August 14, 2024

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

RE: Comments in Docket No. FDA-2014-N-1051, Modified Risk Tobacco Product Applications: Renewal Applications for General Snus Smokeless Tobacco Products Submitted by Swedish Match U.S.A., Inc.

The American Academy of Pediatrics, American Cancer Society Cancer Action Network, American Heart Association, American Lung Association, and Campaign for Tobacco-Free Kids submit these comments in the above-referenced docket. The renewal applications seek authorization to continue to make the following modified risk claim with respect to the General Snus products: "Using General Snus instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis." For the reasons given below, the undersigned organizations oppose the renewal applications for General Snus.

I. INTRODUCTION AND LEGAL BACKGROUND

The General Snus applications are governed by the standards set out in Section 911 of the Food, Drug and Cosmetic Act, as amended by the Family Smoking Prevention and Tobacco Control Act of 2009 (Tobacco Control Act).[1] Under the Tobacco Control Act, a "modified risk tobacco product" is defined as a tobacco product that is sold or distributed for use to reduce harm or the risk of tobacco-related disease associated with commercially marketed tobacco products. A product is "sold or distributed" for such a use if, in relevant part,

> (i) [its] label, labeling, or advertising . . . represents explicitly or implicitly that—
>
> > (I) the tobacco product presents a lower risk of tobacco-related disease or is less harmful than one or more other commercially marketed tobacco products;
> >
> > (II) the tobacco product or its smoke contains a reduced level of a substance or presents a reduced exposure to a substance; or

[1] Codified at 21 U.S.C. § 387k.

(III) the tobacco product or its smoke does not contain or is free of a substance; . . . or

(iii) the tobacco product manufacturer . . . has taken any action directed to consumers through the media or otherwise, other than by means of the tobacco product's label, labeling, or advertising . . . that would be reasonably expected to result in consumers believing that the tobacco product or its smoke may present a lower risk of disease or is less harmful than one or more commercially marketed tobacco products, or presents a reduced exposure to, or does not contain or is free of, a substance or substances.

Thus, a modified risk product is defined in terms of the manufacturer's *claims* of reduced risk or reduced exposure in marketing the product, as well as its *actions that may suggest to consumers that a product reduces risk or exposure to hazardous substances*.

Under Section 911(g)(1), the burden is on the applicant seeking an order allowing the marketing of the product with a modified risk claim to demonstrate that the product "*as it is actually used by consumers* will (A) significantly reduce harm and the risk of tobacco-related disease to individual tobacco users; and (B) 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." (emphasis added).

Section 911(g)(4) further requires the U.S. Food and Drug Administration (FDA) to take into account the following specific empirical factors in determining whether the (g)(1) standard has been met:

(A) the relative health risks to individuals of the tobacco product that is the subject of the application;

(B) the increased or decreased likelihood that existing users of tobacco products who would otherwise stop using such products will switch to the tobacco product that is the subject of the application;

(C) the increased or decreased likelihood that persons who do not use tobacco products will start using the tobacco product that is the subject of the application; [and]

(D) the risks and benefits to persons from the use of the tobacco product that is the subject of the application as compared to the use of products for smoking cessation approved under subchapter V to treat nicotine dependence.

Thus, FDA must consider not only the effects of the asserted modified risk product, including its claims of reduced risk, on those who use it, but also its population-wide impact on tobacco use initiation, cessation and relapse, including an assessment of the likelihood that people who smoke

would actually switch to the modified risk product. It is not enough for an applicant to show that the product is less hazardous to users than other tobacco products; in order for a modified risk application to be granted, the applicant is required to show that the benefits of risk reduction (considering the likelihood that people who smoke will completely switch to the modified risk product) outweigh the risks of increased initiation or diminished cessation. In short, the statute requires FDA to make scientific judgments not only about the physical effect of the product's use, but also about the likely responses of potential consumers (both those who smoke and those who do not) to the product's marketing as a modified risk product, i.e., a product marketed with a reduced risk or reduced exposure claim.

For renewal applications, the burden remains on the applicant to demonstrate, through postmarket surveillance, that the justifications for the original modified risk order are still valid. Under Section 911(i)(1), such surveillance is required "to determine the impact of the order issuance on consumer perception, behavior, and health, to enable the Secretary to review the accuracy of the determinations upon which the order was based and to provide information that the Secretary determines is otherwise necessary regarding the use or health risks involving the tobacco product."

As explained more fully below, Swedish Match's application does not provide sufficient evidence to renew the modified risk orders. Because Swedish Match's studies did not examine the impact of the modified risk claim on people who smoke, its purported target consumer, the evidence base does not meet the evidentiary standard in the statute sufficient to support the use of modified risk messaging. In addition, Swedish Match is requesting expanding the use of the messaging. Without sufficient support, FDA cannot renew or expand this order.

II. REASONS FOR DENIAL OF THE RENEWAL APPLICATION

A. Swedish Match's Studies Were Insufficient and Poorly Executed.

Swedish Match received the modified risk orders for its General Snus products in July 2019 and has been required to submit postmarket data to FDA since then. Thus, the company should have several years of data to inform whether or not the claim would impact product use and perceptions. However, findings from its General Snus Patterns of Use (POU) Study failed to answer the key question about whether or not the existing modified risk claim had any impact on perceptions or use patterns, particularly on people who smoke, its purported target consumer. At the June 26, 2024 Tobacco Product Scientific Advisory Committee (TPSAC) meeting evaluating the renewal applications, the TPSAC Chair Dr. Cristine Delnevo stated, "And so I do think that, and . . . I'm hearing other folks say it as well, . . . there was quite a bit of disappointment in the

execution of the postmarket surveillance study. As a survey methodologist myself, I was disappointed to see how that was executed."[2]

The company's studies were designed merely to monitor trends in patterns of use, to see if the statements about disease relative risk in the message remained accurate, and to determine consumer understanding about disease risk of General Snus. They were not designed to determine the population impact of the reduced risk claim itself. These design flaws prevent any conclusions about "the impact of the order issuance" from being made, as required by Section 911(i)(1).

1. Swedish Match's studies did not expose participants to the modified risk claim.

As noted by FDA,[3] Swedish Match's postmarket surveillance studies did not even expose participants to the modified risk claim, which would be the obvious way to test the impact of that message on beliefs and actions of potential users – especially the company's purported target users, people who smoke. Indeed, at the June 26th TPSAC meeting, in response to a direct question about whether or not the impact of the claim was measured, Swedish Match's general counsel Gerry Roerty stated that "it was an intentional choice" to not expose participants to the claim, which means the studies were not intended to assess how people interpreted or reacted to the claim.[4] This is a fatal flaw in this renewal application. Without providing data on exposure to the claim, FDA cannot determine whether or not the claim actually has an impact on beliefs and behavior.

In its renewal request submission to FDA, Swedish Match claimed, "As demonstrated in seven years of periodic PMTA reporting and three years of periodic MRTPA reporting by Swedish Match, these authorizations contributed to reducing the harm caused by combustible tobacco products by providing reduced risk options to adult consumers."[5] However, at the TPSAC meeting, the company also revealed that the authorized claim is currently only on one webpage on its age-gated website, which limits exposure to Swedish Match's reduced risk claim only to a subset of the company's intended audience of "current, legal age smokers,"[6] In fact, there is no evidence showing that these authorizations have "contributed to reducing the harm" because the reduced risk claim is not visible to people who smoke unless they are registered on the Swedish

[2] Tobacco Products Scientific Advisory Committee (TPSAC) Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 193-194.
[3] FDA Briefing Document for TPSAC, at 20.
[4] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 81.
[5] Swedish Match renewal document, at 10.
[6] Swedish Match, U.S. Food and Drug Administration Tobacco Products Scientific Advisory Committee Briefing Materials, June 26, 2024, at 12.

Match website. In addition, in its postmarket surveillance studies, Swedish Match did not present the claim to people who smoke and did not already use General Snus.

Indeed, other conclusions reached by Swedish Match in its renewal materials also remain unproven because of the limited use of the claim and the lack of testing. On page 12 of its renewal request, Swedish Match wrote, "In terms of tobacco use behavior, the presence of the modified risk claim on these products (1) has continued to transition intended consumers 'down that continuum of risk' (Gottlieb 2017) and (2) does not demonstrate significant use of snus by young adults (NYTS 2022)."[7] Again, however, Swedish Match did not show that the claim itself was causally connected to these results. Given that the claim is barely visible, any noted changes in tobacco use behavior occurred essentially in the absence of the claim.

Several participants in the June 26th meeting raised and reiterated this point. TPSAC member Dr. Lucy Popova and consultant Dr. Olivia Wackowski, both experts in health communications, called attention to this deficiency in Swedish Match's studies. Dr. Popova stated, "So this is the mandated thing where . . . you need to assess the impact the MRTP claim has on consumer behavior, including uptake, dual use and complete switch[ing]. … What we're seeing is absence of evidence."[8] Later she elaborated, "In this study, what it tells us is this sample of heavy users, what do they think? This is not in any way . . . connected to the impact of the claim on their perceptions. We don't even know if they saw them. How much they've seen it, if they were exposed or not. This could be their pre-existing belief. It could be an effect of the claim. We do not know. So in that sense, none of the information presented answers the question of how the consumers – the effect of the claim on the consumers. . . . So nothing changed. So we're kind of like back where we were before, but no new information that can allow us to make any claims on how consumers perceive this . . . can be drawn from this data."[9] Dr. Wackowski stated, "I think one issue I have with the study in general is that we don't know the extent to which any of this is actually related to exposure to the claim,"[10] and then again later, "the issue is . . . we don't know to what extent this understanding is attributable to the claim or these people who were users to begin with already had kind of favorable and accurate perceptions. And that might be . . . because

[7] Swedish Match renewal document, at 12.
[8] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 192-193.
[9] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 219-220.
[10] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 216.

of the design."[11] Indeed, Swedish Match's Roerty even admitted that its study was not meant to look at switching, but rather meant to confirm previous CTP conclusions.[12]

Separately, TPSAC member Dr. Adam Leventhal questioned whether the style of the modified risk claim could also impact consumer understanding of the message, stating, "For instance, one of the things that I noted when reviewing some of the example marketing is the word 'lower risk' was bolded, and that was the only bold statement. And so I wondered whether that type of presentation of the information could lead people to focus in on lower risk and not really read the rest of the statement as clearly."[13] Again, because study participants were not shown the claim, this information is not known.

In the absence of data from Swedish Match that exposed people to the claim, it is instructive to look at outside research. A newly published study in which young adults were shown advertisements with and without the General Snus modified risk claim found that the presence of the claim did not change intentions to use snus products, even though it did improve some participants' understanding of relative risk of snus compared to cigarettes. The authors stated, "Taken together, among younger aged populations, there is not any strong evidence that snus MRTP claims attract those who do not use tobacco products, nor is there evidence that such claims could encourage those who smoke to switch to snus."[14] Thus if evidence shows that this modified risk claim does not induce people who smoke to switch completely to this product, then renewing this order is unnecessary because it would not benefit public health.

To summarize, Swedish Match's studies merely show users' existing beliefs about relative risks and health risks, and existing use patterns, *regardless of whether the product is marketed with a reduced risk claim*. Such studies have not demonstrated that General Snus, as a modified risk product, benefits people who smoke by causing them to stop smoking, especially given the messages' very limited use and exposure.

2. Studies were weak and rife with limitations.

FDA's background document raised some limitations of Swedish Match's submitted data, but TPSAC members repeatedly expressed concerns with the quality of the studies and analyses, including the recruitment methods, high attrition rates, problematic questions, and general lack of scientific rigor.

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[11] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 229-230.
[12] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 77.
[13] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 228.
[14] Whaley, RC, et al., "Effects of exposure to snus marketing with versus without modified risk tobacco product claims on snus use intention and perceived harm among young adults," *Tobacco Control,* Published Online First: 31 July 2024, doi: 10.1136/tc-2024-058651.

a. Study participant recruitment

Swedish Match's POU study only recruited people who currently use General Snus, rather than people who exclusively smoke cigarettes or those who do not use snus (whether or not they use any tobacco products). As a result, only the perceptions and use patterns among people who were already using the product were recorded. Excluding the company's intended audience – people who exclusively smoke cigarettes – prevents an adequate assessment of this population's reaction to the modified risk claim under review. In addition, the use of a convenience sample limits the ability to generalize any of the findings to the larger population.

Swedish Match also proactively excluded respondents who did not provide their gender, which further narrows the generalizability of the results. As TPSAC member Dr. Scout noted, "considering snus is the sole category of tobacco products that I know of that has a particularly targeted marketing campaign for the queer communities, it's particularly disappointing to think that the queer information was willfully not collected in any of the data provided here."[15]

b. High loss-to-follow-up rates

FDA's background document for the TPSAC meeting found that the attrition rate in the POU study was "significant" and "suggest[s] that observed tobacco use transitions may not accurately represent the actual likelihood of transition when the data appears to not be missing at random (i.e., associated with tobacco use)."[16] In her presentation to TPSAC, FDA Epidemiologist Nicole Tashakkori described the loss of participants as "differential attrition," in that a certain type of user tended to drop out and "people who exhibited a higher readiness to quit" remained in the study. This finding creates considerable doubt about the reliability of the reported data and the generalizability of the findings. As Dr. Tashakkori stated, "These findings suggest that the observed tobacco use transitions may not accurately represent the actual likelihood of transition when the data appears to not be missing at random."[17] For reasons that were not articulated by the company, Swedish Match did not try to adjust for the dropout rate.

TPSAC members raised concerns about this serious shortcoming in the company's research, with TPSAC Chair Dr. Delnevo describing it as a "huge, huge problem" and suggesting that the company should have replenished the sample.[18]

c. Additional issues with studies

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[15] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 222.
[16] FDA Briefing Document for TPSAC, at 17.
[17] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 107.
[18] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 201.

In addition to agreeing with other comments about the postmarket surveillance research being "problematic" and "concerning,"[19] TPSAC member Dr. Mignonne Guy expressed several critiques about Swedish Match's studies, including that they "did not adequately address the dual use of combustible tobacco products or other noncombustible tobacco products such as electronic cigarettes"[20] and that they did not include "biochemical verification,"[21] even though the study sample was small enough to collect those data. She stated, "I'm just not seeing a lot of compelling evidence that – at this moment – not to say that it cannot be produced in the future – that we can actually issue a renewal with the data that's been presented."[22]

Written comments submitted by UCSF researchers highlighted problems with the wording in Swedish Match's question to assess participants' understanding about cigarette use and reduced risk. In their original comment to FDA in 2019, the researchers stated, "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."[23] The question has not been altered in the survey for the renewal application.[24]

In FDA's own analysis of switching rates among those who used General Snus and cigarettes at baseline, more people who used General Snus and another non-cigarette tobacco product switched completely from cigarettes compared to those using only General Snus.[25] Thus the data do not indicate if the switching was due to General Snus or another product. Even more, without exposure to the modified risk claim, it is clear that the claim itself was not necessary to drive people to switch, which creates doubt that this renewal satisfies the statutory requirement of a population-wide benefit.

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[19] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 202.
[20] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 203.
[21] FDA, *Tobacco Products Scientific Advisory Committee (TPSAC) Meeting P2 – 6/26/2024*, at 28:49, YOUTUBE (July 29, 2024), https://www.youtube.com/watch?v=V4SmC9f9kx8.
[22] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 204.
[23] Popova, L, 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, https://www.regulations.gov/comment/FDA-2014-N-1051-0931.
[24] Lempert, LK, et al., 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, June 20, 2024, https://profglantz.com/wp-content/uploads/2024/06/fda-should-not-renew-the-general-snus-mrtp-orders-ucsf-comment-062024.pdf.
[25] FDA Briefing Document for TPSAC, at 16.

B. Swedish Match Did Not Alter the Claim Based on the Latest Data on Consumer Perceptions About Switching.

Swedish Match's currently authorized claim states, "Using General Snus instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis." Since the company did not actually study the impact of the modified risk claim on consumer perceptions, it is not surprising that it did not seek to modify the language to maximize its impact on public health. The wording "instead of cigarettes" in the claim does not sufficiently explain to consumers that only complete switching could achieve lower risks.

Independent studies published since the order was granted recommend using clearer messaging about switching completely. For instance, Wackowski, et al. (2021) stated that "it is important that future MRTP communications make clear that harm reduction is conditional on complete product switching, not dual product use."[26] Swedish Match did include a short summary of this study in its 2020 annual report to FDA, yet did not seem to acknowledge that recommendation.[27]

TPSAC members and consultants had a lengthy discussion about the limitations of the current claim. Several members expressed confusion over the "instead of cigarettes" wording because it did not clearly communicate that users had to completely switch in order to lower one's risk of the listed diseases, with FDA's Dr. Benjamin Apelberg agreeing that "Yes. There's different language that you could use to imply" exclusive use.[28] Several participants also suggested that the claim language needed to be improved to accurately convey that message:

> Dr. Deirdre Kittner: "I'd like to really encourage FDA to work with the applicant to change the language of the claim to be clear. And clarify that we're talking about exclusive use or completely switching so that consumers really understand how they're able to gain the best public health benefit."[29]
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> Dr. Sven Jordt: "I concur with several of the other panel members in that the language of the reduced risk claim needs to be more precise."[30]

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[26] Wackowski, O, et al., "Smokers' Exposure to Perceived Modified Risk Claims for E-Cigarettes, Snus, and Smokeless Tobacco in the United States," *Nicotine & Tobacco Research* 23(3):605-608, 2021, doi: 10.1093/ntr/ntaa159.
[27] Swedish Match, Periodic Report for STN PM0000012, October 30, 2020, at 7.
[28] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 236.
[29] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 248.
[30] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 253.

> Dr. Dona Upson: "I think it's important to change the wording, but with great care."[31]
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> Dr. Guy: "I am also concerned about the potential for confusion on the part of consumers as my other colleagues have expressed about the MRTP claim. I agree that FDA and the manufacturer both have to be very, very clear about . . . exclusive use at this table, using that term. But also knowing that we have to modify that language and ensure that it's acceptable to the individuals that are actually using these products."[32]

The problem is that Swedish Match requested renewal of its previously authorized claim when there is more recent evidence that a different wording would make the switching message clearer to consumers. FDA should deny these renewal applications and give the company the option of submitting a new modified risk application with a revised, clearer claim. FDA should require data proving that use of the new claim would actually impact consumer perceptions and patterns of use, including switching.

C. The Request for Expanded Use of the Message Is Not Supported by the Evidence Provided by the Applicant.

Swedish Match indicated that it seeks expanded use of the modified risk claim beyond the current limited use on its website. However, Swedish Match's decision not to study the impact of the message itself limits FDA's ability to evaluate whether or not people who smoke would benefit from seeing General Snus modified risk messaging in different media, such as at points of sale, in direct mail, or in other channels. Given that the company failed to show any beneficial impact from its reduced risk claim, there is no basis to permit the expansion of the claim to additional venues.

As Roerty described at the TPSAC meeting, the company originally used the authorized modified risk message in many venues, but then rolled back to only one section of the website – not even throughout the age-gated website – in order to better measure exposure that the claim was not being seen by unintended audiences.[33] However, this means that Swedish Match is missing a significant portion of its intended audience, which it has identified as "current, legal age smokers,"[34] who, unless they registered on the website, would not otherwise see this claim. As

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[31] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 259.
[32] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 261.
[33] TPSAC Meeting, June 26, 2024, Transcript, https://www.fda.gov/media/180480/download?attachment, at 85.
[34] Swedish Match, U.S. Food and Drug Administration Tobacco Products Scientific Advisory Committee Briefing Materials, June 26, 2024, at 12.

noted, this self-imposed restriction further limits Swedish Match's ability to assert that its authorized claim has had any impact on the population as a whole.

III. CONCLUSION

In applying for renewal of its modified risk order, Swedish Match made the intentional choice not to expose its study participants to its reduced risk claim. It also has used this claim to such a limited extent in marketing its General Snus products that no reliable real-world evidence could be provided to show a benefit to people who smoke. While it is important to check the validity of the claim, as Swedish Match did, that alone is not sufficient to show that a modified risk claim provides any benefit to the public health.

As Swedish Match has continually boasted, it is the first company to receive a modified risk order from FDA, which means that it is also the first one to go through the renewal process. If FDA renews the modified risk order with this low-caliber evidence, it will send a signal to other companies that they do not need to show the impact of the modified risk message in order to use it, thus undermining the standards established by the Tobacco Control Act for authorization of modified risk products.

For these reasons, FDA should deny the modified risk renewal application for General Snus.

Respectfully submitted,

American Academy of Pediatrics

American Cancer Society Cancer Action Network

American Heart Association

American Lung Association

Campaign for Tobacco-Free Kids