July 27, 2022

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

Submitted to: https://www.federalregister.gov/documents/2022/05/04/2022-08994/tobacco-product-standard-for-menthol-in-cigarettes#open-comment

RE: Docket No. FDA-2021-N-1349, Tobacco Product Standard for Menthol in Cigarettes

To Whom It May Concern:

On behalf of the American Association for Cancer Research’s (AACR) more than 50,000 laboratory researchers, physician-scientists, other health professionals, and patient advocates who constitute our national and international membership, we thank the U.S. Food and Drug Administration (FDA) for the opportunity to express our support for FDA’s proposed tobacco product standard that prohibits menthol cigarettes and to suggest some additional ways to strengthen the overall proposal.

Tobacco use is responsible for more than 480,000 premature deaths in the United States every year (1). Smoking tobacco products is known to cause 18 types of cancer, accounting for 19 percent of all cancers diagnosed in the United States and nearly 30 percent of cancer deaths each year (2). In addition, more than 85 percent of annual lung cancer cases and deaths are attributed to smoking. These effects are driven by the incredibly addictive nature of nicotine and the high levels of carcinogens resulting from burning tobacco (3–5). As detailed below and in the draft product standard, menthol increases the addictiveness of nicotine and associated harms of inhaling combustion-related carcinogens.

The Family Smoking Prevention and Tobacco Control Act (TCA) required FDA to determine if the continued market availability of menthol was “appropriate for the protection of public health.” Scientific evidence has strongly supported the public health benefits of prohibiting menthol in cigarettes for more than a decade, as determined by the FDA Tobacco Products Scientific Advisory Committee in 2011 (6). Partially due to the relatively steady levels of menthol cigarette use while non-mentholated cigarette use declined (7), the market share of menthol cigarettes increased from 29 percent of all cigarettes sold in 2009 to 37 percent in 2020 (8). Additionally, predatory advertising practices from the tobacco industry have resulted in disproportionately high rates of menthol cigarette smoking among racial and ethnic minority groups. For example, 84.6 percent of African Americans who smoke use menthol cigarettes (9). Between 1980 and 2018, menthol cigarettes were responsible for an additional 10.1 million Americans initiating smoking, and an estimated additional 378,000 premature deaths (10). Furthermore, 157,000 of the additional premature deaths (41 percent) caused by menthol cigarettes were among African Americans, despite only comprising approximately 12 percent of the U.S. population (11). These health disparities caused by the tobacco industry’s business practices are unacceptable.

A large body of evidence demonstrates menthol increases the harms of tobacco use by increasing the ease of initiation and decreasing success of cessation attempts (12–18). Increased abundance of nicotinic acetylcholine receptors in human brains and inhibition of nicotine metabolism by menthol cigarette use are key mechanisms that enhance the addictiveness of nicotine (19–21). For these reasons, AACR issued a policy statement in 2010 and also joined 17 other organizations in signing a Citizen’s Petition in 2013 urging the FDA to take the much needed action it is now proposing (22,23). AACR appreciates the opportunity to once again support this important regulation.
AACR Strongly Supports a Tobacco Product Standard that Prohibits Menthol-Flavored Cigarettes, and It Should be Strengthened to Prohibit Any Amount of Natural or Synthetic Cooling Agent

Overall, the proposed product standard is very strong and clearly details the scientific and legal justification for prohibiting menthol as a characterizing flavor. It is estimated this product standard would prevent 650,000 premature deaths from tobacco related illness in the United States by 2060 (24). AACR particularly appreciates and supports that the product standard includes tobacco product accessories, flavoring added to packaging, and product labeling. These provisions will help address loopholes used by the tobacco industry to circumvent the spirit of a similar menthol cigarette ban in the European Union (25). However, the definition of characterizing flavor could be improved with further clarification that sets clear limits on allowable levels of small molecule cooling agents. AACR is concerned about a potential loophole whereby tobacco manufacturers could argue the presence of a low level of menthol or odorless and tasteless synthetic cooling agents do not constitute a “characterizing flavor,” but nonetheless reduce irritation from smoke and increase appeal of harmful products (26). The cooling and analgesic properties of menthol contribute significantly to tobacco product appeal and initiation, according to independent scientific studies as well as the tobacco industry’s own findings (17,27–30).

It is notable that nearly all cigarettes contain amounts of menthol greater than levels naturally occurring in tobacco plants, whether marketed as mentholated cigarettes or not (31–34). In tobacco plants, Paschke, et al. detected very low naturally occurring levels of the cooling agents menthol (0.30 ppm), linalool (0.31 ppm), and carvone (0.28 ppm) (34). Concentrations of menthol vapors as low as 8 ppm have been shown to significantly attenuate the irritating effects of smoke and smoke constituents in mice via activation of the TRPM8 receptor (21,35), the primary protein responsible for a cold sensation in mammals. At least one type of cigarette branded as a non-menthol cigarette had detectable menthol concentrations greater than 100 ppm prior to burning (32). Furthermore, following a ban on menthol as a characterizing flavor in the European Union, alternative natural and synthetic cooling agents have been detected in combustible cigarettes (33), representing a significant loophole based on a definition of characterizing flavor instead of a clear threshold of cooling agent concentrations. Of particular concern are the synthetic Wilkinson Sword (WS) cooling agents that are odorless and flavorless, but still capable of providing a cooling sensation via activation of the TRPM8 receptor (33,34,36,37). Setting definitive thresholds for the amount of TRPM8 agonists, within the proposed characterizing flavor definition would enable more effective and objective implementation of the product standard by creating clear metrics for enforcement actions. For these reasons, AACR recommends FDA specify maximum allowed concentrations of natural and synthetic cooling agents within the product standard that do not exceed natural levels of cooling agents found in tobacco plants (i.e., no flavoring or cooling agents may be added to cigarettes in any way). In summary, the tobacco industry should not be allowed to increase the addictiveness of their products by masking the taste or harshness of cigarette smoke with any amount of added small molecules. FDA should revisit specific thresholds on cooling agents and cellular receptors if new biological insights suggest alternate receptors can elicit these effects.

Examples of menthol cigarette bans demonstrate they are effective at reducing smoking. A recent analysis of a menthol cigarette ban in Canada found that 21.2 percent of adults who mainly smoked menthol cigarettes had quit smoking compared to 13.2 percent of adults who did not smoke menthol cigarettes between 2016 and 2018 (38). Extrapolating this effect size to U.S. adults who mainly smoke menthol cigarettes on a daily basis would estimate nearly 800,000 more adults quitting smoking due to a ban on menthol cigarettes. In June 2020, Massachusetts implemented a comprehensive ban on flavored cigarettes and cigars. In the year following the ban, per capita menthol cigarette sales declined 92 percent and overall cigarette sales declined 33 percent (39). In comparison states during the same time frame, per
capita menthol sales declined 3 percent and overall cigarette sales declined 4 percent. These real-world results demonstrate that prohibition of menthol flavors benefits and promotes public health.

Responses to Solicited Questions:

AACR Supports Further Efforts to Emphasize the Product Standard Does Not Criminalize Personal Use or Possession of Tobacco Products

The draft product standard and the TCA clearly delineate that the FDA’s current authority regarding enforcement of tobacco regulations pertains exclusively to the manufacture, distribution, importation, and sale of tobacco products. AACR recognizes there are concerns regarding local law enforcement efforts for tobacco products and related violence disproportionately affecting historically marginalized racial and ethnic minority groups. However, these concerns are not applicable to FDA’s current jurisdiction regarding the development of federal tobacco product standards to promote public health. Historical predatory marketing practices of the tobacco industry targeted vulnerable populations as a business strategy to maintain market share as overall smoking rates declined (27,40). It is important to emphasize that the proposed product standard will rectify the tobacco industry’s damage done to the health of African Americans and other historically marginalized groups. AACR encourages FDA to continue emphasizing its specific role to enforce federal tobacco regulations as well as engage with the U.S. Department of Justice, state and local agencies, and community stakeholders to address disparate enforcement of local and state tobacco laws and regulations.

AACR Strongly Disagrees with Exempting Certain Cigarette Products from the Menthol Rule

Exempting any cigarette product from this product standard would allow a dangerous loophole for the tobacco industry to exploit. While very low nicotine cigarettes (VLNCs) reduce smoking and increase abstinence compared to standard cigarettes, menthol significantly reduces these effects. A secondary analysis of a clinical trial examining the effect of switching to VLNCs found that compared to standard nicotine content cigarettes, those who chose to smoke non-mentholated VLNCs had an odds ratio of 9.11 for abstinence at week 20, while participants who chose to smoke mentholated VLNCs had an odds ratio of 1.88 (41). This finding suggests that allowing an exemption for mentholated VLNCs would reduce the cessation promoting effects of VLNCs substantially. This finding supports the inclusion of VLNCs in the proposed product standard.

In conclusion, AACR supports the proposed product standard to prohibit menthol flavored cigarettes. However, the proposed definition of characterizing flavor could be further strengthened by specifying a threshold amount of natural or synthetic cooling agents allowed in cigarettes, based on naturally occurring levels in tobacco plants. This clarification would increase the ease of regulatory enforcement and ensure the tobacco industry does not violate the spirit of the new rule with alternative cooling agents that may not meet the criteria of having a characterizing flavor. It would also benefit public health if FDA were to establish a similar threshold for tobacco product sweeteners. Additionally, the TCA tasks FDA with developing product standards appropriate for public health based on scientific evidence, and therefore concerns regarding local law enforcement agencies outside of FDA’s jurisdiction should not impact the federal rule making process. Lastly, AACR believes there should be no exemptions from the product standard. These comments are based on careful discussion and evaluation by the AACR’s Tobacco Products and Cancer Subcommittee (roster attached) and are approved by AACR’s CEO, Chair of the Tobacco Products and Cancer Subcommittee, and Chair of the Science Policy and Government Affairs
Committee. If AACR can provide any additional information or assistance to FDA, please do not hesitate to contact Dana Acton, Director of Science Policy and Legislative Affairs, at dana.acton@aacr.org.

Thank you again for the opportunity to comment on this important issue.

Sincerely,

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