May 26, 2026

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Comments in Docket No. 2026-N-264, "Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke; Established List Additions and Request for Comments," 91 Fed. Reg. 21,824 (April 23, 2026)

The American Academy of Pediatrics, American Cancer Society Cancer Action Network, American Heart Association, American Lung Association, Campaign for Tobacco-Free Kids, and Truth Initiative submit these comments in the above-designated docket concerning FDA's proposed additions to its list of harmful and potentially harmful constituents ("HPHC") in tobacco products and tobacco smoke. Our organizations strongly support FDA's efforts to evaluate and update its HPHC list and firmly urge the agency to do so whenever the science supports the addition of new constituents to the list. Updating the list in a timely manner is critical for the agency to be able to keep up with the dynamic tobacco product marketplace. We also support FDA's proposal to add pulegone, furfuryl alcohol, and methyl eugenol to the HPHC list at this time.

Background

The Family Smoking Prevention and Tobacco Control Act requires FDA to "establish, and periodically revise, as appropriate," a list of HPHCs, including smoke constituents, in tobacco products.[1] It also requires tobacco product manufacturers to report to FDA any constituents on the HPHC list that are present in its tobacco products.[2]

FDA established its HPHC list in 2012 when it designated 93 constituents in cigarettes and smokeless tobacco as HPHCs.[3] In 2019, the agency requested comments on whether 19 additional constituents should be added to the list to reflect the full range of products now under FDA's authorities as well as on whether FDA should apply an additional criterion for inclusion on the list, namely constituents identified by the National Institute for Occupational Safety and

[1] 21 U.S.C. § 387d(e).

[2] *Id.* § 387d(a)(3).

[3] *See* Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke; Established List, 77 Fed. Reg. 20,034 (2012).

Health ("NIOSH") as having adverse respiratory effects.[4] In the present notice, FDA has announced that it is adding 18 of the 19 proposed constituents to the HPHC list and has finalized its conclusion that constituents identified by NIOSH as respiratory constituents will be an additional criterion for inclusion on the HPHC list.[5] The present notice also requests comments on whether three additional constituents—pulegone, furfuryl alcohol, and methyl eugenol—should be added to the list.[6]

When FDA established the HPHC list in 2012, the agency's tobacco authority only covered cigarettes, roll-your-own, and smokeless tobacco. In 2016, that authority was extended to include all products made or derived from tobacco, including such products as e-cigarettes, heated tobacco products, and nicotine pouches.[7] Of note, e-cigarettes have been the most commonly used tobacco products among youth since 2014, while nicotine pouches have been the second most commonly used product for the past two years.[8] Additionally, in 2022, in response to the rising popularity of so-called synthetic nicotine products, Congress expanded FDA's tobacco authorities to include all products containing nicotine, regardless of whether the nicotine is derived from tobacco.[9] Despite these significant expansions of FDA's authority over tobacco products, FDA's HPHC list has been frozen since 2012 and limited to constituents only found in cigarettes or smokeless tobacco made from tobacco-derived nicotine.

The HPHC List Must Keep Pace with the Evolving Tobacco Product Market

An updated and accurate HPHC list, which reflects the evolving nature of the tobacco products landscape, is essential for FDA to exercise its jurisdiction effectively, particularly when the agency is deciding whether to grant applications to market tobacco products, grant modified risk applications, or establish product standards. An updated list is also necessary for FDA to fully and accurately evaluate products' risk profiles across different product categories. For example, during the October 7, 2025 meeting of FDA's Tobacco Product Scientific Advisory Committee ("TPSAC") to review Philip Morris International's application for renewed

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[4] *See* Harmful and Potentially Harmful Constituents in Tobacco Products; Established List; Proposed Additions; Request for Comments, 84 Fed. Reg. 38,032 (2019).

[5] 91 Fed. Reg. at 21,826.

[6] *Id.* at 21,827.

[7] Deeming Tobacco Products to be Subject to the Federal Food, Drug and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act: Restrictions on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products; Final Rule, 81 Fed. Reg. 28,974 (May 10, 2016).

[8] Jamal, A., Park-Lee, E., Birdsey, J., West, A., Cornelius, M., Cooper, M. R., Cowan, H., Wang, J., Sawdey, M. D., Cullen, K. A., & Navon, L. (2024). Tobacco Product Use Among Middle and High School Students - National Youth Tobacco Survey, United States, 2024. *MMWR. Morbidity and mortality weekly report*, *73*(41), 917–924. https://doi.org/10.15585/mmwr.mm7341a2. Food and Drug Administration. 2025 National Youth Tobacco Survey, March 4, 2026; https://www.fda.gov/tobacco-products/youth-and-tobacco/national-youth-tobacco-survey-nyts. Accessed: March 13, 2026.

[9] Consolidated Appropriations Act, 2022, Pub. L. No. 117-103, Division P, Title I, Subtitle B, § 111, 136 Stat. 49, 789-90 (2022).

authorization to claim that its heated tobacco products, IQOS and HeatSticks, "significantly reduce[s]" a consumer's "exposure to harmful and potentially harmful constituents" as compared to cigarettes, Committee members raised concerns that FDA's established list of HPHCs was inadequate. They noted that the list, at that time, only included HPHCs in cigarettes and smokeless tobacco—and thus the health effects of the IQOS heated tobacco products were likely not being accurately accounted for.[10]

Research shows that some toxicants that were not on FDA's HPHC list but are still associated with health harms are found in the IQOS aerosol at higher levels than found in cigarette smoke.[11] Further, FDA's briefing document to TPSAC during the original evaluation of PMI's modified risk tobacco product application in 2018 described a study that found 82 compounds from HeatStick aerosol that had not been previously reported in cigarette smoke.[12] Another study analyzing used HeatSticks and devices found that the filters in the HeatSticks melt from the heated device and release formaldehyde cyanohydrin, a highly toxic chemical, which is not on FDA's HPHC list but which, when metabolized in the body, produces formaldehyde, a constituent that is on the HPHC list.[13] FDA should review all of these chemicals to see if they should be added to the HPHC list.

As Dr. Sven-Eric Jordt commented during the October 2025 TPSAC meeting, use of the outdated list means that "FDA has insufficient tools to make conclusions . . . and neglects concerns related to these compounds that are not on the list but are known carcinogens or cardiovascular toxicants."[14] This situation illustrates the importance of an updated, comprehensive, and accurate HPHC list on FDA's decision-making.

To that end, we support FDA's proposed additions of pulegone, furfuryl alcohol, and methyl eugenol to the HPHC list. Research shows the presence of these chemicals in e-cigarettes and indicates potential health concerns. In particular, mint- and menthol-flavored e-cigarettes can contain potentially dangerous levels of pulegone, a Group 2B carcinogen (possibly carcinogenic to humans) according to the International Agency for Research on Cancer ("IARC").[15] One study found that pulegone levels in tested mint- and menthol-flavored e-cigarettes were "higher than the FDA considers unacceptable for intake of synthetic pulegone in food, and higher than in

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[10] TPSAC Meeting, Oct. 7, 2025, at 46, 72, 77, https://www.fda.gov/media/189658/download?attachment.

[11] St Helen, G., Jacob Iii, P., Nardone, N., & Benowitz, N. L. (2018). IQOS: examination of Philip Morris International's claim of reduced exposure. *Tobacco control*, *27*(Suppl 1), s30-s36. https://doi.org/10.1136/tobaccocontrol-2018-054321.

[12] FDA Briefing Document, at 14.

[13] Davis, B, Williams, M, & Talbot, P, "iQOS: evidence of pyrolysis and release of a toxicant from plastic," *Tobacco Control* 28:34–41, 2019.

[14] TPSAC Meeting at 77.

[15] Omaiye, E. E., Luo, W., McWhirter, K. J., Pankow, J. F., & Talbot, P. (2020). Electronic Cigarette Refill Fluids Sold Worldwide: Flavor Chemical Composition, Toxicity, and Hazard Analysis. *Chemical research in toxicology*, *33*(12), 2972–2987. https://doi.org/10.1021/acs.chemrestox.0c00266.

smokers of combustible menthol cigarettes."[16] Another study found that pulegone levels measured in tested mint JUUL and PuffBar products "were high enough to present a cancer risk."[17] Additionally, researchers have documented that furfuryl alcohol can be released during the pyrolysis of the e-cigarette wick.[18] This chemical has been found to irritate the respiratory system when inhaled and is harmful if swallowed.[19] Finally, IARC identified methyl eugenol, a flavor additive used in e-liquids,[20] as a Group 2B carcinogen for humans.[21]

Conclusion

In sum, our organizations support the inclusion of pulegone, furfuryl alcohol, and methyl eugenol to the established list of HPHCs and urge FDA to regularly evaluate whether additional or different constituents or criteria should be added to best keep pace with the evolving tobacco product landscape.

Respectfully submitted,

American Academy of Pediatrics

American Cancer Society Cancer Action Network

American Heart Association

American Lung Association

Campaign for Tobacco-Free Kids

Truth Initiative

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[16] Jabba, S. V., & Jordt, S. E. (2019). Risk Analysis for the Carcinogen Pulegone in Mint- and Menthol-Flavored e-Cigarettes and Smokeless Tobacco Products. *JAMA internal medicine*, *179*(12), 1721–1723. https://doi.org/10.1001/jamainternmed.2019.3649.

[17] Omaiye, E. E., Luo, W., McWhirter, K. J., Pankow, J. F., & Talbot, P. (2022). Flavour chemicals, synthetic coolants and pulegone in popular mint-flavoured and menthol-flavoured e-cigarettes. *Tobacco control*, *31*(e1), e3–e9. https://doi.org/10.1136/tobaccocontrol-2021-056582.

[18] Soulet, S., & Sussman, R. A. (2022). Critical Review of the Recent Literature on Organic Byproducts in E-Cigarette Aerosol Emissions. *Toxics*, *10*(12), 714. https://doi.org/10.3390/toxics10120714.

[19] Franko, J., Jackson, L. G., Hubbs, A., Kashon, M., Meade, B. J., & Anderson, S. E. (2012). Evaluation of furfuryl alcohol sensitization potential following dermal and pulmonary exposure: enhancement of airway responsiveness. *Toxicological sciences : an official journal of the Society of Toxicology*, *125*(1), 105–115. https://doi.org/10.1093/toxsci/kfr271 . Australia National Health and Medical Research Council (NHMRC), Inhalation toxicity of non-nicotine e-cigarette constituents: risk assessments, scoping review and evidence map, February 2022, https://www.nhmrc.gov.au/sites/default/files/documents/attachments/ecigarettes/Scoping_review_on_the_inhalation_toxicity_of_non-nicotine_e-cigarette_constituents.pdf.

[20] Taylor, A., Dunn, K., & Turfus, S. (2021). A review of nicotine-containing electronic cigarettes-Trends in use, effects, contents, labelling accuracy and detection methods. *Drug testing and analysis*, *13*(2), 242–260. https://doi.org/10.1002/dta.2998.

[21] IARC, Some Chemicals Present in Industrial and Consumer Products, Food and Drinking-Water, Volume 101, 2013, https://www.ncbi.nlm.nih.gov/books/NBK373192/pdf/Bookshelf_NBK373192.pdf.