

Flavoured tobacco products and the public's health: lessons from the TPSAC menthol report

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ABSTRACT

The menthol report developed by the Tobacco Products Scientific Advisory Committee (TPSAC) of the Center for Tobacco Products elaborated a methodology for considering the public health impact of menthol in cigarettes that has relevance to flavourings generally. The TPSAC report was based on a conceptual framework on how menthol in cigarettes has public health impact results of evidence from related systematic reviews, and an evidence-based statistical model. In extending this approach to flavourings generally, consideration will need to be given to the existence of multiple flavourings, a very dynamic market place and regulatory interventions and industry activities. Now is the time to begin to develop the research strategies and models needed to extend the TPSAC approach to flavoured tobacco products generally.

When the Family Smoking Prevention and Tobacco Control Act was passed in 2009, menthol was the only characterising flavouring permitted in cigarettes.¹ This exemption for menthol reflected the scope of the market for menthol cigarettes, about one-third of sales at the time, and pressures from the major companies that manufactured them. Consequently, the Act called for a report on menthol in cigarettes by the Tobacco Products Scientific Advisory Committee (TPSAC), the advisory committee to the Food and Drug Administration's (FDA) Center for Tobacco Products constituted under the Act. The report was to be completed within 1 year from TPSAC's establishment. The committee was charged with addressing the following considerations listed in Section 907 (pp. 1799–1801) subsections (a)(3)(B)(i) and (b) of the Act with regard to menthol:

- ▶ The risks and benefits to the population as a whole, including users and non-users of tobacco products
- ▶ The increased or decreased likelihood that existing users of tobacco products will stop using such products and
- ▶ The increased or decreased likelihood that those who do not use tobacco products will start using such products.

These three considerations define overall public health impact, the benchmark for decision-making by the FDA on tobacco products. In approaching its task of characterising public health impact, TPSAC adopted a model (figure 1)² that captured pathways of potential harm and benefit to population health. On the basis of results from that model, TPSAC concluded that 'Menthol cigarettes have an adverse impact on public health in the United States' and that 'There are no public health benefits of menthol compared to non-menthol cigarettes'.

After the passage of the 2009 Act, characterising flavourings other than menthol have emerged as a threat to public health.³ These flavours are now widely used in the manufacture of cigars, waterpipe tobacco, electronic (e-) cigarettes and other alternative tobacco products.^{4–12} Consequently, the FDA has just released its final deeming rule, extending regulatory authority to electronic cigarettes, cigars, pipe tobacco, some dissolvables, gels and waterpipe tobacco.¹³ These products incorporate a wide range of flavourings, including menthol, raising concern about their implications for public health impact. Under Section 907, the FDA has the authority to regulate flavourings in tobacco products, but in the deeming rule it is not taking immediate authority over any flavourings, including menthol, in these products.

Anticipating future regulation of flavourings in a broad range of tobacco products, we consider the evidence and integrative modelling that will be needed for that purpose. Here, we make analogies from the TPSAC menthol report to the challenges that will be faced in considering the population health consequences of having additional flavoured products in the marketplace. We propose that the

menthol framework can be generalised to an extent to the flavoured tobacco products covered in the deeming regulation. Figure 1 presents the TPSAC framework, which was used to estimate the consequences of having menthol available in comparison to a counterfactual, that is, counter to actuality, scenario in which menthol cigarettes are not available, but all other considerations are equivalent. The outcomes considered for public health impact were occurrences of tobacco-caused diseases and premature mortality. The numbered points in the diagram are those steps in the framework where the presence of menthol in cigarettes could affect the public health impact of cigarettes. These points also correspond to parameters in the statistical model used to estimate public health impact; TPSAC turned to the literature to make estimates for the values of these parameters in the model, carrying out systematic reviews to derive the best estimates possible and using committee judgement and sensitivity analyses when needed.

The overall TPSAC approach has general relevance to potential future regulation of flavourings in all tobacco products under FDA's jurisdiction: the formulation of a conceptual framework, the conduct of systematic reviews around the framework and the implementation of an evidence-based statistical model for making estimates related to public health impact. The systematic reviews highlighted gaps in the scientific evidence, pointing to the most critical research needs for strengthening the evidence foundation for potential regulation of menthol. We note that the FDA has not yet taken action on menthol in cigarettes. However, the TPSAC conceptual framework for menthol is limited for future scenarios of regulation of flavoured tobacco products that could involve multiple products and multiple flavourings—scenarios far more complex than the TPSAC menthol framework involving only one product and only one flavouring. Additionally, while considering tobacco industry marketing, the TPSAC framework did not incorporate regulatory and other policy measures that might be used to optimise the product mix in a way most beneficial to public health.

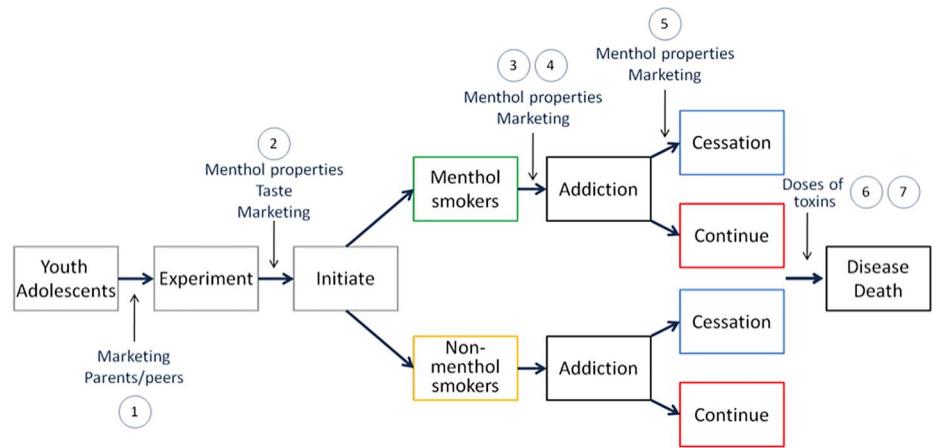
Nonetheless, some elements of the TPSAC model will be relevant to assessing the public health impact of flavourings, to targeting research and to future modelling. The model makes clear how flavourings could impact public health: through encouraging initiation and maintaining

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Figure 1 Model of smoking and health: from experimentation to disease.²



nicotine addiction and through increasing product toxicity, either directly as a consequence of the flavouring itself or of altered dosimetry. The model also indicates multiple points at which marketing (and countering regulation) will affect public health impact.

A broad programme of research on flavourings will be needed to characterise both pharmacological properties, including interactions with nicotine around addiction, and toxicity. There is already a basis for concern around both aspects of flavouring. Menthol, for example, has pharmacological properties that imply adverse consequences for public health impact; its anaesthetic and topical cooling properties may facilitate initiation and maintain addiction.² One flavouring (diacetyl) that appears to be widely present in the liquids ('e-juice') used in e-cigarettes can cause a severe and even fatal disease of the lung's small airways, bronchiolitis obliterans.^{3 14 15} Reports of analyses of flavourings in e-juices indicate the presence of agents with similar structures, along with numerous other flavourings.⁴ E-cigarettes are effective aerosol delivery devices, generating an aerosol that delivers droplets in a size range that reaches the lung's small airways and alveoli. For adolescents, lung growth is not complete, raising further concern about inhaling potentially toxic aerosols beginning during an age of susceptibility and continuing into adulthood.

TPSAC's menthol framework and the related population impact model are a useful starting point for anticipating models that will capture the full complexity of a future with multiple flavourings and flavoured products and with market forces and regulations that will drive patterns of use of flavoured and unflavoured products. The FDA will need models that capture this complexity and its variation

over time as the product mix changes, industry marketing and promotion shift, and product regulation and other tobacco control measures evolve.

TPSAC carried out carefully documented literature reviews to support implementation of its model; gaps in evidence became transparent through this process and pointed to research needs that should be given priority. Anticipating that the FDA will eventually consider the implications of flavourings in non-cigarette products, some research and surveillance needs are clear:

- ▶ Establishing a mechanism for tracking the flavouring agents that are being used so that potential toxicities can be examined
- ▶ Developing in vitro assays that would predict the potential toxicities of flavourings
- ▶ Investigating the implications of flavourings for addiction liability and maintenance of nicotine addiction
- ▶ Determining whether the chemicals in flavouring agents have additional addiction liability, independent of the addiction liability of nicotine
- ▶ Establishing surveillance for sentinel events in users of flavoured products, such as bronchiolitis obliterans
- ▶ Evaluating patterns of use of flavoured tobacco products among adolescents and young adults
- ▶ Determining whether products with flavourings are marketed in a way that attracts youth, young adults, minorities or other vulnerable populations
- ▶ Determining how the presence of various flavours alters users' perceptions of the relative harmfulness of tobacco products and
- ▶ Determining whether the presence of flavours in other nicotine products but not in cigarettes results in product switching (eg, from cigarettes to small cigars).

The TPSAC report on menthol cigarettes indicates the necessity of taking a systematic approach to characterising the population impact of flavoured tobacco products.¹⁶ The framework developed by TPSAC supported the conduct of systematic reviews and the implementation of an evidence-based model; the results of the models led to clear guidance to the FDA on the public health consequences of menthol. In contrast to today's tobacco products marketplace, however, only one flavouring was considered by TPSAC and the landscape of tobacco products was far less dynamic than today. If system-based approaches are to be used to generate evidence to support regulation, then surveillance and research strategies will be needed that are immediately responsive and quickly informative on the most critical points in the 'system'. Now is the time to begin to develop the needed research strategies and models.

Numbers refer to TPSAC questions related to individual smokers. Marketing refers to marketing of menthol cigarettes. (1) Does availability of menthol cigarettes increase the likelihood of experimentation? (2) Does availability of menthol cigarettes increase the likelihood of becoming a regular smoker? (3) Does inclusion of menthol in cigarettes increase the likelihood of the smoker becoming addicted? (4) Does inclusion of menthol in cigarettes increase the degree of addiction of the smoker? (5) Are smokers of menthol cigarettes less likely to quit successfully than smokers of non-menthol cigarettes? (6) Do biomarker studies indicate that smokers of menthol cigarettes receive greater doses of harmful agents per cigarette smoked compared with smokers of non-menthol cigarettes? (7) Do smokers of menthol cigarettes have increased risk for diseases caused by smoking compared with smokers of non-menthol cigarettes?

What this paper adds

- This paper documents the approach taken by the Tobacco Products Scientific Advisory Committee (TPSAC) of the US FDA to estimate the consequences for public health of menthol cigarettes.
- Drawing on lessons learned from the TPSAC report, the paper offers insights into approaches for assessing the public health impact of flavoured tobacco products generally.

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