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Dockets Management Staff (HFA-305)
U.S. Food and Drug Administration
5630 Fishers Lane, Rm. 2061
Rockville, MD 20852

RE: Modified Risk Tobacco Product Application: Application for Copenhagen Snuff Fine Cut Submitted by Altria Clients Services LLC on behalf of U.S. Smokeless Tobacco Company LLC, Docket No. FDA-2018-N-3261

The undersigned public health organizations submit these additional comments on the above-referenced modified risk tobacco product application ("MRTPA") submitted by Altria Client Services LLC ("Altria") on behalf of U.S. Smokeless Tobacco Co. LLC ("USSTC") for Copenhagen Snuff Fine Cut, a loose moist snuff tobacco product.[1] The application should be denied for the reasons both articulated in previous comments[2] and further detailed in these comments.

I. SUMMARY OF ADDITIONAL REASONS THE COPENHAGEN SNUFF FINE CUT MODIFIED RISK APPLICATION SHOULD BE DENIED

In the MRTPA, Altria seeks a modified risk tobacco product ("MRTP") order under section 911(g)(1) of the Family Smoking Prevention and Tobacco Control Act's ("TCA") for the following claim: "IF YOU SMOKE, CONSIDER THIS: Switching completely to this product from cigarettes reduces risk of lung cancer." If granted, this would be the first grandfathered tobacco product to receive an MRTP order and only the second tobacco product to receive a section 911(g)(1) risk modification order. Such an order would be accompanied by an FDA finding that the product, as actually used by consumers, will significantly reduce harm and the risk of tobacco-related disease to individual tobacco users and benefit the health of the population as a whole.[3]

In addition to the bases discussed in previous comments,[4] the subject application should be denied for the following reasons:

[1] *See* 83 Fed. Reg. 47,925 (September 21, 2018).
[2] Comment from Campaign for Tobacco-Free Kids et al. in Docket No. FDA-2018-N-3261 (Jan. 22, 2020), https://www.regulations.gov/comment/FDA-2018-N-3261-0060.
[3] *See* Modified Risk Granted Orders—Risk Modification for Swedish Match's General Snus products (Oct. 22, 2019), https://www.fda.gov/media/131922/download.
[4] Campaign for Tobacco-Free Kids et al., *supra* note 2.

- **It is unclear whether Altria has provided sufficient information to fully characterize the product and allow FDA to adequately assess the product's risk profile and its public health impact.**

- **Altria has not demonstrated that the specific product meets the requirements of section 911.**

    - Because the MRTPA lacks evidence specific to the product that is the subject of the application, FDA cannot make the required statutory findings under section 911(g)(4) of the TCA.

    - Because the MRTPA lacks sufficient product-specific evidence regarding both users and non-users of tobacco products, FDA cannot find the subject product, as actually used by consumers, will significantly reduce harm and the risk of tobacco-related disease to individual tobacco users and benefit the health of the population as a whole taking into account both users of tobacco products and persons who do not currently use tobacco products.

    - Because the applicant has not corrected other important deficiencies identified by FDA, the agency cannot conclude that the product meets the section 911 public health standard, and it cannot ensure consumers will not be misled into believing other Copenhagen products are FDA-authorized MRTPs when in fact they are not.

II. THE APPLICATION SHOULD BE DENIED BECAUSE IT IS UNCLEAR WHETHER ALTRIA HAS PROVIDED SUFFICIENT INFORMATION TO FULLY CHARACTERIZE THE PRODUCT AND ALLOW FDA TO ADEQUATELY ASSESS THE PRODUCT'S RISK PROFILE AND ITS PUBLIC HEALTH IMPACT

Copenhagen Snuff Fine Cut is a grandfathered tobacco product not subject to the premarket review requirement for new tobacco products under section 910 of the TCA.[5] Still, to make modified risk claims and be marketed as an MRTP, the product must be authorized by FDA to meet the TCA's public health standard.[6] The public health standard is central to FDA's review under both sections 910 and 911.

For MRTP authorizations specifically, applicants are "held to a more robust public health standard than a manufacturer of an ordinary new tobacco product."[7] With section 911 of the TCA, Congress sought to ensure the public would not be deceived, as it had been in the past, by tobacco manufacturers' fraudulent health claims.[8] This purpose is important for FDA's review of all MRTPAs, but

[5] https://www.fda.gov/tobacco-products/advertising-and-promotion/us-smokeless-tobacco-company-modified-risk-tobacco-product-mrtp-application
[6] 21 U.S.C. 387k.
[7] *Nicopure Labs, LLC v. FDA*, 944 F.3d 267, 278 (D.C. Cir. 2019).
[8] *See* Campaign for Tobacco-Free Kids et al., *supra* note 2, at sections II and III.

it is especially paramount for the subject application which, by virtue of simply being an older product already on the market, escapes the TCA's threshold premarket review requirement.

Because the TCA's public health standard applies to both sections 910 and 911, and the factors bearing on whether the public health standard is met are either the same or similar, it is reasonable for FDA to request information under section 911 that it would also require for a section 910 review. It has not yet had to do so for the other authorized MRTPs, but the statute clearly empowers FDA to require as part of MRTPAs "such other information as the Secretary may require."[9] This is entirely appropriate and is not "import[ing] Section 910 requirements into Section 911," as asserted by Altria.[10]

And indeed, FDA issued a deficiency letter on March 26, 2021 requesting additional information from the applicant to more fully characterize the product so the agency could sufficiently assess both the product's risk profile and its public health impact.[11] Altria's responses to the identified deficiencies are heavily redacted, but given that the agency requested basic information needed to characterize the product (e.g., the identity, quantity, purity, and purpose of flavoring ingredients and quantities of harmful and potentially harmful constituents ("HPHCs") of the product as it as actually used by consumers), it is impossible for the public to be certain that FDA has the information it needs to assess the product's risks accurately and thoroughly. Without such information, the FDA cannot fulfill the purpose of section 911: to ensure that the public is not misled by the reduced risk claims and that the product, marketed with those claims, benefits the health of the population as a whole.

III. THE APPLICATION SHOULD BE DENIED BECAUSE ALTRIA HAS NOT DEMONSTRATED THAT THE SPECIFIC PRODUCT MEETS THE REQUIREMENTS OF SECTION 911

A. The MRTPA lacks product-specific data.

To grant a section 911(g)(1) risk modification order, the applicant must demonstrate that the ***specific product***, as it is actually used by consumers, will significantly reduce harm and the risk of tobacco-related disease to individual tobacco users and benefit the health of the population as a whole taking into account both users of tobacco products and persons who do not currently use tobacco products.[12] In setting out the required considerations that FDA must take into account when making its

[9] 21 U.S.C. 387k(d)(7). There is also no qualifying language or limitation placed on requiring "such other information" under section 911 as there is under section 910: "such other information *relevant to the subject matter of the application* as the Secretary may require." 21 U.S.C 387j(b)(1)(G) (emphasis added).

[10] Copenhagen Snuff Fine Cut MRTPA ("Copenhagen MRTPA") – September 29, 2021 Amendment ("September 2021 Amendment"), at 5 of "2 CSFC MRTPA Deficiency Letter Response_Combined Narrative_Redacted," available at https://www.fda.gov/tobacco-products/advertising-and-promotion/us-smokeless-tobacco-company-modified-risk-tobacco-product-mrtp-application.

[11] *See, e.g.*, Questions 2-6 and 8 of the March 26, 2021 FDA Deficiency Letter as captured in the applicant's September 2021 Amendment. *Id.* at 11, 14, 17, 20, 30, 38.

[12] In its September 2021 Amendment, Altria argues that section 911 violates the First Amendment by imposing these evidentiary burdens even as to speech that is true and not misleading: "… once an applicant has demonstrated that a proposed MRTP claim is accurate and non-misleading, that should be the end of the matter, and FDA should authorize the application." *Id.* at 3. But this identical attack on section 911 was rejected in

determination under section 911(g)(1), the statute repeatedly uses the phrase "the tobacco product that is the subject of the application."[13] Thus, there is no doubt the TCA requires product-specific information.

Despite the clear statutory mandate, Altria's MRTPA lacks evidence specific to the product that is the subject of the application. The candidate product is a grandfathered product (FDA Grandfather Status # GF1200194),[14] but much of the data submitted was for modified versions of the product. This was the subject of the February 1, 2019 amendment to the MRTPA.[15] The more recent tobacco blend, ingredient, and HPHC data (i.e., since 2008) were for modified versions of the candidate product, including a product that was—and still appears to be—the subject of a pending Substantial Equivalence ("SE") review ("the Provisional Product").[16] Altria described the Provisional Product as the "currently-marketed version of Copenhagen® Snuff Fine Cut."[17]

Muddying matters more, in a later amendment to the MRTPA, Altria stated both that "the MRTPA remains applicable to the [redacted], as the tobacco product inside the can will still be the same grandfathered product (GF1200194),"[18] and that the subject MRTPA is "for one of its previously marketed moist smokeless tobacco products (Copenhagen Snuff Fine Cut). USSTC now markets a different product under the same product name as the one for which the MRTPA was submitted."[19] Altria's vague and incomplete descriptions of the various products that were the subject of data used to support the MRTPA, taken with their admissions that the grandfathered product that is the subject of the application is no longer on the market and that the currently-marketed version of Copenhagen Snuff Fine Cut is the Provisional Product,[20] make it clear that FDA cannot, with assurance, make the product-

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Nicopure Labs, LLC, where the Court distinguished *Sorrell v. IMS Health Inc.*, 564 U.S. 552 (2011) and held that the application of section 911 to the marketing of e-cigarettes as reduced risk products satisfied the elements established by the Supreme Court in *Central Hudson Gas & Electric Corp. v. Public Serv. Commission of N.Y.,* 447 U.S. 557 (1980) that must be met to uphold a statute regulating commercial speech that is neither misleading nor related to unlawful activity. 944 F.3d 267, 284-89. *Accord, Discount Tobacco City & Lottery, Inc. v. U.S.,* 674 F.3d 509, 534-37 (6th Cir. 2012).

[13] 21 U.S.C. 387k(g)(4)(A)-(D).

[14] Copenhagen MRTPA Executive Summary, at 5, https://digitalmedia.hhs.gov/tobacco/static/mrtpa/Copenhagen/2.3-executive%20summary%20_Redacted.pdf.

[15] Copenhagen MRTPA – February 1, 2019 Amendment ("February 2019 Amendment), available at https://www.fda.gov/tobacco-products/advertising-and-promotion/us-smokeless-tobacco-company-modified-risk-tobacco-product-mrtp-application.

[16] *Id.* at 2.

[17] *Id.*

[18] Copenhagen MRTPA – September 2021 Amendment, *supra* note 10, at 7 of "2 CSFC MRTPA Deficiency Letter Response_Combined Narrative_Redacted."

[19] *Id.* at 8 of Appendix 1.2.

[20] Copenhagen MRTPA – February 2019 Amendment, *supra* note 15. We note there is also an SE order from May 2019 for a Copenhagen Snuff Fine Cut product that does not seem to be mentioned in the MRTPA. FDA Technical Project Lead (TPL) Review: SE0015098-SE0015099, SE0015101-SE0015102, SE0015104-SE0015105, https://www.fda.gov/media/132852/download. The existence of distinct tobacco products with the same name is likely to contribute to consumer confusion as discussed below at section III.C. of these comments.

specific statutory findings required by section 911(g)(4) to grant an MRTP order for the grandfathered product that is the subject of the application.

B. The MRTPA lacks convincing product-specific evidence regarding both users and non-users of tobacco products.

Studies released since our previous comments continue to demonstrate our concern that cigarette smokers and dual users of cigarettes and smokeless tobacco rarely transition to exclusive smokeless tobacco use.[21] As a threshold matter, dual use is primarily a concern among young people: a study authored by FDA and National Institutes of Drug Abuse (NIDA) researchers, among others, looked at longitudinal data from the PATH study, Waves 1 to 3 (2013-2016), and found that youth (12-17 years old) and young adults (18-24 years old) were more likely to be dual users of cigarettes and smokeless tobacco compared to older adults.[22] Another study by FDA and NIDA researchers, using PATH Waves 3-5 (2015-2019) data, concluded: "Very few cigarette smokers transition to smokeless tobacco use, and among those who do, dual use is more common than exclusive smokeless tobacco use. Further, the majority of exclusive cigarette smokers who transition to dual use at Wave 4 continue smoking cigarettes at Wave 5, either as dual users or as exclusive smokers."[23]

Recent studies also build on past studies showing that dual use provides little to no health benefit compared to exclusive smoking. A study of dual users (cigarette and smokeless tobacco) in West Virginia found that they used more cigarettes per day on dual use days than on days when they didn't use smokeless tobacco. Increased number of cigarettes also meant higher cotinine levels on dual use days. The authors stated that "[t]he patterns of dual use among these samples do not support the idea of product replacement."[24] These findings are reinforced by another study using national PATH Wave 1 (2013-2014) data showing dual users who used either smokeless tobacco or cigarettes daily had higher nicotine metabolites compared to exclusive daily cigarette smokers. The authors of this study stated, "This suggests that dual users may be supplementing their nicotine intake, rather than substituting products to maintain higher nicotine concentrations."[25]

A different study using PATH Wave 1 (2013-2014) data found similar levels of all measured biomarkers of potential harm ("BOPH") among dual users compared to exclusive cigarette smokers after adjusting for demographics and health characteristics. In addition, while exclusive smokeless tobacco users showed comparable BOPH levels with former and never smokers, dual users showed significantly

[21] *See* Campaign for Tobacco-Free Kids et al., *supra* note 2, at section VI.
[22] Sharma, E, et al., "Longitudinal pathways of exclusive and polytobacco smokeless use among youth, young adults and adults in the USA: findings from the PATH Study Waves 1–3 (2013–2016)," Tobacco Control 2020;29:s170-s177.
[23] Jackson, RA, et al., "Transitions to smokeless tobacco use among adult cigarette smokers in the Population Assessment of Tobacco and Health (PATH) Study, Waves 3–5 (2015– 2019)," Tobacco Control, online ahead of print, doi: 10.1136/tobaccocontrol-2021-056907, December 22, 2021.
[24] Felicione, NJ, et al., "Cigarette smokers' concurrent use of smokeless tobacco: dual use patterns and nicotine exposure," Tobacco Control 2021;30:24-29.
[25] Cheng, Y, et al., "Biomarkers of Exposure among Adult Smokeless Tobacco Users in the Population Assessment of Tobacco and Health Study (Wave 1, 2013–2014)," Cancer Epidemiol Biomarkers Prev 2020;29:659-67.

higher levels of some BOPH (soluble intercellular adhesion molecule-1, Interleukin 6, and F2-isoprostane) compared to never smokers.[26] The data consistently show that smokers do not switch to exclusive smokeless tobacco use but are instead more likely to use both products, and that dual use does not reduce health risks. The applicant did not provide evidence that the subject product has, or will, change these patterns of use and risks. Thus, FDA should deny the MRTPA because the evidence does not support that cigarette smokers will completely switch to the proposed MRTP.

We have also commented extensively on the failure of the applicant to provide data on youth perceptions of the proposed MRTP, which is the population of primary concern among non-users.[27] That failure has not been rectified in any of the application's amendments. Altria also has not submitted data demonstrating youth perceptions of the name and packaging change for the proposed MRTP. This remains an improper oversight by both the FDA for not requiring it, and Altria for not providing it, because before the National Survey on Drug Use and Health stopped collecting data on smokeless tobacco brands in 2015, Copenhagen was consistently in the top three preferred brands named by youth (12-17 years old) smokeless tobacco users.[28]

C. The applicant has not corrected other important deficiencies identified by FDA.

Citing concerns about Altria's comparison of the proposed MRTP to the marketplace of smokeless tobacco products, FDA conducted its own product-specific analysis and identified elevated levels of HPHCs relative to other smokeless tobacco products.[29] However, rather than being responsive to FDA's request to address the specific product's impact to "the population of tobacco users that may completely switch to or begin to dual use their current product(s) with the proposed MRTP,"[30] Altria continued to ignore the fact that the real-world marketplace of smokeless tobacco products is not limited to just moist smokeless tobacco.[31] Its improper narrowing of the category for purposes of HPHC exposure is just one example of convenient line drawing in its application. In other instances, Altria acknowledged that dual users (i.e., smokers who also use smokeless tobacco products) are "another logical audience" and an "opportunity" for transitioning to the proposed MRTP.[32] If the applicant itself expects to market its modified risk product to dual users who may be using other smokeless tobacco products, this itself supports the relevance of the broader category of smokeless tobacco products to the population health impact determination.

[26] Chang, JT, et al., "Biomarkers of Potential Harm among Adult Cigarette and Smokeless Tobacco Users in the PATH Study Wave 1 (2013–2014): A Cross-sectional Analysis," Cancer Epidemiology Biomarkers and Prevention 2021;30:1320-7.
[27] *See* Campaign for Tobacco-Free Kids et al., *supra* note 2, at section V.
[28] Substance Abuse and Mental Health Services Administration (SAMHSA)'s public online data analysis system (PDAS), National Survey on Drug Use and Health, 1999-2014.
[29] Copenhagen MRTPA – September 2021 Amendment, *supra* note 10, at 38 of "2 CSFC MRTPA Deficiency Letter Response_Combined Narrative_Redacted."
[30] *Id.*
[31] *Id.* at 39-51.
[32] *Id.* at 2.

Finally, we previously raised the concern that viewers of the proposed marketing for the proposed MRTP "may misinterpret the modified risk message to apply to any and all Copenhagen snuff products."[33] This concern is heightened by the revelation that multiple versions of Copenhagen Snuff Fine Cut products are on the market, including the Provisional Product that the applicant asserts is the currently-marketed version,[34] and that USSTC has renamed the subject product.[35]

The agency also raised a similar concern regarding whether consumers would be able to distinguish between the aforementioned versions of the product, and thus, would not be misled that they're using an authorized MRTP when they are not.[36] The applicant responded by renaming the subject product and producing a bridging study, but that study did not demonstrate that consumers are able to "distinguish the proposed MRTP from the currently marketed product," which was FDA's stated concern.[37] Instead, Altria's results showed "that renaming the proposed MRTP has little impact on adult tobacco users' and nonusers' behavioral intentions and risk perceptions."[38] In other words, Altria argued it need not demonstrate that consumers can distinguish between the products because their perceptions were the same regardless of the name of the product. This only reinforces FDA's concern that consumers will be misled that other Copenhagen products are authorized MRTPs when in fact they are not—a concern that we share.

Altria's non-responsiveness to the deficiencies identified by FDA and obfuscation about which product would be subject to the MRTP order makes it impossible for FDA to find that section 911's requirements have been met. Accordingly, FDA should deny the application.

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

[33] Campaign for Tobacco-Free Kids et al., *supra* note 2, at 23.
[34] Copenhagen MRTPA – February 2019 Amendment, *supra* note 15.
[35] Copenhagen MRTPA – September 2021 Amendment, *supra* note 19.
[36] *Id.*
[37] *Id.*
[38] Copenhagen MRTPA – September 2021 Amendment, *supra* note 10, at 7-8 of "2 CSFC MRTPA Deficiency Letter Response_Combined Narrative_Redacted."