

FDA should prohibit all menthol flavor additives, compounds, constituents, and ingredients in cigarettes, and should not limit the proposed standard to prohibiting menthol as a “characterizing flavor”

**Docket No. FDA-2021-N-1349
for “Tobacco Product Standard for Menthol in Cigarettes”**

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The Food and Drug Administration’s proposed rule to prohibit menthol in cigarettes is justified by solid scientific evidence and we generally support its quick finalization and implementation. Prohibiting menthol in cigarettes “will reduce initiation rates of smoking cigarettes, particularly for youth and young adults, and thereby decrease the likelihood that nonusers of cigarettes who experiment with these tobacco products would progress to regular cigarette smoking. Additionally, the proposed tobacco product standard is anticipated to improve the health of current smokers of menthol cigarettes by decreasing cigarette consumption and increasing the likelihood of cessation among this population.”¹

FDA correctly pointed out that the effects of menthol are not limited to providing a pleasing taste, reducing the harshness of nicotine, and making it easier to initiate and continue smoking. Rather, menthol interacts with nicotine at the level of receptors in the brain which makes the nicotine even more addictive, particularly to the developing brains of adolescents and young adults.² Therefore, ***FDA should not limit the proposed standard to prohibiting menthol merely as a “characterizing flavor,” but should instead extend the proposed standard to prohibiting all menthol flavor additives, compounds, constituents, and ingredients in cigarettes to ensure that the proposed standard protects the public health, especially the health of young people.***

¹ US Food and Drug Administration, Tobacco Product Standard for Menthol in Cigarettes, May 4, 2022, Proposed Rule, 87 FR 26454 at 26458.

² US Food and Drug Administration, Tobacco Product Standard for Menthol in Cigarettes, May 4, 2022, Proposed Rule, 87 FR 26454 at 26457.

1. Menthol contributes to a greater risk of nicotine dependence and should be prohibited as an ingredient in cigarettes

In the preamble to the proposed rule, FDA reported that in addition to its flavor and sensory effects:

“menthol contributes to a greater risk of nicotine dependence by enhancing the addictive effects of nicotine in the brain by affecting mechanisms involved in nicotine addiction (Refs. 10-13). Clinical data show that menthol cigarette smokers have higher levels of brain nicotinic receptors compared to non-menthol smokers (Ref. 14). Studies demonstrate that menthol, like nicotine, binds to nicotinic receptors in the brain (Refs. 15 and 16), and menthol alone can increase the number of nicotinic receptors in the brain (Refs. 10 and 11). Evidence demonstrates that the combined effects of menthol and nicotine in the brain are associated with behaviors indicative of greater addiction to nicotine compared to nicotine alone (Refs. 10 and 12). [emphasis added]”³

Indeed, the tobacco industry’s own research shows that menthol can be “tuned” to compensate for lowered nicotine levels.^{4, 5, 6}

Because the FDA understands the biological mechanisms for how menthol and nicotine interact to produce nicotine addictiveness and dependence, FDA should prohibit menthol and menthol analogues as ingredients in cigarettes.

2. FDA should ensure that the tobacco industry does not evade the menthol prohibition by prohibiting menthol and menthol analogs as ingredients.

Any current or future menthol analogs should also be prohibited as ingredients.

Because the biological effects depend on the molecular structure of menthol, it would be possible to design different molecules that, while different in other aspects from menthol, would be similar enough to have the same interaction with nicotine at the brain receptor level. For example, menthone is a keto derivative of menthol (i.e., a menthol analogue). There are also indications in the literature that other substances would also be menthol analogues or participate in the synthesis of this compound or mentholated aroma, for example, methyl salicylate, bornyl

³ US Food and Drug Administration, Tobacco Product Standard for Menthol in Cigarettes, May 4, 2022, Proposed Rule, 87 FR 26454 at 26457.

⁴ Yerger, Valerie B. "Menthol's potential effects on nicotine dependence: a tobacco industry perspective." Tobacco control 20.Suppl 2 (2011): ii29-ii36.

⁵ Yerger, Valerie B., and Phyllis M. McCandless. "Menthol sensory qualities and smoking topography: a review of tobacco industry documents." Tobacco control 20.Suppl 2 (2011): ii37-ii43.

⁶ Low Level Menthol. Opportunity Summary, 1986. RJ Reynolds Records; Master Settlement Agreement. Available: <https://www.industrydocuments.ucsf.edu/docs/#id=rtgn0056>

acetate, para-anisyl alcohol, l-carvone, citronellol, linalool, citral, eucalyptol, beta-pinene, alpha-pinene, geraniol and alpha-terpineol.⁷

FDA requested additional comments regarding any alternatives to prohibiting menthol as a characterizing flavor (e.g., prohibiting all menthol flavor additives, compounds, constituents, or ingredients).⁸ ***Because the menthol's nicotine addiction-enhancing ability depends on its chemical structure and biological interaction with nicotine at the receptor level, FDA should prohibit menthol and menthol analogs as flavor additives, compounds, constituents, and ingredients, and not just as a characterizing flavor.***

Menthol is an important ingredient in many “non-menthol” cigarettes that are not marketed with menthol as a characterizing flavor and is added to increase addictiveness. Under the rule as proposed, tobacco companies could evade the intent of the rule and continue to add menthol to cigarettes as an ingredient, additive, or constituent to maximize their addictiveness if they simply stopped calling them “menthol cigarettes.” Even low concentrations present in products that are not characterized as “menthol” are able to activate the cold receptor TRPM8.⁹

Brian King, the new director of the Center for Tobacco Products, recognized that “policies based on characterizing flavor might not cover constituents added by the manufacturer that provide a cooling sensory experience (e.g., similar to menthol) that can increase appeal, but are not the characterizing flavor.”¹⁰ Indeed, many tobacco companies are now adding menthol analogs and constituents that provide a cooling sensation similar to menthol in addition to menthol, and studies have shown that they increase the appeal of the tobacco products, especially among young people.^{11, 12, 13} Menthol is the dominant flavor chemical in both mint- and menthol-flavored e-cigarettes, so youth interchange mint and menthol products to achieve a “minty”

⁷ R Balaji Rao. 6: Strategies in (-)-Menthol Synthesis [Internet]. Chemistry LibreTexts. 2014. Available from: [https://chem.libretexts.org/Bookshelves/Organic_Chemistry/Book%3A_Logic_of_Organic_Synthesis_\(Rao\)/06%3A_A_Strategies_in_\(-\)-Menthol_Synthesis](https://chem.libretexts.org/Bookshelves/Organic_Chemistry/Book%3A_Logic_of_Organic_Synthesis_(Rao)/06%3A_A_Strategies_in_(-)-Menthol_Synthesis)

Surburg, H., Panten, J. Common Fragrance and Flavor Materials: Preparation, Properties and Uses. WILEY- VCH Verlag GmbH, Germany, 5th ed, 2006.

⁸ US Food and Drug Administration, Tobacco Product Standard for Menthol in Cigarettes, May 4, 2022, Proposed Rule, 87 FR 26454 at 26488.

⁹ Paschke M, Tkachenko A, Ackermann K, Hutzler C, Henkler F, Luch A. Activation of the cold-receptor TRPM8 by low levels of menthol in tobacco products. *Toxicol Lett.* 2017 Apr 5;271:50–7.

¹⁰ King, BA. Flavors remain a major driver of youth e-cigarette use. *Am J Public Health.* Published online ahead of print May 26, 2022:e1-e2. DOI: <https://doi.org/10.2105/AJPH.2022.306895>.

¹¹ Davis DR, Morean ME, Bold KW, et al. Cooling e-cigarette flavors and the association with e-cigarette use among a sample of high school students. *PLoS One.* 2021;16(9):e0256844. <https://doi.org/10.1371/journal.pone.0256844>.

¹² Tackett AP, Barrington-Trimis JL, Leventhal AM. ‘Flavour ban approved’: new marketing strategies from tobacco-free nicotine pouch maker Zyn. *Tob Control* 2022;0:1–2. Epub ahead of print: 22 April 2022. doi:10.1136/tobaccocontrol-2021-057222

¹³ Leventhal AM, Tackett AP, Whitted L, et al. Ice flavours and non-menthol synthetic cooling agents in e-cigarette products: a review. *Tob Control* 2022;0:1–9. doi:10.1136/tobaccocontrol-2021-057073 Epub ahead of print: 28 April 2022. doi:10.1136/tobaccocontrol-2021-057073.

flavor.¹⁴ Manufacturers can evade flavor restrictions^{15, 16} without removing mint/menthol and fruit ingredients just by using “concept flavor” names (e.g., “Lush Ice,” “O.M.G” [Orange, mango and guava]) and associated packaging which contributes to the appeal of tobacco products.¹⁷

Because the proposed rule prohibits menthol as a “characterizing flavor” but not as an ingredient, additive, or constituent, tobacco companies could evade the rule by using menthol substitutes and/or renaming their products.

The tobacco industry has a long and shameful history of deceiving the public about the addictiveness and other harmful health effects of smoking and evading FDA regulations, resulting in the landmark 2006 federal court judgment which found the major US tobacco companies had violated the Racketeer Influenced and Corrupt Organizations Act (RICO). Judge Kessler described in detail how the tobacco companies “have marketed and sold their lethal products with zeal, with deception, with a single-minded focus on their financial success, and without regard for the human tragedy or social costs that success exacted,” and that they continue to engage in misconduct that “misleads consumers in order to maximize Defendants’ revenues by recruiting new smokers (the majority of whom are under the age of 18), preventing current smokers from quitting, and thereby sustaining the industry.”¹⁸

We urge FDA to ensure that the tobacco industry does not continue to deceive the public and evade the menthol prohibition by strengthening the rule to not only prohibit menthol as a “characterizing flavor,” but also prohibiting menthol and menthol analogs as flavor additives, compounds, constituents, and ingredients.

3. FDA’s provision in the proposed rule that includes components, parts, and other menthol flavorings that can be added to non-menthol cigarettes is essential for an effective rule that is necessary to decrease opportunities for evasion

FDA states that the proposed rule in 21 CFR section 1162.5 would establish a tobacco product standard that would not only prohibit the use of menthol as a characterizing flavor in cigarettes, but would also specifically state that ***the rule extends to a cigarette or any of its components or parts, and would cover menthol flavoring that is separate from the cigarette.*** For example, menthol flavoring that is added to non-menthol cigarettes via drops, capsules, filter tips for roll-your-own tobacco, and cards that can be inserted into a cigarette pack or pouch of

¹⁴ Omaiye, E. E., Luo, W., McWhirter, K. J., Pankow, J. F., & Talbot, P. (2021). Flavour chemicals, synthetic coolants and pulegone in popular mint-flavoured and menthol-flavoured e-cigarettes. *Tob Control*. Published Online First: 30 June 2021. doi: 10.1136/tobaccocontrol-2021-056582.

¹⁵ Gaiha, Shivani Mathur, et al. "E-cigarette devices, brands, and flavors attract youth: Informing FDA's policies and priorities to close critical gaps." *Addictive Behaviors* 126 (2022): 107179.

¹⁶ N. Hemmerich, K.M. Ribisl, S.M. Noar. A list of permissible electronic nicotine delivery systems ingredients would be more effective. *American Journal of Public Health*, 110 (6) (2020), pp. 774-775, 10.2105/AJPH.2020.305677.

¹⁷ Erinoso O, Smith KC, Iacobelli M, Saraf S, Welding K, Cohen JE. Global review of tobacco product flavour policies. *Tob Control* 2021 Jul 1;30(4):373-9.

¹⁸ US v Philip Morris USA Inc, 9 F. Supp. 2d 1, (D.D.C. 2006).

rolling tobacco would be considered components or parts of cigarettes under proposed section 1162.3 and would be prohibited.”¹⁹ We strongly support this essential provision.

This provision is justified by experience in the European Union,²⁰ the United Kingdom,²¹ and Canada²² where tobacco companies have made design changes and developed aftermarket products that allow smokers to add menthol to cigarettes. These products allow companies to evade the menthol prohibition and thereby limit the effectiveness of the menthol prohibition by maintaining menthol cigarette customers and attracting new smokers who may initiate with menthol. *The FDA’s rule as proposed would prohibit such work-arounds.*

4. FDA should model the proposed rule on Brazil’s law that prohibits tobacco products that contain additives including menthol

The *Agência Nacional de Vigilância Sanitária* (ANVISA, Brazilian Health Regulatory Agency) adopted a resolution²³ (regulation) in March 2012 that applies to all tobacco products sold in Brazil, whether made in Brazil or imported, that prohibits the importation or sale in Brazil of tobacco products that contain additives, including:

- I. synthetic and natural substances in any form (pure substances, extracts, oils, distillates, balms, among others), with flavoring properties that can impart, intensify, modify or enhance the flavor of the product, including additives identified as flavoring agents...
- II. processing aids for flavorings;
- ...
- IX. ameliorants [defined as “a substance that reduces irritating aspects of the smoke of tobacco products]

“Additives” is defined in the resolution to include “any substance or compound that is not tobacco or water, used in the processing of tobacco leaf and reconstituted tobacco, in the

¹⁹ US Food and Drug Administration, Tobacco Product Standard for Menthol in Cigarettes, May 4, 2022, Proposed Rule, 87 FR 26454 at 26488.

²⁰ Brink AL, Glahn AS, Kjaer NT. Tobacco companies’ exploitation of loopholes in the EU ban on menthol cigarettes: a case study from Denmark. *Tobacco Control*. 2022 Mar 20; Available from: <https://tobaccocontrol.bmj.com/content/early/2022/03/20/tobaccocontrol-2021-057213>

Hiscock R, Silver K, Zatoński M, Gilmore AB. Tobacco industry tactics to circumvent and undermine the menthol cigarette ban in the UK. *Tobacco Control*. 2020 Dec 1;29(e1):e138–42.

²¹ [Hiscock, R., K. Silver, Mateusz Zatoński, et al. “Tobacco Industry Tactics to Circumvent and Undermine the Menthol Cigarette Ban in the UK.” *Tobacco Control*, 29:e138–e142, 2020. Available at <http://dx.doi.org/10.1136/tobaccocontrol-2020-055769>.](https://doi.org/10.1136/tobaccocontrol-2020-055769)

²² Chaiton, M.O., R. Schwartz, J.E. Cohen, et al. “The Use of Flavour Cards and Other Additives After a Menthol Ban in Canada.” *Tobacco Control*, 30:601–602, 2020. Available at <https://doi.org/10.1136/tobaccocontrol-2020-055698>

²³ Agência Nacional de Vigilância Sanitária, Collegiate Directorate. Resolution – RDC No. 14, of March 15, 2012. Available: https://bvsms.saude.gov.br/bvs/saudelegis/anvisa/2012/rdc0014_15_03_2012.pdf

manufacture and packaging of a tobacco product, including sugars, sweeteners, flavoring agents and (ameliorants).”

“Flavoring agents” is defined as “a natural or synthetic substance or mixture of substances that imparts, modifies, enhances or intensifies the flavor of tobacco products.”

“Ameliorants” is defined as “a substance that reduces irritating aspects of the smoke of tobacco products.”

Eight categories of additives (sugars, exclusively for the restitution of the sugar originally present in tobacco leaf prior to the curing process; adhesives; binders; combustion agents; processing aids that are not for flavorings; pigments or coloring agents used to whiten the paper or the filter and for other express purposes; glycerol and propylene glycol; and potassium sorbate) are exempted from the rule. However, because menthol is both a flavoring agent and an ameliorant, it squarely conforms with the rule’s definition of a prohibited additive and is not permitted in tobacco products in Brazil.

FDA should adopt language similar to that in Brazil’s rule and prohibit menthol as an additive in all cigarettes because it is used to enhance the flavors and to reduce the irritating aspects of nicotine and thereby increase the appeal of cigarettes, especially to young people and never-smokers.

5. Conclusion

In addition to its flavor and sensory effects that makes menthol-flavored tobacco products less harsh and more appealing, especially to youth, menthol contributes to a greater risk of nicotine dependence by enhancing the addictive effects of nicotine in the brain by affecting brain receptors. For this reason, menthol is an important ingredient and added to many “non-menthol” cigarettes as well as cigarettes marketed as “menthol flavored” to increase their addictiveness. The tobacco industry has a long history of deceiving the public about the addictiveness of smoking, and tobacco companies have already devised ways to try to evade menthol prohibitions that are based on “characterizing flavors.”

Therefore, we urge FDA to strengthen the proposed rule and prohibit all menthol flavor additives, compounds, constituents, and ingredients in cigarettes, and not limit the proposed standard to “characterizing flavors” and maintain the provisions prohibiting components and parts that could be used to introduce menthol to cigarettes.