruit, candy, and mint flavors, and sustained by high-nicotine formulations. Nicotine exposure during childhood and adolescence harms the developing brain, disrupting learning, memory, attention, mood regulation, and impulse control.ⁱⁱⁱ And the harms of ENDS use compound quickly. E-cigarette aerosol contains volatile organic compounds, fine particulates, heavy metals, and flavoring chemicals that damage lung tissue. Adolescents who use e-cigarettes experience significantly higher rates of respiratory symptoms, wheezing, shortness of breath, asthma, and cardiovascular risks.^{iv} Mental health impacts further intensify this risk profile. CDC analyses show that more than 40% of youth e-cigarette users report moderate to severe symptoms of depression or anxiety, which is nearly double the rate observed among non-users. Further, many youths report vaping to cope with stress or emotional distress, however nicotine dependence and withdrawal actually exacerbate these symptoms, creating a reinforcing cycle of harm.^v

Flavors are a major driver of youth initiation and sustained ENDS use in the United States.^{vi} In 2024, nearly 90% of middle and high school students who used e-cigarettes reported using flavored products, consistent with similarly high proportions in prior years.^{vii} Several qualitative studies further demonstrate that flavored, high-nicotine products mask the harshness of tobacco, lowering barriers to experimentation and promoting continued use among youth.^{viii,ix}

Flavored ENDS use in early life creates a pathway toward sustained nicotine dependence and subsequent chronic disease in adulthood. Longitudinal evidence from the Population Assessment of Tobacco and Health (PATH) study found that youth whose first tobacco product was flavored were significantly more likely to become current tobacco users later in adulthood, compared to those whose first product was flavorless.^x Beyond the well-documented respiratory effects of ENDS, emerging longitudinal research has also demonstrated associations between exclusive e-cigarette use and increased risk of conditions such as chronic obstructive pulmonary disease and hypertension in adulthood.^{xi} These health outcomes impose significant and growing costs to the health care system. E-cigarette use is already associated with approximately \$15 billion in annual U.S. health care spending, and these costs are expected to rise as youth users age, particularly if even a fraction transition to long-term combustible tobacco use in adulthood. These burdens are most immediately felt in primary care, where family physicians manage the longitudinal progression of nicotine-related chronic diseases, and within public programs such as Medicaid. In 2024, combined federal and state spending attributable to smoking-related illness reached an estimated \$72.7 billion, underscoring the long-term fiscal implications of youth-initiated nicotine addiction.^{xii}

At the same time, manufacturers have lowered costs and intensified the addictive potential of ENDS products. Data from the CDC Foundation and Truth Initiative show that between February 2020 and June 2024, while monthly e-cigarette unit sales increased by

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approximately 35%, the total amount of nicotine sold each month increased by more than 240%.^{xiii} This divergence reflects deliberate product design choices that increase nicotine delivery per unit and is driven largely by the rapid expansion of disposable e-cigarettes on the market, which have surged in popularity among young users and are now the most commonly used ENDS product among youth.^{xiv} However, as of April 2026, the FDA has only authorized 41 ENDS products. The remainder of products flooding the market, often flavored and disposable, are likely sold unlawfully. The scale of this illicit market is well documented, including the large-scale federal seizure of more than four million unauthorized e-cigarettes in September 2025.^{xv}

Further, vape manufacturers are releasing “smart” vapes which are commonly used by young people, with nearly one third of youth who currently use e-cigarettes reporting that they used a “smart” vape in the past 30 days in 2024.^{xvi} ENDS products that incorporate gamification features raise heightened public health concerns because they entwine nicotine addiction with multiple reinforcing behavioral mechanisms. By coupling pharmacologic dependence with reward-based digital engagement, screen use, and gaming mechanics, these products intensify use frequency, psychological reinforcement, and habit formation, effectively locking youth into durable patterns of nicotine dependence.^{xvii}

Accordingly, while we appreciate the FDA’s stringent evidentiary threshold for PMTAs for ENDS products, we urge the FDA to explicitly clarify that this framework applies to all ENDS products, including disposable ENDS, “smart” vapes, and single-use products. In parallel, we encourage FDA to continue strengthening coordination with DOJ and DEA to disrupt the illegal importation and distribution of unauthorized disposable ENDS products.

The convergence of flavor-driven initiation, widespread access to disposable ENDS products, intensified nicotine delivery, and increasingly sophisticated product design collectively increase the magnitude and complexity of risks to youths. Thus, **the AAFP reaffirms our [recommendation](#) that the marketing and advertising of ENDS to children and youth cease immediately, and [opposes](#) all forms of advertisement of tobacco products, including ENDS.** Further, we reiterate our [strong support](#) for FDA’s finalization of the [proposed](#) tobacco product standard establishing a maximum nicotine yield of 0.7 milligrams per gram of total tobacco in cigarettes and other combusted tobacco products to reduce continued harm.

FDA ENDS proposed regulatory framework

The AAFP [believes](#) the tobacco industry must be stringently and comprehensively regulated to protect the health of the public. Recent research found that youth and young adults living in jurisdictions with comprehensive local or state flavor restrictions reported lower use of any tobacco product as well as lower use of flavored products.^{xviii} As of 2025, six states and nearly 400 counties, cities, towns, and tribal governments have adopted policies restricting the sale of flavored tobacco products.^{xix} However, the public health impact of these policies is substantially constrained by widespread exemptions: more than 40% of

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individuals covered by flavor policies live in jurisdictions with significant retailer, product, or flavor carveouts.^{xx} **These findings demonstrate the importance of a robust federal regulatory framework that moves beyond patchwork state policies to uniformly addresses the youth appeal of flavored ENDS products.**

The AAFP therefore supports FDA's application of a graduated, risk-proportionate evidentiary standard based on the relative youth appeal of specific flavor categories. We agree with the FDA's recognition that fruit and candy/dessert flavored ENDS warrant close scrutiny due to their disproportionate contribution to youth initiation. However, recent raw [data](#) from the 2025 National Youth Tobacco Survey indicate candy and mint flavors may be associated with comparable levels of youth ENDS use. This evidence makes clear that youth appeal is not always confined to any single flavor category and cautions against regulatory approaches that rely on flavor-based distinctions alone. Although flavor categories certainly contribute to varying levels of initiation, flavor is only one component of a broader risk profile. **Accordingly, as the FDA develops a risk-proportionate evidentiary standard, it should evaluate flavor alongside other critical factors, most notably nicotine content and delivery characteristics, rather than treating flavor as an exclusive determinant of youth risk.** By scaling evidentiary expectations to multifactorial youth risk, FDA aligns the burden of proof with the magnitude of potential population-level harm, consistent with the statutory requirement under Section 910(c)(4) of the FD&C Act to evaluate risks and benefits at the population level.

We also cautiously support FDA's position that applicants for flavored ENDS products must demonstrate an added benefit relative to tobacco-flavored ENDS. While tobacco-flavored products represent comparatively lower risk to youths compared to non-tobacco flavors, **current evidence does *not* consistently demonstrate that non-tobacco flavors confer meaningful improvements in long-term cessation outcomes.** Requiring a product-specific demonstration of added benefit appropriately prevents authorization based on speculative or generalized assumptions.

Additionally, the AAFP strongly supports the FDA's expectation that applicants submit robust, product-specific evidence, including well-controlled studies and valid data on behavioral outcomes such as initiation, switching, cessation, and relapse. Given the limitations of the existing literature, this emphasis is essential to ensure that "Appropriate for the Protection of the Public Health" (APPH) determinations necessary for PMTAs are grounded in high-quality causal evidence.

While we acknowledge FDA's recognition that flavored ENDS products may facilitate switching among some adult smokers, we agree with the FDA's conclusion in the draft guidance that the population-level harms driven by youth initiation and sustained nicotine dependence outweigh the methodologically limited evidence of incremental cessation benefit associated with flavored ENDS products. **The AAFP's longstanding policy on ENDS does [not recommend](#) the use of ENDS as a smoking cessation device.** Youth initiation of

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ENDS products introduces entirely new nicotine users into the population, resulting in long-term addiction and an expanded population-level burden of disease. By contrast, adult use of ENDS products generally reflects switching or substitution among individuals who are already nicotine-dependent and does not reliably result in complete or sustained cessation. For these reasons, the AAFP cautiously supports FDA's regulatory framework for evaluating flavored ENDS products and urges the FDA to make explicit in its final guidance that flavored ENDS products with high youth-appeal should be presumed to *not* meet the APPH standard absent exceptionally strong, causal evidence of sustained adult cessation benefit.

We also recognize the significant operational demands facing federal tobacco regulatory and public health agencies. While the vast majority of recent staffing reductions at FDA's Center for Tobacco Products (CTP) were ultimately [rescinded](#) as of April 2026, staffing and resource constraints affecting the Centers for Disease Control and Prevention's Office on Smoking and Health (OSH) persist. Given the scientific complexity of tobacco regulation and the critical role of tobacco use surveillance and population-level prevention efforts, effective implementation of the proposed evidentiary framework depends on sustained, coordinated investment across agencies. To fully protect public health, the AAFP urges HHS to maintain adequate staffing and resources for CTP and to ensure that CDC's OSH has the capacity necessary to support robust surveillance, evaluation, and prevention activities that complement the FDA's regulatory work.

We thank you for the opportunity to provide comments on this important issue. Should you have any questions, please contact Sahana Chakravarti, Regulatory Specialist, at schakravarti@aaafp.org.

Sincerely,

A handwritten signature in black ink that reads "J Brull, MD". The signature is written in a cursive, flowing style.

Jen Brull, MD, FAAFP
American Academy of Family Physicians, Board Chair

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