FDA should not grant exemptions to the proposed standard on a case-by-case basis for certain cigarettes such as heated tobacco products or low nicotine cigarettes

Docket No. FDA-2021-N-1349
for "Tobacco Product Standard for Menthol in Cigarettes"

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We generally support the Food and Drug Administration's proposed rule to prohibit menthol in cigarettes because it is justified by solid scientific evidence, will reduce initiation rates of smoking cigarettes, particularly for adolescents and young adults, reduce disease and death caused by cigarette smoking, increase the likelihood that current menthol smokers will quit, and will reduce tobacco-related disparities and advance health equity. For these reasons, ***there is no justification for FDA to include in the final product standard rule a provision that would allow firms to request an exemption from the standard for certain menthol cigarettes such as "noncombusted cigarettes" (e.g., heated tobacco products) or reduced nicotine cigarettes on a case-by-case basis.***

1. Menthol contributes to a greater risk of nicotine dependence and should be prohibited as an ingredient in all cigarettes, regardless of whether or not they are combusted, so there is no scientific justification to exempt heated tobacco products

FDA's proposed product standard would cover all products meeting the statutory definition of "cigarette." As FDA points out, this definition "includes all types, sizes, nicotine strengths and formulations of cigarettes, cigarette tobacco and RYO [roll-your-own] tobacco, as well as HTPs [heated tobacco products, e.g. IQOS] that meet the definition of a cigarette in the FD&C Act (cigarettes that are HTPs)."[1] Nevertheless, FDA is considering including a provision in the proposed product standard that would allow companies to request an exemption from the

[1] US Food and Drug Administration, Tobacco Product Standard for Menthol in Cigarettes, May 4, 2022, Proposed Rule, 87 FR 26454 at 26486.

standard for certain cigarettes on a case-by-case basis, and requests comments on exemptions.[2] ***Because there is no scientific evidence that combustion is necessary for menthol to have the effects and interactions with nicotine that the FDA describes, there is no evidence to support exempting certain cigarettes from the menthol prohibitions.***

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). 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]

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.[6] These consequences grow out of the biological effects of menthol and how menthol amplifies the addictive properties of nicotine, not as a result of combustion. In its proposed rule, FDA demonstrates with significant scientific details that it understands the biological mechanisms for how menthol and nicotine interact to make nicotine more addictive and why menthol in cigarettes produce nicotine dependence.

There is no evidence, and FDA does not advance any scientific justification to support the notion, that combustion changes menthol or nicotine in a way that affects the underlying biological mechanisms that lead to the adverse effects of menthol. Therefore, there is no scientific justification for exempting any product meeting the definition of "cigarette," regardless of whether they are combusted or electronically heated. FDA should not allow manufacturers of so-called "noncombusted" or heated tobacco products to request an exemption to the menthol standard.

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[2] US Food and Drug Administration, Tobacco Product Standard for Menthol in Cigarettes, May 4, 2022, Proposed Rule, 87 FR 26454 at 26487.
[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 Phyra M. McCandless. "Menthol sensory qualities and smoking topography: a review of tobacco industry documents." Tobacco control 20.Suppl 2 (2011): ii37-ii43.
[6] US Food and Drug Administration, Tobacco Product Standard for Menthol in Cigarettes, May 4, 2022, Proposed Rule, 87 FR 26454 at 26457.

Further, without offering any scientific justification, FDA posits that tobacco products exist on a "continuum of risk" and that certain kinds of cigarettes such as heated tobacco products may pose less risk to individual or population health. We do not agree. FDA's marketing and modified exposure authorizations for IQOS heated tobacco products (which are available in two menthol flavors) failed to address significant concerns found in the published literature about the health impacts of IQOS and the FDA did not make a good case that IQOS is safer than a conventional cigarette.[7]

The evidence Philip Morris used to support its supplemental modified risk tobacco product application for IQOS 3 was the same evidence it used to support its modified risk application for IQOS 2.4. However, Philip Morris failed to demonstrate reductions in pulmonary toxicity among IQOS users as compared to conventional cigarette smokers and IQOS emissions may create novel risks of immunosuppression not observed with conventional cigarettes, failed to show that IQOS aerosol exposure leads to less vascular endothelial dysfunction than cigarette smoke exposure, and failed to address IQOS's potential appeal to adolescents and young adults. Additionally, FDA's decision was based on Philip Morris's applications that did not adequately address new published research providing scientific evidence regarding the potential pulmonary, vascular, and other health harms of IQOS. We attach and incorporate by reference three public comments we submitted to the IQOS 3 MRTP docket that provide scientific evidence of these health harms and a list of published literature on the health harms of IQOS that were not included in the IQOS applications.

2. FDA should not allow manufacturers of reduced nicotine products or any other tobacco product to request an exemption to the menthol standard

The biological mechanisms that lead to menthol's interaction with nicotine that create a greater risk of nicotine dependence exist in all nicotine products, including reduced nicotine products. FDA provides no scientific justification to support the notion that the interaction of menthol with nicotine at the level of brain receptors is absent or reduced in any significant way in products that contain reduced levels of nicotine. Indeed, because menthol amplifies the addictive effects of nicotine, if FDA were to grant an exemption to the menthol standard for reduced nicotine products, manufacturers of reduced nicotine products may have more reason to add or increase menthol additives in these products to increase their addictiveness. Such an outcome would defeat the purpose of any standard FDA might adopt requiring reduce nicotine levels in tobacco products.

Therefore, FDA should not include an exemption to the proposed rule that would allow manufacturers to request an exemption for reduced nicotine products.

[7] Lempert LK, Glantz S. Analysis of FDA's IQOS marketing authorisation and its policy impacts *Tobacco Control* 2021;**30:**413-421.

3. FDA should not allow tobacco companies to evade regulations intended to protect public health

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."[8]

By permitting companies to seek exemptions for certain products on a case-by-case basis, FDA would open the door to more deceit, delay, and evasion. ***We urge FDA to ensure that the tobacco industry does not continue to deceive the public and evade the menthol prohibition by not allowing companies to seek exemptions from the rule on a case-by case basis.***

4. Conclusion

FDA's proposed rule to prohibit menthol in cigarettes will reduce initiation rates of smoking cigarettes, particularly for adolescents and young adults, reduce disease and death caused by cigarette smoking, increase the likelihood that current menthol smokers will quit, and will reduce tobacco-related disparities and advance health equity. There is no scientific evidence that the harmful effects of menthol are different for different kinds of cigarettes. Therefore, ***there is no scientific evidence to support exempting certain cigarettes on a case-by-case basis from the menthol prohibitions. We urge FDA to not include any such exemptions in the product standard.***

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