FDA should not renew the Modified Risk Granted Order for eight Swedish Match General Snus modified risk tobacco product application for General Snus products because as actually used by consumers, these products will not benefit the health of the population as a whole

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BACKGROUND

FDA granted Modified Risk Tobacco Product (MRTP) marketing authorization for eight Swedish Match General Snus smokeless tobacco products (including four mint-flavored products) on October 22, 2019, permitting Swedish Match (which is wholly owned by Philip Morris International (PMI)) to market these products with the following modified risk information:

> "Using General Snus instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis."[1]

The MRTP marketing order included requirements related to conditions of marketing and postmarket surveillance and studies. The order expires 5 years from the issue date (i.e., October 22, 2024), with an opportunity for renewal. On July 17, 2023, Swedish Match submitted an application requesting renewal of the MRTP order.[2] On May 6, 2024, FDA announced it would convene a meeting of the Tobacco Products Scientific Advisory Committee (TPSAC) on June 26, 2024, to discuss Swedish Match's application for renewal of the General Snus MRTP order and to also discuss "broader Modified Risk Tobacco Products program developments related to the conceptualization and measurement of consumer understanding."[3]

[1] US Food & Drug Administration, Modified Risk Granted Orders – Risk Modification for eight General Snus Smokeless Tobacco Products, October 22, 2019. Available: https://www.fda.gov/media/131922/download?attachment

[2] Swedish Match USA, Inc. MRTP Renewal Request, July 17, 2023. Available https://digitalmedia.hhs.gov/tobacco/hosted/mrtpa/swedish/1%20MR%20Renewal%20July%2017%2C%202023.zip

[3] Food and Drug Administration, The Tobacco Products Scientific Advisory Committee; Notice of Meeting, May 6, 2024. 89 FR 37231. Available: https://www.federalregister.gov/documents/2024/05/06/2024-09786/the-tobacco-products-scientific-advisory-committee-notice-of-meeting

To be granted a renewal of its MRTP order permitting Swedish Match to market its products with its modified risk claim, the company must demonstrate that the product, *as actually used by consumers*, will continue to both:

1) Significantly reduce harm and the risk of tobacco-related disease to individual tobacco users; and

2) 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.[4]

In particular, Swedish Match must demonstrate with scientific evidence that consumers, including youth and nonusers, continue to understand what is meant by the MRTP claim, are not misled by it, and that marketing these products with MRTP claims do not lead to initiation by youth or other nonusers.

It is especially important that the evidence demonstrates reduction of harms and addition of benefits to the whole population based on how the products are *actually used by consumers*. This means Swedish Match must address whether consumers, including youth, understand that to obtain the purported benefits, General Snus *must be used exclusively, not with cigarettes* or other tobacco products. Additionally, Swedish Match must not only demonstrate *understanding* but also that MRTP claims will affect behavior, leading to exclusive use of General Snus in place of cigarettes. In particular, Swedish Match must address the likelihood of dual- and poly-use of smokeless tobacco products with cigarettes, nicotine pouches, e-cigarettes, and other tobacco products. Further, it is essential that Swedish Match consider the impact, especially on youth, of marketing mint-flavored tobacco products and of co-marketing these products with the PMI ZYN nicotine pouches that are popular with youth (which we discuss more fully in a separate comment).

As we discuss in detail below, ***Swedish Match did not meet these statutory burdens. Therefore, FDA should allow the current marketing order to lapse and not renew the MRTP authorization for its General Snus products.***[5]

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[4] Family Smoking Prevention and Tobacco Control Act, section 911(g)(1), Public Law 111-31, 21 USC 387k (June 22, 2009).

[5] UCSF TCORS submitted comments opposing Swedish Match's original 2014 MRTP application and its amended 2018 MRTP application. Those comments continue to be relevant and are incorporated by reference and attached to this comment. Popova L, Sung H-Y, Chaffee B, et al. The revised Swedish Match modified risk tobacco product application for General Snus fails to provide evidence that the claim is not misleading and will have a beneficial effect on the population as a whole, January 16, 2019. Available: https://www.regulations.gov/comment/FDA-2014-N-1051-0931; Four UCSF comments to FDA on Swedish Match's original 2014 MRTP application, including: Popova L, Glantz S, Swedish Match's Consumer Perception Study Provides No Evidence for the Population-Level Effects of Modified Snus Labels, November 24, 2014; Popova L, Ling P, Swedish Match's claim that perceptions of health risks of snus are exaggerated
is likely incorrect, November 24, 2014; Glantz S, Popova L, Lempert L, "Swedish Experience" extolled in this MRTP application is not transferrable to the US because of the dual use with cigarettes and differences in the tobacco advertising environment, November 25, 2014; Glantz S, FDA should require that all communications from tobacco manufacturers regarding MRTPs be done in a way that narrowly target smokers, November 25, 2014. All available at: https://tobacco.ucsf.edu/summary-ucsf-public-comments-fda-swedish-match-mrtp-application

Swedish Match's July 2023 MRTP Renewal Request[6] states, "The scientific evidence in our initial application demonstrated consumer comprehension of the claim (i.e., fully switching to these products from combustible products would provide risk reduction), as well as a correct consumer perception of risk associated with the MRTP products (i.e., relative to cigarettes)." However, as we explained in our January 16, 2019, comment to FDA and TPSAC[7] asking FDA to deny Swedish Match's request for its initial MRTP order, Swedish Match did not provide sufficient evidence to support issuance of such an order.

FDA's authorization of Swedish Match's proposed MRTP claim would not benefit public health because:

- Consumers are likely not to understand that the language "instead of cigarettes" in the then-proposed advertising and labeling means a ***complete switch*** to General Snus and may instead interpret this statement as saying General Snus is compatible with dual use with cigarettes or other tobacco products.

- Swedish Match presented no evidence that the modified risk claim would result in current smokers completely switching to General Snus.

- Swedish Match only tested a limited number of their products seeking MRTP orders, not all eight sub-brands.

- Swedish Match's studies failed to test the effects of the modified risk claim on dual users.

- Swedish Match failed to present information on the impact of their proposed modified risk claim on youth.

- The modified risk claim misleads consumers about the health risks of General Snus.

- Because the studies presented in the original MRTP application, the postmarket surveillance, and studies submitted in support of the MRTP renewal application use hypotheses with flawed wording and flawed testing procedures, FDA should not rely on conclusions reached in these studies.

- The results of Swedish Match's studies submitted with its original MRTP application suggest that their proposed modified risk claims can be misunderstood to indicate "no risk" or reduced risk of various health conditions that were not included in the claim, such as gum disease.

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[6] Swedish Match USA, Inc., MRTP Renewal Request for MR0000020 - MR0000022, MR0000024- MR0000025, MR0000027- MR0000029, July 17, 2023, pp 9-10. Available: https://digitalmedia.hhs.gov/tobacco/hosted/mrtpa/swedish/1%20MR%20Renewal%20July%2017%2C%202023.zip

[7] Popova L, Sung H-Y, Chaffee B, et al. The revised Swedish Match modified risk tobacco product application for General Snus fails to provide evidence that the claim is not misleading and will have a beneficial effect on the population as a whole, January 16, 2019. Available: https://www.regulations.gov/comment/FDA-2014-N-1051-0931

• The Dynamic Population Model used by Swedish Match in its original MRTP application is inappropriate to assess the population health impact of the proposed modified risk claim for a product which is already marketed in the U.S.

• Swedish Match failed to provide details about its post-market surveillance plan.

Therefore, FDA should *not* have issued an order in 2019 permitting Swedish Match to market its General Snus products with the proposed MRTP claim because marketing General Snus with the then-proposed modified risk claim might actually harm public health by promoting more use of this tobacco product, including more dual use with cigarettes and other tobacco products.

Further, as we describe in more detail below, the "General Snus Patterns of Use Study, Baseline Study Report, SMU 19-01GENS"[8] which Swedish Match submitted on December 13, 2023 as part of its required postmarket surveillance and studies (PMSS) reporting failed to provide the evidence that is necessary to support a determination that the marketing of General Snus products with modified risk claims is appropriate for the protection of the public health. ***As of June 19, 2024, FDA has not posted any additional evidence from or reporting by Swedish Match to support this claim. Therefore, FDA should not renew the MRTP order now.***

1. Consumers are likely not to understand that the language "instead of cigarettes" in the MRTP claim means a *complete switch* to General Snus and may instead interpret this statement as compatible with dual use of General Snus with cigarettes or other tobacco products.

As we stated in our January 2019 comment,[9] Tobacco Control Act section 911(h)(1) requires that any advertising or labeling concerning modified risk products "enable the public to comprehend the information concerning modified risk and to understand the relative significance of such information in the context of total health and in relation to all of the diseases and health-related conditions associated with the use of tobacco products." The scientific studies submitted by the MRTP applicant "should inform FDA's evaluation of the product's marketing on consumer perception and understanding, including:

- The ability of consumers to understand the modified risk claims and the significance of the information in the context of one's health;
- Consumers' beliefs about the health risks of using the product relative to other tobacco products, including those within the same class of products;
- Consumer beliefs about the health risks of using the product relative to cessation aids; and

[8] December 13, 2023, Amendment: Response to FDA Request for Clarification, General Snus Patters of Use Study, Baseline Study Report, SMU 19-01GENS Available: https://digitalmedia.hhs.gov/tobacco/hosted/mrtpa/swedish/2022%20Periodic%20Reports/MR000258%2012-13-2023%20NEW.zip

[9] Popova L, Sung H-Y, Chaffee B, et al. The revised Swedish Match modified risk tobacco product application for General Snus fails to provide evidence that the claim is not misleading and will have a beneficial effect on the population as a whole, January 16, 2019. Available: https://www.regulations.gov/comment/FDA-2014-N-1051-0931

- Consumer beliefs about the risks of using the product relative to quitting all tobacco use."[10]

In particular, "the scientific studies submitted by the applicant should inform FDA's evaluation of the tobacco product's impact on tobacco use behavior, including:

- The likelihood that current tobacco product users will start using the product;
- The likelihood that tobacco users who adopt the product will switch to or switch back to other tobacco products that present higher levels of individual health risk;
- The likelihood that consumers will use the product in conjunction with other tobacco products;
- The likelihood that users who may have otherwise quit using tobacco products will instead use the product; and
- The likelihood that consumers will use the product as intended or designed."[11]

If the modified risk claim is not communicated properly, it could lead to misperception about the safety of the product.

There is a well-developed literature addressing relative risk perceptions of smokeless tobacco and cigarettes. A systematic review demonstrated misperceptions of the risks of smokeless tobacco were common in the scientific literature, and can be sensitive to measurement methods.[12] Furthermore, studies have shown that exposure to reduced-risk claims can decrease harm perception of smokeless tobacco among adolescents and increase their willingness to try these products, as well as among current tobacco users.[13] Data from the Population Assessment of Tobacco and Health (PATH) study indicate that lower risk perceptions were associated with subsequent use of multiple non-cigarette tobacco products, including smokeless tobacco.[14] Furthermore, evidence shows that FDA authorization claims can lead both adults and youth to perceive tobacco products as safe, potentially increasing their use.[15]

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[10] FDA, Guidance for Industry, Modified Risk Tobacco Product Applications, Draft Guidance, March 2012. Available at: https://www.fda.gov/downloads/TobaccoProducts/Labeling/UCM297751.pdf

[11] FDA, Guidance for Industry, Modified Risk Tobacco Product Applications, Draft Guidance, March 2012. Available at: https://www.fda.gov/downloads/TobaccoProducts/Labeling/UCM297751.pdf

[12] Czoli CD, Fong GT, Mays D*, et al.* How do consumers perceive differences in risk across nicotine products? A review of relative risk perceptions across smokeless tobacco, e-cigarettes, nicotine replacement therapy and combustible cigarettes. *Tobacco Control* 2017;**26:**e49-e58.

[13] Chaffee BW, Couch ET, Popova L, Halpern-Felsher B. Effects of a Reduced Risk Claim on Adolescents' Smokeless Tobacco Perceptions and Willingness to Use. J Adolesc Health. 2023 Sep;73(3):445-451. doi: 10.1016/j.jadohealth.2023.04.025. Epub 2023 Jun 9. PMID: 37294249; PMCID: PMC10527275.

[14] Elton-Marshall T, Driezen P, Fong GT, Cummings KM, Persoskie A, Wackowski O, Choi K, Kaufman A, Strong D, Gravely S, Taylor K. Adult perceptions of the relative harm of tobacco products and subsequent tobacco product use: Longitudinal findings from waves 1 and 2 of the population assessment of tobacco and health (PATH) study. Addictive behaviors. 2020 Jul 1;106:106337.

[15] Olivia A Wackowski, Michelle Jeong, Stefanie K Gratale, Caitlin Weiger, Julia Chen-Sankey, Andrew A Strasser, Cristine D Delnevo, The impact of exposure to FDA e-cigarette authorization messages on product perceptions and interest – an experiment with adults who smoke and youth, *Nicotine & Tobacco Research*, 2024;, ntae141, https://doi.org/10.1093/ntr/ntae141

Therefore, it is essential that the General Snus modified risk claim is properly communicated, that consumers understand that they must completely switch to General Snus and not dual use these products with cigarettes or other tobacco products, and that Swedish Match demonstrate that consumers do not have misperceptions about the safety of the product. Swedish Match failed to meet these burdens, so FDA should deny reauthorization of its MRTP order.

Our January 2019 comment[16] explained that Swedish Match evaluated "comprehension" of the claim by asking:

> For General Snus to put you at a lower risk of disease, how many cigarettes can you smoke on a day when you also use General Snus?
>
> 1 Zero (0) cigarettes
> 2 Up to 5 cigarettes
> 3 Up to 20 cigarettes
> 4 As many as you want to smoke
> 5 None of the above
> 99 Don't know
> 999 Decline to answer[17]

The wording of this question is problematic because it implies that switching on some days while continuing to smoke on other days is compatible with complete switching.

As we explain in our earlier comment, only between 37.4% and 56.2% of participants selected the correct number (zero cigarettes) (Table 1 from the Kantar Health study Swedish Match submitted to support its original MRTP application[18]). The detailed breakdown of proportions for other answer options has only been provided for current smokers after FDA requested it, but examining the raw data shows that across all groups, among other answers, the largest proportions were for "don't know" and "none of the above". The current renewal application fails to correct the problems with the question and wording from 2019, and FDA should not renew the MRTP order. While the renewal application does report a higher percentage of survey respondents identifying that smoking zero cigarettes would lower their risk of disease, this finding was based on a highly selective population that does not represent cigarette smokers in general, as we discuss below.

Table 1. Proportion of participants who selected "zero cigarettes" in response to the question regarding the number of cigarettes one can smoke a day to lower risk of disease when using General Snus.

Participant category	Test (claim 1)	Control	p-value

[16] Popova L, Sung H-Y, Chaffee B, et al. The revised Swedish Match modified risk tobacco product application for General Snus fails to provide evidence that the claim is not misleading and will have a beneficial effect on the population as a whole, January 16, 2019. Available: https://www.regulations.gov/comment/FDA-2014-N-1051-0931
[17] Kantar Health, General Snus MRTPA Study, p. 30, 04-study-smna-report-section-172_Release in Full.pdf
[18] Kantar Health, General Snus MRTPA Study, pp. 155-160, 04-study-smna-report-section-01-through 16_Redacted.pdf

Never tobacco users - legal age to 24 years	42.3%	37.2%	0.055
Never tobacco users – older than 24 years	37.4%	31.2%	0.020**
Former cigarette smokers - legal age and older	49.7%	37.0%	<0.001***
Current cigarette smokers - legal age to 24 years	56.2%	45.0%	<0.001***
Current cigarette smokers - older than 24 years of age	43.7%	33.9%	0.001*
Current smokeless tobacco users - legal age and older	53.9%	49.4%	0.160

Source: pp. 155-160, 04-study-smna-report-section-01-through-16_Redacted.pdf
P-values were reported from one-tailed independent two-sample proportion tests.
Statistical significance was adjusted according to the Holm procedure, whereby p-values ordered from lowest to highest are compared (in that order) against target, adjusted p-values of ***-p<0.017, ** -p<0.025, and * -p<0.050, respectively. Testing ends with the first non-significant comparison.

In addition, Altria tested consumer understanding of the phrase "instead of cigarettes" has been tested in Altria's 2018 Copenhagen Moist Snuff MRTP application.[19] Altria found that: "some 21–34-year-old adult smokers who do not reject MST [moist smokeless tobacco] disliked Prefix, [wording of the question] 'Using this product instead of cigarettes…,' because it connoted ideas of switching to MST from cigarettes. A few participants in this group, however, thought 'instead of' was as open-ended as 'alternative to' and found the phrasing acceptable as a way of suggesting choice."[20] In particular, ***Altria found in its Copenhagen MRPT qualitative study, that participants understood "alternative" to be compatible with continued smoking and not necessarily requiring complete switching from cigarettes to the smokeless tobacco product: "Across the board, the participants in this study tended to prefer a prefix that frames MST as an alternative to cigarettes rather than a replacement"[21].***

PMI's current General Snus application does not appear to take note of this study, which is publicly available, or present any evidence that the proposed MRTP statement would yield any different results.

To support their current MRTP renewal application for four mint flavors and four tobacco flavors of General Snus, PMI/Swedish Match cites the FDA's March 2023 MRTPA authorization of tobacco-flavored Copenhagen Classic Snuff[22] which permits Altria's U.S. Smokeless Tobacco Company to market its loose moist snuff product Copenhagen Classic Snuff

[19] Altria Client Services. (2018). *USSTC MRTP Application for Copenhagen Snuff Fine Cut: 6.2.: Effect of Marketing on Consumer Understanding and Perceptions*. Available at http://digitalmedia.hhs.gov/tobacco/static/mrtpa/Copenhagen/6-2-risk-perceptions_Release%20in%20Full.pdf
[20] Copenhagen MRTP application, 7.3.3-1: CS-01- Claims Qualitative Study; p. 17, app-7-3-3-1-cs-01-claims-qual-study_Redacted.pdf
[21] Copenhagen MRTP application, 7.3.3-1: CS-01- Claims Qualitative Study; p. 6, app-7-3-3-1-cs-01-claims-qual-study_Redacted.pdf
[22] US Food and Drug Administration, Modified Risk Granted Order – Risk Modification for US Smokeless Tobacco Company's Copenhagen Classic Snuff, March 16, 2023. Available: https://www.fda.gov/media/166254/download?attachment

with the claim, "IF YOU SMOKE, CONSIDER THIS: Switching completely to this product from cigarettes reduces risk of lung cancer."

As we noted in an earlier public comment,[23] the "Claim Comprehension and Intentions" study[24] (CCI) originally submitted by Altria Client Services LLC, on behalf of US Smokeless Tobacco Company LLC (a subsidiary of Altria Group, Inc.) to support the MRTPA authorization of Copenhagen Classic found few statistically significant changes in harm perceptions among study participants shown the proposed reduced risk statement. Notably, the only subset of the CCI study population for which the test group reported a statistically significant decrease in the perception that smokeless tobacco "negatively impacts health" was young adult tobacco non-users.

More importantly, compared to viewing a control image, viewing an advertisement with the reduced risk claim (MRTP image) did not increase intentions to try Copenhagen snuff among any of the tobacco user or nonuser subgroups included in the analysis.

This finding is important because it shows that while consumers may <u>understand</u> the MRTP claim, there is no evidence supporting the assumption that viewing the MRTP claim encourages cigarette smokers to switch to the purportedly less harmful product.

Swedish Match provides no additional evidence that the MRTP claim for General Snus will encourage cigarette smokers to switch to snus use.

Our own research independently supports this conclusion. Specifically, we conducted a study[25] of California adolescents in which participants were randomized to view a Copenhagen snuff image with or without the MRTP reduced risk claim. Adolescents exposed to the MRTP claim were less likely to perceive smokeless tobacco to cause "a lot" of harm. In addition, among adolescents who were past 30-day users of at least one nicotine product (predominantly consisting of e-cigarette users), viewing the MRTP claim increased willingness to try moist snuff. ***These findings suggest that smokeless tobacco MRTP claims increase interest in using smokeless tobacco among youth.***

Because youth, as a whole, have a low prevalence of cigarette smoking and smokeless tobacco use, increased susceptibility to smokeless tobacco in this population is likely to harm public health.

The lack of evidence that MRTP claims increase interest in switching to smokeless tobacco among adult cigarette smokers means that there is no evidence for an offsetting adult benefit

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[23] Chaffee B, Popova L, Lempert L, et al. FDA should not permit the U.S. Smokeless Tobacco Company to market Copenhagen Snuff with modified risk claims, January 16, 2019, Docket Number FDA-2018-N-3261, available: https://www.regulations.gov/comment/FDA-2018-N-3261-0014

[24] Copenhagen MRTP application, 7.3.3-1: CS-01- Claims Qualitative Study; app-7-3-3-1-cs-01-claims-qual-study_Redacted.pdf

[25] Chaffee BW, Couch ET, Popova L, Halpern-Felsher B. Effects of a Reduced Risk Claim on Adolescents' Smokeless Tobacco Perceptions and Willingness to Use. J Adolesc Health. 2023 Sep;73(3):445-451. doi: 10.1016/j.jadohealth.2023.04.025. Epub 2023 Jun 9. PMID: 37294249; PMCID: PMC10527275.

to overcome the increased risk to youth that could result from authorizing the proposed MRTP statement.

The quantitative findings from the Swedish Match study that not all users understand the message that they need to stop smoking all cigarettes are corroborated with results of a qualitative study from Copenhagen moist snuff MRTP application.[26] ***Together, they indicate that at least some adult consumers are likely to understand "instead of cigarettes" to mean using snus in addition to smoking cigarettes, a behavior that is likely to increase harm to the users.***

As of 2024, Swedish Match was continuing to promote its General Snus products using the MRTP claim, including specific reference to the FDA order permitting Swedish Match to make this claim.[27] It is likely that consumers interpret FDA's MRTP authorization as approval or endorsement of this product. As mentioned above, evidence shows that FDA authorization claims can lead both adults and youth to perceive tobacco products as safe, potentially increasing their use.[28] Importantly, ***Swedish Match did not submit evidence that consumers understand that FDA's authorization does not mean that these products are safe or "approved" by FDA.***

In sum, Swedish Match is required to demonstrate in its renewal MRTP application that marketing its products with modified risk claims will continue to benefit the population as a whole, considering both users and non-users of the proposed MRTP product. ***Swedish Match failed to meet its burden of demonstrating population benefit, so FDA must not issue a renewal of the MRTP order for General Snus.***

2. The Postmarket Surveillance and Studies (PMSS) submitted by Swedish Match are flawed and cannot be used to support renewal of its MRTP order.

Postmarket Surveillance and Studies (PMSS) are required under Tobacco Control Act section 911(i)(1) and under the October 2019 MRTP order are a condition for marketing Swedish Match's General Snus products with the MRTP claim. On June 5, 2024, FDA posted the PMSS report Swedish Match submitted on December 13, 2023[29] which includes the General Snus Patterns of Use Study, Baseline Study Report, SMU 19-01GENS. Although this report is heavily redacted, there is enough information to demonstrate that the PMSS lacks key information necessary to support FDA concluding that authorizing renewal of the MRTP application is warranted.

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[26] Copenhagen MRTP application, 7.3.3-1: CS-01- Claims Qualitative Study; app-7-3-3-1-cs-01-claims-qual-study_Redacted.pdf

[27] https://www.generalsnus.com/ModifiedRisk/

[28] Olivia A Wackowski, Michelle Jeong, Stefanie K Gratale, Caitlin Weiger, Julia Chen-Sankey, Andrew A Strasser, Cristine D Delnevo, The impact of exposure to FDA e-cigarette authorization messages on product perceptions and interest – an experiment with adults who smoke and youth, *Nicotine & Tobacco Research*, 2024;, ntae141, https://doi.org/10.1093/ntr/ntae141

[29] December 13, 2023, Amendment: Response to FDA Request for Clarification, General Snus Patters of Use Study, Baseline Study Report, SMU 19-01GENS Available: https://digitalmedia.hhs.gov/tobacco/hosted/mrtpa/swedish/2022%20Periodic%20Reports/MR000258%2012-13-2023%20NEW.zip

The PMSS report provides a description of the frequency of snus use and other tobacco product use among a convenience sample of General Snus users. ***As a result, the PMSS report cannot be considered to represent the patterns in the use of snus and other tobacco and nicotine products in the general population or the overall public health impact of MRTP authorization, or even whether and how the existing MRTP General Snus authorization has affected these patterns.***

In particular, the PMSS report cannot answer whether:

- MRTP authorization has encouraged cigarette smokers to switch completely to snus use;
- Tobacco non-users (youth or adults) have initiated snus use because of MRTP authorization;
- Any cigarette smokers switched to snus who would have otherwise quit all tobacco use;
- Any snus users continued to use snus who would have otherwise quit all tobacco use.

Specifically, the PMSS report (study SMU 19-01GENS) analyzed a convenience sample of 1655 individuals who purchased General Snus from one of approximately 10,600 retail locations and completed an online survey.

This is not a representative sample. Respondents joined the study by answering a study invitation on stickers placed on snus packages at those retail locations. The number of stickers per location is not reported. The response percentage is not reported but is likely to be very small. If we assume that 20 consumers per location received the sticker, the participation percentage would be <0.8% (i.e., 1655 out of 10,600 x 20); if 100 consumers per location received the sticker, the participation percentage would be <0.2% (i.e., 1655 out of 10,600 x 100). As Swedish Match acknowledged, that meant the study sample was a convenience sample that included those "who were more interested in research, or perhaps healthy enough to participate, may be over-represented, hence the possibility of selection bias." In addition, it is unclear how the data were processed before analysis, which may lead to selection bias during the data processing and analysis phase.

There is self-selection bias inherent in this study design. As stated in the Amendment, this sample is likely healthier and more interested in research than the general population. Not stated, but important, this sample is likely more interested in snus and committed to the General Snus brand to self-select into consumer research about it. Similarly, consumers who made multiple General Snus purchases would have more opportunities to view the study invitation. It is not stated in the Amendment whether there were any mechanisms to protect against the same individual submitting multiple responses to the survey. In total, this sample likely overestimates snus use frequency, familiarity with snus, and favorable perceptions of snus compared to the general population. Indeed, in this survey sample, 82% of snus users reported using General Snus every day. In nationally representative surveys of adult men from a mature snus market (Norway), pooled from 2005-2010, only ~60% of current snus users reported using snus every day.[30]

[30] Lund KE, McNeill A. Patterns of dual use of snus and cigarettes in a mature snus market. Nicotine Tob Res. 2013 Mar;15(3):678-84. doi: 10.1093/ntr/nts185. Epub 2012 Sep 18. PMID: 22990221; PMCID: PMC3572872.

At each wave of the survey, a substantial portion of potential respondents was excluded for reasons not presented in the public (unredacted) application materials. At baseline, nearly as many participants were terminated (N=1048) as were retained in the analytic sample (N=1655). Quotas were used, presumably to control the demographic distribution of the survey sample, but it is not clear what variables were used to set the quotas. It is unclear why quotas were then used in follow-up waves of the survey. For example, another N=159 potential respondents were terminated from the 6-month follow-up survey "based inclusion/exclusion criteria/quota filled/Intellectual Property blocker." It is not stated why these participants, who were deemed eligible for the baseline survey, were deemed to no longer be eligible at follow-up. At the least, removing these responses decreased the sample size and contributed to losses to follow-up. The specific reasons that these potential participants were excluded and how their exclusion affected the reported findings are unclear.

There were extremely large losses to follow-up at each wave of the survey, making the survey population less representative in each subsequent wave. After 6 months, less than half of the baseline sample was retain for analysis (695 out of 1655; 42%). By the final wave of the survey, only 27% of the initial analytic sample was included in the data (451 out of 1655).

The application notes that the prevalence of cigarette smoking is lower in the survey follow-up waves than at baseline, but due to losses to follow-up, this does not necessarily mean that individual consumers changed their smoking behaviors over time. Alternatively, it is plausible that cigarette smokers were less likely to complete a follow-up survey about snus than were dedicated snus users. With such high percentages of losses to follow-up, differences between who does and does not respond can have a major impact on the characteristics of the retained sample. This could have easily been examined in the data but was not presented in the renewal application.

In the application, assessments of change in cigarette smoking behavior are made among non-representative sub-sets of the data. For example, consider General Snus® POU Study Report; Section 7.3.5; Primary Objective. In this analysis, changes in cigarette smoking behaviors are assessed but only among respondents who maintained the same frequency of General Snus use. Excluded are any participants who increased or maintained their cigarette smoking frequency while decreasing (or increasing) their frequency of snus use. Examining only this narrow subset of the sample precludes broad conclusions about the impact of MRTP authorization.

Completely ignored is the key question of whether the MRTP claim authorized for General Snus has caused any cigarette smokers to switch completely to a less harmful product and whether that switching has been counterbalanced by dual use, less total cessation, and snus uptake among non-smokers.

It was stated that "current General Snus® users include a significant number of former cigarette smokers (67.2%) suggesting that use of General Snus® may support a reduction in smoking." However, the use of smoking cessation methods, particularly evidence-based ones, was not clearly addressed. It is not valid to claim General Snus® as an effective smoking cessation aid without clarifying these influencing factors. In fact, it is possible that some of these former

cigarette smokers had quit smoking long ago and only initiated use of General Snus more recently.

Table 7. Outcomes Table for Secondary Objective 1 – Perceptions of absolute risk.

Measurement Domain	Subcategory	Measurement Details	Metric
Absolute risk attributed to using *General* Snus® and to smoking cigarettes daily but using no other TNPs (Baseline, Month 6, Year 1, Year 2)	Mouth cancer	One item for each health condition (3 health conditions total) will assess the perception of the absolute risk from: a) daily use of only *General* Snus® and no other TNP; b) daily use of only cigarettes and no other TNP.	Absolute risk perception of a person suffering from each health condition will be assessed with "Very low chance," "Low chance," "Moderate chance," "High chance" and "Very high chance." "Don't know" is also available as a response option.
	Heart disease		
	Lung cancer		

Source: December 13, 2023, Amendment: Response to FDA Request for Clarification

Table 7 from the "Amendment - Postmarket Surveillance Studies Wave Reports" submitted by Swedish Match supporting its MRTP renewal MR0000256 *on* December 13, 2023,[31] reproduced above, shows the statements used to assess the absolute risk perception of using General Snus® and of smoking cigarettes daily. The actual results were redacted, but Swedish Match claimed that "results demonstrated that respondents perceived that cigarettes presented the greatest risk of health conditions which include mouth cancer, heart disease and lung cancer. Moreover, usage of General Snus® products alone was associated with some risk of health conditions, although at a lower rate than smoking." It is important to note that these measures leave out the important behavior of dual use of both General Snus and cigarettes, and the risk perceptions of dual use.

Since the postmarket surveillance studies fail to address risk perceptions of dual use, there is insufficient evidence to support renewal of the MRTP order.

3. Swedish Match did not address dual- or poly- use of General Snus with cigarettes and/or other tobacco products.

As we noted in our January 2019 comment,[32] in Swedish Match's "Perceptions and Behavioral Intentions Study," submitted as part of an amendment to the 2019 MRTP application, participants were either non-users, exclusive cigarette smokers, or exclusive smokeless users. Dual users were not included. However, it is important to include dual users as study participants because dual use of smokeless tobacco products (including snus) and other products is common. The 2012-14 National Adult Tobacco Survey showed that 3.6% of U.S. adults aged 18+ were current smokeless tobacco users and 52.4% of these current smokeless tobacco users were dual users, i.e., concurrently used one or more other tobacco products.[33] A detailed study of tobacco

[31] December 13, 2023, Amendment: Response to FDA Request for Clarification, General Snus Patters of Use Study, Baseline Study Report, SMU 19-01GENS, PDF p. 32. Available: https://digitalmedia.hhs.gov/tobacco/hosted/mrtpa/swedish/2022%20Periodic%20Reports/MR000258%2012-13-2023%20NEW.zip

[32] Popova L, Sung H-Y, Chaffee B, et al. The revised Swedish Match modified risk tobacco product application for General Snus fails to provide evidence that the claim is not misleading and will have a beneficial effect on the population as a whole, January 16, 2019. Available: https://www.regulations.gov/comment/FDA-2014-N-1051-0931

[33] See Table 2, Sung HY, Wang Y, Yao T, Lightwood J, Max W. Polytobacco Use and Nicotine Dependence Symptoms Among US Adults, 2012-2014. Nicotine Tob Res. 2018;20(suppl_1):S88-S98. PMCID: PMC6093419.

use patterns among dual users of cigarettes and smokeless tobacco among adult dual users in West Virginia conducted in 2015-2017 found the average number of cigarettes smoked per day and cotinine levels were higher on days when cigarettes were used concurrently with smokeless tobacco, suggesting that product replacement was not occurring.[34] Another study of dual tobacco users in the military found that dual users had earlier age at smoking initiation, longer duration of smoking and heavier smoking, all higher risk behavior patterns.[35]

FDA cannot ignore this substantial group of tobacco users, particularly since dual use is riskier than smoking or snus use alone.

For example, dual use increases the risk of myocardial infarction more than cigarette smoking alone.[36]

National Youth Tobacco Survey data from 2014-2020 also found that dual and polytobacco use of e-cigarette with other tobacco products including smokeless tobacco is increasing.[37]

General Snus has been marketed in the US since Swedish Match North America (SMNA) received market authorization for General Snus in November 2015, and has been marketed with the MRTP claim since October 2019. ***Given this lengthy marketing period, there is no reason that Swedish Match could not present updated epidemiological data demonstrating real-world use of the product, particularly the rates of initiation, switching, dual use, and cessation.***

The lack of such data is another reason that FDA should deny the MRTP renewal.

The December 13, 2023 amendment[38] purported to present co-use rates across four waves of the postmarket surveillance and studies (PMSS). Based on the data presented in the PMSS, at the baseline (Wave 1), the percentage of co-use was 14.5% (sum of everyday and some-day cigarette smokers who also use General Snus). At Wave 2, there was a slight reduction to 12.3%. At Wave 3 the co-use rate was 14.1%, and Wave 4 was 13.5%. Overall, while there were fluctuations, the percentage of dual users remained relatively stable around 12-14% over the course of the study. These percentages are lower than presented in studies of the general population, largely because the PMSS was conducted among a non-representative convenience sample of individuals who purchased General Snus and self-selected to be in a study about it. Despite this self-selection, a substantial portion of responds used General Snus in combination with cigarette smoking.

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[34] Felicione NJ, Ozga-Hess JE, Ferguson SG*, et al.* Cigarette smokers' concurrent use of smokeless tobacco: dual use patterns and nicotine exposure. *Tobacco Control* 2021;**30:**24-29.

[35] Lin, J., Zhu, K., Soliván-Ortiz, A. M., Larsen, S. L., Irwin, S. P., Schneid, T. R., ... & Lee, S. (2022). Dual use of cigarettes and smokeless tobacco among active duty service members in the US military. *Military Psychology*, *34*(4), 432-444.

[36] Teo KK, Ounpuu S, Hawken S, et al. Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case-control study. Lancet. 2006;368(9536):647–658.

[37] Cook, S., Ortiz Chavez, S., Zavala-Arciniega, L., Hirschtick, J. L., & Fleischer, N. L. (2023). Trends of single, dual, and polytobacco use among school-based students in the United States: an analysis of the national youth tobacco survey. *American Journal of Health Promotion*, *37*(8), 1078-1090

[38] December 13, 2023, Amendment: Response to FDA Request for Clarification, General Snus Patters of Use Study, Baseline Study Report, SMU 19-01GENS Available: https://digitalmedia.hhs.gov/tobacco/hosted/mrtpa/swedish/2022%20Periodic%20Reports/MR000258%2012-13-2023%20NEW.zip

Additionally, in its Summary of Wave 4 Results, Swedish Match reported that of those respondents who endorsed that use of General Snus presented less risk to health than cigarette smoking, 79.8% understood that no cigarettes can be smoked while using General Snus to benefit from it being lower risk. Again, despite this being a convenience sample likely to be more dedicated to and interested in General Snus than the general population of tobacco users and non-users, ***approximately one-fifth (20.2%) of these General Snus users do not understand that they must completely switch from cigarettes to General Snus to obtain the lower risk of some adverse health effects described in the authorized MRTP claim.***[39]

As noted above, postmarket surveillance and studies (PMSS) are required under Tobacco Control Act section 911(i)(1) and under the October 2019 MRTP order for continued marketing Swedish Match's General Snus products with the MRTP claim. In its MRTP Renewal Request, Swedish Match states that "Seven years of post-market tracking and annual reporting continue to support the conclusion that consumers of General Snus, even while reducing the amount of the product they use longitudinally, remain committed to a reduction of combustible products."[40] However, FDA redacted the Swedish Match data PMI submitted to substantiate this claim. In any case, ***Swedish Match's contention in the PMSS that it remains "committed to a reduction of combustible products" does not indicate complete switching from cigarettes to General Snus, but instead strongly suggests that consumers continue to use General Snus concurrently with cigarettes and/or other tobacco products (i.e., dual- or poly- use).***

4. **Marketing Swedish Match General Snus products does not benefit the health of the population as a whole.**

The law is clear. To renew the existing MRTP order permitting Swedish Match to market its products with its modified risk claim, FDA must make a determination that General Snus products will benefit the health of individuals and the population as a whole, taking into account:

> (1) The increased or decreased likelihood that existing users of tobacco products who would otherwise stop using such products will switch to [General Snus];
> (2) The increased or decreased likelihood that person who do not use tobacco products will start using [General Snus]; and
> (3) The risks and benefits to persons from the use [General Snus] as compared to the use of [FDA approved smoking cessation and nicotine dependence treatments].[41]

There is no support for the claim that, among the general population, existing adult users of tobacco products will switch completely to General Snus. As discussed in more detail above, the

[39] General Snus Patterns of Use Study, Wave 4 Technical Report – Final, at PDF p. 186. Available: https://digitalmedia.hhs.gov/tobacco/hosted/mrtpa/swedish/2022%20Periodic%20Reports/MR000258%2012-13-2023%20NEW.zip

[40] Popova L, Sung H-Y, Chaffee B, et al. The revised Swedish Match modified risk tobacco product application for General Snus fails to provide evidence that the claim is not misleading and will have a beneficial effect on the population as a whole, January 16, 2019, p. 10. Available: https://www.regulations.gov/comment/FDA-2014-N-1051-0931

[41] Family Smoking Prevention and Tobacco Control Act, section 911(g)(4), Public Law 111-31, 21 USC 387k (June 22, 2009).

PMSS report submitted in support of ***Swedish Match's MRTP renewal application was not based on a representative sample and did not provide sufficient evidence that the MRTP claim increased switching to smokeless tobacco among adults.***

Additionally, as discussed above, independent research[42] suggests that ***smokeless tobacco MRTP claims increase interest in using smokeless tobacco among youth. As a result, marketing Swedish Match with the MRTP claim may increase the likelihood that youth non-users of tobacco products will start using General Snus and/or other tobacco products.***

Of particular concern, Swedish Match General Snus is available in four mint flavors which include flavor ingredients that have potential adverse effects. Sucralose, a high intensity sweetener, is included in high levels in many snus products which makes the otherwise aversive flavors of tobacco ingredients more attractive to adolescents and other users and can lead to higher rates of initiation and continued use.[43, 44]

Further, the applicant does not present any evidence that using General Snus would present greater benefits to current users of tobacco products than completely ending all tobacco use or as compared to using FDA-approved nicotine replacement therapies.

5. Conclusion

FDA should not renew the Modified Risk Granted Order for eight Swedish Match General Snus products because Swedish Match failed to demonstrate that, as actually used by consumers, these products will benefit the health of the population as a whole.

In particular:

1. Consumers are likely not to understand that the language "instead of cigarettes" in the MRTP claim means a *complete switch* to General Snus, and may instead interpret this statement as compatible with dual use of General Snus with cigarettes or other tobacco products.
2. The postmarket surveillance and studies Swedish Match relied on to support its renewal application are flawed and cannot be considered to represent the patterns in the use of snus and other tobacco and nicotine products in the general population.
3. Swedish Match did not address dual- or poly- use of General Snus with cigarettes and/or other tobacco products.

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[42] Chaffee BW, Couch ET, Popova L, Halpern-Felsher B. Effects of a Reduced Risk Claim on Adolescents' Smokeless Tobacco Perceptions and Willingness to Use. J Adolesc Health. 2023 Sep;73(3):445-451. doi: 10.1016/j.jadohealth.2023.04.025. Epub 2023 Jun 9. PMID: 37294249; PMCID: PMC10527275.

[43] Miao S, Beach ES, Sommer TJ, Zimmerman JB, Jordt SE. High-intensity sweeteners in alternative tobacco products. *Nicotine Tob Res*. 2016;18(11):2169–73.

[44] Rezk-Hanna M, Talhout R, Jordt SE. Sugars and Sweeteners in Tobacco and Nicotine Products: Food and Drug Administration's Regulatory Implications. Nicotine Tob Res. 2023 Mar 22;25(4):838-840. doi: 10.1093/ntr/ntac222. PMID: 36148496; PMCID: PMC10032193.

4. Marketing Swedish Match General Snus products does not benefit the health of the population as a whole.

In addition, FDA's October 22, 2019, MRTP orders[45] state unequivocally: "These orders expire 5 years from the issue date of this letter [October 22, 2024]." Because Swedish Match did not offer sufficient evidence to support renewal of those orders, FDA should simply allow the current marketing order to lapse and enforce against Swedish Match/PMI if it continues marketing General Snus with unauthorized MRTP claims.

[45] US Food & Drug Administration, Modified Risk Granted Orders – Risk Modification for eight General Snus Smokeless Tobacco Products, October 22, 2019. Available: https://www.fda.gov/media/131922/download?attachment