U.S. FOOD AND DRUG ADMINISTRATION

Tobacco Products Scientific Advisory Committee

BRIEFING MATERIALS

Swedish Match USA, Inc.

General Snus Products

MR0000020-MR0000022

MR0000024-MR0000025

MR0000027-MR0000029

June 26, 2024

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Acronyms

µg	Microgram
ACM	All-Cause Mortality
AE	Adverse Experience
APPH	Appropriate for the Protection of Public Health
ATPs	Alternative Tobacco Products
B[a]P	Benzo[a]pyrene
CDC	Centers for Disease Control and Prevention
CHD	Coronary Heart Disease
CPD	Cigarettes per Day
CTP	Center for Tobacco Products
CVD	Cardiovascular Disease
DWB	Dry Weight Basis
ENDS	Electronic Nicotine Delivery Systems
FDA	Food and Drug Administration
FD&C Act	Food, Drug, and Cosmetic Act
FTC	Federal Trade Commission
g	Gram
HPHCs	Harmful and Potentially Harmful Constituents
MGO	Marketing Granted Order
MRGO	Modified Risk Granted Order
MRTP	Modified Risk Tobacco Product
MRTPA	Modified Risk Tobacco Product Application
MST	Moist Smokeless Tobacco
ng	Nanogram
NIH	National Institutes of Health
NNK	4-(Methylnitrosamino)-1-(3-Pyridyl)-1-Butanone
NNN	N-Nitrosonornicotine
NRT	Nicotine Replacement Therapy
NYTS	National Youth Tobacco Survey
OSH	Office on Smoking and Health
P30D	Past-30-Day
PAD	Peripheral Artery Disease
PATH	Population Assessment of Tobacco and Health
PMSS	Postmarket Surveillance and Studies
PMTA	Premarket Tobacco Product Application
POU	Patterns of Use
SLT	Smokeless Tobacco
STN	Submission Tracking Number
TNP	Tobacco and Nicotine Product
TPL	Technical Project Lead
TPSAC	Tobacco Products Scientific Advisory Committee
TSNAs	Tobacco-Specific Nitrosamines
U.S.	United States
WHO	World Health Organization

1. EXECUTIVE SUMMARY

We, Swedish Match USA, Inc. (Swedish Match)[1], submitted applications on July 17, 2023, under section 911(g)(1) of the FD&C Act to request renewal of the MRGO issued on October 22, 2019, for eight *General Snus* products. These MRGOs authorized us 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."*

When authorizing the products, FDA (or "the Agency") concluded:

> *"The FDA's review determined that the claim proposed by the company in its application **is supported by scientific evidence**, that consumers understand the claim and appropriately perceive the relative risk of these products compared to cigarettes, and that the modified risk products, 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."*[2]

As a function of receiving authorizations for the *General Snus* products, FDA required us to conduct certain PMSS and submit data in Annual Reports. FDA reviewed and approved all study designs before PMSS were conducted. The submitted PMSS data required by FDA includes the following:

- Serious and unexpected adverse experience (AE) monitoring
- *General Snus* patterns of use (POU) study
- Secondary analysis of nationally representative survey data on tobacco product use
- Surveillance of new research study findings

We also collected additional postmarket evidence not specifically requested by the FDA, including product monitoring against the GOTHIATEK® standard.

Throughout the postmarket period, we continually monitor marketing and sales data to understand the consumer reach for *General Snus*. In the 2023 calendar year, we sold approximately 3.3 million cans of *General Snus* in about 13,000 retail locations in the U.S. We do not sell *General Snus* via e-commerce and employ extensive responsible marketing practices and controls within these confines. *General Snus* currently makes up around 7% of the overall U.S. snus market.

We submitted Annual Reports with PMSS data and all other new data generated, monitoring the impact of the authorized products and the respective reduced risk modification information on public health, including the impact on individual health risks, consumer understanding and perceptions, and tobacco use behavior and impact to the population on the whole.

[1] Swedish Match USA, Inc. was previously known as Swedish Match North America, Inc.

[2] Scientific Review of MRTPA under Section 911(d) of the FD&C Act – Technical Project Lead, available at: https://www.fda.gov/media/131923/download

FDA's original determination that the *General Snus* products, as actually used by consumers, will significantly reduce harm and the risk of tobacco-related disease continues to hold true today. Based on our PMSS:

- The authorized products continue to be appropriate for the protection of public health (APPH). FDA has not exercised their authority to withdraw any of the *General Snus* authorizations, indicating that FDA does not believe the currently available data raises any public health concerns.
- The available data demonstrates *General Snus* promotes consumer's complete switching from and reduction of combusted products.
- Surveillance of the U.S. market shows *General Snus* does not appeal to nonusers of tobacco and nicotine products, including youth.
- We have complied with all aspects of the PMSS requirements since authorization. FDA has not communicated concerns to us regarding any of the new data and information submitted.

Finally, we employ effective and responsible marketing controls to ensure the products are not taken up by unintended user populations (e.g., youth), and these measures have helped to ensure that there is no significant youth use of snus, as confirmed by nationally representative, government funded surveys. Therefore, the TPSAC should recommend FDA authorize the MRGO renewal for the *General Snus* products.

2. PRODUCTS IN SCOPE OF RENEWAL

The MRTPA renewal encompasses eight authorized *General Snus* products (**Table 1**), which are smokeless tobacco (SLT) products for oral use traditionally produced in Sweden. The products (**Figure 1**) are placed between the upper lip and the gum and do not require expectoration. Swedish snus was developed in the early 1800s and has been in continuous use since.[3] *General Snus* has been marketed in the U.S. since 2004.

Table 1. Product Name and FDA Authorization Information

Product Name	Product Category	STN
General Loose	Smokeless Tobacco	MR0000020
General Dry Mint Portion Original Mini	Smokeless Tobacco	MR0000021
General Portion Original Large	Smokeless Tobacco	MR0000022
General Classic Blend Portion White Large-12 ct	Smokeless Tobacco	MR0000024
General Mint Portion White Large	Smokeless Tobacco	MR0000025
General Nordic Mint Portion White Large-12 ct	Smokeless Tobacco	MR0000027
General Portion White Large	Smokeless Tobacco	MR0000028
General Wintergreen Portion White Large	Smokeless Tobacco	MR0000029

[3] For additional history, see Rutqvist, L.E., Curvall, M., Hassler, T. *et al.* Swedish snus and the GothiaTek® standard. *Harm Reduct J* **8**, 11 (2011). https://doi.org/10.1186/1477-7517-8-11

Figure 1. Sample *General Snus* Products

2.1 Other Product Monitoring Studies (GOTHIATEK Standard)

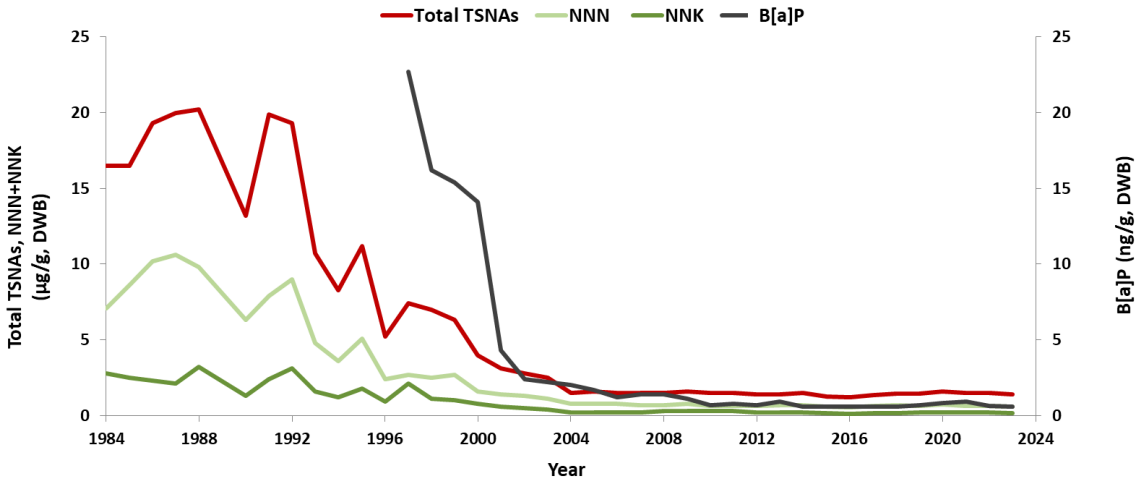
While FDA did not require additional health risk studies as part of the PMSS requirements, we routinely collect data to monitor the *General Snus* products. Specifically, we test the *General Snus* products' continued conformance with the GOTHIATEK standard, our proprietary quality standard for snus products, which, in part, ensures extremely low levels of TSNAs, NNN, NNK, polyaromatic hydrocarbons (B[a]P), and metals.[4] To date, we are not aware of any other manufacturer that has voluntarily committed to ongoing monitoring against maximum constituent levels through a similar standard.

Recognizing the importance of TSNA levels, in 2017, FDA proposed an NNN product standard that would limit the level of NNN in SLT products to no more than 1 microgram per gram (µg/g) of tobacco on a dry weight basis. The exceptionally low levels of TSNAs in *General Snus* meet this proposed standard and offer consumers who switch to these products a substantial reduction in harmful and potentially harmful constituents (HPHCs), which is likely to translate into improved health outcomes.

We conduct this extensive testing annually to confirm the *General Snus* products maintain their exceptionally low HPHC levels consistently over time. **Figure 2** demonstrates the initial reduction and continued maintenance of exceptionally low TSNA and B[a]P levels in the *General Snus* portfolio over the past 20 years. Since the MRGOs were issued in 2019, the average observed levels of these HPHCs have remained low. This suggests the products, when used exclusively in place of cigarettes, will continue to reduce death and disease, consistent with the original authorization. Therefore, while not requested by FDA in PMSS, these data further support the TPSAC should recommend FDA authorize renewal of the MRGOs for these products.

[4] https://www.swedishmatch.com/Snus-and-health/GOTHIATEK/ and https://www.coresta.org/sites/default/files/abstracts/2014_ST13_Lindholm.pdf

Figure 2. Annual Measured Values for *General Snus* TSNA and B[a]P Levels (GOTHIATEK Monitoring)



3. SUMMARY OF PRIOR AUTHORIZATIONS

On June 10, 2014, and March 11, 2015, we submitted MRTPAs[5] and PMTAs, respectively, for *General Snus* products. FDA issued MGOs for the products on November 10, 2015, concluding the products meet the APPH standard and should be authorized. The FDA decision[6] was primarily predicated on the following:

- The products comply with the **GOTHIATEK quality standard**, which includes constituent standards that must not be exceeded in finished products, manufacturing standards, manufacturing process requirements, and consumer package labeling requirements.
- The products contain **significantly lower levels of TSNAs** (NNN and NNK) compared to over 97% of the SLT products currently on the U.S. market, and individuals using these products with reduced NNN levels could decrease their excess cancer risk[7] by 90% compared to use of moist snuff.
- The levels of other HPHCs are similar to or lower than levels of SLT products currently on the U.S. market.
- There are significant **reductions in oral cancer risk** when the products are used exclusively instead of other SLT products or cigarettes on the U.S. market.

[5] 77 Fed. Reg. 20226, April 3, 2012 (https://www.fda.gov/media/83300/download). We submitted applications that conform to this nonbinding guidance.

[6] Premarket Tobacco Application (PMTA) Technical Project Lead (TPL) Review (fda.gov)

[7] The excess lifetime cancer risk is a toxicological tool to estimate the probability of cancer incidence in a population of individuals for a specific lifetime from projected intakes (and exposures) and dose-response data (i.e., slope factors) for a specific chemical.

- There are significantly **lower risks of developing respiratory diseases and cancers** when the products are used exclusively instead of combusted tobacco products.

- There is a low likelihood of nonuser uptake of these products, decreased or delayed cessation, or other significant shifts in user demographics.

FDA issued MRGOs for the submitted modified risk statements (**Section 1**) on October 22, 2019. The FDA decision[8] was based on many of the same reasons listed above for the MGOs, as well as evidence demonstrating both the products' potential to reduce death and disease amongst tobacco product users and consumer understanding of the modified risk information and relative risk of the products.

In total, FDA reviewed the extensive scientific evidence leading to the authorized PMTAs/MRTPAs and eight years of postmarket reporting. The postmarket data continue to support FDA's conclusion that *General Snus* reduces risk of tobacco-related diseases and does not appeal to youth or nonusers of tobacco and nicotine products. *General Snus* continues to have tremendous potential to reduce the death and disease caused by continued combusted cigarette smoking and improve the lives of smokers in the U.S. by providing an acceptable alternative product.

4. SUMMARY OF POSTMARKET SURVEILLANCE AND STUDIES CONDUCTED BY SWEDISH MATCH

In the authorizations for each *General Snus* product, FDA outlined a series of PMSS to be conducted and submitted to FDA in Annual Reports. We conducted and submitted the required PMSS as well as additional postmarket studies to further characterize the impact of the products on health, beyond those required by the FDA. This evidence allows FDA to assess the continued appropriateness of the products for public health on a routine basis and, if necessary, exercise their authority to withdraw an authorization if these requirements are not met or if the submitted data raise new questions of public health.

As part of our PMSS, FDA required us to conduct an additional POU study to examine the impact of the orders on consumer health risks, perception, and behavior. FDA also required monitoring of awareness and use by youth and other unintended user populations (e.g., nonusers). In accordance with section 911(i)(2) of FD&C Act, FDA reviewed and approved all PMSS study plans before we executed the studies. We submitted comprehensive Annual Reports to the FDA demonstrating compliance with these PMSS requirements over the eight years following the first *General Snus* MGO.

The submitted PMSS data required by FDA during authorization are summarized in the remaining sections and include the following:

- Serious and unexpected AE monitoring
- *General Snus* POU study
- Secondary analysis of the Population Assessment of Tobacco and Health (PATH) survey
- Secondary analysis of the National Youth Tobacco Survey (NYTS)

[8] Scientific Review of MRTPA under Section 911(d) of the FD&C Act – Technical Project Lead, available at: https://www.fda.gov/media/131923/download?attachment

- Surveillance of new research study findings

Additional evidence not specifically requested by the FDA was also collected and submitted to FDA. These data are also summarized in the remaining sections and include the following:

- Annual product monitoring to ensure GOTHIATEK standard compliance
- Responsible marketing and controls in place to prevent use of these products amongst unintended populations (e.g., youth, tobacco nonusers)

FDA accepted the submitted Annual Reports containing this evidence without major comment on the scientific data. The original orders remain in effect, indicating that FDA finds the submitted data sufficient to demonstrate the authorized products do not raise new questions of public health and thus, remain APPH.

4.1 Relative Health Risks of the MRTP to Individual Tobacco Users

4.1.1 Serious and Unexpected Adverse Experiences

When the *General Snus* products were authorized in 2015, we established a safety surveillance process to collect and manage all safety information related to the use of *General Snus* products. The aim of the safety surveillance process is to monitor and analyze, in a timely manner, all new safety information related to the use of our products.

Throughout the postmarket surveillance period from Oct. 1, 2015, to Oct. 31, 2023, no serious[9] or unexpected[10] AEs were reported for these products. There have been no changes in the nature and frequency of AEs. Further, we continue to comply with all FDA-required AE reporting. Therefore, when considering these data, the cumulative AEs support renewal of MRGOs for the authorized *General Snus* products.

4.2 Consumer Understanding and Perceptions

As outlined in the series of MRGOs for each *General Snus* product, FDA required us to conduct postmarket studies assessing consumer understanding and perceptions of the product over time to ensure users remain able to adequately understand the modified risk information. FDA stated this study must

> *"include an assessment of consumers' understanding of the claim and perceptions of the products. In particular, PMSS must assess the extent to which users of these products understand that, to reduce their risk of disease relative to smoking as described in the modified risk*

[9] Per the MGO letters for *General Snus*, "a serious adverse experience means an adverse experience that results in any of the following outcomes: death; a life-threatening adverse event; inpatient hospitalization or prolongation of existing hospitalization; a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, a congenital anomaly/birth defect; or any other adverse experience that, based upon appropriate medical judgement, may jeopardize the health of a person and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition."

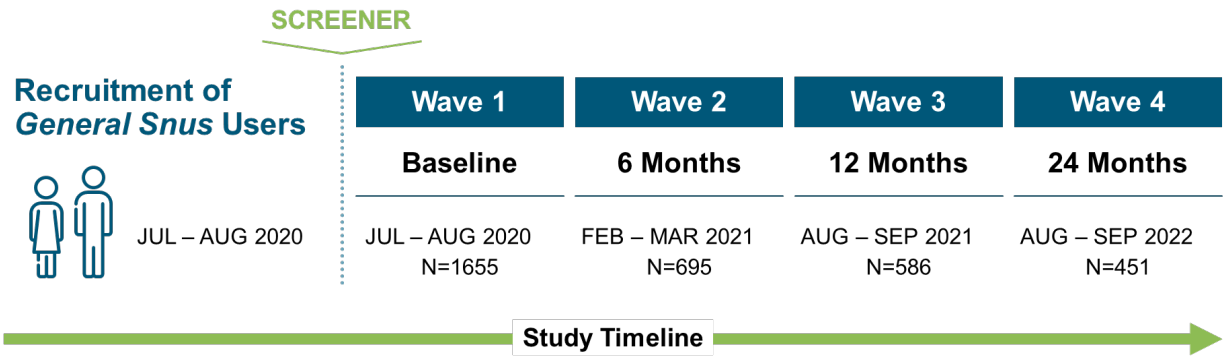
[10] Per the MGO letters for *General Snus*, an "unexpected adverse experience means an adverse experience occurring in one or more persons in which the nature, severity, or frequency of the experience is not consistent with: the known or foreseeable risks associated with the use or exposure to the tobacco product as described in the PMTA and other relevant sources of information, such as postmarket reports and studies; the expected natural progression of any underlying disease, disorder, or condition of the person experiencing the adverse experience and the person's predisposing risk factor profile for the adverse experience; or the results of nonclinical laboratory studies."

> *information, they must use General Snus exclusively.* ***To adequately assess these impacts, you must conduct PMSS that include assessing users' behavior and consumer understanding at multiple time points.***[11]"

To accomplish this, we provided FDA with a study plan to conduct a POU study, which FDA approved in April 2020.

The POU study assessed consumer perception of risk associated with the MRTPs (i.e., relative risk compared to cigarettes), as well as understanding of elements of the modified risk information (i.e., the need to completely switch from cigarettes) post-MRTP authorization. The study consisted of a self-reported longitudinal survey examining patterns of past-30-day (P30D) tobacco and nicotine product (TNP) use among *General Snus* users in a baseline assessment (Wave 1, N = 1,655) and again, among the same *General Snus* users, at 6 months (Wave 2, N = 695), 1 year (Wave 3, N = 586), and 2 years (Wave 4, N = 451) after baseline (Figure 1**Figure 3**).

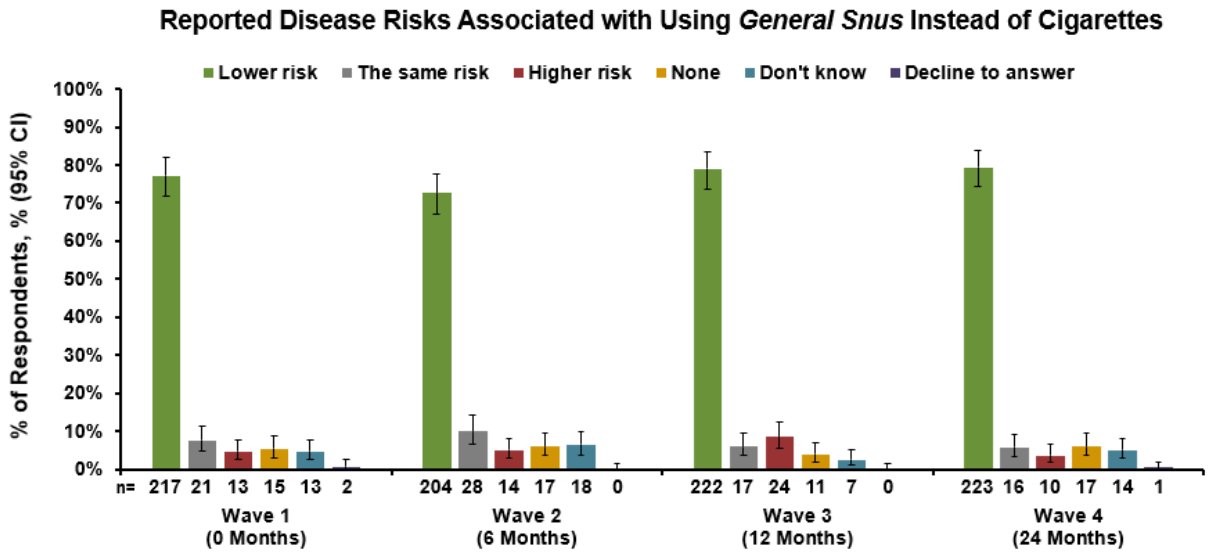
Figure 3. *General Snus* Patterns of Use Study Experimental Design



Across all four waves, surveyed consumers accurately maintained the correct relative risk perception associated with the MRTP product relative to cigarettes. When asked how using *General Snus* instead of cigarettes affects your risk for mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis, the vast majority of consumer were able to identify that using *General Snus* puts you at a lower risk of these conditions (**Figure 4**). The longitudinal results also demonstrate consumers understand that fully switching to *General Snus* from cigarettes is needed to achieve risk reduction. Over the 24 months, greater than 80% of those who understood the modified risk messaging correctly responded that cigarette smokers must switch completely to *General Snus* (answered "zero cigarettes") in order to reduce their risks of diseases (**Figure 5**). These results suggest the modified risk information is effectively educating consumers on the relative health risks of the product and the importance of completely substituting cigarettes with *General Snus*, and that consumer perceptions remain consistent over time.

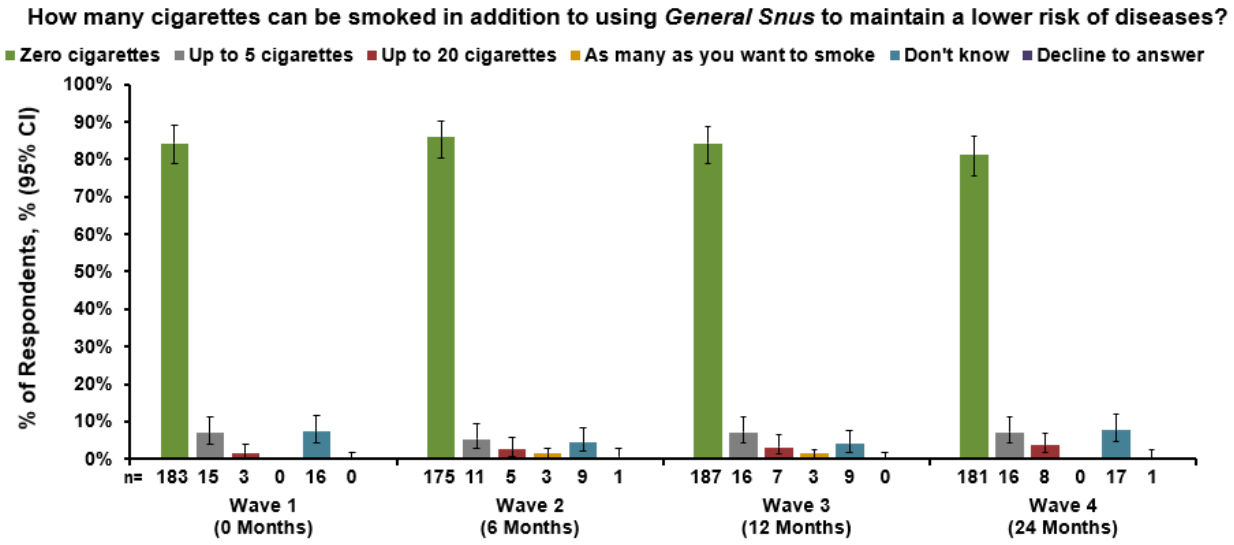
[11] https://www.fda.gov/media/131923/download?attachment

Figure 4. Respondents Overwhelmingly Comprehend Relative Risk of Using *General Snus* Instead of Smoking Cigarettes



n = number of respondents. Error bars = 95% CI.
Source: *General Snus* POU study. This analysis was conducted using data from the 281 participants who completed all 4 waves. Participants were asked "Does using *General Snus* instead of cigarettes place you at a lower risk, the same risk, a higher risk, or no risk?"

Figure 5. Respondents Overwhelmingly Understand Necessity of Eliminating or Significantly Limiting Cigarette Smoking in Addition to Using *General Snus* to Maintain a Lower Risk of Disease



n = number of respondents. Error bars = 95% CI.
Source: *General Snus* POU study. This analysis was conducted using data from the 281 participants who completed all four waves. This question was asked of only those respondents who correctly identified that using *General Snus* instead of cigarettes puts you at a lower risk of disease (see **Figure 4**).

Therefore, the results of postmarket studies continue to support previously submitted premarket evidence showing all of the following:

- The perceived health risks associated with using *General Snus* are lower than the perceived health risks associated with smoking cigarettes, which is in line with the epidemiological data.
- There is a high level of understanding that completely switching to *General Snus* reduces the risk of disease compared to smoking.

Therefore, the availability of *General Snus* along with the modified risk information is improving legal age smokers' ability to make informed, personal choices that could reduce their risk of tobacco-related disease. These study results were communicated to FDA in our Annual Report.

4.3 Tobacco Use Behavior and Impact to the Population as a Whole

FDA required us to also evaluate consumers' use behaviors over time, which were intended to

> *"…assess the extent to which new MRTP users were non-users, smokers, or other tobacco product users before initiating the MRTPs and the extent to which new users of the MRTPs become exclusive users or dual users with cigarettes or other tobacco products over time."*[12]

We assessed use behaviors among U.S. *General Snus* users and nonusers as part of the previously described *General Snus* POU study. We provided FDA with the study plan, which they agreed to in April 2020. We also designed secondary analyses of nationally representative survey data to assess use patterns in *General Snus* users and nonusers, including monitoring youth uptake of the products. The relevant studies include the following:

- The *General Snus* POU study: Longitudinal survey of legal age *General Snus* users to assess use behaviors over time
- Secondary analysis: Estimation of prevalence of *General Snus* use by adults overall and by flavor category using the PATH study
- Secondary analysis: Estimation of use of *General Snus* among youth using the NYTS

4.3.1 Benefit to Legal Age Smokers

Legal age smokers who completely switch to *General Snus* are likely to reduce their risk of disease by replacing their cigarette consumption with a reduced risk alternative. Therefore, it is critical to ensure that *General Snus* is being used by the intended consumers (current, legal age smokers) and to monitor how they are using *General Snus* relative to cigarettes. These data inform the likelihood of consumers becoming complete switchers or dual users of *General Snus* and combusted cigarettes. These product use patterns were monitored using a combination of data collected from the POU study and the PATH survey.

Per the POU study, *General Snus* is primarily used by middle-aged, legal age consumers and does not have high rates of uptake in historically vulnerable populations (**Table 2).** Additionally, less than 8% of

[12] https://www.fda.gov/media/131923/download?attachment

General Snus users were 21–24 years old, suggesting a continued low exposure to the products by those under the age of 25.

Table 2. Demographics of *General Snus* Users Completing All Four Waves

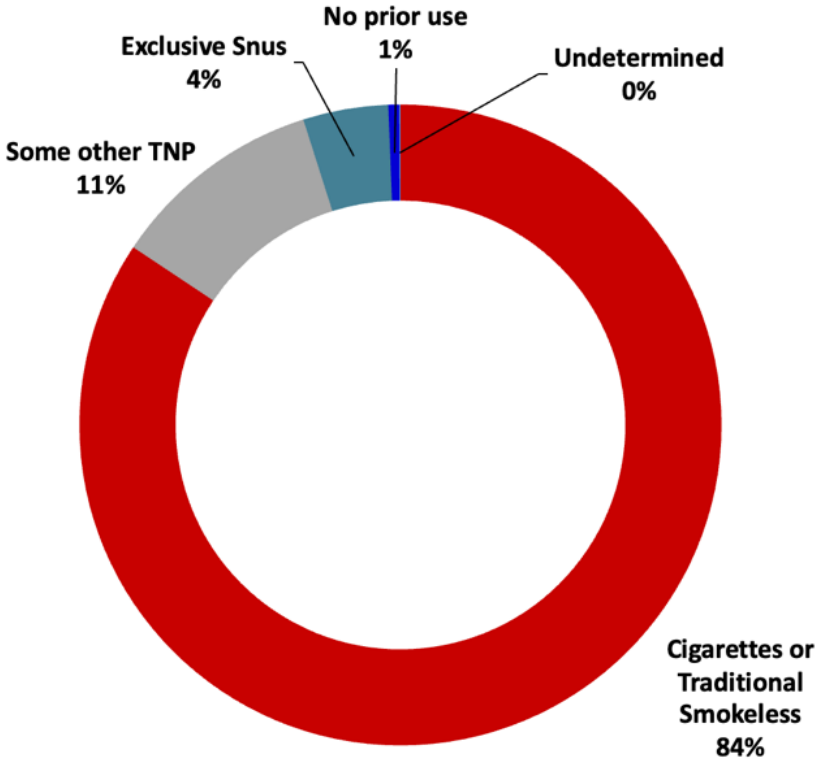
	***General Snus*® Users**
	n=281
Geographic Region	
Northeast (%)	39 (13.9%)
Midwest (%)	87 (31.0%)
South (%)	89 (31.7%)
West (%)	66 (23.5%)
Respondent Age	
Mean age (years) + Std Dev	*37 ± 10*
21-24 (%)	21 (7.5%)
25-34 (%)	105 (37.4%)
35-44 (%)	103 (36.7%)
45-54 (%)	35 (12.5%)
55+ (%)	17 (6.0%)
Gender	
Male (%)	263 (93.6%)
Female (%)	18 (6.4%)
Racial or Ethnic Background	
Caucasian/White (%)	252 (89.7%)
Black/African American (%)	2 (0.7%)
Hispanic (e.g., Latin American, Mexican, Puerto Rican, Cuban) (%)	7 (2.5%)
Asian or Pacific Islander (%)	5 (1.8%)
Native American or Alaskan native (%)	3 (1.1%)
Mixed racial background (%)	11 (3.9%)
Other (%)	1 (0.4%)
Highest Grade or Level of School Completed	
Less than high school (%)	0 (0.0%)
Some high school, no diploma (%)	0 (0.0%)
General Educational Development (GED) (%)	13 (4.6%)
High school graduate - diploma (%)	14 (5.0%)
Some college but no degree (%)	72 (25.7%)
Associate degree (%)	38 (13.6%)
Bachelor's degree (e.g., BA, AB, BS) (%)	101 (36.1%)
Post-graduate degree (e.g., MBA, PhD, JD, etc.) (%)	42 (15.0%)
Marital Status	
Now married (%)	158 (56.2%)
Widowed (%)	4 (1.4%)
Divorced (%)	25 (8.9%)
Separated (%)	3 (1.1%)
Never married (%)	90 (32.0%)
Decline to answer (%)	1 (0.4%)
Household Income in the Past 12 Months	
Less than $24,999 (%)	20 (7.1%)
$25,000 to $49,999 (%)	49 (17.4%)
$50,000 to $74,999 (%)	51 (18.1%)
$75,000 to $99,999 (%)	49 (17.4%)
$100,000 or more (%)	101 (35.9%)
Don't know (%)	2 (0.7%)
Decline to answer (%)	9 (3.2%)

n = number of respondents

Source: *General Snus* POU study. This analysis was conducted using data from the 281 participants who completed all four waves.

Almost all *General Snus* users reported prior fairly regular use of TNPs (**Figure 6**) at Wave 1. The vast majority of established *General Snus* users reported prior use of cigarettes or traditional smokeless products, comprising 84% of users studied. Fairly regular users of other TNPs accounted for 15% of established *General Snus* users, with 4% reporting prior usage of other snus products, and 11% reporting prior use of another TNP. Only 1% of all established *General Snus* user study participants reported no prior use of TNPs. These data suggest that the vast majority of established *General Snus* users have a history of cigarette and/or SLT use and, therefore, could benefit from transitioning to *General Snus* based on the available epidemiological data.

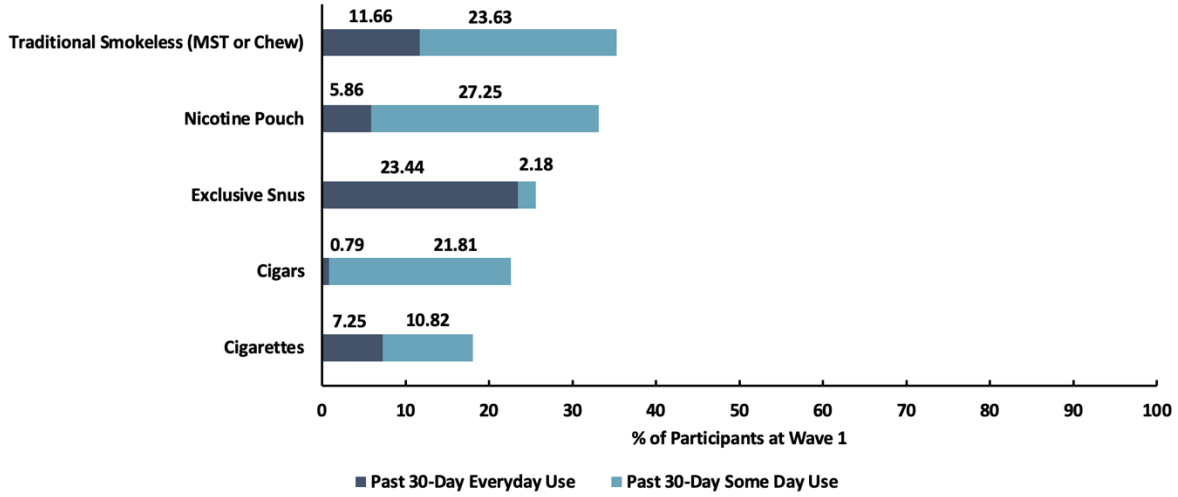
Figure 6. Established *General Snus* Users Report Prior Fairly Regular Use of TNPs



Source: *General Snus* POU study. This analysis was conducted using participants' reported tobacco use history at Wave 1. Participants were asked "Have you ever used any of the following tobacco or nicotine products fairly regularly?" Definition of fairly regular use was adapted from the PATH study.

Poly use of other TNPs was reported by several established *General Snus* users at Wave 1 (Figure **7**). The five most common TNP categories used in the past 30 days were traditional smokeless products (MST or chew), nicotine pouches, snus (exclusive), and combustible products (such as cigars and cigarettes). When assessing past-30-day everyday use, the rates of poly use were dramatically lower for all categories except snus. Rates of poly use were particularly reduced for cigars and nicotine pouches. This suggests that much of the reported poly use of *General Snus* is likely due to situational use of TNPs and may be a temporary, transitional state as users transition from one product category or product to another. This highlights the importance of the modified risk information as it details the need to use snus instead of cigarettes, making it an important tool to encourage TNP users to adopt exclusive use of snus.

Figure 7. Five Most Reported TNP Use Categories (Past-30-Day) Among Established *General Snus* Users at Wave 1 (Everyday and Some Day)

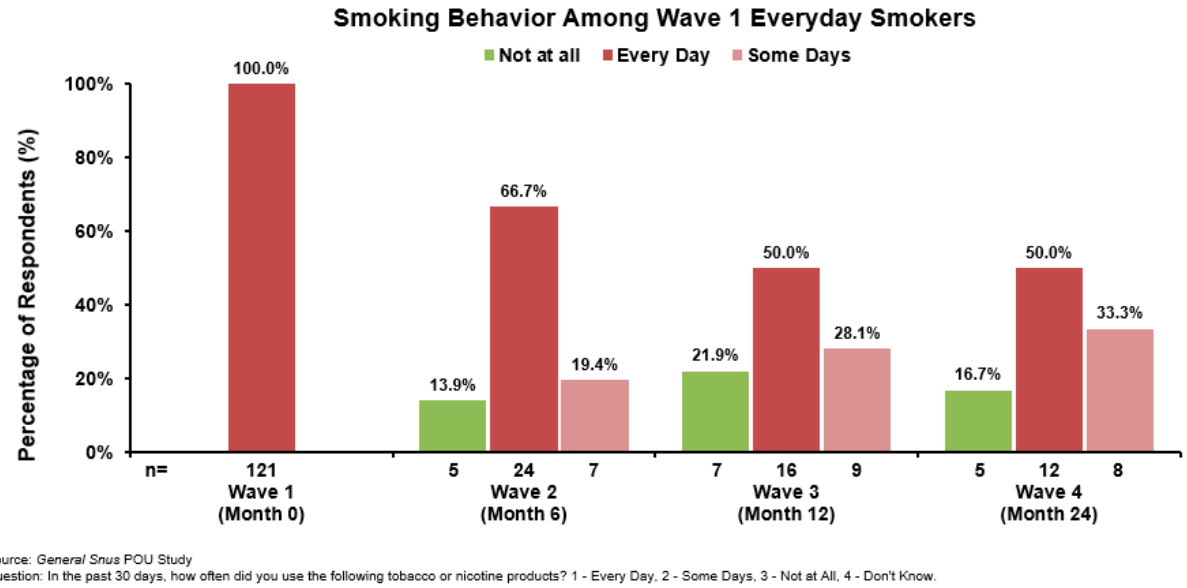


Source: *General Snus* POU study. This analysis was conducted using participants' reported tobacco use history at Wave 1. Categories are not mutually exclusive.

When examining cigarette use among everyday smokers at Wave 1, 16.7% were no longer smoking at Wave 4, and an additional 33.3% had reduced their use from every day to some days (**Figure 8**). In this same subpopulation, a reduction of more than 50% in the mean cigarettes per day (CPD) was observed at Wave 4 (6.29 CPD) in comparison to Wave 1 (12.31 CPD) (**Figure 9**). *General Snus* consumers also demonstrated a reduction in the usage of noncombustible TNPs. When examining usage of other SLT products (MST or chewing tobacco), over 16% of prior fairly regular users were no longer using these products at Wave 1, and an additional 15% reported cessation of use at Wave 4.

We also rely on evidence collected in the PATH survey to monitor adult snus use and identify important factors that influence use behaviors. PATH queried adult established users about their use of flavored products, and roughly 80% of adult established snus users reported regularly using a flavored product (**Figure 10**). This indicates snus consumers have a clear preference for flavored products. Of these established adult users, roughly 80% used only mint and related flavors over the past 30 days, while roughly 10% reported use of only non-mint flavors (**Figure 11**). The other roughly 10% of established adult users reported using both mint and non-mint flavors. Therefore, maintaining a robust selection of noncombustible options with MRTP authorization, including flavored options, is likely to benefit consumers interested in switching to these products. These category-level data are consistent with our product-specific sales data that shows predominate adoption of mint-flavored *General Snus* varieties, which account for approximately two thirds of total sales volume (data not shown).

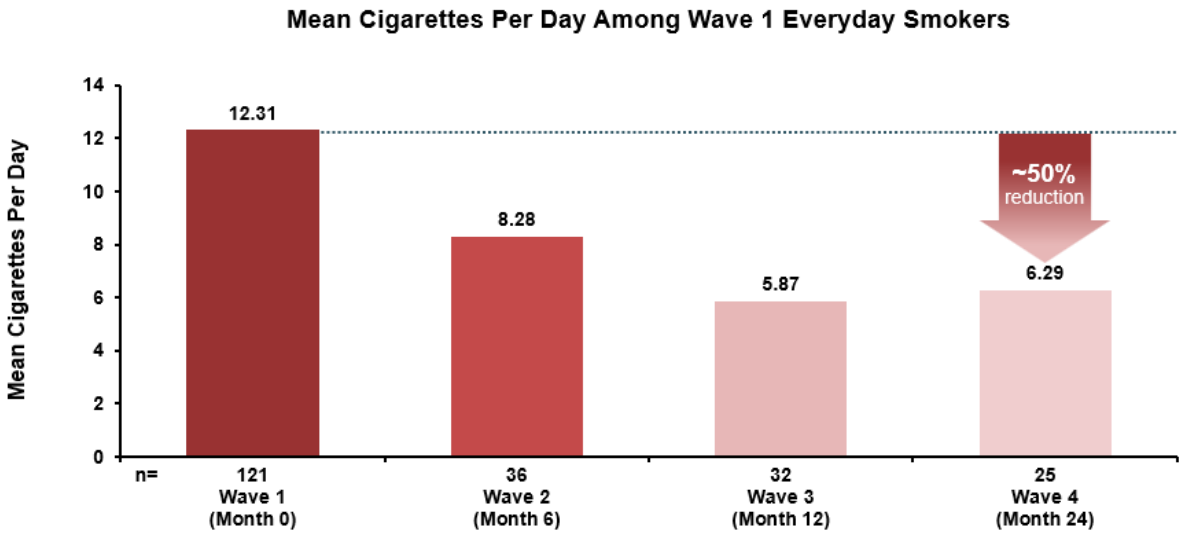
Figure 8. Switching and Reduction in Smoking Among Everyday Smokers at Wave 1



Source: *General Snus* POU Study
Question: In the past 30 days, how often did you use the following tobacco or nicotine products? 1 - Every Day, 2 - Some Days, 3 - Not at All, 4 - Don't Know.

n = number of respondents
Source: *General Snus* POU study

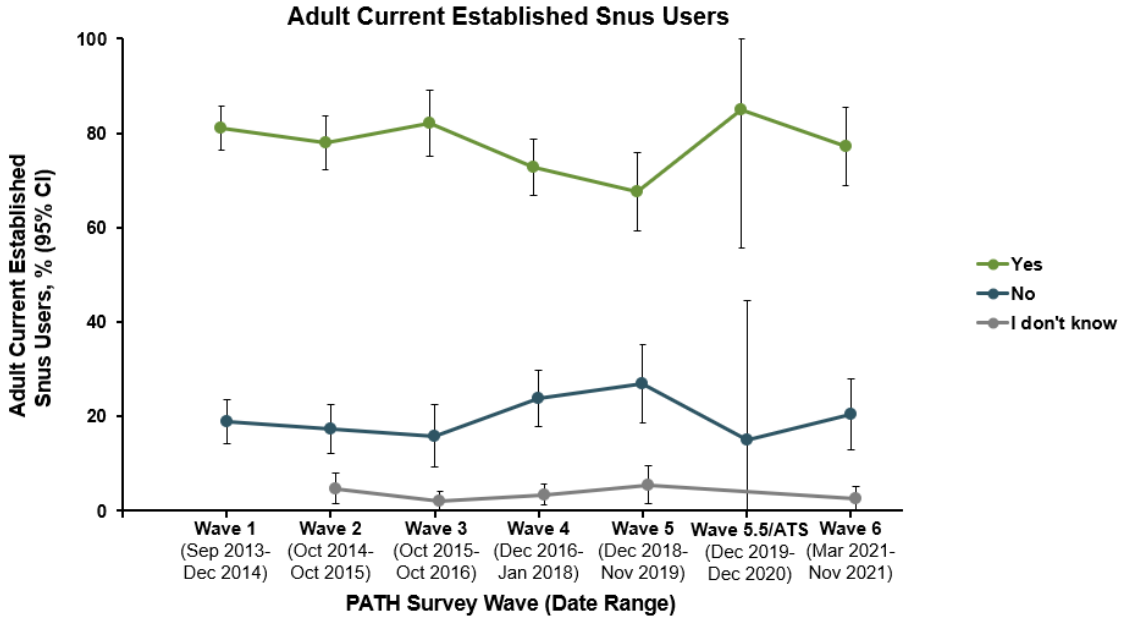
Figure 9. Reduction in Cigarettes per Day Among Everyday Smokers at Wave 1



Source: *General Snus* POU Study
Question: On average, about how many cigarettes do you now smoke each day? A pack usually has 20 cigarettes in it. ____# of cigarettes per day [RANGE = 0-80]

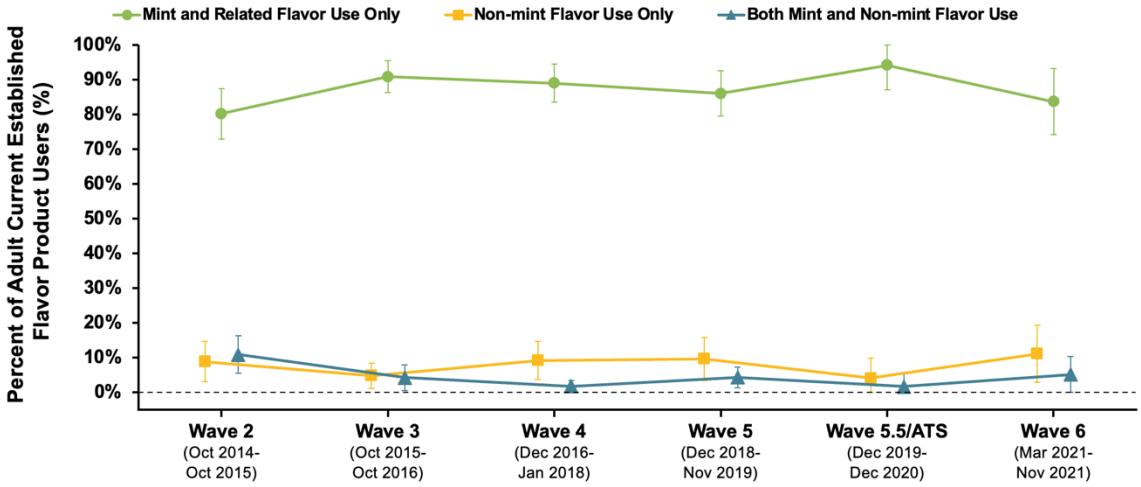
n = number of respondents
Source: *General Snus* POU study

Figure 10. Use of Flavored and Unflavored Snus Products by Adults in the PATH Survey



PATH is a nationally representative survey of youth (age 12 and older) and adults in the U.S. This survey is a collaboration between the National Institutes of Health (NIH) and the FDA.

Figure 11. Past-30-Day Use of Flavored Snus Products by Adults in the PATH Survey



PATH is a nationally representative survey of youth (age 12 and older) and adults in the U.S. This survey is a collaboration between the NIH and the FDA.

The surveillance of new research also suggests the availability of reduced risk products with adequate nicotine delivery and in a variety of flavors is associated with switching away from combusted products.[13] Furthermore, evidence has indicated the use of more than one flavor of product was common among users of reduced risk products and could potentially lead to greater rates of switching away from combusted cigarettes.[14,15,16] Real-world data are supportive of these conclusions with sales data indicating a preference for flavored snus products, including mint varieties.[17]

Overall, the data from these postmarket studies are consistent with the data collected in premarket studies and demonstrate *General Snus* is providing a benefit to adult smokers and does not appeal to nonusers.

- *General Snus* consumers largely consist of existing tobacco users, especially those with a prior history of cigarette smoking and SLT use.

- Established *General Snus* users displayed cigarette switching and overall reduction in cigarette consumption. When examining cigarette use among everyday smokers at Wave 1, 16.7% were no longer smoking at Wave 4 (24 months), and an additional 33.3% had reduced their use from every day to some days. Additionally, the average number of cigarettes consumed per day decreased by approximately 50% from Wave 1 to Wave 4.

- *General Snus* does not appeal to adult nonusers of TNPs based on low prevalence of *General Snus* use among adults.

We reported these collective results to the FDA as part of annual reporting and received no feedback related to these scientific findings from the Agency. This further supports that these findings do not raise new questions of public health and are consistent with the prior evidence leading to authorization.

4.3.2 Risk to Youth

When authorizing the MRTPs, FDA noted the available evidence did not demonstrate significant youth initiation of snus products. We have continued to monitor youth TNP use patterns based on nationally representative survey data collected in both the NYTS and PATH surveys. Postmarket data continues to demonstrate an absence of appeal and uptake of snus among youth.

From 2011 to 2023, NYTS shows a consistently low and declining prevalence of snus use among high school students (**Figure 12**). In 2022, 0.5% of respondents indicated they have used snus at least

[13] Gades MS, Alcheva A, Riegelman AL, Hatsukami DK. The Role of Nicotine and Flavor in the Abuse Potential and Appeal of Electronic Cigarettes for Adult Current and Former Cigarette and Electronic Cigarette Users: A Systematic Review. *Nicotine Tob Res*. 2022 Aug 6;24(9):1332-1343. doi: https://doi.org/10.1093/ntr/ntac073 PMID: 35305014; PMCID: PMC9356694

[14] Farsalinos KE, Romagna G, Tsiapras D, Kyrzopoulos S, Spyrou A, Voudris V. Impact of flavour variability on electronic cigarette use experience: an internet survey. *Int J Environ Res Public Health*. 2013 Dec 17;10(12):7272-82. doi: https://doi.org/10.3390/ijerph10127272.PMID: 24351746; PMCID: PMC3881166

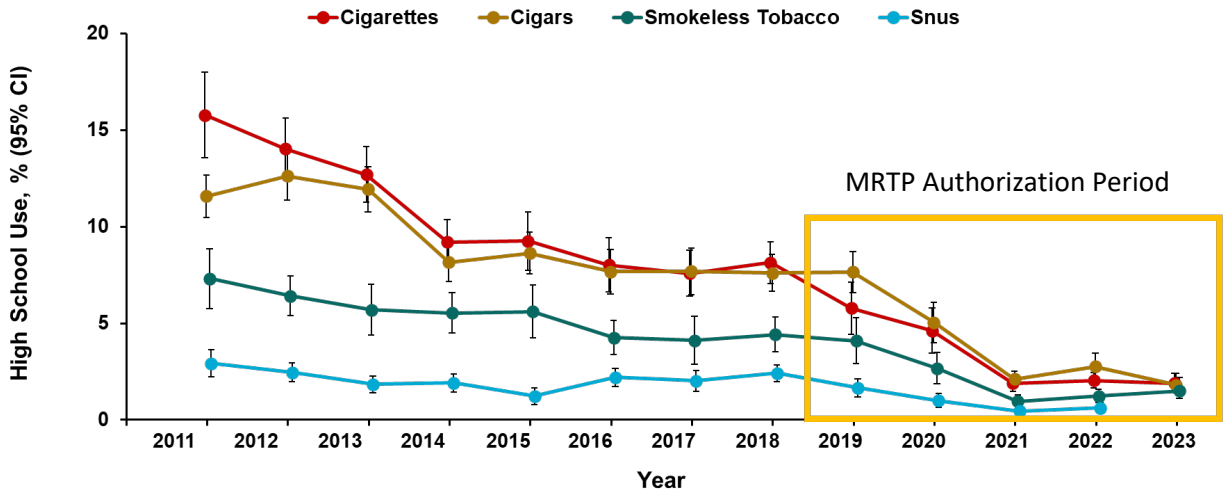
[15] Romijnders KA, Krüsemann EJ, Boesveldt S, Graaf K, Vries H, Talhout R. E-Liquid Flavor Preferences and Individual Factors Related to Vaping: A Survey among Dutch Never-Users, Smokers, Dual Users, and Exclusive Vapers. *Int J Environ Res Public Health*. 2019 Nov 22;16(23):4661. doi: https://doi.org/10.3390/ijerph16234661. PMID: 31766776; PMCID: PMC6926905

[16] Gentry SV, Ward E, Dawkins L, Holland R, Notley C. Reported patterns of vaping to support long-term abstinence from smoking: a cross-sectional survey of a convenience sample of vapers. *Harm Reduct J*. 2020 Oct 6;17(1):70. doi: https://doi.org/10.1186/s12954-020-00418-8. PMID: 33023583; PMCID: PMC7541214

[17] Liber AC, Seidenberg AB, Pesko MF. Tob Contrl Epub ahead of print: [accessed 7/13/2023]. doi:10.1136/tc-2022-057890

once in the past 30 days. When considering ever use of snus, only 1% reported trying snus (even just one time). Furthermore, snus has the lowest prevalence of use among the other major categories of TNPs. These data are consistent with the prevalence of P30D use among youth in the PATH survey, which also shows low and declining rates of snus use among youth (data not shown). Taken together, data from NYTS and PATH demonstrate very low prevalence of snus use, including *General Snus* among underage individuals in the U.S.

Figure 12. NYTS P30D Use of Traditional Tobacco Products, Including Snus



Current youth use of TNPs in NYTS is defined as use on one or more of the past 30 days. Recently published 2023 SLT use estimates include snus. Independent snus use data is not yet available. NYTS is a nationally representative survey of middle and high school youth in the U.S. This survey is a collaboration between the Centers for Disease Control and Prevention, Office on Smoking and Health (CDC, OSH) and the U.S. Food and Drug Administration, Center for Tobacco Products (FDA, CTP). The **yellow** box denotes the MRTP authorization period.

4.3.3 Impact to the Population on the Whole

We support FDA's position on the continuum of risk across tobacco products, specifically that moving users of combusted products down the continuum of risk benefits the population at large.[18] For tobacco harm reduction to be successful, there must be a diverse marketplace of innovative, FDA-authorized, reduced risk products. In this context, having multiple varieties and flavors of *General Snus* can help legal age consumers transition to products lower on the continuum of risk.

In terms of tobacco use behavior, postmarket surveillance has continued to support the conclusions made in the initial MRGOs:

- The *General* Snus products are primarily used by consumers with a tobacco use history (cigarettes and SLT), with low rates of uptake among nonusers.

[18] A recent publication authored by the current Director of the Center for Tobacco Products states that "the health risks for tobacco products exist on a continuum, with combustible products such as cigarettes being the most harmful. Decades of research have documented that cigarette smoking harms nearly every organ of the body; cigarette smoke contains nearly 7,000 chemicals, approximately 70 of which cause cancer. Non-combustible tobacco products, such as e-cigarettes, generally have lower health risks to the user than combusted tobacco products." Toll BA, Smith TT, King BA. *Nat Med*. Epub ahead of print: [accessed 4/16/2024]. doi: https://doi.org/10.1038/s41591-024-02926-7

- *General Snus* can facilitate switching from and reduction of combustible products that are high on the continuum of risk (e.g., cigarettes).

- There are consistently low levels of youth use of snus products.

The evidence demonstrates *General Snus* can benefit the health of the population as a whole by transitioning legal age cigarette smokers away from cigarettes. There is clear evidence of sustained long-term switching from combusted cigarette smoking among legal age *General Snus* users and, based on prevalence of *General Snus* among legal age nicotine users overall, the initiation of *General Snus* by nonusers of tobacco is unlikely. Further, the data demonstrate that snus use amongst youth and underage young adults is very low. Therefore, the continued marketing of *General Snus* as a MRTP will significantly reduce harm and the risk of tobacco-related diseases, and the modified risk order renewal should be granted.

5. SURVEILLANCE OF NEW RESEARCH STUDY FINDINGS IN PUBLISHED SCIENTIFIC LITERATURE

We continually monitor the published scientific literature for new data on *General Snus* and provide our literature review to FDA in Annual Reports. The most recent literature review was conducted to summarize postmarket data focusing on the impact of Swedish snus, including *General Snus*, on health risks, consumer understanding and perceptions, and tobacco use behavior and impact to the population as a whole.

The original PMTAs and MRTPAs included long-term scientific evidence (e.g., decades of Swedish epidemiological studies) demonstrating consumers who exclusively used Swedish snus products had a lower risk of developing tobacco-related disease than consumers who smoked cigarettes. The well-established Swedish experience with snus continues to provide real-world evidence and epidemiological data demonstrating that these smoke-free products reduce tobacco-related morbidity and mortality. [19,20] Public health data show Sweden has the lowest smoking rate and incidence of tobacco-related diseases among men in Europe, due in large part to snus, which many Swedish men began switching to approximately 50 years ago.

Ongoing surveillance of the literature reinforces the reduced health risks associated with *General Snus* use in comparison to cigarettes and the continued validity of the modified risk claim. A complete list of the studies identified in the literature review is provided in the appendix (See Surveillance of Published Literature), with additional relevant publications being summarized in the remainder of this section.

5.1 Health Risks

As part of our surveillance efforts, Swedish Match identified numerous postmarket publications that provide additional evidence surrounding the health risks associated with *General Snus* use for the specific disease outcomes addressed in the modified risk claim.

[19] Ramström, L., Borland, R., & Wikmans, T. (2016). Patterns of Smoking and Snus Use in Sweden: Implications for Public Health. *International journal of environmental research and public health*, 13(11), 1110. https://doi.org/10.3390/ijerph13111110

[20] Snus Commission (2022). Relative Health Risks of Tobacco and Nicotine Products. https://snuskommissionen.se/wp-content/uploads/2023/01/A-report-from-Swedens-Snus-Commission_2022.pdf

In a systematic global review and meta-analysis of 37 studies examining associations between SLT use and oral cancer, Asthana et al. (2019)[21] found that although many SLT products significantly increased oral cancer risk, there was no increased risk associated with snus. Additionally, in a similar meta-analysis of all SLT products sold in World Health Organization (WHO) regions, Gupta et al. (2022)[22] linked many global SLT products to oral cancer but did not identify any association with snus. Although, in a previous meta-analysis of SLT products from WHO regions, Gupta et al. (2019)[23] linked SLT products to increased risk of coronary heart disease (CHD), though a difference between SLT product types was not reported.

In another study of oral cancer risk, Araghi et al. (2020)[24] found no association between snus use and oral cancer using the pooled analysis of nine prospective observational studies from the Swedish Collaboration on Health Effects of Snus Use Study. Kopperud et al. (2023)[25] examined a small group (n = 1,363) of adolescents (18-20 years old) in southeastern Norway and found an increased instance of oral lesions and gingival retractions. Due to the small size of the study (only 216 participants used snus daily) and the homogenous population, this study does not provide conclusive evidence that can be extrapolated to the U.S. population. Further, in an analysis of Wave 1 through Wave 5 data from the PATH study examining the effects of tobacco product use on oral health, Silveira et al. (2022)[26] found no associations between snus users and incidence of oral health outcomes.

In a study of peripheral artery disease (PAD), Yuan et al. (2022)[27] found no increased risk of PAD for snus users. The study, which examined data from over 20,000 Swedish men across a decade (2009-2019), found while cigarette smoking was associated with higher risk of PAD, snus use did not increase PAD risk. Antoniewicz et al. (2022)[28] examined the impact of chronic snus use on endothelial function and arterial stiffness. Although the results showed that chronic snus use altered endothelial function and increased arterial stiffness, it is important to note the extremely limited sample size of 50 healthy men. Additionally, the chronic snus user data were compared only to nonsmokers and the data indicated alcohol use as a statistically significant confounder.

[21] Asthana, S., Labani, S., Kailash, U., Sinha, D. N., & Mehrotra, R. (2019). Association of Smokeless Tobacco Use and Oral Cancer: A Systematic Global Review and Meta-Analysis. Nicotine & tobacco research : *official journal of the Society for Research on Nicotine and Tobacco*, 21(9), 1162–1171. https://doi.org/10.1093/ntr/nty074

[22] Gupta, A. K., Kanaan, M., Siddiqi, K., Sinha, D. N., & Mehrotra, R. (2022). Oral Cancer Risk Assessment for Different Types of Smokeless Tobacco Products Sold Worldwide: A Review of Reviews and Meta-analyses. *Cancer prevention research* (Philadelphia, Pa.), 15(11), 733–746. https://doi.org/10.1158/1940-6207.CAPR-21-0567

[23] Gupta, R., Gupta, S., Sharma, S., Sinha, D. N., & Mehrotra, R. (2019). Risk of Coronary Heart Disease Among Smokeless Tobacco Users: Results of Systematic Review and Meta-Analysis of Global Data. Nicotine & tobacco research : *official journal of the Society for Research on Nicotine and Tobacco*, 21(1), 25–31. https://doi.org/10.1093/ntr/nty002

[24] Araghi et al. 2020. No association between moist oral snuff (snus) use and oral cancer: pooled analysis of nine prospective observational studies. Scand J Public Health 2021 Vol. 49 Issue 8 Pages 833-840. https://www.ncbi.nlm.nih.gov/pubmed/32466721

[25] Kopperud, S. E., Ansteinsson, V., Mdala, I., Becher, R., & Valen, H. (2023). Oral lesions associated with daily use of snus, a moist smokeless tobacco product. A cross-sectional study among Norwegian adolescents. *Acta odontologica Scandinavica*, 81(6), 473–478. https://doi.org/10.1080/00016357.2023.2178502

[26] Silveira, M. L., Everard, C. D., Sharma, E., Lauten, K., Alexandridis, A. A., Duffy, K., Taylor, E. V., Tolliver, E. A., Blanco, C., Compton, W. M., Kimmel, H. L., Iafolla, T., Hyland, A., & Chaffee, B. W. (2022). Tobacco Use and Incidence of Adverse Oral Health Outcomes Among US Adults in the Population Assessment of Tobacco and Health Study. *JAMA network ope*n, 5(12), e2245909. https://doi.org/10.1001/jamanetworkopen.2022.45909

[27] Yuan, S., Titova, O. E., Damrauer, S. M., Åkesson, A., & Larsson, S. C. (2022). Swedish snuff (snus) dipping, cigarette smoking, and risk of peripheral artery disease: a prospective cohort study. *Scientific reports*, 12(1), 12139. https://doi.org/10.1038/s41598-022-16467-x

[28] Antoniewicz, L., Kabele, M., Nilsson, U., Pourazar, J., Rankin, G., Bosson, J. A., & Lundbäck, M. (2022). Chronic snus use in healthy males alters endothelial function and increases arterial stiffness. *PloS one*, 17(6), e0268746. https://doi.org/10.1371/journal.pone.0268746

Two publications found no association between snus use and CVD, when controlling for confounders. Specifically, Titova et al. (2021)[29] found no increase in CVD mortality in a prospective cohort study of middle-aged and older individuals. The authors conclude "In this middle-aged and elderly Swedish population, current Swedish snus use was not associated with the risk of major heart and valvular diseases, abdominal aortic aneurysm, or CVD mortality in the entire study population, but was linked to increased risk of stroke in never smokers." They explain this finding as follows "[t]he possible explanation that we see the effect of snus use on the risk of stroke only in never smokers is that the majority of snus users in our study are former smokers (69%). Cigarette smoking is a well-established strong risk factor for CVDs and may mask the effect of snus in the analysis based on the entire cohort, i.e. residual confounding takes place." Similarly, Frobert et al. (2019)[30] found no increase in CVD mortality using data from the Swedish Coronary Angiography and Angioplasty Registry. The authors conclude "[s]nus use at admission for a first [Percutaneous Coronary Intervention] was not associated with a higher occurrence of all-cause mortality, new revascularization or heart failure hospitalization."

In contrast, Byhamre et al. (2020)[31] found an increase in CVD mortality in a pooled analysis of eight prospective studies of exclusive, Swedish male snus users compared to never tobacco users for data covering 1978-2010. Study design limitations and confounders include fixing tobacco use state at baseline (does not account for never-users initiating), the participants in the control group were not smokers, and the data were collected during a dramatic reduction in constituents. Further, the study observed an inverse-dose-response relationship between snus use and increased risk of CVD mortality. Overall and relative to the other publications, this study provides relatively weak evidence and does not address the risk of CVD in snus users relative to smokers. Rodu et al. (2021)[32] published a critique of this paper, noting several methodological flaws "…that render their results uninformative and possibly misleading."

In a systematic review of SLT products, Hajat et al. (2021)[33] examined data collected from 53 studies from numerous geographical regions. There were significant differences in association with all-cause mortality (ACM), CVD, and cancer between SLT products in different regions. In regions where snus is not the predominate SLT used, such as Asia, the Middle East, and Africa, there is a correlation between SLT use and increased ACM, CVD, and cancer. In European regions where snus is used, there was no increased risk of ACM, CVD, or cancer. Although, in a systematic review assessing cancer risk and mortality for snus users, Valen et al. (2023)[34] showed an association between snus use and increased cancer risk and cancer-specific mortality; the 15 studies included in the review spanned over 10 types of cancer and was limited to male data of snus users compared with nontobacco users. The study

[29] Titova et al. 2021. Swedish snuff (snus) and risk of cardiovascular disease and mortality: prospective cohort study of middle-aged and older individuals. *BMC Med* 2021 Vol. 19 Issue 1 Pages 111. https://www.ncbi.nlm.nih.gov/pubmed/33957912

[30] Frobert, O., Reitan, C., Hatsukami, D. K., Pernow, J., Omerovic, E., & Andell, P. (2019). Smokeless tobacco, snus, at admission for percutaneous coronary intervention and future risk for cardiac events. *Open heart*, *6*(2), e001109. https://doi.org/10.1136/openhrt-2019-001109

[31] Byhamre et al. 2020. Swedish snus use is associated with mortality: a pooled analysis of eight prospective studies. https://doi.org/10.1093/ije/dyaa197

[32] Rodu B and Plurphanswat N. Heterogeneity and other problems in a pooled analysis of snus use and mortality [version 1; peer review: 2 approved]. *F1000Research* 2021, 10:388 (https://doi.org/10.12688/f1000research.52127.1)

[33] Hajat, C., Stein, E., Ramstrom, L., Shantikumar, S., & Polosa, R. (2021). The health impact of smokeless tobacco products: a systematic review. *Harm reduction journal*, 18(1), 123. https://doi.org/10.1186/s12954-021-00557-6

[34] Valen, H., Becher, R., Vist, G. E., Holme, J. A., Mdala, I., Elvsaas, I. Ø., Alexander, J., Underland, V., Brinchmann, B. C., & Grimsrud, T. K. (2023). A systematic review of cancer risk among users of smokeless tobacco (Swedish snus) exclusively, compared with no use of tobacco. *International journal of cancer*, 153(12), 1942–1953. https://doi.org/10.1002/ijc.34643

concluded that the use of snus carries a cancer risk, however, the magnitude of the risk may be affected by user history and individual susceptibility.

These individual studies should be evaluated in context of the totality of evidence surrounding the health risks associated with snus use, and in context of the modified risk claim, which communicates a modified risk in comparison to combusted cigarette smoking and does not communicate an absence of risk. Therefore, this postmarket evidence reinforces the validity of the modified risk claim and does not raise new questions regarding the health risks associated with snus use.

5.2 Consumer Understanding and Perceptions

We also examined the impact of snus messaging on consumer understanding and perceptions in the scientific literature. Wackowski and colleagues (2022)[35] assessed MRTP claims related to snus and electronic nicotine delivery system (ENDS) products, with a focus on quantifying reductions in risk. A study of 57 current smokers and young adult nonsmokers participating in 12 focus groups, six of which focused on snus messaging and perceptions, found that messages stating snus and ENDS products have been estimated to be 90% and 95% less harmful than smoking cigarettes, respectively, are easy to understand and clearly communicate these products are less harmful than smoking cigarettes. The authors conclude such quantitative claims may be effective in gaining attention and persuading some audiences to switch to less harmful products like snus, although attribution to credible sources and active monitoring for unintended consequences (i.e., initiation by nonusers of tobacco) remain important considerations.

A separate study by Wackowski and colleagues (2021)[36] used Wave 3 PATH data (collection period 2015-2016 prior to MRTP claim authorization in 2019) to assess the extent to which cigarette smokers had seen advertising for ENDS, SLT, or snus indicating using these products is less harmful than cigarette smoking. Such advertising was less commonly perceived among cigarette smokers for SLT and snus (approximately 5% for each product category, respectively) than for ENDS (nearly 30%). Nevertheless, 24-27% of smokers who noticed 'less harmful' claims indicated they would use such products in the future, leading the authors to conclude MRTP claims may be an important motivator for some smokers to use reduced risk products. Lee et al. (2020) examined Wave 1-3 PATH data to find that use of SLT and snus was reported to predict increased quitting amongst smokers.

One study related to snus and consumer understanding and perceptions reported an analysis of 11,631 snus-related Twitter posts collected between March 11, 2021, and February 26, 2022.[37] The frequency of snus-related posts remained within a consistent range throughout the study period (generally 25-50 tweets per day), and a sentiment analysis indicated a positive sentiment was more prominent than a negative sentiment. Positive tweets focused on the harm reduction and smoking alternative properties of snus, whereas negative tweets focused on health concerns. Oral health concerns were the most commonly mentioned health category, although these were relatively

[35] Wackowski OA, O'Connor RJ, Diaz D, et al '95% less harmful'? Exploring reactions to quantitative modified risk claims for snus and e-cigarettes. *Tobacco Control* 2022; 31:730-736. https://doi.org/10.1136/tobaccocontrol-2020-056303

[36] Wackowski, O. A., O'Conner, R.J., and Pearson, J.L. (2021): Smokers' Exposure to Perceived Modified Risk Claims for E-Cigarettes, Snus, and Smokeless Tobacco in the United States, *Nicotine & Tobacco Research* 2021; 23:605-608, retrieved from https://doi.org/10.1093/ntr/ntaa159

[37] Chen, J., Xue, S., Xie, Z., Li, D. (2022): Perceptions and Discussions of Snus on Twitter: Observational Study. *JMIR Med Inform* 2022;10(8):e38174. Retrieved from: https://doi.org/10.2196/38174.

infrequent at less than 5% of the total set of snus-related tweets. Taken together, the findings from this study related to snus and consumer understanding and perceptions are consistent with the position that *General Snus* (and snus overall) remain APPH.

Numerous additional studies highlight the importance of including modified risk claims[38, 39, 40, 41] and demonstrate comprehension of the MRTP claims.[42] DeAtley et al. (2023)[43] examined the effects of MRTP claims on perceptions among racial and ethnic groups using three products authorized to include MRTP claims (General Snus Classic White, Philip Morris IQOS, and 22nd Century Group VLN cigarettes) and one not authorized (Juul Labs JUUL e-cigarette). This study found that "[n]ot including an MRTP claim resulted in an increased likelihood of trying a product, decreased concern of serious disease, lower perceived addictiveness" demonstrating consumers may misunderstand modified risk claims.

After the FDA authorized the MRTP claim for *General Snus*, Neilsen data from 19 U.S. states found no sales advantage gained from the claim relative to snus competitors but a relative increase in sales for all snus products. This indicates consumers may make determinations regarding product risk across the entire product class rather than attributing the modified risk to individual products[44].

We also monitor the literature to ensure that there are no deficiencies in the responsible marketing and controls implemented to restrict access to unintended audiences, particularly youth. Recent studies show that the exclusive use of SLT products amongst school-based youth trended downwards[45, 46]. Cheng et al. (2023)[47] found that "[l]ess than a quarter of youth (13–17 year olds) and less than a third of underage young adults (18–20 year olds) had heard of, or seen, snus", illustrating the efficacy of the responsible marketing and controls.

[38] Clarke, E., Thompson, K., Weaver, S., Thompson, J., & O'Connell, G. (2019). Snus: a compelling harm reduction alternative to cigarettes. *Harm reduction journal*, 16(1), 62. https://doi.org/10.1186/s12954-019-0335-1

[39] Wackowski, O. A., Manderski, M. T. B., Lewis, M. J., & Delnevo, C. D. (2019). The Impact of Smokeless Tobacco Risk Information on Smokers' Risk Perceptions and Use Intentions: A News Media Experiment. *Health communication*, 34(3), 325–332. https://doi.org/10.1080/10410236.2017.1407226

[40] Wackowski, O. A., Rashid, M., Greene, K. L., Lewis, M. J., & O'Connor, R. J. (2020). Smokers' and Young Adult Non-Smokers' Perceptions and Perceived Impact of Snus and E-Cigarette Modified Risk Messages. *International journal of environmental research and public health*, 17(18), 6807. https://doi.org/10.3390/ijerph17186807

[41] Lund, K. E., & Vedoy, T. F. (2019). Relative Risk Perceptions between Snus and Cigarettes in a Snus-Prevalent Society-An Observational Study over a 16 Year Period. *International journal of environmental research and public health*, 16(5), 879. https://doi.org/10.3390/ijerph16050879

[42] Pillitteri, J. L., Shiffman, S., Sembower, M. A., Polster, M. R., & Curtin, G. M. (2020). Assessing comprehension and perceptions of modified-risk information for snus among adult current cigarette smokers, former tobacco users, and never tobacco users. *Addictive behaviors reports*, 11, 100254. https://doi.org/10.1016/j.abrep.2020.100254

[43] DeAtley, T., Johnson, A. C., Stone, M. D., Audrain-McGovern, J., Mercincavage, M., & Strasser, A. A. (2023). Effects of Modified Tobacco Risk Products with Claims and Nicotine Features on Perceptions among Racial and Ethnic Groups. *International journal of environmental research and public health*, 20(15), 6454. https://doi.org/10.3390/ijerph20156454

[44] Liber, A. C., Seidenberg, A. B., & Pesko, M. F. (2023). MRTP claim authorisation and *General Snus* sales in the USA: evidence from a difference-in-differences model. *Tobacco control*, tc-2022-057890. Advance online publication. https://doi.org/10.1136/tc-2022-057890

[45] Dai, H. D., & Leventhal, A. M. (2023). Use of Traditional Smokeless, Snus, and Dissolvable Tobacco Among U.S. Youth. *American journal of preventive medicine*, 64(2), 204–212. https://doi.org/10.1016/j.amepre.2022.09.011

[46] 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*: *AJHP*, 37(8), 1078–1090. https://doi.org/10.1177/08901171231191557

[47] Cheng, H. G., Vansickel, A. R., & Largo, E. G. (2023). Awareness and use of tobacco products among underage individuals: findings from the altria client services underage tobacco use survey 2020-2022. *BMC public health*, 23(1), 662. https://doi.org/10.1186/s12889-023-15610-1

5.3 Tobacco Use Behavior and Impact to the Population as a Whole

We also monitor the literature for emerging evidence on population health impact of snus. One newly identified publication reported on the relationship between snus and alcohol use in a matched controlled population study of Norwegians (Watten and Watten, 2021).[48] Alcohol consumption and drinking habits in a sample of snus users was compared to a sample of age- and gender-matched nonusers (n = 1,043 in both samples). Users of snus had higher frequencies of drinking, intoxication, and excess drinking when compared to the matched nonusers. However, the snus user group also differed significantly in several socioeconomic and health-related variables, including general mental health, that were found to be related to alcohol consumption habits. While this study on snus and use behavior has implications for alcohol and nicotine treatment and rehabilitation, the findings do not conflict with the position that *General Snus* remains APPH.

In addition to monitoring the literature, the recently established Rutgers Center of Excellence in Rapid Surveillance in Tobacco will provide FDA with unprecedented, real-time data on tobacco and nicotine marketing, products, and consumer behaviors. This comprehensive data will allow FDA to monitor the market and consumer changes as close to real time as possible and intervene as necessary.[49]

We have not received feedback from the Agency on the provided literature, indicating the required literature search does not raise new questions of public health. In fact, the literature and decades of epidemiological data continue to reinforce and strengthen the original FDA determination that *General Snus* products are APPH and that the products remain APPH, with smoke-free alternatives playing a critical role in helping legal age nicotine users abandon cigarettes and accelerate progress at the population level. Based on the collective findings in the published scientific literature and the studies and surveillance we conducted, renewal of the modified risk order should be granted.

6. RESPONSIBLE MARKETING AND CONTROLS

Upon MRGO renewal by FDA, under section 911(g)(1) of the FD&C Act, we intend to continue to market the products in a manner that restricts access to *General Snus* products by unintended audiences, particularly youth.

Our responsible marketing practices encompass labeling, advertising, marketing, promotion, and other consumer-directed activities. We conform with the requirements and marketing restrictions included in the MGOs and MRGOs, respectively, for those products, and we report to the FDA annually. In addition to annual reporting, Swedish Match also complies with all FDA-mandated marketing rules and regulations, as well as those required by law. Specifically, all *General Snus* product labeling carries the congressionally required, rotating warnings at 30% of the two primary panels. We also require retailers to merchandise *General Snus* in non-self-serve locations unless the facility is an adult-only facility.

In addition to these requirements, we take additional voluntary measures to ensure responsible marketing practices are applied to our entire portfolio of TNPs, including *General Snus* products. We

[48] Watten R.G. and Watten, V.P. (2021): Snus and Alcohol: Mutually Rewarding Effects in the Brain? A Matched Controlled Population Study, Substance Abuse: *Research and Treatment* Volume 15: 1–9, retrieved from https://doi.org/10.1177/11782218211027124.

[49] https://www.fda.gov/tobacco-products/ctp-newsroom/fda-and-nih-award-funding-new-center-rapid-surveillance-tobacco

value transparency with our consumers and regulators, and we have a history of being proactive with marketing controls, including instituting age-gated marketing practices before they were required.

Specifically, we apply the following responsible marketing practices:

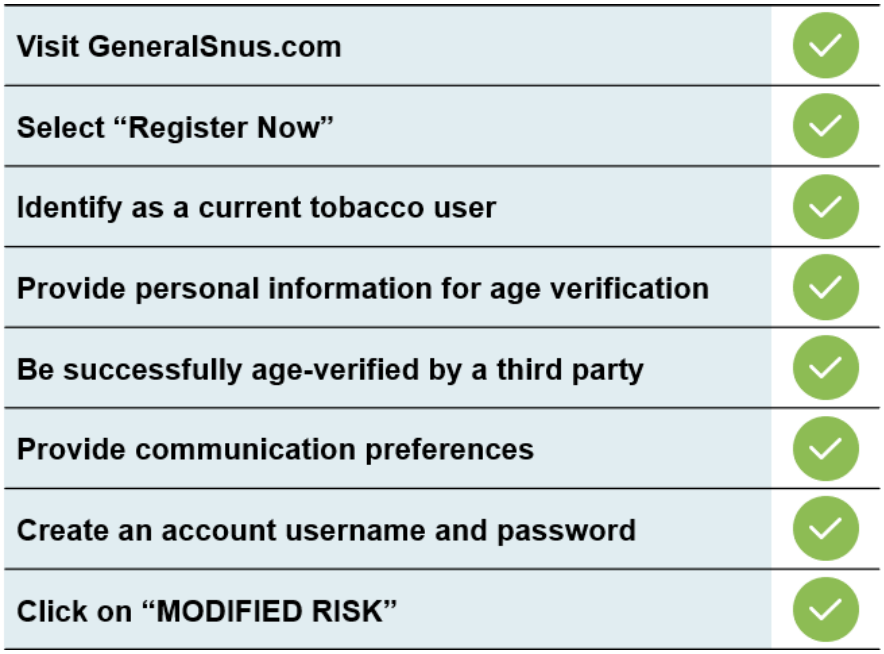
- We limit access to our website (GeneralSnus.com) to ONLY those confirmed to be at least 21 years old. We accomplish this through use of third-party age verification partners who match consumer information with government databases to confirm individuals' identity and age;
- We limit access to our website to self-reported current users of TNPs;
- We do NOT advertise outdoors or through television and other mass media vehicles;
- We use models/talent who are visibly over the age of 35;
- We do NOT engage with consumers on social media platforms that are not age-restricted;
- We do NOT use paid professional athlete endorsements or sponsorship; and
- We do NOT use social influencers in our marketing.

We also routinely analyze data on sales and distribution, product purchasers, delivery of advertising impressions, and media tracking and optimization. The data shows 99.3% of *General Snus* purchasers who provided their age were over age 25, and none were reported to be under age 21, consistent with the practice of restricting owned-retail store entry and purchase, face-to-face engagement, and e-commerce purchase to adults verified as age 21+. Where tracking is available, advertising impressions were delivered predominantly (over 99.2% in all tracked channels) to persons over age 25. These results are consistent with implementation of responsible age restriction and verification practices.

We have also been conservative in our use of the authorized modified risk claim. Currently, the claim, which was authorized as part of our 2019 MRTP, is currently only communicated on the *General Snus* website behind the previously discussed age-gate. To view the claim, a consumer would need to take a series of steps to gain access to the webpage where the claim is visible (**Figure 13**). They must visit GeneralSnus.com, select "Register Now", identify as a current tobacco user, provide personal information for age verification, be successfully age-verified, provide their communication preferences, create a username and password, and click on "Modified Risk."

While this process drastically limits the likelihood that the claim will be viewed by unintended audiences, it also limits the utility of the claim, making it difficult to reach intended consumers, who could achieve a reduction in health risks by switching completely to the products. We remain open to discussion with the FDA on ways to adjust the use of the claim to reach more smokers and SLT product users who could benefit from using our products.

Figure 13. Steps Required to Access the Modified Risk Claim



7. CONCLUSIONS

There is great opportunity to minimize harm from the use of combusted tobacco products by providing opportunities for legal age nicotine users to switch to modified risk alternatives like the authorized *General Snus* products. In addition, there is a need for effective education on the continuum of risk and ready access to authorized MRTP information by consumers. As Kozlowski and Abrams conclude, "[a] new reframing can align action plans to more powerfully and rapidly achieve population-level benefit and minimize harm to eliminate in our lifetime the use of the most deadly combustible tobacco products and thus prevent the premature deaths of 1 billion people projected to occur worldwide by 2100."[50]

The combined evidence from the original and renewal applications submitted in support of these products demonstrate *General Snus* products continue to satisfy the requirements of section 911(g)(1) of the FD&C Act. These products are appropriate to promote public health 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.

On March 16, 2023, FDA authorized U.S. Smokeless Tobacco Company's Copenhagen Classic Snuff as an MRTP[51], allowing the company to market the product with the claim, "IF YOU SMOKE, CONSIDER THIS: Switching completely to this product from cigarettes reduces risk of lung cancer." While *General Snus* is not identical to Copenhagen Classic Snuff, they are both SLT products, and this authorization provides additional support for the continued use of products like *General Snus* as less harmful alternatives to combusted tobacco products.

[50] Kozlowski, L.T., Abrams, D.B. Obsolete tobacco control themes can be hazardous to public health: the need for updating views on absolute product risks and harm reduction. *BMC Public Health* **16**, 432 (2016). https://doi.org/10.1186/s12889-016-3079-9

[51] https://www.fda.gov/media/166254/download?attachment

There is converging public health consensus that non-combusted SLT is less hazardous than combusted cigarettes:

- "On the continuum of risk, non-combustible tobacco products are more likely to reduce harm than a smoked form of tobacco for individuals who would otherwise be using conventional cigarettes."[52]

- "[U]sers of smokeless tobacco products generally have lower risk for tobacco-related morbidity and mortality than users of combustible tobacco products such as cigarettes."[53]

- "[T]hough SLT products are generally considered higher-risk than NRT, they are of considerably lower risk than continued smoking. The overall epidemiological literature supports that cigarette smokers who completely switch to SLT products are likely to substantially lower their risks of cardiovascular disease, lung cancer, and respiratory disease compared to smoking."[54]

As quoted in the last bullet, FDA's evaluation of SLT tobacco products as a class only reinforces its initial evaluation of *General Snus* as a modified risk product and provides additional justification to renew this MRTP claim authorization.

The accuracy of the determinations upon which the original orders were based has not changed. The PMSS submitted over the past eight years have provided FDA ample time and data to review the information upon which the orders were based, and the FDA has not taken any enforcement action to remove the products from market or to remove the MRTP designations. We continue to provide real-world evidence and data over the past decade demonstrating *General Snus* is a viable tobacco harm reduction approach for legal age nicotine users who currently smoke but are either unable or unwilling to quit the use of combustible products. There is no new scientific evidence to change FDA's original decision to grant these applications. The hierarchy of evidence supporting the modified risk information and authorization remains unchanged. Therefore, TPSAC should recommend FDA grant the MRGO renewals.

8. APPENDICES

- MGO Letters
- MRGO Letters
- TPL Executive Summaries
- Surveillance of Published Literature

[52] Zeller, Hatsukami et al. *The Strategic Dialogue on Tobacco Harm Reduction: A vision and blueprint for action in the US*, Tobacco Control, 18(4), 324-332, 2009. http://www.jstor.org/stable/27798615

[53] WHO Study Group on Tobacco Product Regulation (TobReg): The Scientific Basis for Tobacco Product Regulation, 951 Technical Reports Series (2008). https://books.google.com/books?id=-WpeaDp8sbcC

[54] FDA memorandum from September 10, 2020, entitled "Summary of Health Effects of Smokeless Tobacco Products for Epidemiology Branch Product Application Review" https://vaping.org/wp-content/uploads/2023/02/SLTComparativeHealthEffects.pdf

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Center for Tobacco Products
10903 New Hampshire Avenue
Silver Spring, MD 20993

November 10, 2015

MARKETING ORDER

Swedish Match North America, Inc.
Attention: Gerard Roerty, Jr., Vice President, General Counsel & Secretary
Two James Center
1021 East Cary Street, Suite 1600
Richmond, VA 23219
via Certified Mail

FDA Submission Tracking Number (STN): PM0000013

Dear Mr. Roerty:

The Food and Drug Administration (FDA) completed the review of your Premarket Tobacco Product Application (PMTA) submitted under section 910(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), for the following tobacco product:

Applicant:	Swedish Match North America, Inc.
Tobacco Product Name:[1]	General Classic Blend Portion White Large - 12ct
Tobacco Product Category:	Smokeless Tobacco
Tobacco Product Sub-Category:	Portioned Snus
Package Type:	Plastic Can
Package Quantity:	10.8 g
Characterizing Flavor:	None
Portion Count:	12 pouches
Portion Mass:	900 mg
Portion Length:	34 mm
Portion Width:	14 mm
Portion Thickness:	5 mm
Tobacco Cut Size:[2]	(b)(4) (b)(4) (b)(4)

[1] Brand/sub-brand or other commercial name used in commercial distribution
[2] The applicant provided (b)(4) to characterize the tobacco cut size. Therefore, the tobacco cut size cannot be represented with a single value and corresponding range limit.

Based on our review of your PMTA, we find permitting the new tobacco product specified above to be marketed is appropriate for the protection of public health, and that you have met the other requirements of section 910(c) of the FD C Act. Under the provisions of section 910, you may introduce or deliver for introduction into interstate commerce the new tobacco product specified above with the enclosed labeling.

RECORD RETENTION

Under section 910(f) of the FD C Act, we are requiring in this order that you retain the records listed below for a period of not less than 4 years from the date of distribution of the last batch of the new tobacco product specified above. These records must be legible, in the English language, and available for inspection and copying by officers or employees duly designated by the Secretary, upon request:

- PMTA submitted prior to product order
- Postmarket reports/postmarket status reports submitted to FDA, including adverse experiences and all relevant documentation associated with the experience
- Correspondence with FDA pertaining to authorized product
- Nonclinical or clinical study documentation including:
    - study protocols (including statistical analysis plan);
    - amendments showing the dates and reasons for each protocol revision;
    - Institutional Review Board (IRB) or Independent Ethics Committee (IEC) approvals;
    - Informed consent forms;
    - Correspondence with study monitors/investigators/contract research organizations/sponsors/IRB/IEC;
    - Investigator financial disclosure statements;
    - Progress reports;
    - Monitoring reports;
    - Adverse experience reports;
    - Case report forms/subject diaries/medical records/laboratory reports;
    - Subject data line listings/observations records;
    - Test article accountability records;
    - Study results/protocol summaries/study reports; and
    - Certifications and amendments to certifications.
- Records pertaining to the manufacture, in process and release testing, process (including any changes to the process, facility, or controls), packaging, and storage of product
- Records pertaining to the sale, marketing, distribution, or other disposition of the product
- Specimens of all labeling, labels, inserts/onserts, instructions, and other accompanying information
- Hazard analysis

POSTMARKET REPORTS

I. Serious and Unexpected Adverse Experiences Reporting

Under section 910(f) of the FD C Act, we are requiring in this order that you report to the FDA all adverse experiences that are both serious and unexpected and your analysis of the association between the adverse experience and the tobacco product **within 15 calendar days** after the report is received by you. These experiences may become known to you through a response to a customer complaint, request, or suggestion made as a result of an adverse experience, tobacco product defect, or failure reported to you; or identified in the literature or media. Your information should be submitted with a cover letter that includes the following text in the subject line: **SERIOUS UNEXPECTED ADVERSE EXPERIENCE REPORT for STN PM0000013**.

For purposes of reporting under this order, serious adverse experience means an adverse experience that results in any of the following outcomes:

- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect; or
- Any other adverse experience that, based upon appropriate medical judgment, may jeopardize the health of a person and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

For purposes of reporting under this order, unexpected adverse experience means an adverse experience occurring in one or more persons in which the nature, severity, or frequency of the experience is not consistent with:

- The known or foreseeable risks associated with the use or exposure to the tobacco product as described in the PMTA and other relevant sources of information, such as postmarket reports and studies;
- The expected natural progression of any underlying disease, disorder, or condition of the persons(s) experiencing the adverse experience and the person's predisposing risk factor profile for the adverse experience; or
- The results of nonclinical laboratory studies.

II. Manufacturing Deviations

You should promptly investigate all manufacturing deviations, including but not limited to those associated with processing, testing, packing, labeling, storage, holding and distribution. For products that have been distributed, if the deviation may negatively impact public health, you must promptly identify and report that deviation to the Center for Tobacco Products. See instructions below for submitting your regulatory correspondence.

III. Periodic Reporting

Under section 910(f) of the FD C Act, we are requiring in this order that you submit, on an annual basis, beginning October 2016, unless otherwise notified, the following information in a postmarketing annual report to help FDA determine whether continued marketing of your tobacco product is appropriate for the protection of public health or whether there are or may be grounds for withdrawing or temporarily suspending such order. For the 12- month reporting period, the report must include:

1. A single submission with a cover letter that includes the following text in your subject line: **PERIODIC REPORT for STN PM0000013**. The cover letter should include the STN and corresponding tobacco product name, applicant name, date of report, reporting period, and marketing order status outside the United States.
2. A summary of how the tobacco product continues to be appropriate for the protection of the public health which includes:
    a. A status report of ongoing studies and a summary of completed studies about the tobacco product conducted by, or on behalf of, the applicant;
    b. A summary of significant findings on publications not previously reported and include full articles. Any new scientific data (published or otherwise) should also be reported on the likelihood of product use by current users of tobacco products within the same tobacco product category, current users of tobacco products in other tobacco product categories, former users of any tobacco product, and youth and young adults;
    c. A summary of adverse experiences with this tobacco product reported to you, providing a listing and analysis (accompanied by a statement of any changes to the reference risk information and a summary of important risks, including the nature, frequency, and potential risk factors) of all adverse experiences including those serious and unexpected adverse experiences reported previously.
    d. A summary of sales and distribution of the tobacco product: Total U.S. sales reported in dollars, units, and volume with breakdowns by US census region, major retail markets, and channels in which the product is sold (e.g., convenience stores, food and drug markets, big box retailers, internet/online sales, tobacco specialty shops);
    e. Data on current product users. Data should be collected about new users, current users, those who have switched tobacco products, and multiple product users. The results should be broken down by key demographic variables including age, gender, and race/ethnicity. Also, any change in the intended target market for the product should be reported. The data described above may include sales data and post-marketing analysis.
3. A description of each change made to the manufacturing, facilities or controls during the reporting period, including:
    a. A comparison of each change to what was described in the PMTA;
    b. The rationale for making each change; and
    c. A certification that the reported change did not result in any modification (including a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient) of the tobacco product; the basis for concluding that each change did not result in any modification to the final product.

4.&A summary of all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution and indicate a deviation that may affect the characteristics of the final product.

5.&Full-color copies of all advertising for the tobacco product that has not been previously submitted, along with the original date the advertisements were first disseminated and the date the advertisements were discontinued; and

6. In all annual reports, include a description of any or all labeling changes and submit revised full color final printed labeling.
    a. The labeling should include all the panels, be presented in the actual size and color with legible text.
    b.&For the first annual report only, submit all final printed labeling (actual labeling for each required warning distributed with the product); include labels, inserts/onserts, instructions, and other accompanying information or materials for this product.

In accordance with 40 CFR 1506.6, we will make your environmental assessment publicly available.

This order authorizing the marketing of this new tobacco product does not mean FDA "approved" the new tobacco product specified above; therefore, you may not make any express or implied statement or representation directed to consumers that conveys, or misleads or would mislead consumers into believing, among other things, that the new tobacco product specified above is "approved" by FDA. See Section 301(tt) of the FD&C Act. This marketing order is subject to withdrawal or temporary suspension under section 910(d) of the FD&C Act.

We remind you that all regulated tobacco products, including the new tobacco product specified above, are subject to the requirements of Chapter IX of the FD C Act and its regulations. These requirements currently include, but are not limited to, annual registration, listing of products, listing of ingredients, reporting of harmful and potentially harmful constituents, and payment of user fees. There are also packaging, labeling, and advertising requirements with which you must comply. It is your responsibility to ensure the tobacco product specified above complies with all applicable statutory and regulatory requirements. FDA will monitor your compliance with these applicable statutes and regulations.

If you discontinue the manufacture, preparation, compounding or processing for commercial distribution this tobacco product and later decide to reintroduce the product into the market, please contact the Office of Science to discuss if additional information is necessary.

For more information on your responsibilities under the FD&C Act, we encourage you to visit our website at http://www.fda.gov/TobaccoProducts. You may also obtain information by contacting FDA's Center for Tobacco Products at 1-877-CTP-1373, AskCTP@fda.hhs.gov, or SmallBiz.Tobacco@fda.hhs.gov.

We remind you all regulatory correspondence can be submitted via the FDA Electronic Submission Gateway (http://www.fda.gov/esg) using eSubmitter or by mail to:

Food and Drug Administration
Center for Tobacco Products
Document Control Center
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

We are unable to accept regulatory submissions by electronic mail.

If you have questions, you may contact Asia Brown, MHSA, Regulatory Health Project Manager, at (240) 402-3833.

Sincerely,

Digitally signed by David Ashley -S
Date: 2015.11.10 06:01:52 -05'00'

David L. Ashley, Ph.D.
RADM, US Public Health Service
Director
Office of Science
Center for Tobacco Products

Enclosure

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Center for Tobacco Products
10903 New Hampshire Avenue
Silver Spring, MD 20993

November 10, 2015

MARKETING ORDER

Swedish Match North America, Inc.
Attention: Gerard Roerty, Jr., Vice President, General Counsel & Secretary
Two James Center
1021 East Cary Street, Suite 1600
Richmond, VA 23219
via Certified Mail

FDA Submission Tracking Number (STN): PM0000011

Dear Mr. Roerty:

The Food and Drug Administration (FDA) completed the review of your Premarket Tobacco Product Application (PMTA) submitted under section 910(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), for the following tobacco product:

Applicant:	Swedish Match North America, Inc.
Tobacco Product Name:[1]	General Dry Mint Portion Original Mini
Tobacco Product Category:	Smokeless Tobacco
Tobacco Product Sub-Category:	Portioned Snus
Package Type:	Plastic Can
Package Quantity:	6.0 g
Characterizing Flavor:	Mint
Portion Count:	20 pouches
Portion Mass:	300 mg
Portion Length:	28 mm
Portion Width:	14 mm
Portion Thickness:	5 mm
Tobacco Cut Size:[2]	(b)(4) (b)(4) (b)(4)

Based on our review of your PMTA, we find permitting the new tobacco product specified above to be marketed is appropriate for the protection of public health, and that you have met the other requirements of section 910(c) of the FD&C Act. Under the provisions of section 910, you may introduce or deliver for introduction into interstate commerce the new tobacco product specified above with the enclosed labeling.

---

[1] Brand/sub-brand or other commercial name used in commercial distribution
[2] The applicant provided (b)(4) to characterize the tobacco cut size. Therefore, the tobacco cut size cannot be represented with a single value and corresponding range limit.

RECORD RETENTION

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- Correspondence with FDA pertaining to authorized product
- Nonclinical or clinical study documentation including:
    - study protocols (including statistical analysis plan);
    - amendments showing the dates and reasons for each protocol revision;
    - Institutional Review Board (IRB) or Independent Ethics Committee (IEC) approvals;
    - Informed consent forms;
    - Correspondence with study monitors/investigators/contract research organizations/sponsors/IRB/IEC;
    - Investigator financial disclosure statements;
    - Progress reports;
    - Monitoring reports;
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    - Case report forms/subject diaries/medical records/laboratory reports;
    - Subject data line listings/observations records;
    - Test article accountability records;
    - Study results/protocol summaries/study reports; and
    - Certifications and amendments to certifications.
- Records pertaining to the manufacture, in process and release testing, process (including any changes to the process, facility, or controls), packaging, and storage of product
- Records pertaining to the sale, marketing, distribution, or other disposition of the product
- Specimens of all labeling, labels, inserts/onserts, instructions, and other accompanying information
- Hazard analysis

POSTMARKET REPORTS

I. Serious and Unexpected Adverse Experiences Reporting

Under section 910(f) of the FD C Act, we are requiring in this order that you report to the FDA all adverse experiences that are both serious and unexpected and your analysis of the association between the adverse experience and the tobacco product **within 15 calendar days** after the report is received by you. These experiences may become known to you through a response to a customer complaint, request, or suggestion made as a result of an adverse experience, tobacco product defect, or failure reported to you; or identified in the literature or media. Your information should be submitted with a cover letter that includes the following text in the subject line: **SERIOUS UNEXPECTED ADVERSE EXPERIENCE REPORT for STN PM0000011**.

For purposes of reporting under this order, serious adverse experience means an adverse experience that results in any of the following outcomes:

- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect; or
- Any other adverse experience that, based upon appropriate medical judgment, may jeopardize the health of a person and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

For purposes of reporting under this order, unexpected adverse experience means an adverse experience occurring in one or more persons in which the nature, severity, or frequency of the experience is not consistent with:

- The known or foreseeable risks associated with the use or exposure to the tobacco product as described in the PMTA and other relevant sources of information, such as postmarket reports and studies;
- The expected natural progression of any underlying disease, disorder, or condition of the persons(s) experiencing the adverse experience and the person's predisposing risk factor profile for the adverse experience; or
- The results of nonclinical laboratory studies.

II. Manufacturing Deviations

You should promptly investigate all manufacturing deviations, including but not limited to those associated with processing, testing, packing, labeling, storage, holding and distribution. For products that have been distributed, if the deviation may negatively impact public health, you must promptly identify and report that deviation to the Center for Tobacco Products. See instructions below for submitting your regulatory correspondence.

III. Periodic Reporting

Under section 910(f) of the FD C Act, we are requiring in this order that you submit, on an annual basis, beginning October 2016, unless otherwise notified, the following information in a postmarketing annual report to help FDA determine whether continued marketing of your tobacco product is appropriate for the protection of public health or whether there are or may be grounds for withdrawing or temporarily suspending such order. For the 12- month reporting period, the report must include:

1.&A single submission with a cover letter that includes the following text in your subject line: **PERIODIC REPORT for STN PM0000011**. The cover letter should include the STN and corresponding tobacco product name, applicant name, date of report, reporting period, and marketing order status outside the United States.
2. A summary of how the tobacco product continues to be appropriate for the protection of the public health which includes:
    a. A status report of ongoing studies and a summary of completed studies about the tobacco product conducted by, or on behalf of, the applicant;

b.&A summary of significant findings on publications not previously reported and include full articles. Any new scientific data (published or otherwise) should also be reported on the likelihood of product use by current users of tobacco products within the same tobacco product category, current users of tobacco products in other tobacco product categories, former users of any tobacco product, and youth and young adults;

c.&A summary of adverse experiences with this tobacco product reported to you, providing a listing and analysis (accompanied by a statement of any changes to the reference risk information and a summary of important risks, including the nature, frequency, and potential risk factors) of all adverse experiences including those serious and unexpected adverse experiences reported previously.

d.&A summary of sales and distribution of the tobacco product: Total U.S. sales reported in dollars, units, and volume with breakdowns by US census region, major retail markets, and channels in which the product is sold (e.g., convenience stores, food and drug markets, big box retailers, internet/online sales, tobacco specialty shops);

e.&Data on current product users. Data should be collected about new users, current users, those who have switched tobacco products, and multiple product users. The results should be broken down by key demographic variables including age, gender, and race/ethnicity. Also, any change in the intended target market for the product should be reported. The data described above may include sales data and post-marketing analysis.

3.&A description of each change made to the manufacturing, facilities or controls during the reporting period, including:

a. A comparison of each change to what was described in the PMTA;
b. The rationale for making each change; and
c. A certification that the reported change did not result in any modification (including a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient) of the tobacco product; the basis for concluding that each change did not result in any modification to the final product.

4.&A summary of all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution and indicate a deviation that may affect the characteristics of the final product.

5.&Full-color copies of all advertising for the tobacco product that has not been previously submitted, along with the original date the advertisements were first disseminated and the date the advertisements were discontinued; and

6. In all annual reports, include a description of any or all labeling changes and submit revised full color final printed labeling.

a. The labeling should include all the panels, be presented in the actual size and color with legible text.

b.&For the first annual report only, submit all final printed labeling (actual labeling for each required warning distributed with the product); include labels, inserts/onserts, instructions, and other accompanying information or materials for this product.

In accordance with 40 CFR 1506.6, we will make your environmental assessment publicly available.

This order authorizing the marketing of this new tobacco product does not mean FDA "approved" the new tobacco product specified above; therefore, you may not make any express or implied statement or representation directed to consumers that conveys, or misleads or would mislead consumers into believing, among other things, that the new tobacco product specified above is "approved" by FDA. See Section 301(tt) of the FD&C Act. This marketing order is subject to withdrawal or temporary suspension under section 910(d) of the FD&C Act.

We remind you that all regulated tobacco products, including the new tobacco product specified above, are subject to the requirements of Chapter IX of the FD C Act and its regulations. These requirements currently include, but are not limited to, annual registration, listing of products, listing of ingredients, reporting of harmful and potentially harmful constituents, and payment of user fees. There are also packaging, labeling, and advertising requirements with which you must comply. It is your responsibility to ensure the tobacco product specified above complies with all applicable statutory and regulatory requirements. FDA will monitor your compliance with these applicable statutes and regulations.

If you discontinue the manufacture, preparation, compounding or processing for commercial distribution this tobacco product and later decide to reintroduce the product into the market, please contact the Office of Science to discuss if additional information is necessary.

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We remind you all regulatory correspondence can be submitted via the FDA Electronic Submission Gateway (http://www.fda.gov/esg) using eSubmitter or by mail to:

Food and Drug Administration
Center for Tobacco Products
Document Control Center
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

We are unable to accept regulatory submissions by electronic mail.

If you have questions, you may contact Asia Brown, MHSA, Regulatory Health Project Manager, at (240) 402-3833.

Sincerely,

Digitally signed by David Ashley -S
Date: 2015.11.10 05:59:58 -05'00'

David L. Ashley, Ph.D.
RADM, US Public Health Service
Director
Office of Science
Center for Tobacco Products

Enclosure

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Center for Tobacco Products
10903 New Hampshire Avenue
Silver Spring, MD 20993

November 10, 2015

MARKETING ORDER

Swedish Match North America, Inc.
Attention: Gerard Roerty, Jr., Vice President, General Counsel & Secretary
Two James Center
1021 East Cary Street, Suite 1600
Richmond, VA 23219
via Certified Mail

FDA Submission Tracking Number (STN): PM0000010

Dear Mr. Roerty:

The Food and Drug Administration (FDA) completed the review of your Premarket Tobacco Product Application (PMTA) submitted under section 910(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), for the following tobacco product:

Applicant:	Swedish Match North America, Inc.
Tobacco Product Name:[1]	General Loose
Tobacco Product Category:	Smokeless Tobacco
Tobacco Product Sub-Category:	Loose Snus
Package Type:	Cardboard Can with Plastic Lid
Package Quantity:	45.0 g
Characterizing Flavor:	None
Tobacco Cut Size:[2]	(b)(4) (b)(4) (b)(4)

Based on our review of your PMTA, we find permitting the new tobacco product specified above to be marketed is appropriate for the protection of public health, and that you have met the other requirements of section 910(c) of the FD&C Act. Under the provisions of section 910, you may introduce or deliver for introduction into interstate commerce the new tobacco product specified above with the enclosed labeling.

[1] Brand/sub-brand or other commercial name used in commercial distribution
[2] The applicant provided (b)(4) to characterize the tobacco cut size. Therefore, the tobacco cut size cannot be represented with a single value and corresponding range limit.

RECORD RETENTION

Under section 910(f) of the FD C Act, we are requiring in this order that you retain the records listed below for a period of not less than 4 years from the date of distribution of the last batch of the new tobacco product specified above. These records must be legible, in the English language, and available for inspection and copying by officers or employees duly designated by the Secretary, upon request:

- PMTA submitted prior to product order
- Postmarket reports/postmarket status reports submitted to FDA, including adverse experiences and all relevant documentation associated with the experience
- Correspondence with FDA pertaining to authorized product
- Nonclinical or clinical study documentation including:
    - study protocols (including statistical analysis plan);
    - amendments showing the dates and reasons for each protocol revision;
    - Institutional Review Board (IRB) or Independent Ethics Committee (IEC) approvals;
    - Informed consent forms;
    - Correspondence with study monitors/investigators/contract research organizations/sponsors/IRB/IEC;
    - Investigator financial disclosure statements;
    - Progress reports;
    - Monitoring reports;
    - Adverse experience reports;
    - Case report forms/subject diaries/medical records/laboratory reports;
    - Subject data line listings/observations records;
    - Test article accountability records;
    - Study results/protocol summaries/study reports; and
    - Certifications and amendments to certifications.
- Records pertaining to the manufacture, in process and release testing, process (including any changes to the process, facility, or controls), packaging, and storage of product
- Records pertaining to the sale, marketing, distribution, or other disposition of the product
- Specimens of all labeling, labels, inserts/onserts, instructions, and other accompanying information
- Hazard analysis

POSTMARKET REPORTS

I. Serious and Unexpected Adverse Experiences Reporting

Under section 910(f) of the FD C Act, we are requiring in this order that you report to the FDA all adverse experiences that are both serious and unexpected and your analysis of the association between the adverse experience and the tobacco product **within 15 calendar days** after the report is received by you. These experiences may become known to you through a response to a customer complaint, request, or suggestion made as a result of an adverse experience, tobacco product defect, or failure reported to you; or identified in the literature or media. Your information should be submitted with a cover letter that includes the following text in the subject line: **SERIOUS UNEXPECTED ADVERSE EXPERIENCE REPORT for STN PM0000010**.

For purposes of reporting under this order, serious adverse experience means an adverse experience that results in any of the following outcomes:

- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect; or
- Any other adverse experience that, based upon appropriate medical judgment, may jeopardize the health of a person and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

For purposes of reporting under this order, unexpected adverse experience means an adverse experience occurring in one or more persons in which the nature, severity, or frequency of the experience is not consistent with:

- The known or foreseeable risks associated with the use or exposure to the tobacco product as described in the PMTA and other relevant sources of information, such as postmarket reports and studies;
- The expected natural progression of any underlying disease, disorder, or condition of the persons(s) experiencing the adverse experience and the person's predisposing risk factor profile for the adverse experience; or
- The results of nonclinical laboratory studies.

II. Manufacturing Deviations

You should promptly investigate all manufacturing deviations, including but not limited to those associated with processing, testing, packing, labeling, storage, holding and distribution. For products that have been distributed, if the deviation may negatively impact public health, you must promptly identify and report that deviation to the Center for Tobacco Products. See instructions below for submitting your regulatory correspondence.

III. Periodic Reporting

Under section 910(f) of the FD C Act, we are requiring in this order that you submit, on an annual basis, beginning October 2016, unless otherwise notified, the following information in a postmarketing annual report to help FDA determine whether continued marketing of your tobacco product is appropriate for the protection of public health or whether there are or may be grounds for withdrawing or temporarily suspending such order. For the 12- month reporting period, the report must include:

1.&A single submission with a cover letter that includes the following text in your subject line: **PERIODIC REPORT for STN PM0000010**. The cover letter should include the STN and corresponding tobacco product name, applicant name, date of report, reporting period, and marketing order status outside the United States.
2. A summary of how the tobacco product continues to be appropriate for the protection of the public health which includes:
    a. A status report of ongoing studies and a summary of completed studies about the tobacco product conducted by, or on behalf of, the applicant;

b.&A summary of significant findings on publications not previously reported and include full articles. Any new scientific data (published or otherwise) should also be reported on the likelihood of product use by current users of tobacco products within the same tobacco product category, current users of tobacco products in other tobacco product categories, former users of any tobacco product, and youth and young adults;

c.&A summary of adverse experiences with this tobacco product reported to you, providing a listing and analysis (accompanied by a statement of any changes to the reference risk information and a summary of important risks, including the nature, frequency, and potential risk factors) of all adverse experiences including those serious and unexpected adverse experiences reported previously.

d.&A summary of sales and distribution of the tobacco product: Total U.S. sales reported in dollars, units, and volume with breakdowns by US census region, major retail markets, and channels in which the product is sold (e.g., convenience stores, food and drug markets, big box retailers, internet/online sales, tobacco specialty shops);

e.&Data on current product users. Data should be collected about new users, current users, those who have switched tobacco products, and multiple product users. The results should be broken down by key demographic variables including age, gender, and race/ethnicity. Also, any change in the intended target market for the product should be reported. The data described above may include sales data and post-marketing analysis.

3.&A description of each change made to the manufacturing, facilities or controls during the reporting period, including:

a. A comparison of each change to what was described in the PMTA;
b. The rationale for making each change; and
c. A certification that the reported change did not result in any modification (including a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient) of the tobacco product; the basis for concluding that each change did not result in any modification to the final product.

4.&A summary of all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution and indicate a deviation that may affect the characteristics of the final product.

5.&Full-color copies of all advertising for the tobacco product that has not been previously submitted, along with the original date the advertisements were first disseminated and the date the advertisements were discontinued; and

6. In all annual reports, include a description of any or all labeling changes and submit revised full color final printed labeling.

a. The labeling should include all the panels, be presented in the actual size and color with legible text.

b.&For the first annual report only, submit all final printed labeling (actual labeling for each required warning distributed with the product); include labels, inserts/onserts, instructions, and other accompanying information or materials for this product.

In accordance with 40 CFR 1506.6, we will make your environmental assessment publicly available.

This order authorizing the marketing of this new tobacco product does not mean FDA "approved" the new tobacco product specified above; therefore, you may not make any express or implied statement or representation directed to consumers that conveys, or misleads or would mislead consumers into believing, among other things, that the new tobacco product specified above is "approved" by FDA. See Section 301(tt) of the FD&C Act. This marketing order is subject to withdrawal or temporary suspension under section 910(d) of the FD&C Act.

We remind you that all regulated tobacco products, including the new tobacco product specified above, are subject to the requirements of Chapter IX of the FD C Act and its regulations. These requirements currently include, but are not limited to, annual registration, listing of products, listing of ingredients, reporting of harmful and potentially harmful constituents, and payment of user fees. There are also packaging, labeling, and advertising requirements with which you must comply. It is your responsibility to ensure the tobacco product specified above complies with all applicable statutory and regulatory requirements. FDA will monitor your compliance with these applicable statutes and regulations.

If you discontinue the manufacture, preparation, compounding or processing for commercial distribution this tobacco product and later decide to reintroduce the product into the market, please contact the Office of Science to discuss if additional information is necessary.

For more information on your responsibilities under the FD&C Act, we encourage you to visit our website at http://www.fda.gov/TobaccoProducts. You may also obtain information by contacting FDA's Center for Tobacco Products at 1-877-CTP-1373, AskCTP@fda.hhs.gov, or SmallBiz.Tobacco@fda.hhs.gov.

We remind you all regulatory correspondence can be submitted via the FDA Electronic Submission Gateway (http://www.fda.gov/esg) using eSubmitter or by mail to:

Food and Drug Administration
Center for Tobacco Products
Document Control Center
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

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If you have questions, you may contact Asia Brown, MHSA, Regulatory Health Project Manager, at (240) 402-3833.

Sincerely,

Digitally signed by David Ashley -S
Date: 2015.11.10 05:58:03 -05'00'

David L. Ashley, Ph.D.
RADM, US Public Health Service
Director
Office of Science
Center for Tobacco Products

Enclosure

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Center for Tobacco Products
10903 New Hampshire Avenue
Silver Spring, MD 20993

November 10, 2015

MARKETING ORDER

Swedish Match North America, Inc.
Attention: Gerard Roerty, Jr., Vice President, General Counsel & Secretary
Two James Center
1021 East Cary Street, Suite 1600
Richmond, VA 23219
via Certified Mail

FDA Submission Tracking Number (STN): PM0000015

Dear Mr. Roerty:

The Food and Drug Administration (FDA) completed the review of your Premarket Tobacco Product Application (PMTA) submitted under section 910(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), for the following tobacco product:

Applicant:	Swedish Match North America, Inc.
Tobacco Product Name:[1]	General Nordic Mint Portion White Large - 12ct
Tobacco Product Category:	Smokeless Tobacco
Tobacco Product Sub-Category:	Portioned Snus
Package Type:	Plastic Can
Package Quantity:	10.8 g
Characterizing Flavor:	Mint
Portion Count:	12 pouches
Portion Mass:	900 mg
Portion Length:	34 mm
Portion Width:	14 mm
Portion Thickness:	5 mm
Tobacco Cut Size:[2]	(b)(4) (b)(4) (b)(4)

[1] Brand/sub-brand or other commercial name used in commercial distribution
[2] The applicant provided (b)(4) to characterize the tobacco cut size. Therefore, the tobacco cut size cannot be represented with a single value and corresponding range limit.

Based on our review of your PMTA, we find permitting the new tobacco product specified above to be marketed is appropriate for the protection of public health, and that you have met the other requirements of section 910(c) of the FD C Act. Under the provisions of section 910, you may introduce or deliver for introduction into interstate commerce the new tobacco product specified above with the enclosed labeling.

RECORD RETENTION

Under section 910(f) of the FD C Act, we are requiring in this order that you retain the records listed below for a period of not less than 4 years from the date of distribution of the last batch of the new tobacco product specified above. These records must be legible, in the English language, and available for inspection and copying by officers or employees duly designated by the Secretary, upon request:

- PMTA submitted prior to product order
- Postmarket reports/postmarket status reports submitted to FDA, including adverse experiences and all relevant documentation associated with the experience
- Correspondence with FDA pertaining to authorized product
- Nonclinical or clinical study documentation including:
    - study protocols (including statistical analysis plan);
    - amendments showing the dates and reasons for each protocol revision;
    - Institutional Review Board (IRB) or Independent Ethics Committee (IEC) approvals;
    - Informed consent forms;
    - Correspondence with study monitors/investigators/contract research organizations/sponsors/IRB/IEC;
    - Investigator financial disclosure statements;
    - Progress reports;
    - Monitoring reports;
    - Adverse experience reports;
    - Case report forms/subject diaries/medical records/laboratory reports;
    - Subject data line listings/observations records;
    - Test article accountability records;
    - Study results/protocol summaries/study reports; and
    - Certifications and amendments to certifications.
- Records pertaining to the manufacture, in process and release testing, process (including any changes to the process, facility, or controls), packaging, and storage of product
- Records pertaining to the sale, marketing, distribution, or other disposition of the product
- Specimens of all labeling, labels, inserts/onserts, instructions, and other accompanying information
- Hazard analysis

POSTMARKET REPORTS

I. Serious and Unexpected Adverse Experiences Reporting

Under section 910(f) of the FD C Act, we are requiring in this order that you report to the FDA all adverse experiences that are both serious and unexpected and your analysis of the association between the adverse experience and the tobacco product **within 15 calendar days** after the report is received by you. These experiences may become known to you through a response to a customer complaint, request, or suggestion made as a result of an adverse experience, tobacco product defect, or failure reported to you; or identified in the literature or media. Your information should be submitted with a cover letter that includes the following text in the subject line: **SERIOUS UNEXPECTED ADVERSE EXPERIENCE REPORT for STN PM0000015**.

For purposes of reporting under this order, serious adverse experience means an adverse experience that results in any of the following outcomes:

- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect; or
- Any other adverse experience that, based upon appropriate medical judgment, may jeopardize the health of a person and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

For purposes of reporting under this order, unexpected adverse experience means an adverse experience occurring in one or more persons in which the nature, severity, or frequency of the experience is not consistent with:

- The known or foreseeable risks associated with the use or exposure to the tobacco product as described in the PMTA and other relevant sources of information, such as postmarket reports and studies;
- The expected natural progression of any underlying disease, disorder, or condition of the persons(s) experiencing the adverse experience and the person's predisposing risk factor profile for the adverse experience; or
- The results of nonclinical laboratory studies.

II. Manufacturing Deviations

You should promptly investigate all manufacturing deviations, including but not limited to those associated with processing, testing, packing, labeling, storage, holding and distribution. For products that have been distributed, if the deviation may negatively impact public health, you must promptly identify and report that deviation to the Center for Tobacco Products. See instructions below for submitting your regulatory correspondence.

III. Periodic Reporting

Under section 910(f) of the FD C Act, we are requiring in this order that you submit, on an annual basis, beginning October 2016, unless otherwise notified, the following information in a postmarketing annual report to help FDA determine whether continued marketing of your tobacco product is appropriate for the protection of public health or whether there are or may be grounds for withdrawing or temporarily suspending such order. For the 12- month reporting period, the report must include:

1. A single submission with a cover letter that includes the following text in your subject line: **PERIODIC REPORT for STN PM0000015**. The cover letter should include the STN and corresponding tobacco product name, applicant name, date of report, reporting period, and marketing order status outside the United States.
2. A summary of how the tobacco product continues to be appropriate for the protection of the public health which includes:
    a. A status report of ongoing studies and a summary of completed studies about the tobacco product conducted by, or on behalf of, the applicant;
    b. A summary of significant findings on publications not previously reported and include full articles. Any new scientific data (published or otherwise) should also be reported on the likelihood of product use by current users of tobacco products within the same tobacco product category, current users of tobacco products in other tobacco product categories, former users of any tobacco product, and youth and young adults;
    c. A summary of adverse experiences with this tobacco product reported to you, providing a listing and analysis (accompanied by a statement of any changes to the reference risk information and a summary of important risks, including the nature, frequency, and potential risk factors) of all adverse experiences including those serious and unexpected adverse experiences reported previously.
    d. A summary of sales and distribution of the tobacco product: Total U.S. sales reported in dollars, units, and volume with breakdowns by US census region, major retail markets, and channels in which the product is sold (e.g., convenience stores, food and drug markets, big box retailers, internet/online sales, tobacco specialty shops);
    e. Data on current product users. Data should be collected about new users, current users, those who have switched tobacco products, and multiple product users. The results should be broken down by key demographic variables including age, gender, and race/ethnicity. Also, any change in the intended target market for the product should be reported. The data described above may include sales data and post-marketing analysis.
3. A description of each change made to the manufacturing, facilities or controls during the reporting period, including:
    a. A comparison of each change to what was described in the PMTA;
    b. The rationale for making each change; and
    c. A certification that the reported change did not result in any modification (including a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient) of the tobacco product; the basis for concluding that each change did not result in any modification to the final product.

4.&A summary of all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution and indicate a deviation that may affect the characteristics of the final product.

5.&Full-color copies of all advertising for the tobacco product that has not been previously submitted, along with the original date the advertisements were first disseminated and the date the advertisements were discontinued; and

6. In all annual reports, include a description of any or all labeling changes and submit revised full color final printed labeling.
    a. The labeling should include all the panels, be presented in the actual size and color with legible text.
    b.&For the first annual report only, submit all final printed labeling (actual labeling for each required warning distributed with the product); include labels, inserts/onserts, instructions, and other accompanying information or materials for this product.

In accordance with 40 CFR 1506.6, we will make your environmental assessment publicly available.

This order authorizing the marketing of this new tobacco product does not mean FDA "approved" the new tobacco product specified above; therefore, you may not make any express or implied statement or representation directed to consumers that conveys, or misleads or would mislead consumers into believing, among other things, that the new tobacco product specified above is "approved" by FDA. See Section 301(tt) of the FD&C Act. This marketing order is subject to withdrawal or temporary suspension under section 910(d) of the FD&C Act.

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If you discontinue the manufacture, preparation, compounding or processing for commercial distribution this tobacco product and later decide to reintroduce the product into the market, please contact the Office of Science to discuss if additional information is necessary.

For more information on your responsibilities under the FD&C Act, we encourage you to visit our website at http://www.fda.gov/TobaccoProducts. You may also obtain information by contacting FDA's Center for Tobacco Products at 1-877-CTP-1373, AskCTP@fda.hhs.gov, or SmallBiz.Tobacco@fda.hhs.gov.

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Food and Drug Administration
Center for Tobacco Products
Document Control Center
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

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If you have questions, you may contact Asia Brown, MHSA, Regulatory Health Project Manager, at (240) 402-3833.

Sincerely,

Digitally signed by David Ashley -S
Date: 2015.11.10 06:04:40 -05'00'

David L. Ashley, Ph.D.
RADM, US Public Health Service
Director
Office of Science
Center for Tobacco Products

Enclosure

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Center for Tobacco Products
10903 New Hampshire Avenue
Silver Spring, MD 20993

November 10, 2015

MARKETING ORDER

Swedish Match North America, Inc.
Attention: Gerard Roerty, Jr., Vice President, General Counsel & Secretary
Two James Center
1021 East Cary Street, Suite 1600
Richmond, VA 23219
via Certified Mail

FDA Submission Tracking Number (STN): PM0000014

Dear Mr. Roerty:

The Food and Drug Administration (FDA) completed the review of your Premarket Tobacco Product Application (PMTA) submitted under section 910(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), for the following tobacco product:

Applicant:	Swedish Match North America, Inc.
Tobacco Product Name:[1]	General Mint Portion White Large
Tobacco Product Category:	Smokeless Tobacco
Tobacco Product Sub-Category:	Portioned Snus
Package Type:	Plastic Can
Package Quantity:	24.0 g
Characterizing Flavor:	Mint
Portion Count:	24 pouches
Portion Mass:	1000 mg
Portion Length:	34 mm
Portion Width:	18 mm
Portion Thickness:	5.5 mm
Tobacco Cut Size:[2]	(b)(4) (b)(4) (b)(4)

Based on our review of your PMTA, we find permitting the new tobacco product specified above to be marketed is appropriate for the protection of public health, and that you have met the other requirements of section 910(c) of the FD&C Act. Under the provisions of section 910, you may introduce or deliver for introduction into interstate commerce the new tobacco product specified above with the enclosed labeling.

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[1] Brand/sub-brand or other commercial name used in commercial distribution
[2] The applicant provided (b)(4) to characterize the tobacco cut size. Therefore, the tobacco cut size cannot be represented with a single value and corresponding range limit.

RECORD RETENTION

Under section 910(f) of the FD C Act, we are requiring in this order that you retain the records listed below for a period of not less than 4 years from the date of distribution of the last batch of the new tobacco product specified above. These records must be legible, in the English language, and available for inspection and copying by officers or employees duly designated by the Secretary, upon request:

- PMTA submitted prior to product order
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- Correspondence with FDA pertaining to authorized product
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    - study protocols (including statistical analysis plan);
    - amendments showing the dates and reasons for each protocol revision;
    - Institutional Review Board (IRB) or Independent Ethics Committee (IEC) approvals;
    - Informed consent forms;
    - Correspondence with study monitors/investigators/contract research organizations/sponsors/IRB/IEC;
    - Investigator financial disclosure statements;
    - Progress reports;
    - Monitoring reports;
    - Adverse experience reports;
    - Case report forms/subject diaries/medical records/laboratory reports;
    - Subject data line listings/observations records;
    - Test article accountability records;
    - Study results/protocol summaries/study reports; and
    - Certifications and amendments to certifications.
- Records pertaining to the manufacture, in process and release testing, process (including any changes to the process, facility, or controls), packaging, and storage of product
- Records pertaining to the sale, marketing, distribution, or other disposition of the product
- Specimens of all labeling, labels, inserts/onserts, instructions, and other accompanying information
- Hazard analysis

POSTMARKET REPORTS

I. Serious and Unexpected Adverse Experiences Reporting

Under section 910(f) of the FD C Act, we are requiring in this order that you report to the FDA all adverse experiences that are both serious and unexpected and your analysis of the association between the adverse experience and the tobacco product **within 15 calendar days** after the report is received by you. These experiences may become known to you through a response to a customer complaint, request, or suggestion made as a result of an adverse experience, tobacco product defect, or failure reported to you; or identified in the literature or media. Your information should be submitted with a cover letter that includes the following text in the subject line: **SERIOUS UNEXPECTED ADVERSE EXPERIENCE REPORT for STN PM0000014**.

For purposes of reporting under this order, serious adverse experience means an adverse experience that results in any of the following outcomes:

- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect; or
- Any other adverse experience that, based upon appropriate medical judgment, may jeopardize the health of a person and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

For purposes of reporting under this order, unexpected adverse experience means an adverse experience occurring in one or more persons in which the nature, severity, or frequency of the experience is not consistent with:

- The known or foreseeable risks associated with the use or exposure to the tobacco product as described in the PMTA and other relevant sources of information, such as postmarket reports and studies;
- The expected natural progression of any underlying disease, disorder, or condition of the persons(s) experiencing the adverse experience and the person's predisposing risk factor profile for the adverse experience; or
- The results of nonclinical laboratory studies.

II. Manufacturing Deviations

You should promptly investigate all manufacturing deviations, including but not limited to those associated with processing, testing, packing, labeling, storage, holding and distribution. For products that have been distributed, if the deviation may negatively impact public health, you must promptly identify and report that deviation to the Center for Tobacco Products. See instructions below for submitting your regulatory correspondence.

III. Periodic Reporting

Under section 910(f) of the FD C Act, we are requiring in this order that you submit, on an annual basis, beginning October 2016, unless otherwise notified, the following information in a postmarketing annual report to help FDA determine whether continued marketing of your tobacco product is appropriate for the protection of public health or whether there are or may be grounds for withdrawing or temporarily suspending such order. For the 12- month reporting period, the report must include:

1.&A single submission with a cover letter that includes the following text in your subject line: **PERIODIC REPORT for STN PM0000014**. The cover letter should include the STN and corresponding tobacco product name, applicant name, date of report, reporting period, and marketing order status outside the United States.
2. A summary of how the tobacco product continues to be appropriate for the protection of the public health which includes:
    a. A status report of ongoing studies and a summary of completed studies about the tobacco product conducted by, or on behalf of, the applicant;

b.&A summary of significant findings on publications not previously reported and include full articles. Any new scientific data (published or otherwise) should also be reported on the likelihood of product use by current users of tobacco products within the same tobacco product category, current users of tobacco products in other tobacco product categories, former users of any tobacco product, and youth and young adults;

c.&A summary of adverse experiences with this tobacco product reported to you, providing a listing and analysis (accompanied by a statement of any changes to the reference risk information and a summary of important risks, including the nature, frequency, and potential risk factors) of all adverse experiences including those serious and unexpected adverse experiences reported previously.

d.&A summary of sales and distribution of the tobacco product: Total U.S. sales reported in dollars, units, and volume with breakdowns by US census region, major retail markets, and channels in which the product is sold (e.g., convenience stores, food and drug markets, big box retailers, internet/online sales, tobacco specialty shops);

e.&Data on current product users. Data should be collected about new users, current users, those who have switched tobacco products, and multiple product users. The results should be broken down by key demographic variables including age, gender, and race/ethnicity. Also, any change in the intended target market for the product should be reported. The data described above may include sales data and post-marketing analysis.

3.&A description of each change made to the manufacturing, facilities or controls during the reporting period, including:

a. A comparison of each change to what was described in the PMTA;
b. The rationale for making each change; and
c. A certification that the reported change did not result in any modification (including a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient) of the tobacco product; the basis for concluding that each change did not result in any modification to the final product.

4.&A summary of all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution and indicate a deviation that may affect the characteristics of the final product.

5.&Full-color copies of all advertising for the tobacco product that has not been previously submitted, along with the original date the advertisements were first disseminated and the date the advertisements were discontinued; and

6. In all annual reports, include a description of any or all labeling changes and submit revised full color final printed labeling.

a. The labeling should include all the panels, be presented in the actual size and color with legible text.

b.&For the first annual report only, submit all final printed labeling (actual labeling for each required warning distributed with the product); include labels, inserts/onserts, instructions, and other accompanying information or materials for this product.

In accordance with 40 CFR 1506.6, we will make your environmental assessment publicly available.

This order authorizing the marketing of this new tobacco product does not mean FDA "approved" the new tobacco product specified above; therefore, you may not make any express or implied statement or representation directed to consumers that conveys, or misleads or would mislead consumers into believing, among other things, that the new tobacco product specified above is "approved" by FDA. See Section 301(tt) of the FD&C Act. This marketing order is subject to withdrawal or temporary suspension under section 910(d) of the FD&C Act.

We remind you that all regulated tobacco products, including the new tobacco product specified above, are subject to the requirements of Chapter IX of the FD C Act and its regulations. These requirements currently include, but are not limited to, annual registration, listing of products, listing of ingredients, reporting of harmful and potentially harmful constituents, and payment of user fees. There are also packaging, labeling, and advertising requirements with which you must comply. It is your responsibility to ensure the tobacco product specified above complies with all applicable statutory and regulatory requirements. FDA will monitor your compliance with these applicable statutes and regulations.

If you discontinue the manufacture, preparation, compounding or processing for commercial distribution this tobacco product and later decide to reintroduce the product into the market, please contact the Office of Science to discuss if additional information is necessary.

For more information on your responsibilities under the FD&C Act, we encourage you to visit our website at http://www.fda.gov/TobaccoProducts. You may also obtain information by contacting FDA's Center for Tobacco Products at 1-877-CTP-1373, AskCTP@fda.hhs.gov, or SmallBiz.Tobacco@fda.hhs.gov.

We remind you all regulatory correspondence can be submitted via the FDA Electronic Submission Gateway (http://www.fda.gov/esg) using eSubmitter or by mail to:

Food and Drug Administration
Center for Tobacco Products
Document Control Center
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

We are unable to accept regulatory submissions by electronic mail.

If you have questions, you may contact Asia Brown, MHSA, Regulatory Health Project Manager, at (240) 402-3833.

Sincerely,

Digitally signed by David Ashley -S
Date: 2015.11.10 06:03:46 -05'00'

David L. Ashley, Ph.D.
RADM, US Public Health Service
Director
Office of Science
Center for Tobacco Products

Enclosure

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Center for Tobacco Products
10903 New Hampshire Avenue
Silver Spring, MD 20993

November 10, 2015

MARKETING ORDER

Swedish Match North America, Inc.
Attention: Gerard Roerty, Jr., Vice President, General Counsel & Secretary
Two James Center
1021 East Cary Street, Suite 1600
Richmond, VA 23219
via Certified Mail

FDA Submission Tracking Number (STN): PM0000012

Dear Mr. Roerty:

The Food and Drug Administration (FDA) completed the review of your Premarket Tobacco Product Application (PMTA) submitted under section 910(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), for the following tobacco product:

Applicant:	Swedish Match North America, Inc.
Tobacco Product Name:[1]	General Portion Original Large
Tobacco Product Category:	Smokeless Tobacco
Tobacco Product Sub-Category:	Portioned Snus
Package Type:	Plastic Can
Package Quantity:	24.0 g
Characterizing Flavor:	None
Portion Count:	24 pouches
Portion Mass:	1000 mg
Portion Length:	33 mm
Portion Width:	18 mm
Portion Thickness:	6 mm
Tobacco Cut Size:[2]	(b)(4) (b)(4) (b)(4)

Based on our review of your PMTA, we find permitting the new tobacco product specified above to be marketed is appropriate for the protection of public health, and that you have met the other requirements of section 910(c) of the FD&C Act. Under the provisions of section 910, you may introduce or deliver for introduction into interstate commerce the new tobacco product specified above with the enclosed labeling.

---

[1] Brand/sub-brand or other commercial name used in commercial distribution
[2] The applicant provided (b)(4) to characterize the tobacco cut size. Therefore, the tobacco cut size cannot be represented with a single value and corresponding range limit.

RECORD RETENTION

Under section 910(f) of the FD C Act, we are requiring in this order that you retain the records listed below for a period of not less than 4 years from the date of distribution of the last batch of the new tobacco product specified above. These records must be legible, in the English language, and available for inspection and copying by officers or employees duly designated by the Secretary, upon request:

- PMTA submitted prior to product order
- Postmarket reports/postmarket status reports submitted to FDA, including adverse experiences and all relevant documentation associated with the experience
- Correspondence with FDA pertaining to authorized product
- Nonclinical or clinical study documentation including:
    - study protocols (including statistical analysis plan);
    - amendments showing the dates and reasons for each protocol revision;
    - Institutional Review Board (IRB) or Independent Ethics Committee (IEC) approvals;
    - Informed consent forms;
    - Correspondence with study monitors/investigators/contract research organizations/sponsors/IRB/IEC;
    - Investigator financial disclosure statements;
    - Progress reports;
    - Monitoring reports;
    - Adverse experience reports;
    - Case report forms/subject diaries/medical records/laboratory reports;
    - Subject data line listings/observations records;
    - Test article accountability records;
    - Study results/protocol summaries/study reports; and
    - Certifications and amendments to certifications.
- Records pertaining to the manufacture, in process and release testing, process (including any changes to the process, facility, or controls), packaging, and storage of product
- Records pertaining to the sale, marketing, distribution, or other disposition of the product
- Specimens of all labeling, labels, inserts/onserts, instru.ctions, and other accompanying information
- Hazard analysis

POSTMARKET REPORTS

I. Serious and Unexpected Adverse Experiences Reporting

Under section 910(f) of the FD C Act, we are requiring in this order that you report to the FDA all adverse experiences that are both serious and unexpected and your analysis of the association between the adverse experience and the tobacco product **within 15 calendar days** after the report is received by you. These experiences may become known to you through a response to a customer complaint, request, or suggestion made as a result of an adverse experience, tobacco product defect, or failure reported to you; or identified in the literature or media. Your information should be submitted with a cover letter that includes the following text in the subject line: **SERIOUS UNEXPECTED ADVERSE EXPERIENCE REPORT for STN PM0000012**.

For purposes of reporting under this order, serious adverse experience means an adverse experience that results in any of the following outcomes:

- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect; or
- Any other adverse experience that, based upon appropriate medical judgment, may jeopardize the health of a person and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

For purposes of reporting under this order, unexpected adverse experience means an adverse experience occurring in one or more persons in which the nature, severity, or frequency of the experience is not consistent with:

- The known or foreseeable risks associated with the use or exposure to the tobacco product as described in the PMTA and other relevant sources of information, such as postmarket reports and studies;
- The expected natural progression of any underlying disease, disorder, or condition of the persons(s) experiencing the adverse experience and the person's predisposing risk factor profile for the adverse experience; or
- The results of nonclinical laboratory studies.

II. Manufacturing Deviations

You should promptly investigate all manufacturing deviations, including but not limited to those associated with processing, testing, packing, labeling, storage, holding and distribution. For products that have been distributed, if the deviation may negatively impact public health, you must promptly identify and report that deviation to the Center for Tobacco Products. See instructions below for submitting your regulatory correspondence.

III. Periodic Reporting

Under section 910(f) of the FD C Act, we are requiring in this order that you submit, on an annual basis, beginning October 2016, unless otherwise notified, the following information in a postmarketing annual report to help FDA determine whether continued marketing of your tobacco product is appropriate for the protection of public health or whether there are or may be grounds for withdrawing or temporarily suspending such order. For the 12- month reporting period, the report must include:

1.&A single submission with a cover letter that includes the following text in your subject line: **PERIODIC REPORT for STN PM0000012**. The cover letter should include the STN and corresponding tobacco product name, applicant name, date of report, reporting period, and marketing order status outside the United States.
2. A summary of how the tobacco product continues to be appropriate for the protection of the public health which includes:
    a. A status report of ongoing studies and a summary of completed studies about the tobacco product conducted by, or on behalf of, the applicant;

b.&A summary of significant findings on publications not previously reported and include full articles. Any new scientific data (published or otherwise) should also be reported on the likelihood of product use by current users of tobacco products within the same tobacco product category, current users of tobacco products in other tobacco product categories, former users of any tobacco product, and youth and young adults;

c.&A summary of adverse experiences with this tobacco product reported to you, providing a listing and analysis (accompanied by a statement of any changes to the reference risk information and a summary of important risks, including the nature, frequency, and potential risk factors) of all adverse experiences including those serious and unexpected adverse experiences reported previously.

d.&A summary of sales and distribution of the tobacco product: Total U.S. sales reported in dollars, units, and volume with breakdowns by US census region, major retail markets, and channels in which the product is sold (e.g., convenience stores, food and drug markets, big box retailers, internet/online sales, tobacco specialty shops);

e.&Data on current product users. Data should be collected about new users, current users, those who have switched tobacco products, and multiple product users. The results should be broken down by key demographic variables including age, gender, and race/ethnicity. Also, any change in the intended target market for the product should be reported. The data described above may include sales data and post-marketing analysis.

3.&A description of each change made to the manufacturing, facilities or controls during the reporting period, including:

a. A comparison of each change to what was described in the PMTA;
b. The rationale for making each change; and
c. A certification that the reported change did not result in any modification (including a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient) of the tobacco product; the basis for concluding that each change did not result in any modification to the final product.

4.&A summary of all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution and indicate a deviation that may affect the characteristics of the final product.

5.&Full-color copies of all advertising for the tobacco product that has not been previously submitted, along with the original date the advertisements were first disseminated and the date the advertisements were discontinued; and

6. In all annual reports, include a description of any or all labeling changes and submit revised full color final printed labeling.

a. The labeling should include all the panels, be presented in the actual size and color with legible text.

b.&For the first annual report only, submit all final printed labeling (actual labeling for each required warning distributed with the product); include labels, inserts/onserts, instructions, and other accompanying information or materials for this product.

In accordance with 40 CFR 1506.6, we will make your environmental assessment publicly available.

This order authorizing the marketing of this new tobacco product does not mean FDA "approved" the new tobacco product specified above; therefore, you may not make any express or implied statement or representation directed to consumers that conveys, or misleads or would mislead consumers into believing, among other things, that the new tobacco product specified above is "approved" by FDA. See Section 301(tt) of the FD&C Act. This marketing order is subject to withdrawal or temporary suspension under section 910(d) of the FD&C Act.

We remind you that all regulated tobacco products, including the new tobacco product specified above, are subject to the requirements of Chapter IX of the FD C Act and its regulations. These requirements currently include, but are not limited to, annual registration, listing of products, listing of ingredients, reporting of harmful and potentially harmful constituents, and payment of user fees. There are also packaging, labeling, and advertising requirements with which you must comply. It is your responsibility to ensure the tobacco product specified above complies with all applicable statutory and regulatory requirements. FDA will monitor your compliance with these applicable statutes and regulations.

If you discontinue the manufacture, preparation, compounding or processing for commercial distribution this tobacco product and later decide to reintroduce the product into the market, please contact the Office of Science to discuss if additional information is necessary.

For more information on your responsibilities under the FD&C Act, we encourage you to visit our website at http://www.fda.gov/TobaccoProducts. You may also obtain information by contacting FDA's Center for Tobacco Products at 1-877-CTP-1373, AskCTP@fda.hhs.gov, or SmallBiz.Tobacco@fda.hhs.gov.

We remind you all regulatory correspondence can be submitted via the FDA Electronic Submission Gateway (http://www.fda.gov/esg) using eSubmitter or by mail to:

Food and Drug Administration
Center for Tobacco Products
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Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

We are unable to accept regulatory submissions by electronic mail.

If you have questions, you may contact Asia Brown, MHSA, Regulatory Health Project Manager, at (240) 402-3833.

Sincerely,

Digitally signed by David Ashley -S
Date: 2015.11.10 06:00:57 -05'00'

David L. Ashley, Ph.D.
RADM, US Public Health Service
Director
Office of Science
Center for Tobacco Products

Enclosure

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Center for Tobacco Products
10903 New Hampshire Avenue
Silver Spring, MD 20993

November 10, 2015

MARKETING ORDER

Swedish Match North America, Inc.
Attention: Gerard Roerty, Jr., Vice President, General Counsel & Secretary
Two James Center
1021 East Cary Street, Suite 1600
Richmond, VA 23219
via Certified Mail

FDA Submission Tracking Number (STN): PM0000016

Dear Mr. Roerty:

The Food and Drug Administration (FDA) completed the review of your Premarket Tobacco Product Application (PMTA) submitted under section 910(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), for the following tobacco product:

Applicant:	Swedish Match North America, Inc.
Tobacco Product Name:[1]	General Portion White Large
Tobacco Product Category:	Smokeless Tobacco
Tobacco Product Sub-Category:	Portioned Snus
Package Type:	Plastic Can
Package Quantity:	24.0 g
Characterizing Flavor:	None
Portion Count:	24 pouches
Portion Mass:	1000 mg
Portion Length:	34 mm
Portion Width:	18 mm
Portion Thickness:	5.5 mm
Tobacco Cut Size:[2]	(b)(4) (b)(4) (b)(4) (b)(4)

Based on our review of your PMTA, we find permitting the new tobacco product specified above to be marketed is appropriate for the protection of public health, and that you have met the other requirements of section 910(c) of the FD&C Act. Under the provisions of section 910, you may introduce or deliver for introduction into interstate commerce the new tobacco product specified above with the enclosed labeling.

---

[1] Brand/sub-brand or other commercial name used in commercial distribution
[2] The applicant provided (b)(4) to characterize the tobacco cut size. Therefore, the tobacco cut size cannot be represented with a single value and corresponding range limit.

RECORD RETENTION

Under section 910(f) of the FD C Act, we are requiring in this order that you retain the records listed below for a period of not less than 4 years from the date of distribution of the last batch of the new tobacco product specified above. These records must be legible, in the English language, and available for inspection and copying by officers or employees duly designated by the Secretary, upon request:

- PMTA submitted prior to product order
- Postmarket reports/postmarket status reports submitted to FDA, including adverse experiences and all relevant documentation associated with the experience
- Correspondence with FDA pertaining to authorized product
- Nonclinical or clinical study documentation including:
    - study protocols (including statistical analysis plan);
    - amendments showing the dates and reasons for each protocol revision;
    - Institutional Review Board (IRB) or Independent Ethics Committee (IEC) approvals;
    - Informed consent forms;
    - Correspondence with study monitors/investigators/contract research organizations/sponsors/IRB/IEC;
    - Investigator financial disclosure statements;
    - Progress reports;
    - Monitoring reports;
    - Adverse experience reports;
    - Case report forms/subject diaries/medical records/laboratory reports;
    - Subject data line listings/observations records;
    - Test article accountability records;
    - Study results/protocol summaries/study reports; and
    - Certifications and amendments to certifications.
- Records pertaining to the manufacture, in process and release testing, process (including any changes to the process, facility, or controls), packaging, and storage of product
- Records pertaining to the sale, marketing, distribution, or other disposition of the product
- Specimens of all labeling, labels, inserts/onserts, instructions, and other accompanying information
- Hazard analysis

POSTMARKET REPORTS

I. Serious and Unexpected Adverse Experiences Reporting

Under section 910(f) of the FD C Act, we are requiring in this order that you report to the FDA all adverse experiences that are both serious and unexpected and your analysis of the association between the adverse experience and the tobacco product **within 15 calendar days** after the report is received by you. These experiences may become known to you through a response to a customer complaint, request, or suggestion made as a result of an adverse experience, tobacco product defect, or failure reported to you; or identified in the literature or media. Your information should be submitted with a cover letter that includes the following text in the subject line: **SERIOUS UNEXPECTED ADVERSE EXPERIENCE REPORT for STN PM0000016**.

For purposes of reporting under this order, serious adverse experience means an adverse experience that results in any of the following outcomes:

- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect; or
- Any other adverse experience that, based upon appropriate medical judgment, may jeopardize the health of a person and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

For purposes of reporting under this order, unexpected adverse experience means an adverse experience occurring in one or more persons in which the nature, severity, or frequency of the experience is not consistent with:

- The known or foreseeable risks associated with the use or exposure to the tobacco product as described in the PMTA and other relevant sources of information, such as postmarket reports and studies;
- The expected natural progression of any underlying disease, disorder, or condition of the persons(s) experiencing the adverse experience and the person's predisposing risk factor profile for the adverse experience; or
- The results of nonclinical laboratory studies.

II. Manufacturing Deviations

You should promptly investigate all manufacturing deviations, including but not limited to those associated with processing, testing, packing, labeling, storage, holding and distribution. For products that have been distributed, if the deviation may negatively impact public health, you must promptly identify and report that deviation to the Center for Tobacco Products. See instructions below for submitting your regulatory correspondence.

III. Periodic Reporting

Under section 910(f) of the FD C Act, we are requiring in this order that you submit, on an annual basis, beginning October 2016, unless otherwise notified, the following information in a postmarketing annual report to help FDA determine whether continued marketing of your tobacco product is appropriate for the protection of public health or whether there are or may be grounds for withdrawing or temporarily suspending such order. For the 12- month reporting period, the report must include:

1.&A single submission with a cover letter that includes the following text in your subject line: **PERIODIC REPORT for STN PM0000016**. The cover letter should include the STN and corresponding tobacco product name, applicant name, date of report, reporting period, and marketing order status outside the United States.
2. A summary of how the tobacco product continues to be appropriate for the protection of the public health which includes:
    a. A status report of ongoing studies and a summary of completed studies about the tobacco product conducted by, or on behalf of, the applicant;

b.&A summary of significant findings on publications not previously reported and include full articles. Any new scientific data (published or otherwise) should also be reported on the likelihood of product use by current users of tobacco products within the same tobacco product category, current users of tobacco products in other tobacco product categories, former users of any tobacco product, and youth and young adults;

c.&A summary of adverse experiences with this tobacco product reported to you, providing a listing and analysis (accompanied by a statement of any changes to the reference risk information and a summary of important risks, including the nature, frequency, and potential risk factors) of all adverse experiences including those serious and unexpected adverse experiences reported previously.

d.&A summary of sales and distribution of the tobacco product: Total U.S. sales reported in dollars, units, and volume with breakdowns by US census region, major retail markets, and channels in which the product is sold (e.g., convenience stores, food and drug markets, big box retailers, internet/online sales, tobacco specialty shops);

e.&Data on current product users. Data should be collected about new users, current users, those who have switched tobacco products, and multiple product users. The results should be broken down by key demographic variables including age, gender, and race/ethnicity. Also, any change in the intended target market for the product should be reported. The data described above may include sales data and post-marketing analysis.

3.&A description of each change made to the manufacturing, facilities or controls during the reporting period, including:

a. A comparison of each change to what was described in the PMTA;
b. The rationale for making each change; and
c. A certification that the reported change did not result in any modification (including a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient) of the tobacco product; the basis for concluding that each change did not result in any modification to the final product.

4.&A summary of all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution and indicate a deviation that may affect the characteristics of the final product.

5.&Full-color copies of all advertising for the tobacco product that has not been previously submitted, along with the original date the advertisements were first disseminated and the date the advertisements were discontinued; and

6. In all annual reports, include a description of any or all labeling changes and submit revised full color final printed labeling.

a. The labeling should include all the panels, be presented in the actual size and color with legible text.

b.&For the first annual report only, submit all final printed labeling (actual labeling for each required warning distributed with the product); include labels, inserts/onserts, instructions, and other accompanying information or materials for this product.

In accordance with 40 CFR 1506.6, we will make your environmental assessment publicly available.

This order authorizing the marketing of this new tobacco product does not mean FDA "approved" the new tobacco product specified above; therefore, you may not make any express or implied statement or representation directed to consumers that conveys, or misleads or would mislead consumers into believing, among other things, that the new tobacco product specified above is "approved" by FDA. See Section 301(tt) of the FD&C Act. This marketing order is subject to withdrawal or temporary suspension under section 910(d) of the FD&C Act.

We remind you that all regulated tobacco products, including the new tobacco product specified above, are subject to the requirements of Chapter IX of the FD C Act and its regulations. These requirements currently include, but are not limited to, annual registration, listing of products, listing of ingredients, reporting of harmful and potentially harmful constituents, and payment of user fees. There are also packaging, labeling, and advertising requirements with which you must comply. It is your responsibility to ensure the tobacco product specified above complies with all applicable statutory and regulatory requirements. FDA will monitor your compliance with these applicable statutes and regulations.

If you discontinue the manufacture, preparation, compounding or processing for commercial distribution this tobacco product and later decide to reintroduce the product into the market, please contact the Office of Science to discuss if additional information is necessary.

For more information on your responsibilities under the FD&C Act, we encourage you to visit our website at http://www.fda.gov/TobaccoProducts. You may also obtain information by contacting FDA's Center for Tobacco Products at 1-877-CTP-1373, AskCTP@fda.hhs.gov, or SmallBiz.Tobacco@fda.hhs.gov.

We remind you all regulatory correspondence can be submitted via the FDA Electronic Submission Gateway (http://www.fda.gov/esg) using eSubmitter or by mail to:

Food and Drug Administration
Center for Tobacco Products
Document Control Center
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

We are unable to accept regulatory submissions by electronic mail.

If you have questions, you may contact Asia Brown, MHSA, Regulatory Health Project Manager, at (240) 402-3833.

Sincerely,

Digitally signed by David Ashley -S
Date: 2015.11.10 06:05:34 -05'00'

David L. Ashley, Ph.D.
RADM, US Public Health Service
Director
Office of Science
Center for Tobacco Products

Enclosure

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Center for Tobacco Products
10903 New Hampshire Avenue
Silver Spring, MD 20993

November 10, 2015

MARKETING ORDER

Swedish Match North America, Inc.
Attention: Gerard Roerty, Jr., Vice President, General Counsel & Secretary
Two James Center
1021 East Cary Street, Suite 1600
Richmond, VA 23219
via Certified Mail

FDA Submission Tracking Number (STN): PM0000017

Dear Mr. Roerty:

The Food and Drug Administration (FDA) completed the review of your Premarket Tobacco Product Application (PMTA) submitted under section 910(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), for the following tobacco product:

Applicant:	Swedish Match North America, Inc.
Tobacco Product Name:[1]	General Wintergreen Portion White Large
Tobacco Product Category:	Smokeless Tobacco
Tobacco Product Sub-Category:	Portioned Snus
Package Type:	Plastic Can
Package Quantity:	24.0 g
Characterizing Flavor:	Wintergreen
Portion Count:	24 pouches
Portion Mass:	1000 mg
Portion Length:	34 mm
Portion Width:	18 mm
Portion Thickness:	5.5 mm
Tobacco Cut Size:[2]	(b)(4) (b)(4) (b)(4) (b)(4)

Based on our review of your PMTA, we find permitting the new tobacco product specified above to be marketed is appropriate for the protection of public health, and that you have met the other requirements of section 910(c) of the FD&C Act. Under the provisions of section 910, you may introduce or deliver for introduction into interstate commerce the new tobacco product specified above with the enclosed labeling.

---

[1] Brand/sub-brand or other commercial name used in commercial distribution
[2] The applicant provided (b)(4) to characterize the tobacco cut size. Therefore, the tobacco cut size cannot be represented with a single value and corresponding range limit.

RECORD RETENTION

Under section 910(f) of the FD C Act, we are requiring in this order that you retain the records listed below for a period of not less than 4 years from the date of distribution of the last batch of the new tobacco product specified above. These records must be legible, in the English language, and available for inspection and copying by officers or employees duly designated by the Secretary, upon request:

- PMTA submitted prior to product order
- Postmarket reports/postmarket status reports submitted to FDA, including adverse experiences and all relevant documentation associated with the experience
- Correspondence with FDA pertaining to authorized product
- Nonclinical or clinical study documentation including:
    - study protocols (including statistical analysis plan);
    - amendments showing the dates and reasons for each protocol revision;
    - Institutional Review Board (IRB) or Independent Ethics Committee (IEC) approvals;
    - Informed consent forms;
    - Correspondence with study monitors/investigators/contract research organizations/sponsors/IRB/IEC;
    - Investigator financial disclosure statements;
    - Progress reports;
    - Monitoring reports;
    - Adverse experience reports;
    - Case report forms/subject diaries/medical records/laboratory reports;
    - Subject data line listings/observations records;
    - Test article accountability records;
    - Study results/protocol summaries/study reports; and
    - Certifications and amendments to certifications.
- Records pertaining to the manufacture, in process and release testing, process (including any changes to the process, facility, or controls), packaging, and storage of product
- Records pertaining to the sale, marketing, distribution, or other disposition of the product
- Specimens of all labeling, labels, inserts/onserts, instructions, and other accompanying information
- Hazard analysis

POSTMARKET REPORTS

I. Serious and Unexpected Adverse Experiences Reporting

Under section 910(f) of the FD C Act, we are requiring in this order that you report to the FDA all adverse experiences that are both serious and unexpected and your analysis of the association between the adverse experience and the tobacco product **within 15 calendar days** after the report is received by you. These experiences may become known to you through a response to a customer complaint, request, or suggestion made as a result of an adverse experience, tobacco product defect, or failure reported to you; or identified in the literature or media. Your information should be submitted with a cover letter that includes the following text in the subject line: **SERIOUS UNEXPECTED ADVERSE EXPERIENCE REPORT for STN PM0000017**.

For purposes of reporting under this order, serious adverse experience means an adverse experience that results in any of the following outcomes:

- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect; or
- Any other adverse experience that, based upon appropriate medical judgment, may jeopardize the health of a person and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

For purposes of reporting under this order, unexpected adverse experience means an adverse experience occurring in one or more persons in which the nature, severity, or frequency of the experience is not consistent with:

- The known or foreseeable risks associated with the use or exposure to the tobacco product as described in the PMTA and other relevant sources of information, such as postmarket reports and studies;
- The expected natural progression of any underlying disease, disorder, or condition of the persons(s) experiencing the adverse experience and the person's predisposing risk factor profile for the adverse experience; or
- The results of nonclinical laboratory studies.

II. Manufacturing Deviations

You should promptly investigate all manufacturing deviations, including but not limited to those associated with processing, testing, packing, labeling, storage, holding and distribution. For products that have been distributed, if the deviation may negatively impact public health, you must promptly identify and report that deviation to the Center for Tobacco Products. See instructions below for submitting your regulatory correspondence.

III. Periodic Reporting

Under section 910(f) of the FD C Act, we are requiring in this order that you submit, on an annual basis, beginning October 2016, unless otherwise notified, the following information in a postmarketing annual report to help FDA determine whether continued marketing of your tobacco product is appropriate for the protection of public health or whether there are or may be grounds for withdrawing or temporarily suspending such order. For the 12- month reporting period, the report must include:

1.&A single submission with a cover letter that includes the following text in your subject line: **PERIODIC REPORT for STN PM0000017**. The cover letter should include the STN and corresponding tobacco product name, applicant name, date of report, reporting period, and marketing order status outside the United States.
2. A summary of how the tobacco product continues to be appropriate for the protection of the public health which includes:
    a. A status report of ongoing studies and a summary of completed studies about the tobacco product conducted by, or on behalf of, the applicant;

b.&A summary of significant findings on publications not previously reported and include full articles. Any new scientific data (published or otherwise) should also be reported on the likelihood of product use by current users of tobacco products within the same tobacco product category, current users of tobacco products in other tobacco product categories, former users of any tobacco product, and youth and young adults;

c.&A summary of adverse experiences with this tobacco product reported to you, providing a listing and analysis (accompanied by a statement of any changes to the reference risk information and a summary of important risks, including the nature, frequency, and potential risk factors) of all adverse experiences including those serious and unexpected adverse experiences reported previously.

d.&A summary of sales and distribution of the tobacco product: Total U.S. sales reported in dollars, units, and volume with breakdowns by US census region, major retail markets, and channels in which the product is sold (e.g., convenience stores, food and drug markets, big box retailers, internet/online sales, tobacco specialty shops);

e.&Data on current product users. Data should be collected about new users, current users, those who have switched tobacco products, and multiple product users. The results should be broken down by key demographic variables including age, gender, and race/ethnicity. Also, any change in the intended target market for the product should be reported. The data described above may include sales data and post-marketing analysis.

3.&A description of each change made to the manufacturing, facilities or controls during the reporting period, including:

a. A comparison of each change to what was described in the PMTA;
b. The rationale for making each change; and
c. A certification that the reported change did not result in any modification (including a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient) of the tobacco product; the basis for concluding that each change did not result in any modification to the final product.

4.&A summary of all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution and indicate a deviation that may affect the characteristics of the final product.

5.&Full-color copies of all advertising for the tobacco product that has not been previously submitted, along with the original date the advertisements were first disseminated and the date the advertisements were discontinued; and

6. In all annual reports, include a description of any or all labeling changes and submit revised full color final printed labeling.

a. The labeling should include all the panels, be presented in the actual size and color with legible text.

b.&For the first annual report only, submit all final printed labeling (actual labeling for each required warning distributed with the product); include labels, inserts/onserts, instructions, and other accompanying information or materials for this product.

In accordance with 40 CFR 1506.6, we will make your environmental assessment publicly available.

This order authorizing the marketing of this new tobacco product does not mean FDA "approved" the new tobacco product specified above; therefore, you may not make any express or implied statement or representation directed to consumers that conveys, or misleads or would mislead consumers into believing, among other things, that the new tobacco product specified above is "approved" by FDA. See Section 301(tt) of the FD&C Act. This marketing order is subject to withdrawal or temporary suspension under section 910(d) of the FD&C Act.

We remind you that all regulated tobacco products, including the new tobacco product specified above, are subject to the requirements of Chapter IX of the FD C Act and its regulations. These requirements currently include, but are not limited to, annual registration, listing of products, listing of ingredients, reporting of harmful and potentially harmful constituents, and payment of user fees. There are also packaging, labeling, and advertising requirements with which you must comply. It is your responsibility to ensure the tobacco product specified above complies with all applicable statutory and regulatory requirements. FDA will monitor your compliance with these applicable statutes and regulations.

If you discontinue the manufacture, preparation, compounding or processing for commercial distribution this tobacco product and later decide to reintroduce the product into the market, please contact the Office of Science to discuss if additional information is necessary.

For more information on your responsibilities under the FD&C Act, we encourage you to visit our website at http://www.fda.gov/TobaccoProducts. You may also obtain information by contacting FDA's Center for Tobacco Products at 1-877-CTP-1373, AskCTP@fda.hhs.gov, or SmallBiz.Tobacco@fda.hhs.gov.

We remind you all regulatory correspondence can be submitted via the FDA Electronic Submission Gateway (http://www.fda.gov/esg) using eSubmitter or by mail to:

Food and Drug Administration
Center for Tobacco Products
Document Control Center
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

We are unable to accept regulatory submissions by electronic mail.

If you have questions, you may contact Asia Brown, MHSA, Regulatory Health Project Manager, at (240) 402-3833.

Sincerely,

Digitally signed by David Ashley -S
Date: 2015.11.10 06:06:25 -05'00'

David L. Ashley, Ph.D.
RADM, US Public Health Service
Director
Office of Science
Center for Tobacco Products

Enclosure

U.S. FOOD & DRUG ADMINISTRATION

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

October 22, 2019

MODIFIED RISK GRANTED ORDERS ––
RISK MODIFICATION

Swedish Match USA, Inc.
Attention: Gerard Roerty, Vice President, General
Counsel & Secretary
Two James Center
1021 East Cary Street, Suite 1600
Richmond, VA 23219

FDA Submission Tracking Numbers (STNs): MULTIPLE STNs, See Appendix A

Dear Mr. Roerty:

We completed review of your MRTPAs[1] and are issuing modified risk granted orders for the tobacco products identified in Appendix A.

Based on our review of your MRTPAs, we find that the modified risk tobacco products, as described in your applications and specified in Appendix A, 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. Therefore, we authorize the marketing of the modified risk tobacco 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."

Under the provisions of section 911, you may introduce or deliver for introduction into interstate commerce the modified risk tobacco products, in accordance with these risk modification orders. These risk modification orders include requirements related to conditions of marketing under section 911(h) and postmarket surveillance and studies under section 911(i) as well as requests related to other record retention and reporting, as outlined in the attached appendices.

These orders expire 5 years from the issue date of this letter. If you wish to renew your orders, we recommend a request for renewal is received by FDA 360 days prior to the expiration date. Your renewal may cross-reference your MRTPAs that are subject to these orders.

The requirements in these risk modification orders are intended to help ensure that your modified risk tobacco products, as actually used by consumers, will continue to 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

[1] Modified Risk Tobacco Product Applications (MRTPAs) submitted under section 911(d) of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

currently use tobacco products. However, compliance with these requirements alone is not a guarantee that the modified risk tobacco products, as actually used by consumers, will continue to significantly reduce harm and the risk of tobacco-related disease to individual tobacco users and benefit the health of the population as a whole, particularly if, despite these measures, there is a significant increase in youth initiation or initiation by non-users. FDA will continue to monitor the marketing of your modified risk tobacco products and their impact on the population.

These orders authorizing the marketing of these modified risk tobacco products do not mean FDA "approved" the modified risk tobacco products specified in Appendix A; therefore, you may not make any express or implied statement or representation directed to consumers that conveys, or misleads, or would mislead consumers into believing, among other things, that the modified risk tobacco products specified in Appendix A are "approved" by FDA.[2] The modified risk tobacco products subject to these risk modification orders are subject to withdrawal as described in section 911(j).

We remind you that all regulated tobacco products, including the modified risk tobacco products specified in Appendix A, are subject to the requirements of the FD&C Act and its implementing regulations. It is your responsibility to ensure the modified risk tobacco products specified in Appendix A comply with all applicable statutory and regulatory requirements. FDA will monitor your compliance with all applicable statutes and regulations.

In accordance with 40 CFR 1506.6, we will make your Environmental Assessment (EA) publicly available.

We encourage you to submit all regulatory correspondence electronically via the CTP Portal[3,4] using eSubmitter.[5] Alternatively, submissions may be mailed to:

Food and Drug Administration
Center for Tobacco Products
Document Control Center (DCC)
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

The CTP Portal and FDA's Electronic Submission Gateway (ESG) are generally available 24 hours a day, seven days a week; if the upload is successful, submissions are considered received by DCC on the day of upload. Submissions delivered to DCC by courier or physical mail will be considered timely if received during delivery hours on or before the due date[6]; if the due date falls on a weekend or holiday, the delivery must be received on or before the preceding business day. We are unable to accept regulatory submissions by e-mail.

[2] See Section 301(tt) of the FD&C Act.
[3] http://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/Manufacturing/ucm515047.htm
[4] FDA's Electronic Submission Gateway (ESG) is still available as an alternative to the CTP Portal.
[5] https://www.fda.gov/industry/fda-esubmitter
[6] https://www.fda.gov/tobacco-products/about-center-tobacco-products-ctp/contact-ctp

If you have any questions regarding these orders, please contact Shireen Fotelargias, Regulatory Health Project Manager, at (240) 402-0435 or Shireen.Fotelargias@fda.hhs.gov.

If you have any questions regarding postmarket activities for the modified risk tobacco products subject of these orders, please contact Eugene Y Chuang, at (240) 402-9302 or Eugene.Chuang@fda.hhs.gov.

Sincerely,

Digitally signed by Matthew R. Holman -S
Date: 2019.10.22 08:58:56 -04'00'

Matthew R. Holman, Ph.D.
Director
Office of Science
Center for Tobacco Products

Enclosures:

Appendix A- List of Tobacco Products That Are Subject of This Letter
Appendix B- Required Postmarket Surveillance and Studies
Appendix C- Advertising and Promotion Requirements
Appendix D- Recordkeeping and Retention
Appendix E- Manufacturing Information

Appendix A

List of Tobacco Products That Are Subject of This Letter

Common Attributes of MRTPAs	
Submission Date:	June 10, 2014
Receipt Date:	June 10, 2014
Product Manufacturer:	Swedish Match USA, Inc.
Product Category:	Smokeless Tobacco Products
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.
MR0000020: General Loose[7]	
Product Subcategory:	Loose Snus
Package Type:	Cardboard Can with Plastic Lid
Package Quantity:	45.0 g
Characterizing Flavor:	None
MR0000021: General Dry Mint Portion Original Mini[7]	
Product Subcategory:	Portioned Snus
Package Type:	Plastic Can
Package Quantity:	6.0 g
Characterizing Flavor:	Mint
MR0000022: General Portion Original Large[7]	
Product Subcategory:	Portioned Snus
Package Type:	Plastic Can
Package Quantity:	24.0 g
Characterizing Flavor:	None
MR0000024: General Classic Blend Portion White Large – 12 ct[7]	
Product Subcategory:	Portioned Snus
Package Type:	Plastic Can
Package Quantity:	10.8 g
Characterizing Flavor:	None
MR0000025: General Mint Portion White Large[7]	
Product Subcategory:	Portioned Snus
Package Type:	Plastic Can
Package Quantity:	24.0 g
Characterizing Flavor:	Mint
MR0000027: General Nordic Mint Portion White Large – 12 ct[7]	
Product Subcategory:	Portioned Snus
Package Type:	Plastic Can
Package Quantity:	10.8 g
Characterizing Flavor:	Mint

[7] STN: Product Name (Brand/sub-brand or other commercial name used in commercial distribution)

MR0000028: General Portion White Large[7]	
Product Subcategory:	Portioned Snus
Package Type:	Plastic Can
Package Quantity:	24.0 g
Characterizing Flavor:	None
MR0000029: General Wintergreen Portion White Large[7]	
Product Subcategory:	Portioned Snus
Package Type:	Plastic Can
Package Quantity:	24.0 g
Characterizing Flavor:	Wintergreen

Appendix B

Required Postmarket Surveillance and Studies (PMSS)

Under Section 911(i)(1) of the FD&C Act, FDA must require postmarket surveillance and studies for any product for which an applicant received an order under 911(g)(1) in order 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."

I. PMSS Content

MRTP Use Behavior and Consumer Understanding and Perception

After receiving authorization, the determination of whether the eight General Snus products that are the subject of these applications, as actually used by consumers, continue to benefit the health of the population as a whole is likely to be driven by use behavior. Therefore, monitoring use of the eight General Snus products that are the subject of these applications in terms of uptake, dual use, and complete switching is required. In particular, your PMSS must assess the extent to which new MRTP users were non-users, smokers, or other tobacco product users before initiating the MRTPs and the extent to which new users of the MRTPs become exclusive users or dual users with cigarettes or other tobacco products over time. Relatedly, such surveillance must include an assessment of consumers' understanding of the claim and perceptions of the products. In particular, PMSS must assess the extent to which users of these products understand that, to reduce their risk of disease relative to smoking as described in the modified risk information, they must use General Snus exclusively. **To adequately assess these impacts, you must conduct PMSS that include assessing users' behavior and consumer understanding at multiple time points**.

In addition, FDA has determined that assessing the impact of your MRTP orders on uptake of the products requires surveillance of MRTP sales and distribution, which provide information to assess tobacco consumption at the population level. Your PMSS protocols must describe procedures for monitoring and reporting MRTP sales and distribution in the U.S. by product, major metropolitan areas, and channels where the products are sold (e.g., convenience stores, food and drug stores, internet and digital retailers, tobacco specialty shops). Your annual PMSS report must include:

- U.S. sales and distribution of the tobacco products by quarter since the granting of your modified risk granted orders (for the initial reporting period) or the previous reporting period (for all reports that follow), including, for each MRTPA STN, total U.S. sales and distribution reported in dollars and units, and broken down by major metropolitan areas, and channels where the products were distributed and sold during the reporting period (e.g., convenience stores, food and drug stores, internet and digital retailers, tobacco specialty shops).
- A brief synthesis and summary of the sales and distribution data for the initial reporting period or the previous reporting period (for all reports that follow), including annual and quarterly growth rate (percent change) in total U.S. sales and distribution of the tobacco products for each MRTPA STN, post-MRTP authorization.

MRTP Use and Adverse Experiences

In order for FDA to determine whether the eight General Snus products that are the subject of these applications, as actually used by consumers, continue to benefit the health of the population as a whole, your PMSS must include ongoing surveillance of all adverse experiences associated with the use of the MRTPs. These experiences may become known to you through any source, including a customer complaint, request, or suggestion made as a result of an adverse experience, tobacco product defect, or failure, reported to you, or identified in the literature or media. Your PMSS protocols must include procedures for monitoring and analyzing adverse experiences and your annual PMSS report must include:

- A summary of reported adverse experiences for the tobacco products, which includes a listing of all adverse experiences during the reporting period and a cumulative list, including all serious and unexpected adverse experiences previously reported. The summary must be accompanied by an analysis of the reports and a statement of any changes to risk information related to the products including nature, frequency, and potential aggravating factors.

In addition, the PMTA orders for your General snus products, issued on November 10, 2015, require you to report to the FDA all adverse experiences that are both serious and unexpected and your analysis of the association between the adverse experience and the tobacco product within 15 calendar days after the report is received by you. These experiences may become known to you through any source, including a customer complaint, request, or suggestion made as a result of an adverse experience, tobacco product defect, or failure, reported to you, or identified in the literature or media. We request that when submitting such reports, you reference both your PMTAs and you MRTPAs for these products. Your information should be submitted with a cover letter that includes the following text in the subject line: **SERIOUS UNEXPECTED ADVERSE EXPERIENCE REPORT FOR STN(s) PM0000010-PM0000017 and MR0000020-MR0000022, MR0000024-MR0000025, and MR0000027-MR0000029.**

For purposes of this reporting, *serious adverse experience* means an adverse experience that results in any of the following outcomes:

- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect; or
- Any other adverse experience that, based upon appropriate medical judgment, may jeopardize the health of a person and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

For purposes of this reporting, *unexpected adverse experience* means an adverse experience occurring in one or more persons in which the nature, severity, or frequency of the experience is not consistent with:

- The known or foreseeable risks associated with the use or exposure to the tobacco product as described in the PMTA (including the results of human subject investigations) and other relevant sources of information, such as postmarket reports and studies;

- The expected natural progression of any underlying disease, disorder, or condition of the person(s) experiencing the adverse experience and the person's predisposing risk factor profile for the adverse experience; or
- The results of nonclinical laboratory studies.

Surveillance of New Research Study Findings the MRTPs and Consumer Perception, Behavior, or Health

In order for FDA to determine whether the eight General Snus products that are the subject of these applications, as actually used by consumers, continue to benefit the health of the population as a whole, your PMSS must include surveillance of new research study information about the MRTPs and consumer perception, behavior, or health. In particular, your PMSS protocol must include procedures for monitoring and assessing findings both in your own studies (i.e., studies conducted by you or on your behalf) and in publications including any new scientific data (published or otherwise) regarding the MRTPs and consumer perception, behavior, or health. Your annual PMSS report must include:

- A summary of significant findings about the tobacco products from research studies conducted by you or on your behalf, whether or not such studies were specifically required under this order. A summary of significant findings in publications not previously reported and full copies of the articles. This must include any new scientific data (published or otherwise) on the MRTPs and consumer perception, behavior, or health.

II. Submitting PMSS Protocols and Reports

Within 30 days of receiving this notice, you must submit complete protocols for your PMSS as required under section 911(i)(2) of the FD&C Act. Label your submission clearly as a "PMSS Protocol," and reference your MRTPA Submission Tracking Numbers (STNs). If you have more than one protocol, submit each protocol as a separate submission. If applicable, each protocol should include the name(s) of the principal investigator(s) and materials that demonstrate the relevant professional credentials and training that qualify them to lead the study. Within 60 days of receipt of the protocol(s), FDA will determine if the principal investigator proposed to be used in the surveillance has sufficient qualifications and experience to conduct the surveillance and if the protocol(s) will result in collection of the data or other information that FDA designates as necessary to protect public health, pursuant to section 911(i)(2) of the FD&C Act. FDA will notify you of and provide opportunities to address, any deficiency in the submission. If the PMSS protocol is amended subsequent to FDA approval, FDA must receive the amended protocol promptly. For protocol amendments that are administrative in nature (e.g., corrections in punctuation or titles), the amended protocol must be received by FDA within 30 days of the update. For protocol amendments that seek to modify the study design (including endpoints, sites, questionnaires, methodology, etc.) or other scientific parameters, you may not initiate the change until you receive FDA approval.

As part of the requirement to conduct PMSS, you must initiate and conduct your PMSS per timeframes established in your protocols and approved by FDA. Note that for PMSS that involve human subjects, the anticipated start date for each study must account for the time required for securing IRB approval, as needed. In addition to specifying the start date, your protocols must contain timelines for completion of major study milestones including, as applicable, the start and completion of participant recruitment, initiation of data collection (per wave, if applicable), completion of data collection, analysis, and report writing. If you deviate from these timelines, we request that you report the deviation within 30 days to FDA.

Section 911(i) requires that the results of PMSS be submitted on an annual basis. These reports must be identified as "PMSS Report", and the MRTPA STNs should be referenced for each report. The PMSS Report must indicate the beginning and ending date of the period covered by the report and must include accomplishments since the last reporting period. For quantitative updates on studies in progress (e.g., participant accrual), reports should describe both interim (since the last reporting period) as well as cumulative (since study initiation) accomplishments. The PMSS Report describing studies in progress must describe the status of PMSS, including, as applicable the status of recruitment, data collection, and analysis; a summary of the study milestones achieved and any deviations from the agreed upon timelines in the protocol; a summary of protocol amendments; and a summary of any preliminary analyses conducted. Once a study is completed, the PMSS Report should include the complete final study report.

Appendix C

Advertising and Promotion Requirements

I. Recordkeeping and Retention

Under section 911(h)(5) of the FD&C Act, these risk modification orders require you to establish and maintain the following records:

- Records pertaining to the products' labeling, advertising, marketing, and/or promotion – whether conducted by you, on your behalf, or at your direction – including:
  - Specimens of all labeling, labels, inserts/onserts, instructions, and other accompanying information;
  - Copies of all advertising, marketing, and/or promotional materials published, disseminated to consumers, or for use in engaging or communicating with consumers;
  - Copies of any formative research studies conducted among any audiences in the formation of the labeling, advertising, marketing, and/or promotional materials, including qualitative and quantitative research studies used to determine message effectiveness, consumer knowledge, attitudes, beliefs, intentions, and behaviors toward using the products, and including copies of the stimuli used in testing;
  - Copies of any consumer evaluation research studies conducted among any audiences to determine the effectiveness of labeling, advertising, marketing, and/or promotional materials and any shifts in consumer knowledge, attitudes, beliefs, intentions, and behaviors toward using the products, and including copies of the stimuli used in testing;
  - Copies of any contractual agreements regarding the creation and/or dissemination of the products' labeling, advertising, marketing, and/or promotional materials;
  - Copies of all advertising and marketing plans, including strategic creative briefs and paid media plans, by channel and by product, and the dollar amount(s) and flighting of such plans, by channel and by product, including any:
    - Use of competent and reliable data sources, methodologies, and technologies to establish, maintain, and monitor highly targeted advertising and marketing plans and media buys;
    - Targeting of specific adult audiences by age-range(s), including young adult audiences, ages 18-24, and other demographic and/or psychographic characteristics that reflect your intended target audience;
    - Actions taken to restrict youth-access and limit youth-exposure to the products' labeling, advertising, marketing, and/or promotion;
    - Use of owned, earned, shared, and/or paid social media to create labeling for, advertise, market, and/or promote the products;
    - Use of partners, influencers, bloggers, and/or brand ambassadors to create labeling for, advertise, market, and/or promote the products;
    - Consumer engagements – whether conducted by you, on your behalf, or at your direction – including events at which the products were demonstrated; and/or
    - Use of earned media and/or public-relations outreach to create labeling for, advertise, market, and/or promote the products
  - Copies of all records pertaining to media tracking and optimization, by channel, by product, and by audience demographics (e.g., age, gender, race/ethnicity, geographic region), and all post-launch delivery-verification reports submitted to you from an accredited source, by channel, by product, and by audience demographics; and

- Policies and procedures for real-time digital media monitoring to identify, correct, and prevent any delivery of advertising impressions to youth, ages 17 years and under, including documentation of such monitoring activities and implementation of corrective and preventive measures

II. Notifications

Under section 911(h)(5) of the FD&C Act these risk modification orders require that for the first six months after the date of your modified risk order you provide FDA a 30-day notification for all labeling, advertising, marketing, and/or promotional materials for which you plan on disseminating to the public. These notifications are not for pre-approval, but are required so that FDA can have timely access to your marketing plans and materials, and if needed, provide you advisory comments, including any concerns about their possible impact on youth appeal and tobacco use initiation and on the finding that continued marketing of your products will benefit the health of the population as a whole. You may begin disseminating the materials 30 days after providing notification to FDA. This notification must be received by FDA **at least 30 days prior** to dissemination, which includes but is not limited to the publication, dissemination to consumers, or use in engaging or communicating with consumers of such materials. The notification must include:

- Full-color copies of all such labeling, advertising, marketing, and/or promotional materials for the products. The materials must include all panels where applicable (e.g., print ads, point of sale signs) and reflect the actual size and colors used. For any materials that would not fit on an 8.5" x 11" piece of paper, you may resize and submit electronic versions of such materials in a format that FDA can review and with sufficient resolution to allow FDA to read lettering clearly. If resizing the advertisement does not allow for text to be read easily, the text may be provided separately and referenced. Digital media, such as videos, must be submitted in a format that FDA is able to open and review.
- All advertising and marketing plans, including strategic creative briefs and paid media plans, by channel and by product, and the details, dollar amount(s) and flighting of such plans, by channel and by product, including any plans to:
  - Use competent and reliable data sources, methodologies, and technologies to establish, maintain, and monitor highly targeted advertising and marketing plans and media buys, including a list of all data sources used to target advertising and marketing plans an media buys;
  - Target specific adult audiences by age-range(s), including young adults, ages 18-24, and other demographic and psychographic characteristics that reflect your intended target audience(s), including how the target audience(s) are defined and the insights used to develop the target audience profile(s) and the source of such insights;
  - Restrict youth-access and limit youth-exposure to the products' labeling, advertising, marketing, and/or promotion;
  - Use owned, earned, shared/social, and/or paid media to create labeling for, advertise, market, and/or promote the products;
  - Use partners, influencers, bloggers, and/or brand ambassadors to create labeling for, advertise, market, and/or promote the products;
  - Conduct any consumer engagements – whether by you, on your behalf, or at your direction – including events at which the products will be demonstrated; and/or
  - Use public-relations outreach to create labeling for, advertise, market, and/or promote the products.

III. Periodic Reporting

Under sections 911(h)(5) of the FD&C Act, these orders require that you submit periodic reports every 6 months to FDA once during the month of June of each year and once during the month of December of each year, beginning June 2020. For the six-month reporting period, the report must include:

- A cover letter that includes the following text in your subject line: **PERIODIC REPORT for MR0000020-MR0000022, MR0000024-MR0000025, MR0000027-MR0000029**. The cover letter should include the STN(s) and corresponding tobacco product name(s), applicant name, date of report, and reporting period.
- All final printed labeling (including all variations, such as those reflecting different required warnings) not previously submitted (e.g., if previously submitted under section 905(i) or previously submitted at the last reporting period and no changes were made, please list the date and manner of submission), including the date the labeling was first disseminated and the date when the labeling was discontinued, and a description of all changes to the labeling. The labeling must include all the panels and be presented in the actual size and color with legible text. The labeling must include labels, inserts/onserts, instructions, and any other accompanying information or materials for the products.
- All final full-color advertising, marketing, and/or promotional materials, published, disseminated to consumers, or for use in engaging or communicating with consumers not previously submitted (e.g., if previously submitted under 905(i) or previously submitted at the last reporting period and no changes were made, please list the date and manner of submission), along with the original date such materials were first disseminated and the date they were discontinued, and a description of all changes to the materials. The materials must be legible, include all panels where applicable (e.g., print ads, point of sale signs) and reflect the actual size and colors used. For any materials that would not fit on an 8.5" x 11" piece of paper, you may resize and submit electronic versions of such materials in a format that FDA can review and with sufficient resolution to allow FDA to read lettering clearly. If resizing the advertisement does not allow for text to be read easily, the complete text may be provided separately and clearly referenced. Digital media, such as videos must be submitted in a format that FDA is able to open and review.

IV. Annual Reporting

Under section 911(h)(5) of the FD&C Act, these risk modification orders require that you submit the following reports to FDA **on an annual basis**, beginning twelve months from the date of this order. For each twelve-month reporting period, these annual reports must include:

- A cover letter that includes the following text in your subject line: **ANNUAL REPORT for MR0000020-MR0000022, MR0000024-MR0000025, MR0000027-MR0000029**. The cover letter should include the STN(s) and corresponding tobacco product name(s), firm name, date of report, reporting period.
- A description of the implementation of all advertising and marketing plans, including strategic creative briefs and paid media plans – whether conducted by you, on your behalf, or at your direction – by channel and by product, and the dollar amount(s) and flighting of such plans, by channel and by product, including a description of any:
  - Use of competent and reliable data sources, methodologies, and technologies to establish, maintain, and monitor highly targeted advertising and marketing plans and media buys, including a list of all data sources used to target advertising and marketing plans and media buys;

  - Targeting of specific adult audiences by age-range(s), including young adults, ages 18-24, and other demographic and/or psychographic characteristics that reflect the intended target audience(s), how the target audience(s) were defined and the insights used to develop the target audience profiles(s) and the source of such insights;
  - Actions taken to restrict youth-access and limit youth-exposure to the products' labeling, advertising, marketing, and/or promotion;
  - Use of owned, earned, shared/social, and/or paid media to create labeling for, advertise, market, and/or promote the products;
  - Use of partners, influencers, bloggers, and/or brand ambassadors to create labeling for, advertise, market, and/or promote the products;
  - Consumer engagements – whether conducted by you, on your behalf, or at your direction – including events at which the products were demonstrated; and/or
  - Use of public-relations outreach to create labeling for, advertise, market, and/or promote the products; including the original date such plans were first used and the date they were discontinued, and a description of all changes to such plans since the last periodic report, by channel and by product.
- An analysis of the actual delivery of advertising impressions, by channel, by product, and by audience demographics (e.g., age, gender, race/ethnicity, geographic location), including a breakout by age-group (i.e., adults, ages 25+; young adults, ages 18-24; and youth, ages 12-17 and ages 11 and under), not previously submitted. This analysis should be verified against post-launch delivery-verification reports submitted to you from an accredited source.
- A summary of media tracking and optimization, by channel, by product, and by audience demographics (e.g., age, gender, race/ethnicity, geographic location), including a summary of real-time digital media monitoring to identify, correct, and prevent delivery of advertising impressions to youth, ages 17 and under, and including a summary of implementation of any corrective and preventive measures, not previously submitted.

V. Additional Conditions for Marketing

Under section 911(h)(5) of the FD&C Act, these risk modification orders require you to:

- For any of the products' labeling, advertising, marketing, and/or promotion appearing in your **owned digital properties** (e.g., your company-owned, consumer-directed, product-branded website(s) and/or mobile applications) – whether conducted by you, on your behalf, or at your direction – establish, maintain, and monitor use of independent age- and identity-verification service(s) that compare consumer information against independent, competent, and reliable data sources, such as public records, at the first point of access to such properties, to restrict access to such labeling, advertising, marketing, and/or promotion to only individuals who are at least of federal minimum legal age to purchase tobacco products.
- For any of the products' labeling, advertising, marketing, and/or promotion appearing in any **shared digital properties** (e.g., your product-branded social media accounts, pages and associated content; content promoting your products on your behalf disseminated through another entity's social media accounts) – whether conducted by you, on your behalf, or at your direction – establish, maintain, and monitor use of the available site-, platform- and content-(e.g., post, video) specific age-restriction controls (e.g., age-restrict an entire product-branded account and all associated content disseminated through such account; ensure age-restriction of a specific video disseminated by an influencer promoting the products on your behalf through the influencer's account), at the first point of access to such properties, to restrict access to such

labeling, advertising, marketing, and/or promotion to only individuals who are at least of federal minimum legal age to purchase tobacco products.

- For any of the products' labeling, advertising, marketing, and/or promotion appearing in **paid digital media** (e.g., paid digital banner advertisements for the product(s) running on another company's website; paid advertising for the product(s) running in social media; paid distribution of influencer content) – whether conducted by you, on your behalf, or at your direction:
  - Establish, maintain, and monitor use of competent and reliable data sources, methodologies, and technologies to precisely target delivery of such labeling, advertising, marketing, and/or promotion to only individuals who are at least of federal minimum legal age to purchase tobacco products. Such targeting must use only first- and/or second-party age-verified data, where:
    - "First-party" age-verified data is data owned by you (e.g., your customer registration data collected via site traffic to your company-owned website; data you use in direct marketing to your adult smoking customers) that you have age-verified through independent, competent, and reliable data sources; and
    - "Second-party" age-verified data is first-party data owned and age-verified by another competent and reliable entity (e.g., another company's first-party user registration data) to which you have access. Such data must be age-verified by the second party.
    - "First-party" and "second-party" data does not include data obtained from data aggregators who categorize consumers based on trackable activities and inferred interests (e.g., internet search terms, video interactions, browsing history, purchasing behaviors) to create demographic and psychographic profiles marketers may use to enhance audience targeting. Such data is not considered age-verified and can only be used in combination with first- and/or second-party age-verified data.
- Establish, maintain, and monitor use of competent and reliable data sources, methodologies, and technologies (e.g., using an embedded tracking pixel in all digital advertising) – whether conducted by you, on your behalf, or at your direction – to **track and measure actual delivery of all advertising impressions**, by channel, by product, and by audience demographics (e.g., age, gender, race/ethnicity, geographic location), including a breakout by age-group (i.e., adults, ages 25+; young adults, ages 18-24; and youth, ages 12-17 and ages 11 and under). Such monitoring requires real-time digital media tracking, and identifying, correcting, and preventing delivery of advertising impressions to youth, ages 17 and under. Such monitoring also requires post-launch delivery verification reports be submitted to you from an accredited source.
- For any use of **partners, influencers, bloggers, and/or brand ambassadors** to create labeling for, advertise, market, and/or promote the products – whether conducted by you, on your behalf, or at your direction – disclose to consumers or viewers, via the use of statements such as "sponsored by [firm name]" in such labeling, advertising, marketing, and/or promotional materials, any relationships between you and entities that create labeling for, advertise, market, and/or promote the products, on your behalf, or at your direction.

The requirements above are intended to help ensure that your modified risk tobacco products, as actually used by consumers, will continue to benefit the health of the population as a whole. Limiting youth initiation of the products and, relatedly, youth exposure to advertising and marketing materials for the products are important factors in the population health benefit analysis. Accordingly, FDA also recommends limiting youth-exposure to any of the tobacco products' labeling, advertising, marketing, and/or promotion appearing in print media publications.

After receiving authorization, the determination of whether the eight modified risk General Snus products, as actually used by consumers, continue to benefit the health of the population as a whole

is likely to be driven by use behavior. An uptake in youth initiation and use of the products would have a significant negative impact on the population health benefit analysis. To help ensure that your products, as actually used by consumers, continue to benefit the health of the population as a whole, we strongly recommend that you take measures to limit youth initiation and use of the products, beyond limiting advertising and promotion as required in this order. For example, we strongly recommend you adopt the following measures related to all digital sales of your products:

- For any **digital sales** – whether conducted by you, on your behalf, or at your direction – establish, maintain, and monitor use of independent age- and identity-verification service(s) that compare customer information against independent, competent, and reliable data sources, such as public records, to prevent the sale of the products to individuals who are under the federal minimum legal age to purchase tobacco products.

Relatedly, we request that you submit the following information to CTP on an annual basis:

- A summary of the implementation and effectiveness of any policies and procedures regarding verification of the age and identity of purchasers of the products.
- A summary of the implementation and effectiveness of any policies and procedures regarding restrictions on youth access to the products.

We remind you that if FDA can no longer make the determination that your products, as actually used by consumers, will benefit the health of the population as a whole, FDA must withdraw the modified risk orders, after an opportunity for an informal hearing. See under section 911(j)(1) of the FD&C Act. Although adopting the measures above is not in itself a guarantee that the products will continue to benefit the health of the population as a whole, it is an important step in helping to ensure that there are no grounds for withdrawal of your orders.

Appendix D

Recordkeeping and Retention

The risk modification orders for your modified risk tobacco products are effective for 5 years from the issue date of the orders. If you wish to renew your orders, we recommend you submit a request for renewal 360 days prior to the end of your effective timeframe. In order to help ensure that your risk modification orders meet the standard for renewal and to help expedite the review of any renewal applications, we request that you establish and maintain the records listed below. The records should be retained for a period of not less than four years from the date of distribution of the last batch of the tobacco products listed in your orders under section 911(g)(1). The records should be legible, written in English, and upon request, available for inspection and copying by officers or employees duly designated by the Secretary. Please note that Appendices B and C require you to periodically submit some of these records to FDA (e.g., in PMSS reports and/or advertising and promotion-related reports). Additionally, we remind you that the PMTA orders for your General snus products issued on November 10, 2015, also require you to establish and maintain records, some of which overlap with the records listed below:

- The MRTPAs submitted prior to the orders
- Postmarket reports, as described in the Required PMSS Appendix, including adverse experience reports and all relevant documentation associated with the experience
- Records of all nonclinical or clinical studies, including:
  - Source data;
  - Study protocols (including statistical analysis plan);
  - Amendments showing the dates and reasons for any protocol revisions;
  - Institutional Review Board (IRB) or Independent Ethics Committee (IEC) approvals or non-approvals;
  - Informed consent forms;
  - Correspondence with study monitors/investigators/contract research organizations/sponsors/IRB/IEC;
  - Investigator financial disclosure statements;
  - Progress reports;
  - Monitoring reports;
  - Adverse experience reports;
  - Case report forms/subject diaries/medical records/laboratory reports;
  - Subject data line listings/observation records;
  - Test article accountability records;
  - Study results/protocol summaries/study reports; and
  - Certifications and amendments to certifications
- Records pertaining to the manufacture, in process and release testing, production process (including any changes to the process, facility, or controls), packaging, storage, and stability monitoring and testing (including protocol and results) of the products
- Records pertaining to the sale, distribution, or other disposition of the products, specifically:
  - A list of distributors and retailers of the products, including brick-and-mortar and digital[8];
  - Any available information (not to include personally identifiable information) about product purchases, such as purchasers' demographics (e.g., age, gender, race/ethnicity, geographic region) and previous or current use of other tobacco products (i.e., dual use);
  - Policies and procedures regarding verification of the age and identity of purchasers of the products; and

[8] For the purposes of this order, here and throughout the document, "digital" includes internet/online and mobile.

  - Policies and procedures regarding restrictions on youth access to the products
- Health hazard analyses, if performed voluntarily or directed by FDA
- Records pertaining to any and all complaints associated with any of the products that you receive or of which you are aware

Appendix E

Manufacturing Information

The PMTA orders for your General Snus products, issued on November 10, 2015, require you to report to the FDA manufacturing information. We request that when submitting such reports, you reference both your PMTAs and you MRTPAs for these products. When cross-referencing, please provide the date of submission and location in the submission where the information is covered. When cross-referencing, please provide the date of submission and location in the submission where the information is covered.

For each twelve-month reporting period, the annual reports should include:

- A cover letter that includes the following text in your subject line: **ANNUAL REPORT for MR0000020-MR0000022, MR0000024-MR0000025, MR0000027-MR0000029**. The cover letter should include the STN(s) and corresponding tobacco product name(s), firm name, date of report, reporting period.
- A description of each change made to the manufacturing process, facilities, or controls during the reporting period including:
  - A comparison of each change to what was described in the MRTPAs;
  - The rationale for making each change; and
  - A certification that the reported change did not result in any modification (including a change in design, any component, any part, or any constituent, including a smoke or aerosol constituent, or in the content, delivery, or form of nicotine, or any other additive or ingredient) of the tobacco products and the basis for concluding that each manufacturing change did not result in any modification to the products.[9]
- A summary of all manufacturing deviations, investigations, and corrective and preventive actions, including, but not limited to, those deviations associated with processing, testing, packing, labeling, storage, holding, and distribution and indicate any deviation(s) that may affect the characteristics of the products. For additional information on manufacturing deviations, see below.

Manufacturing Deviations

You should promptly investigate all manufacturing deviations including, but not limited to, those associated with processing, testing, packing, labeling, storage, holding, and distribution. The PMTA orders for your General snus products, issued on November 10, 2015, require that, for products that have been distributed, if the deviation may negatively impact public health, you promptly identify and report that deviation to CTP. We request that when submitting such reports, you reference both your PMTAs and you MRTPAs for these products.

Discontinuation and Reintroduction

If you discontinue the manufacture, preparation, compounding, or processing for commercial distribution of these modified risk tobacco products and later decide to reintroduce the modified risk tobacco products into the market, please contact the Office of Compliance and Enforcement prior to reintroduction.

[9] We note that any modifications made to a tobacco product would render it a new tobacco product that would be subject to the premarket review requirements under section 910 of the FD&C Act.

Premarket Tobacco Application (PMTA) Technical Project Lead (TPL) Review

Submission Information			
Applicant	Swedish Match North America, Inc.		
Submission Date	March 11, 2015	**FDA Receipt Date**	March 11, 2015
PM0000010: General Loose			
Product Category	Smokeless Tobacco		
Product Sub-Category	Loose Snus		
Package Type	Cardboard Can with Plastic Lid		
Package Quantity	45.0 g		
Tobacco Cut Size:	(b) (4)		
Characterizing Flavor	None		
PM0000011: General Dry Mint Portion Original Mini			
Product Category	Smokeless Tobacco		
Product Sub-Category	Portioned Snus		
Package Type	Plastic Can		
Package Quantity	6.0 g		
Portion Count:	20 pouches		
Portion Mass:	300 mg		
Portion Length:	28 mm		
Portion Width:	14 mm		
Portion Thickness:	5 mm		
Tobacco Cut Size:	(b) (4)		
Characterizing Flavor	Mint		
PM0000012: General Portion Original Large			
Product Category	Smokeless Tobacco		
Product Sub-Category	Portioned Snus		
Package Type	Plastic Can		
Package Quantity	24.0g		
Portion Count:	24 pouches		
Portion Mass:	1000 mg		
Portion Length:	33 mm		
Portion Width:	18 mm		
Portion Thickness:	6 mm		
Tobacco Cut Size:	(b) (4)		
Characterizing Flavor	None		

[1]The applicant provided (b)(4) buckets to characterize the tobacco cut size. Therefore, the tobacco cut size cannot be represented with a single value and corresponding range limit.

PM0000013: General Classic Blend Portion White Large - 12ct	
Product Category	Smokeless Tobacco
Product Sub-Category	Portioned Snus
Package Type	Plastic Can
Package Quantity	10.8 g
Portion Count:	12 pouches
Portion Mass:	900 mg
Portion Length:	34 mm
Portion Width:	14 mm
Portion Thickness:	5 mm
Tobacco Cut Size:	(b) (4)
Characterizing Flavor	None
PM0000014: General Mint Portion White Large	
Product Category	Smokeless Tobacco
Product Sub-Category	Portioned Snus
Package Type	Plastic Can
Package Quantity	24.0 g
Portion Count:	24 pouches
Portion Mass:	1000 mg
Portion Length:	34 mm
Portion Width:	18 mm
Portion Thickness:	5. 5 mm
Tobacco Cut Size:	(b) (4)
Characterizing Flavor	Mint
PM0000015: General Nordic Mint Portion White Large - 12ct	
Product Category	Smokeless Tobacco
Product Sub-Category	Portioned Snus
Package Type	Plastic Can
Package Quantity	10.8 g
Portion Count:	12 pouches
Portion Mass:	900 mg
Portion Length:	34 mm
Portion Width:	14 mm
Portion Thickness:	5 mm
Tobacco Cut Size:	(b) (4)
Characterizing Flavor	Mint

PM0000016: General Portion White Large	
Product Category	Smokeless Tobacco
Product Sub-Category	Portioned Snus
Package Type	Plastic Can
Package Quantity	24.0 g
Portion Count:	24 pouches
Portion Mass:	1000 mg
Portion Length:	34 mm
Portion Width:	18 mm
Portion Thickness:	5.5 mm
Tobacco Cut Size:	(b) (4)
Characterizing Flavor	None

PM0000017: General Wintergreen Portion White Large	
Product Category	Smokeless Tobacco
Product Sub-Category	Portioned Snus
Package Type	Plastic Can
Package Quantity	24.0 g
Portion Count:	24 pouches
Portion Mass:	1000 mg
Portion Length:	34 mm
Portion Width:	18 mm
Portion Thickness:	5.5 mm
Tobacco Cut Size:	(b) (4)
Characterizing Flavor	Wintergreen

	STN	Submission Date	Solicited Y/N
Amendment(s)	PM0000018	3/31/2015	Y
	PM0000019	3/31/2015	Y
	PM0000020	3/31/2015	Y
	PM0000021	3/31/2015	Y
	PM0000022	3/31/2015	Y
	PM0000023	3/31/2015	Y
	PM0000024	3/31/2015	Y
	PM0000025	3/31/2015	Y
	PM0000026	6/3/2015	Y
	PM0000027	6/23/2015	Y
	PM0000029	7/8/2015	Y

	Cross Referenced Submission	Industry Meetings	Other Related Submission STN(s)
Related Submissions	MR0000020		SE0000140, SE0010524
	MR0000021		SE0000139, SE0010525
	MR0000022		SE0000143, SE0010526
	MR0000024		SE0010528
	MR0000025		SE0000141, SE0010529
	MR0000027		SE0010531
	MR0000028		SE0000144, SE0010532
	MR0000029		SE0000145, SE0010533
Product Use	☒ For Consumer Use ☐ For Further Manufacturing		
Product Type	☒ Complete ☐ Component Part, or Accessory		

DISCIPLINES REVIEWED	DATE OF REVIEW
Behavioral Pharmacology	October 21, 2015
Chemistry	October 30, 2015
Clinical Pharmacology	October 21, 2015
Engineering	October 2, 2015
Environmental Science	October 8, 2015
Epidemiology	October 6, 2015
Medical	October 20, 2015
Microbiology	October 15, 2015
OCE Review (DEM & DPAL)	October 6, 2015
Social Science	October 2, 2015
Statistics	September 28, 2015
Toxicology	October 16, 2015

Recommended Action(s)

☒ Issue a Marketing Authorization letter; application contains sufficient evidence to demonstrate the product is appropriate for the protection of public health.

☐ Issue a No Marketing Authorization letter; application does not contain sufficient evidence to demonstrate the product is appropriate for the protection of public health.

Technical Project Lead Name:

CTP/OS Ii-Lun Chen, MD
Director, Division of Individual Health Science

Digitally signed by lilun Chen -S

Signatory Decision:

☒ I concur with TPL recommendation and basis of recommendation

☐ I concur with TPL recommendation and am providing additional comments (see separate memo)

☐ I do not concur with TPL recommendation as stated in my separate memo

Signatory: David Ashley, Ph.D.
CTP/OS RADM, U.S. Public Health Service
Director
Office of Science

Digitally signed by David Ashley -S
Date: 2015.11.03 13:25:56 -05'00'

Premarket Tobacco Application Technical Project Leader Review

I. Executive Summary

On March 11, 2015, Swedish Match North America (SMNA) submitted eight General brand snus premarket tobacco product applications (PMTAs) to FDA seeking authorization under Section 910(b) of the Federal Food, Drug and Cosmetic Act (FD&C Act).

Scientific review of these eight applications demonstrates that these eight products have the following qualities:

- Produced with a voluntary, proprietary standard using acceptable manufacturing processes as confirmed by both application review and on-site inspections. The applicant's heat treatment process distinguishes Swedish snus from other types of smokeless tobacco (ST), including snus-like products sold in the US market. The proprietary quality standard for Swedish snus products was developed to ensure product quality. The principal components of this standard include constituent standards, manufacturing standards, manufacturing process requirements, and consumer package labeling with a "best before" date. The constituent standards set maximum levels that must not be exceeded for selected constituents in the finished products.

  The proposed products contain significantly lower levels of NNN and NNK compared to over 97% the ST products currently on US market. Since NNN and NNK are among the most carcinogenic constituents in tobacco products, reduction of NNN and NNK levels in ST products could reduce the cancer risk for consumers using ST products. Assuming persons who would have used other US ST products use these product instead, an individual using these products with reduced NNN levels could decrease the excess cancer risk[2] by 90% compared to use of moist snuff (market share: 82%), 67% compared to use of chewing tobacco (market share: 15%), 38% compared to use of United States (US)-style snus, and 92% compared to use of dry snuff. Even further reductions in excess cancer risk could occur with the corresponding reductions in NNK; however, a quantitative contribution cannot be determined at this time due to the absence of a NNK cancer slope factor.

- Levels of other harmful and potentially harmful constituents (HPHC)(including As, Cd, acetaldehyde, crotonaldehyde, formaldehyde, and BaP) are similar to or lower than levels of ST products currently on the US market. Certain HPHCs (such as acrolein, acetaldehyde, cadmium, and nickel) have been identified as constituents of more toxic concern in the smoke of combusted products as compared to smokeless products.

- When used as exclusively instead of other smokeless tobacco products or cigarettes on the US market, these products offer potential for reductions in oral cancer risk.

[2]The excess lifetime cancer risk is a toxicological tool to estimate the probability of cancer incidence in a population of individuals for a specific lifetime from projected intakes (and exposures) and dose-response data (i.e., slope factors) for a specific chemical.

- When used as exclusively instead of combusted tobacco products, these products offer lower risk of developing respiratory diseases (i.e., chronic obstructive pulmonary disease (COPD), emphysema, chronic bronchitis) and cancers (such as oral, esophageal, and lung) than smokers.

- If nonusers were to initiate or users decrease cessation, there would be negative health consequences.

- Use of Swedish snus products is not risk-free and its use is associated with adverse health risks such adverse pregnancy outcomes, oral disease, increased risk of fatal cardiovascular events, pancreatic cancer, diabetes, and all-cause mortality.

- It is anticipated that the marketing of the proposed products, as described in the PMTAs, there is a low likelihood of nonuser uptake of these products, decreased or delayed cessation, or other significant shifts in user demographics.

Information from national tobacco use studies and other studies submitted by the applicant indicate that migration of smokers to exclusive use of these proposed snus tobacco products while possible is expected to be limited. It is more likely that uptake of the proposed products occurs among current smokeless tobacco users. Given the above listed justifications based on information gathered from nonclinical and clinical product evaluations as well as substantial epidemiological studies, the totality of evidence provided in the applications support authorization of these products so that current ST product users will have additional options for less toxic tobacco products, thereby potentially decreasing the negative health impact from tobacco product use making the marketing of these proposed products appropriate for the protection of public health.

U.S. FOOD & DRUG ADMINISTRATION

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

Scientific Review of Modified Risk Tobacco Product Application (MRTPA) Under Section 911 (d) of the FD&C Act – Technical Project Lead

SUBMISSION INFORMATION			
Applicant	Swedish Match USA, Inc.		
Product Manufacturer	Swedish Match USA, Inc.		
Submission Date	June 10, 2014	**FDA Receipt Date**	June 10, 2014
Purpose	☒ Risk Modification (911(g)(1) order) ☐ Exposure Modification (911(g)(2) order)		
Claims	Using General Snus instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.		
Primary STN(s)	MR0000020	General Loose	☒Single ☐Co-Packaged **Description** N/A
	MR0000021	General Dry Mint Portion Original Mini	☒Single ☐ Co-Packaged **Description:** N/A
	MR0000022	General Portion Original Large	☒Single ☐ Co-Packaged **Description:** N/A
	MR0000024	General Classic Blend Portion White Large – 12 ct	☒Single ☐ Co-Packaged **Description:** N/A
	MR0000025	General Mint Portion White Large	☒Single ☐ Co-Packaged **Description:** N/A
	MR0000027	General Nordic Mint Portion White Large – 12 ct	☒Single ☐ Co-Packaged **Description:** N/A
	MR0000028	General Portion White Large	☒Single ☐ Co-Packaged **Description** N/A
	MR0000029	General Wintergreen Portion White Large	☒Single ☐ Co-Packaged **Description:** N/A

Amendments			
Amendment STN	**Primary STN**	**Description**	**FDA Receipt Date**
MR0000030	All	Market Tracker raw data	July 31, 2014
MR0000031	All	HPHC raw data	August 1, 2014
MR0000032	All	Background information related to cognitive testing for the premarket consumer perception study	August 5, 2014
MR0000033	All	Raw data for the consumer perception study	August 15, 2014
MR0000035	All	Response to November 12, 2014, FDA Information Request	December 3, 2014

MR0000036	All	Response to November 25, 2014, FDA Information Request	December 9, 2014
MR0000038	All	Response to January 9, 2015, FDA Information Request	January 27, 2015
MR0000039	All	Response to February 6, 2015, FDA Information Request	February 20, 2015
MR0000041	All	Response to March 6, 2015, FDA Information Request	March 11, 2015
MR0000042	All	Response to April 28, 2015, Information Request	May 22, 2015
MR0000044	All	Response to June 5, 2015, Information Request	June 19, 2015
MR0000131	All	Response to December 14, 2016, FDA Information Request	September 17, 2018
MR0000138	All	Response to October 24, 2018, FDA Information Request	November 28, 2018
MR0000148	All	Amended response of November 28, 2018 Amendment	January 30, 2019
MR0000158	All	Response to April 18, 2019, FDA Information Request	April 24, 2019

PROPOSED MODIFIED RISK TOBACCO PRODUCT (SINGLE PRODUCTS)	
STN	MR0000020
Product Name	General Loose
Product Category	Smokeless Tobacco
Product Sub-Category	Loose Snus
Package Type	Cardboard Can with Plastic Lid
Package Quantity	45.0 g
Characterizing Flavor	None
Product Use	☒ For Consumer Use ☐ For Further Manufacturing
STN	MR0000021
Product Name	General Dry Mint Portion Original Mini
Product Category	Smokeless Tobacco
Product Sub-Category	Portioned Snus
Package Type	Plastic Can
Package Quantity	6.0 g
Characterizing Flavor	Mint
Product Use	☒ For Consumer Use ☐ For Further Manufacturing

STN	MR0000022
Product Name	General Portion Original Large
Product Category	Smokeless Tobacco
Product Sub-Category	Portioned Snus
Package Type	Plastic Can
Package Quantity	24.0 g
Characterizing Flavor	None
Product Use	☒ For Consumer Use ☐ For Further Manufacturing
STN	MR0000024
Product Name	General Classic Blend Portion White Large – 12 ct
Product Category	Smokeless Tobacco
Product Sub-Category	Portioned Snus
Package Type	Plastic Can
Package Quantity	10.8 g
Characterizing Flavor	None
Product Use	☒ For Consumer Use ☐ For Further Manufacturing
STN	MR0000025
Product Name	General Mint Portion White Large
Product Category	Smokeless Tobacco
Product Sub-Category	Portioned Snus
Package Type	Plastic Can
Package Quantity	24.0 g
Characterizing Flavor	Mint
Product Use	☒ For Consumer Use ☐ For Further Manufacturing
STN	MR0000027
Product Name	General Nordic Mint Portion White Large – 12 ct
Product Category	Smokeless Tobacco
Product Sub-Category	Portioned Snus
Package Type	Plastic Can
Package Quantity	10.8 g
Characterizing Flavor	Mint
Product Use	☒ For Consumer Use ☐ For Further Manufacturing
STN	MR0000028
Product Name	General Portion White Large
Product Category	Smokeless Tobacco
Product Sub-Category	Portioned Snus
Package Type	Plastic Can
Package Quantity	24.0 g
Characterizing Flavor	None
Product Use	☒ For Consumer Use ☐ For Further Manufacturing

STN	MR0000029
Product Name	General Wintergreen Portion White Large
Product Category	Smokeless Tobacco
Product Sub-Category	Portioned Snus
Package Type	Plastic Can
Package Quantity	24.0 g
Characterizing Flavor	Wintergreen
Product Use	☒ For Consumer Use [ ] For Further Manufacturing

DISCIPLINES REVIEWED	DATE OF REVIEW
Engineering	September 14, 2016
Chemistry	September 15, 2016
Microbiology	September 15, 2016
Toxicology	September 19, 2016
Social Science	October 27, 2016; October 11, 2019
Addiction Clinical Pharmacology	October 28, 2016
Behavioral Clinical Pharmacology	October 31, 2016
Medical	October 26, 2016
Epidemiology	November 2, 2016
Statistics	October 24, 2016; October 27, 2016
Environmental Science	October 3, 2019
OCE Review (DEM & DPAL)	November 12, 2014; September 16, 2016; September 20, 2016; October 17, 2019

Recommended Action(s)

- [X] Issue a Modified Risk Granted letter
- [ ] Issue a Denial letter

Technical Project Lead (TPL):

/S/

Benjamin J. Apelberg, Ph.D.
Director
Division of Population Health Science

Signatory Decision:

- ☒ Concur with TPL recommendation and basis of recommendation
- ☐ Concur with TPL recommendation with additional comments (see separate memo)
- ☐ Do not concur with TPL recommendation (see separate memo)

/S/

Matthew R. Holman, Ph.D.
Director
Office of Science

I. Executive Summary

On June 10, 2014, FDA received applications from Swedish Match North America, Inc. (SMNA)[1] requesting modified risk tobacco product (MRTP) orders under Section 911(g)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for eight General Snus products.

SMNA initially proposed marketing these products as modified risk through the removal and revision of certain health warnings currently required by the Comprehensive Smokeless Tobacco Health Education Act for smokeless tobacco products. In particular, the applicant proposed to:

1. Remove "WARNING: This product can cause gum disease and tooth loss."

2. Remove "WARNING: This product can cause mouth cancer."

3. Revise "WARNING: This product is not a safe alternative to cigarettes" to "WARNING: No tobacco product is safe but this product presents substantially lower risks to health than cigarettes."

The applicant did not propose a change to the warning: "WARNING: Smokeless tobacco is addictive."

The requests to remove warnings were evaluated as implied modified risk claims that the products cannot cause the health outcomes named (gum disease and tooth loss; mouth cancer).

On December 14, 2016, FDA completed its review of the modified risk tobacco product applications (MRTPAs) and issued a partial decision on the applications. The request to remove the gum disease and tooth loss warning was denied, while FDA deferred final action on the other requests. In deferring final action, FDA determined that the applications in their current form did not provide sufficient evidence to meet the standard of 911(g)(1), but they could be amended in a way that would support the issuance of a modified risk order. Accordingly, FDA issued a Response Letter, which included the following three deficiencies:

1. You request to omit from the label and advertising "WARNING: This product can cause mouth cancer." This warning is currently required for smokeless tobacco products generally. Omission of this warning from a subset of smokeless tobacco products indicates that unlike other smokeless tobacco products, the eight General snus products cannot cause mouth cancer. Thus, the request is to market the products with an implied modified risk claim that the products, as compared to other smokeless tobacco products, cannot cause mouth cancer.

   Although the eight General snus products contain significantly lower levels of harmful carcinogens than other smokeless tobacco products currently in the U.S. market, the products contain nitrosamines, including NNN and NNK, which have been demonstrated to cause cancer, including cancers of the mouth. NNN in particular has been found to be a potent oral

[1] The applicant changed its name from Swedish Match North America (SMNA) to Swedish Match USA, Inc. during the period between submission of their initial applications and their September 2018 amendment described below. In this document we will refer to the applicant as SMNA when describing events that took place during the time that was their name. We will refer to the applicant as Swedish Match when describing events occurring subsequent to the name change.

carcinogen, and since, according to the available toxicological evidence, there is no established threshold level for NNN carcinogenicity, the products pose an increased risk of mouth cancer compared to non-use. In addition, the available epidemiological evidence on the products, as actually used by consumers in Sweden and Norway, is not sufficient to conclude that the use of the products themselves does not increase the risk of cancers of the mouth. In fact, the most recent published epidemiological study found an association between snus use and mouth cancer. Accordingly, the totality of the scientific evidence supports the statement that smokeless tobacco products in general and these products in particular "can cause mouth cancer" and the proposed modified risk claim is not substantiated. We therefore conclude that the scientific evidence currently before the agency does not support the removal of the warning related to mouth cancer. Additionally, you did not provide evidence regarding how the modified risk information (i.e., the removal of the mouth cancer warning) would impact consumer behavior or whether consumers would understand the modified risk information in the context of total health. As a result, we are not issuing modified risk orders based on the proposed claim in its current form.

Although your applications do not support the specific request related to removing the warning related to mouth cancer, the evidence you provided may support applications that seek to market the products with other claims about relatively lower risk of mouth cancer for these products as compared to other tobacco products. Compared to the claim in your current applications, any new claim should be more precisely tailored to the supporting science. For example, you may consider pursuing explicit claims that appear outside of the health warning, elsewhere on the label or in advertising, providing information to consumers concerning the differences in mouth cancer risks between the eight General snus products and other tobacco products. These claims will need to be carefully constructed and adequately tested so as to ensure that the products meet the modified risk standards, including the requirement for consumer comprehension. We recommend that you meet with the Office of Science in FDA's Center for Tobacco Products to discuss how your applications could be amended.

2. You request to revise the currently required "WARNING: This product is not a safe alternative to cigarettes" on the label and advertising, by replacing it with an express modified risk claim "WARNING: No tobacco product is safe, but this product presents substantially lower risks to health than cigarettes." Our review concluded that the claim that the eight General snus products present substantially lower risks to health may be substantiated, but only in part. That is, there is evidence to support that the eight General snus products, as actually used by consumers in Sweden and Norway, as compared to smoking cigarettes may substantially reduce the risks of some, but not all, tobacco-related diseases to individual tobacco users. The scientific evidence is insufficient to support that substantial reductions would be observed across the full range of risks posed by tobacco products, as implied by a generalized statement about health risks as compared to smoking (i.e., "substantially lower risks to health than cigarettes"). The evidence is also insufficient that U.S. consumers would use the products in the same manner as consumers in Sweden and Norway (e.g., frequency or intensity of usage; exclusive snus use versus dual use with cigarettes); therefore, we cannot conclude that, as actually used by U.S. consumers, the products would substantially reduce the risks to smokers. In addition, FDA assessed the potential benefits and harms to the health of the population and concluded that the evidence is insufficient to determine that the products will benefit the population as a whole, taking into account, for example, smokers who switch completely to the General snus products, non-users who initiate use, and dual use by current tobacco users. Furthermore, the

scientific evidence is not sufficient to conclude that the modified risk information would be comprehended by the public in the context of total health and in relation to all tobacco-related disease, particularly in the context of a warning. As a result, we are not issuing modified risk orders based on the proposed claim in its current form.

Although your applications do not support the specific request to revise the warning, the evidence you provided may support applications that seek to market the products with other claims about relative health risks compared to cigarettes. Compared to the claim in your current applications, any new claim should be more precisely tailored to the supporting science. For example, you may consider pursuing explicit claims that appear outside of the health warning, elsewhere on the label or in advertising, providing information to consumers concerning the differences in specific health risks between the eight General snus products and cigarettes. These claims will need to be carefully constructed and adequately tested so as to ensure that the products meet the modified risk standards, including the requirement for consumer comprehension. We recommend that you meet with the Office of Science in FDA's Center for Tobacco Products to discuss how your applications could be amended.

3. The Consumer Perception Study you conducted was deficient for purposes of providing insight on potential behavioral impacts of the modified risk information or on consumer comprehension because it did not use appropriate stimuli and the methods used to assess comprehension, perceptions, and behavioral intentions were problematic. If you choose to conduct a new consumer perception and comprehension study (e.g., as part of addressing the deficiencies discussed in 1 and 2 above), you should address the deficiencies identified in our review of the Consumer Perception Study. To best inform an evaluation of the effects of the modified risk information, study stimuli should test the proposed modified risk information verbatim. As noted above, consider providing modified risk information by some means other than through the removal or revision of the warning statements. However, if modified risk information remains in the warning statement itself, your study should also examine the impact of the context of the modified risk information, i.e., how the context of the modified risk information (e.g., whether presented within a warning or as a standalone claim) affects consumer perception and comprehension.

   Although a well-designed study on consumer perception and comprehension will provide indirect information on potential impacts on behavior, we recommend that you also consider assessing consumer perception, comprehension, and intentions in the context of an actual use study designed to address behavioral outcomes, particularly among current users of tobacco products. Such data would provide direct evidence of the impact of the proposed claims on consumer behavior, including evidence that U.S. consumers will use the proposed products as intended, e.g., the products will be used by current tobacco users, in lieu of, and not in addition to, smoking cigarettes.

On September 17, 2018, Swedish Match submitted an amendment to address the FDA Response Letter. The applicant addressed the deficiencies accordingly:

- Deficiencies 1 and 2: The applicant has tested and proposed a revised modified risk claim that is more precisely tailored to the scientific evidence. Specifically, the revised claim conveys specific health risks that are reduced relative to cigarette smoking, describes how the products should be used relative to cigarettes (i.e., "instead of") and *does not* include a subjective qualifier of the

risk reduction (e.g., "substantially"). The revised modified risk claim is explicit and appears outside of the health warning label. The applicant no longer requests to change or remove any warning labels.

- Deficiency 3: The applicant has conducted a new consumer perception study to evaluate the revised modified risk claim and redress the initial study's deficiencies in terms of study stimuli and measures.

To communicate modified risk information to consumers, the applicant proposes to add the following claim to the advertising of the eight General Snus products that are the subject of these applications:

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

The applicant proposes to use the claim in advertisements but does not plan to add it to the products' labels. The applicant submitted a new consumer study, the Perceptions and Behavioral Intentions (PBI) study, to evaluate consumer reactions to the product with the proposed claim, including consumer understanding, perceptions, and intentions to buy the products.

The applicant's request was assessed, per Section 911(g)(1) to determine whether the applicant demonstrated that, as actually used by consumers, the products sold or distributed with the proposed modified risk information 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.

The assessment of whether the products meet the MRTP standard begins with an assessment of the scientific substantiation of the proposed modified risk information. Under Section 911(g)(1), the modified risk inquiry also involves an assessment of whether the proposed modified risk products, as actually used by consumers, will significantly reduce harm and the risk of tobacco-related disease to individual tobacco users. This assessment includes an evaluation of the relative health risks to individual tobacco users, including a broad range of health risks beyond those specifically addressed in the proposed modified risk claim.

The modified risk inquiry further includes an assessment of the potential benefits and harms to 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. This assessment considers the impact of the products with the proposed modified risk information on tobacco use behaviors, such as the potential for adoption of the products on the part of current tobacco users, dual or poly use of tobacco products by current users, the likelihood of product uptake among current non-tobacco users, and the ensuing health outcomes resulting from those behaviors in the population. This evaluation includes assessments of:

- The increased or decreased likelihood that existing tobacco product users who would otherwise stop using such products will switch to using the MRTPs;
- The increased or decreased likelihood that persons who do not use tobacco products will start using the MRTPs;

- The risks and benefits to persons from the use of the MRTPs compared to the use of smoking cessation drug or device products approved by FDA to treat nicotine dependence.

The modified risk standard also involves an assessment of consumer perception, understanding, and comprehension of the modified risk information, which may be an important precursor to consumer behavior and could affect how consumers actually use the products. Relatedly, Section 911(h)(1) of the FD&C Act 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."

To the extent possible, the assessment integrates the various threads of evidence regarding the products and their potential effects on health and tobacco use behavior, including tobacco use initiation, to determine both the net effect of the products on overall tobacco-related morbidity and mortality and the distribution of the benefits and harms across the population, e.g., harms to current non-users that result from significant increases in initiation of tobacco use.

In addition to the information contained in the MRTPAs, the assessment considered the recommendations from the Tobacco Products Scientific Advisory Committee (TPSAC); comments, data, and information submitted to FDA by interested persons; and other scientific information identified by the Agency from other sources.

After conducting a thorough scientific review of all of these materials, I conclude that:

- The applicant **has demonstrated** that, as actually used by consumers, the eight General Snus products sold or distributed with the proposed modified risk information, 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.

The claim "Using General Snus instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis" is scientifically accurate. The available scientific evidence, in particular the long-term epidemiological studies, reviewed under the original submission and summarized again in this review, substantiates that relative to cigarette smoking, exclusive use of the eight General Snus products poses lower risk of the above-named health outcomes. The applicant provided sufficient justification to determine that the epidemiological evidence from Sweden and Norway, although not specific to the products that are subjects of these applications, provides a reasonable characterization of the risks that would be expected to be observed among General Snus users in the U.S. if they used the products in a similar manner.

The available scientific evidence demonstrates that exclusive use of the eight General Snus products will significantly reduce harm and the risk of tobacco-related disease to individual tobacco users. As described above, exclusive use of these products poses lower risks than cigarette smoking for many of the major causes of tobacco-related disease. In addition to these lower risks relative to cigarette smoking, FDA has previously determined that the levels of NNN and NNK, two potent carcinogens in smokeless tobacco products, in these General Snus products are lower than those in the vast majority of smokeless tobacco products on the U.S. market, and when used exclusively instead of other smokeless tobacco products, the General Snus products offer the potential for reductions in oral cancer risk.

Although exposure to harmful and potentially harmful constituents (HPHCs) is lower than many other smokeless tobacco products, exposure is still elevated compared with non-use and, therefore, long-term use of General Snus is not without health risks. FDA's 2016 Technical Project Lead (TPL) review concluded that Swedish snus use (compared with no use of tobacco) has been associated with increased risk of specific disease endpoints in individual epidemiological studies, including pancreatic cancer, fatal MI and stroke, diabetes, and adverse pregnancy outcomes. In addition, there are potential negative effects of nicotine exposure on the developing adolescent brain.

The additional evidence provided in the amendment also supports that, as actually used by consumers, the eight General Snus MRTPs will benefit the health of the population as a whole. The PBI study demonstrated that exposure to the claim positively impacted relative risk perceptions and intentions to buy the product among smokers aged 25 years and older, a group who stands to benefit the most from the marketing of the products. For instance, among adult smokers aged 25 years and older, participants who were exposed to a marketing video with the modified risk claim reported significantly higher intentions to buy the product compared to those who did not see the modified risk claim. Smokers under age 25 years showed a similar pattern, although the impact of the claim on intentions was not statistically significant for this group. Similarly, although not statistically significant, the pattern of results also suggested the claim may have a positive impact on smokeless tobacco users' intentions to buy the product. In addition, smokeless tobacco users across conditions showed the highest mean levels of intentions to buy the product, suggesting that the marketing of the products with the claim could increase the likelihood of current smokeless users transitioning to the eight General Snus products, which are likely to be a less toxic alternative. The applicant also provided evidence to show that consumers can understand the claim and its significance in the context of total health, including understanding that the risk reduction is not achieved via partial switching (i.e., dual use of General Snus with continued use of cigarettes). In fact, the proposed claim improved consumers' understanding of the risks of General Snus relative to cigarettes and their understanding that dual use presents greater health risks than exclusive General Snus use, thereby increasing the likelihood that consumers who use the products will do so exclusively. Together, the demonstrated impact of the claim on understanding, perceptions, and behavioral intentions, even in the context of a relatively brief exposure, supports that the proposed MRTPs will benefit the population as a whole.

The PBI study provided sufficient evidence to support product authorization. However, the results were not without limitations. In particular, although the evidence showed that exposure to the modified risk claim significantly impacted perceptions of the absolute and relative risk of the products—shifting perceptions in line with the claim, towards greater accuracy—this was true, on average, but not necessarily for all participants. In fact, a proportion of participants was not affected by the claim and continued to perceive the product as just as harmful as cigarettes, for instance. Likewise, just as some participants did not perceive General Snus as less harmful compared to cigarettes, a proportion also did not understand that exclusive use of General Snus would be less harmful than dual use of General Snus with cigarettes. Considered in the context of the totality of the evidence, these results do not undermine my conclusion that the product meets the standard in Section 911(g)(1) of the FD&C Act. However, given their relevance to the population health impact of these MRTPs, these are areas that need to be monitored through postmarket surveillance and studies (PMSS).

Finally, the new evidence supports that the population health benefits gained by cigarette smokers (and potentially other smokeless tobacco users) switching to these products will not be outweighed by the risks of initiating new tobacco use. The PBI study found low levels of intentions to buy the product among non-users of tobacco (including young adults) and, importantly, found that the inclusion of the

modified risk claim did *not* affect these intentions. Prevention of youth initiation of tobacco products is a key consideration in FDA's evaluation. Although the available evidence from epidemiological studies does not demonstrate significant youth initiation of snus products at this time, it is possible that marketing the product as a modified risk product could change this. In fact, some studies suggest that risks perceptions predict tobacco product use among youth (e.g., Song et al. 2009; Strong et al. 2019). Thus, it is essential that modified risk marketing be targeted to current tobacco users and disseminated in ways to minimize exposure among youth. Based on these conclusions, the postmarket requirements described below include measures to limit youth exposure to the products' labeling, advertising, and marketing. In addition, reporting requirements will enable FDA to monitor, among other things, the degree to which the implementation of the marketing plans is effectively targeting the intended audience and limiting exposure to youth.

Section 911(h)(4) of the FD&C Act requires an MRTP order to be for a specified time period. I recommend authorization for a period of five years, given that these would be the first MRTP authorizations issued by the Agency. Although this review has found that the products will benefit the health of the population as a whole, that determination may change over time as a function of how the product is actually used by consumers. Therefore, monitoring use of the eight General Snus products that are the subject of these applications in terms of uptake, dual use, and complete switching is required. As described below, postmarket surveillance and studies must include an assessment of MRTP users' behavior and understanding at multiple time points. A five-year period is a reasonable amount of time for trends in use behavior to emerge to evaluate in postmarket surveillance and studies and assess whether the standard continues to be met and whether the order should be renewed.

Briefing Materials Appendix - Surveillance of Published Literature

Swedish Match USA, Inc.

General Snus Products

MR0000020-MR0000022

MR0000024-MR0000025

MR0000027-MR0000029

Literature Search Date Range =

January 1, 2019 – March 29, 2024

Surveillance of Published Literature

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