

January 30, 2024

Gerard J. Roerty, Jr.
Vice President, General Counsel & Secretary
Swedish Match USA, Inc.
Two James Center
1021 East Cary Street, Suite 1600
Richmond, VA 23219
Phone: (b) (6)
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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

SUBJECT: RESPONSE TO DEFICIENCY LETTER – MR0000256.PD1-MR0000256.PD5, MR0000256.PD7-MR0000256.PD9

Dear Sir or Madam:

We received your correspondence dated January 17, 2024 ("Letter") (**see attachment, Attachment A**) regarding FDA's review of the MRTPA Renewal that Swedish Match USA, Inc. ("Swedish Match", "we", "us" or "our") had previously submitted on July 17, 2023, as well as the referenced Amendment Response dated December 13, 2023, for the following products:

- MR0000256.PD1: General Loose
- MR0000256.PD2: General Dry Mint Portion Original Mini
- MR0000256.PD3: General Portion Original Large
- MR0000256.PD4: General Classic Blend Portion White Large – 12ct
- MR0000256.PD5: General Mint Portion White Large
- MR0000256.PD7: General Nordic Mint Portion White Large – 12ct
- MR0000256.PD8: General Portion White Large
- MR0000256.PD9: General Wintergreen Portion White Large

As part of our reply to the Agency's request for additional information, we set forth below, our response ("Response") to each request enumerated in the Letter. This Response and its associated reference and attachments have been constructed as directed by FDA in the Letter. Where appropriate, we have included any previously submitted information, as well as direct FDA to the section(s), page(s), and line number(s) of our prior reports, including amendments, where this information can also be found.

Swedish Match submits that this Response and the information we are supplying in connection with this Response are trade secret, proprietary information that is protected under state and federal law from public disclosure. This information should therefore be handled in accordance with the security procedures adopted by FDA, in connection with enforcement of the FDCA.

We appreciate your consideration and evaluation of this Response concerning our MRTPAs identified above. If you should have any questions, please let me know.

Sincerely yours,

(b) (6)

Gerard J. Roerty, Jr.
Vice President, General Counsel & Secretary

Document Attachments (List)

Attachment A – CTP Correspondence re: MR0000256.PD1-MR0000256.PD5, MR0000256.PD7-MR0000256.PD9 dated January 17, 2024

Attachment B – IRB Review and Exemption Determination Letter

Attachment C – Summary of Previous Periodic Reporting (Excel File Format)

Attachment D – Response to CTP Correspondence dated December 14, 2023

Attachment E – Study Materials for General Snus Patterns of Use Study (see sections E.1 – E.5)

Attachment F – “Readme” Summary of General Snus Patterns of Use Study (Data and Analyses)

Attachment G – Data Maps Files (.xlsx files G.1 – G.4)

Attachment H – Solicited Code (.txt file format H.1 - H.5)

Attachment I – Data Files (.xpt format I.1 - I.4)

Each request for additional information identified by number in the Letter is reproduced below in bold type followed by Swedish Match's Response.

1. Your MRTPA renewal application lacks adequate cross-referencing to include all information that you submitted in support of your application review. On October 19, 2023, you submitted two-post market surveillance reports (PS0000306, PS0000307) and on December 14, 2023, you submitted two additional post-market surveillance reports PS0000314, PS0000315). These four reports are not cross-referenced in your renewal application. Since the post-market surveillance reports contain information that is relevant to scientific review, we are currently unable to continue with a comprehensive scientific review. Submit an amendment that cross-references the four missing post-market surveillance reports. In the future, be sure to submit amendments to your renewal application in parallel when submit new post-market surveillance reports.

Swedish Match Response to Question #1

In **Attachment C**, Swedish Match provides an amended .xlsx file containing cross-referencing for our previous periodic and annual reporting. We previously submitted this .xlsx file with our July 17, 2023 renewal application. This amended file contains cross-referencing for the correspondence we submitted after July 17, 2023, including cross-referencing for the post-market surveillance reports (i.e., PS0000306, PS0000307, PS0000314, PS0000315) submitted on October 19, 2023 and December 14, 2023. Specifically, **Attachment C Tab 2** provides the requested cross-referencing.

This amendment is intended to supersede and replace the previous version of this .xlsx file.

2. Your MRTPA renewal application lacks documents containing all information related to the General Snus Patterns of Use study. Specifically, it is missing line data and relevant files to aid data analysis. These items are important for FDA to replicate applicant findings or conduct alternative statistical analyses. Your renewal also lacks documentation of IRB approval for your General Snus Patterns of Use study. Documentation of IRB approval is needed for FDA to assure any data collection involving participants was conducted with appropriate measure to protect the rights and welfare of human research subjects. Submit line data, data definition files that include the names of the variables, codes, and formats used in each dataset, and copies of programs and any necessary macro programs used to create derived datasets and the results reported in the study reports. Additionally, submit documentation of IRB approval for the study.

Swedish Match Response to Question #2

The requested documents for Swedish Match's General Snus Patterns of Use study have been included in this Response (**please see attachments, Attachment D, Attachment E, Attachment F, Attachment G, Attachment H, Attachment I**). The solicited information provided in this Response include the following items:

- Line data and relevant files to aid data analysis;
- Data definition files that include the names of the variables, codes, and formats used in each data set;

- Copies of programs and any necessary macro programs used to create derived datasheets and the results reported in the study reports.

The inclusion of these items will allow FDA to replicate applicant findings and/or conduct alternative statistical analyses.

Per FDA's request, this Response also includes:

- Documentation of Institutional Review Board ("IRB") review for the study (**see attachment, Attachment B**)

Documented approval from a central IRB in the U.S. was obtained prior to the initiation of the study. Sterling, IRB (Atlanta, Georgia) approved this study. The General Snus Patterns of Use Study received a Category 2 Exemption.

Further:

Per FDA's request, on January 17, 2024, Swedish Match submitted updated Environmental Assessments and corresponding Confidential Appendices for each of the eight (8) General Snus SKUs included in the MRTPA renewal application. Regarding their environmental impact, the assessments continued to demonstrate the appropriateness of the protection of the public health ("APPH") of the proposed modified risk tobacco products. To assist FDA in their assessment of the application, we cross-referenced these recently submitted items into the aforementioned amended Excel file (**see attachment, Attachment C, Tab 9**).



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

January 17, 2024

DEFICIENCY

Swedish Match U.S.A. Inc.
Attention: Gerard J. Roerty, Jr., General Counsel
Two James Center
1021 East Cary Street, Suite 1600
Richmond, VA 23219

FDA Submission Tracking Numbers (STNs): Multiple STNs, see Appendix A

Dear Gerard J. Roerty, Jr.:

We reviewed your July 17, 2023, MRTPAs¹ and concluded that additional information is needed for FDA to make a determination for the tobacco products identified in Appendix A. Refer to Appendix B for a list of amendments received in support of your applications.

We request that you submit all the information identified below within 14 calendar days from the date of this letter. In general, to maximize review efficiency of applications, we do not intend to provide an extension of time for response to deficiency letters. This deficiency letter identifies information that FDA needs to complete its scientific review. It should not be understood to communicate a list of all substantive concerns that may be observed during the review of your application and other information. Providing information to address deficiencies identified in your submission does not guarantee that you will receive a positive renewal decision. A final decision will be made at the end of our scientific review based on the totality of all the information included in your original submission, your timely responses to this letter, and any other information before the Secretary with respect to the tobacco product(s) in question.

We have preliminarily determined that these applications do not in their present form support a positive scientific determination. To maximize review efficiency, we do not intend to issue additional Deficiency letters for these applications.

The following information is necessary for FDA to make a scientific determination:

1. Your MRTPA renewal application lacks adequate cross-referencing to include all information that you submitted in support of your application review. On October 19, 2023, you submitted two post-market surveillance reports (PS0000306, PS0000307) and on December 14, 2023, you submitted two additional post-market surveillance reports (PS0000314, PS0000315). These four reports are not cross-referenced in your renewal application. Since the post-market surveillance reports contain information that is relevant to scientific review, we are currently unable to continue with a comprehensive scientific review. Submit an amendment that cross-references the four missing post-market surveillance reports. In the

future, be sure to submit amendments to your renewal application in parallel when you submit new post-market surveillance reports.

2. Your MRTPA renewal application lacks documents containing all information related to the General Snus Patterns of Use study. Specifically, it is missing line data and relevant files to aid data analysis. These items are important for FDA to replicate applicant findings or conduct alternative statistical analyses. Your renewal also lacks documentation of IRB approval for your General Snus Patterns of Use study. Documentation of IRB approval is needed for FDA to assure any data collection involving participants was conducted with appropriate measures to protect the rights and welfare of human research subjects. Submit line data, data definition files that include the names of the variables, codes, and formats used in each dataset, and copies of programs and any necessary macro programs used to create derived datasets and the results reported in the study reports. Additionally, submit documentation of IRB approval for the study.

When responding to this letter, submit an amendment with a cover letter that includes the following text in your subject line: **"RESPONSE TO DEFICIENCY LETTER for MR0000256.PD1-MR0000256.PD5, MR0000256.PD7-MR0000256.PD9."** Refer to Appendix C for best practices in submitting a response to a Deficiency letter.

If you intend to respond to these deficiencies, clearly state (by STN.PD) that you have responded to each numerated deficiency above. Please be advised that an inadequate resolution of the deficiencies described above will likely result in a denial.

Amendments, which contain a substantial amount of new information (e.g., detailed new analyses of previously submitted data, new manufacturing information), may extend the time required for review. FDA generally does not intend to review amendments received after the due date stated in this letter because the scientific review of the tobacco products will have begun and the evaluation of additional amendments would require significant review time by the agency and would likely delay the completion of the determination of market action. In the circumstance the time required for review is extended, FDA will notify you by letter.

We encourage you to submit all regulatory correspondence electronically via the CTP Portal^{1,2} using eSubmitter.³ 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

¹ For more information about CTP Portal, see

<https://www.fda.gov/tobacco-products/manufacturing/submit-documents-ctp-portal>

² FDA's Electronic Submission Gateway (ESG) is still available as an alternative to the CTP Portal.

³ For more information about eSubmitter, see <http://www.fda.gov/ForIndustry/FDAeSubmitter>

Multiple STN.PDs, see Appendix A

Page 3 of 6

The CTP Portal and FDA's Electronic Submission Gateway (ESG) are generally available 24 hours a day, seven days a week; submissions are considered received by DCC on the day of successful upload. Submissions delivered to DCC by courier or physical mail will be considered timely if received during delivery hours on or before the due date⁴; 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.

If you have any questions, please contact Tamirra Glover M.S., Regulatory Health Project Manager, at (301) 796-6727 or tamirra.glover@fda.hhs.gov.

Sincerely,

Digitally signed by Jennifer K.
Bernat -S
Date: 2024.01.17 12:43:49 -05'00'

Jennifer K. Bernat, Ph.D.
Supervisory Social Scientist, DPHS
Office of Science
Center for Tobacco Products

Enclosures:

- Appendix A – Tobacco Products Subject of This Letter
- Appendix B – Amendment Received for These Applications
- Appendix C – Best Practices for Submitting a Response to a Deficiency Letter

⁴ <https://www.fda.gov/tobacco-products/about-center-tobacco-products-ctp/contact-ctp>

Multiple STN.PDs, see Appendix A

Page 4 of 6

Appendix A
Tobacco Products Subject of This Letter

- MR0000256.PD1: General Loose
- MR0000256.PD2: General Dry Mint Portion Original Mini
- MR0000256.PD3: General Portion Original Large
- MR0000256.PD4: General Classic Blend Portion White Large - 12ct
- MR0000256.PD5: General Mint Portion White Large
- MR0000256.PD7: General Nordic Mint Portion White Large - 12ct
- MR0000256.PD8: General Portion White Large
- MR0000256.PD9: General Wintergreen Portion White Large

Multiple STN,PDs, see Appendix A

Page 5 of 6

Appendix B
Amendment Received for These Applications

| Submission Date | Receipt Date | Applications being amended | Reviewed | Brief Description |
|-------------------|-------------------|----------------------------|----------|---|
| December 13, 2023 | December 13, 2023 | All STNs | Yes | Response to December 13, 2023 FDA Information Request |

Appendix C

Best Practices for Submitting a Response to a Deficiency Letter

We recommend that your submission include consecutively numbered pages and be organized as follows:

- List each number and full deficiency text as stated in this letter, and provide your response immediately following the deficiency.
 - Your response should address all STNs identified in a deficiency; if different information/data is being submitted for different STNs in your response to a given deficiency, the response should clearly correlate information/data to the applicable STNs.
 - If your response applies to a subset of STNs (e.g., 5 out of 10) and you would like us to start scientific review upon receipt of your response, provide a statement to that effect in your cover letter.
 - Submit data as an appendix or appendices and reference the appropriate appendix/appendices in your response.
 - Submit publications as an appendix or appendices and reference the appropriate appendix/appendices in your response.
- If resubmitting information (e.g., tables) to correct earlier omissions/errors, clearly identify what information has been revised. FDA will consider that new information to supersede the information provided in the original submission, except for measured values (e.g., test data, HPHC data). For measured values, applicants should provide rationale for why the updated data are appropriate for consideration. If rationale is not provided, measured values will be combined with previous measured values for evaluation.
- If you have already submitted any of the information requested in the deficiency, identify the date of the prior submission, page numbers, and line numbers where the requested information is located.

(b) (4)

TYPE OF REVIEW – EXEMPTION FROM IRB REVIEW DETERMINATION

Determination

Date: June 17, 2020

IRB ID:

(b) (4)

Protocol: General Snus® Patterns of Use Study

Sponsor:

(b) (4)

Principal Investigator:

(b) (4)

(b) (4) is in receipt of submission materials for the above-referenced study.

Items Reviewed:

- Exemption or Non-Human Subjects Research Determination Request
- Protocol (Date: 15 June 2020)
- Baseline Questionnaire (June 16, 2020)
- Consumer Facing Materials
- Perks Login Process

Based on the information available to the IRB, (b) (4) (or designee) has determined that:

The above-listed study is exempt from IRB review pursuant to the terms of the U.S. Department of Health and Human Service's Policy for Protection of Human Research Subjects at 45 C.F.R. §46.104(d).

(b) (4) has determined that the following exemption category(ies) applies:

- Category 2 Exemption (DHHS)

(b) (4) exemption determination is based on the study-related information available to (b) (4) as of the determination date listed above. Should any changes be made to the study subsequent to (b) (4) determination, this determination is no longer applicable.

As the project applicant you are responsible for following all policies of (b) (4) as described in the Exemption or Non-Human Subjects Research Determination Request Submission Agreement which you accepted with project submission. It is your responsibility to ensure this project is conducted in accordance with applicable regulations (local, state and federal) as well as any requirements established by the IRB at the time of the review determination. Refer to the Investigator Handbook at (b) (4) details of these responsibilities.

December 13, 2023

Gerard J. Roerty, Jr.
Vice President, General Counsel & Secretary
Swedish Match USA, Inc.
1021 East Cary Street, Suite 1600
Richmond, VA 23219
Phone: (b) (6)
e-mail: (b) (6)

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

SUBJECT: [AMENDMENT – POST-MARKET SURVEILLANCE STUDIES WAVE REPORTS] Modified Risk Tobacco Product Application Renewal MR0000256

Dear Sir or Madam:

On July 17, 2023, Swedish Match USA, Inc. ("Swedish Match", "our" or "we") submitted our Modified Risk Tobacco Product Application Renewal to Center for Tobacco Products.

On December 12, 2023, we received an email referencing our renewal submission – MR0000256, explaining that CTP was unable to locate the General Snus Patterns of Use Study - Wave 3 and requesting a timeline as to when each Wave was fielded.

Under the MRTP reporting requirements, Swedish Match had full intention to submit all required study phases with our submission. We believe that due to the timing of when reports were received from our vendor, the Wave 3 study was erroneously omitted and not included in error with our Swedish Match PMTA MRTP Combined Postmarket Annual Report dated Oct 28, 2022. The Wave 4 study was included with that submission.

After reviewing the Wave Report documents in our possession, we now submit ALL Post Market Surveillance Study Wave Reports to fulfill the document requirements for Section 1 – Annual Post-Market Surveillance and Studies Report Summary (please see document summary below).

If further information is required, please feel free to contact me.

Sincerely yours,

(b) (6)

Gerard J. Roerty, Jr.

Vice President, General Counsel & Secretary

45 **Attachment A – General Snus Patterns of Use Study Timeline**

46 **Attachment B - PMSS Wave Technical Report Summary**

47 B.1 - General Snus Patterns of Use Study Wave 1 Technical Report_v1.0_07OCT2020_Final

48 B.2 - General Snus Patterns of Use Study Wave 2 Technical Report_v2.0_13JUL2021_Final

49 B.3 - General Snus Patterns of Use Study Wave 3 Technical Report_v2.0_10FEB2022_Final

50 B.4 - General Snus Patterns of Use Study Wave 4 Technical Report_v1.0_04NOV2022_Final

51 B.5 - General Snus Patterns of Use Study Longitudinal Report_v1.0_10APR2023_Final

M RTP PMSS SUBMISSIONS

M RTP Order – 10/22/19

“Respondents will complete surveys at Baseline, and again at 6 months, 1 year and 2 years post Baseline period”.

PMSS Submission Research Timelines

- **Wave 1 (Baseline; Month 0)** – July 25, 2020 to August 17, 2020
- **Wave 2 (Month 6)** – February 2, 2021 to March 6, 2021
- **Wave 3 (Month 12)** – August 5, 2021 to September 7, 2021
- **Wave 4 (Month 24)** – August 4 2022 to September 5, 2022



***General Snus®* Patterns of Use Study**

Baseline Study Report

SMU 19-01GENS

| | |
|--------------------------|--|
| Product Name: | <i>General Snus®</i> |
| First Subject Enrolled: | July 25, 2020 |
| Last Subject Completed: | August 17, 2020 |
| Principal Investigators: | (b) (4) |
| Sponsor: | Swedish Match North America Tryggve Ljung, MD., Ph.D., Vice President Scientific Affairs |
| Version: | <i>1.0 - Final</i> |
| Report Date: | October 7, 2020 |

Confidentiality Statement

This document and the information it contains is confidential and the proprietary property of Swedish Match North America. The information is not to be disclosed or transmitted to any party without the express approval of Swedish Match North America, or its parent and affiliate companies, and any such unauthorized use or disclosure is expressly prohibited.

2. SYNOPSIS

Sponsor:

Swedish Match North America (SMNA)

Two James Center
1021 East Cary Street, Suite 1600
Richmond, VA 23219

Name of Finished Product: *General Snus*[®]
Name of Active Ingredient: Not applicable

Study Title: *General Snus*[®] Patterns of Use Study

Investigator: (b) (4)

Publication (reference): Not applicable

Studied Period: Wave 1 Baseline

Start of data collection: July 25, 2020

End of data collection: August 17, 2020

Objective: The overarching research questions within this study are as follows: (i) *How do General Snus*[®] *users use tobacco and nicotine products (TNP), and (ii) how do they perceive health risks associated with cigarettes and General Snus*[®]? These questions will be studied using a self-reported survey examining patterns of use for the previous 30 days (Baseline-Wave 1) and assessment of TNP use among the same *General Snus*[®] users again at 6 months (Wave 2), 1-year (Wave 3) and 2-year (Wave 4) intervals post baseline.

Primary Objectives:

Use behavior will be assessed, utilizing data from all 4 waves of the study:

1. Compare TNP patterns of use, between all 4 waves. The study will examine self-reported usage patterns for participants, in aggregate, over time. The study will report on frequency of use of *General Snus*[®] use, as well as other TNP, if multiple TNP use is reported. Of specific interest will be usage patterns of cigarettes. Intent to quit and actual quitting of cigarettes will be assessed at each wave of the study.

2. Among *General Snus*® users, compare consumption patterns of cigarettes and *General Snus*® over the last 30 days (Baseline) with consumption patterns in Waves 2 through 4. Of particular interest is whether usage of *General Snus*® offsets usage of cigarettes.
3. Characterize *General Snus*® users in terms of prior TNP use and demographics and compare this to new users of smokeless TNP as reported in the Population Assessment of Tobacco and Health (PATH)
4. Compare the tendencies of *General Snus*® users to quit cigarettes or use *General Snus*® in an incremental fashion, in a supplemental fashion, or in complete substitution of cigarettes.

Secondary Objectives:

Risk Perception and understanding of the MRTP claim will be assessed utilizing data from all 4 Waves of the study:

1. Assess perceptions of risk of certain health conditions (mouth cancer, heart disease, and lung cancer, separately) among *General Snus*® users.
 - a. Assess the absolute risk attributed to using only *General Snus*® daily, smoking only cigarettes daily, dual use of *General Snus*® and cigarettes daily, and never having used any TNPs.
2. Assess the extent to which *General Snus*® users understand the risk reduction as stated in the modified risk claim

Methodology: *General Snus*® user groups were recruited directly from purchasers of *General Snus*® through invitation stickers placed directly on *General Snus*® canisters

A third-party vendor, (b) (4), was hired to place the study invitation stickers on product packaging (e.g., each individual *General Snus*® canister) for all varieties of *General Snus*® available at retail outlets, from July 25 – August 7, 2020. The sticker initiative targeted approximately 10,600 retail stores carrying *General Snus*® across all locations where *General Snus*® was sold at the time of recruitment. Additionally, the sticker identified a website where users who were interested in participating accessed the survey through a secure and unique survey link. The first set of questions were the survey screener, designed to qualify the participant using the study inclusion and exclusion criteria. Once qualified, all respondents accessed a web survey online via a computer, smartphone, or tablet. The study was a 15-minute survey where participants were asked to self-report TNP use within the past 30 days.

This study will be a longitudinal, prospective study that consists of multiple waves to gain an understanding of how *General Snus*® is used by consumers. Respondents completed surveys at Baseline, and will also be questioned at 6 months, 1 year and 2 years post Baseline period. All participants for the Baseline wave must have reported use of *General Snus*® at least once in the previous 30 days and reported use on some days or every day.

In addition to reporting TNP use, participants will report their perceptions of health risk and their understanding of the modified risk claim.

Number of Patients (Planned and Analyzed):

Planned: The Baseline study was planned to recruit a total sample of 1500 participants but was able to exceed target with 1669 participants. Each participant who participated in the Baseline study agreed to participate in the subsequent waves. Respondents who completed the Baseline study may participate in any of the subsequent waves.

Analyzed: The study retained 1655 participants at baseline: *General Snus*® users. Fourteen out of the 1669 participants were excluded from analysis because they failed the attention check question in the survey. The number of respondents that completed all four study waves will be determined after completion of each wave.

Inclusion Criteria:

In addition to the already mentioned cohort definitions, respondents met the following criteria to be included in the study:

- Have used *General Snus*® at least once or more within past 30 days prior AND use it every day or some days prior to study initiation
- Minimum age of 21 years
- Agree to participate in four surveys over the two-year period
- Able to read and speak English
- Currently a resident of the United States
- Individuals who provide electronic informed consent and personal contact information

Exclusion Criteria:

Respondents who met any of the following criteria were excluded from the study:

- Respond as “don’t know” or “decline to answer” to specific demographics (gender, geographical region)
- Unwilling or unable to provide electronic informed consent and personal contact information
- Employed in any of the following fields or professions: market research, marketing, advertising, manufacturers of TNP, or physicians
- Have taken part in a consumer research study on tobacco in the past 2 weeks

Statistical Methods: All baseline analyses performed for the *General Snus*® Patterns of Use Study were descriptive in nature.

Descriptive analyses provide summary statistics for all variables. Summary statistics include counts and proportions for categorical variables and means, standard deviations, medians, minimums and maximums for ordinal and continuous variables. Descriptive statistics describe the sample as well as verify the quality of the data. Inferential statistical testing will be conducted to evaluate change in primary and secondary outcome measures (i.e., patterns of use, risk perception, understanding of claim) from baseline and each follow-up wave of the study. Baseline vs. each follow-up (waves 2, 3, and 4) will be conducted using paired sample t-tests for continuous variables and McNemar test for categorical variables in order to account for correlated measures

The study team formatted and properly labelled the data sets (including all responses from respondents and the date that the survey was completed) using Statistical Package for the Social Sciences ([IBM SPSS Statistics v23, 2015](#)) and [R software \(version 3.5.2\)](#) so they were suitable for analysis. The data sets contained a subject ID number and did not contain any information that could be used to identify individual respondents.

Results and Discussion:

Overall, the *General Snus*® respondents and New *General Snus*® cohorts were comparable, though the new product user cohort was slightly younger, more were female, more had some college but no degree, and reported an annual household income less than \$49,999. However, due the small sample size of the new users (n=52), this data may be difficult to generalize and make conclusions.

Primary Objective 1: Evaluate baseline TNP use in the past 30 days.

Reported TNP use in the past 30 days: Among the 1655 *General Snus*® respondents, at least 40% of ever users (from 43.3% to 62.3%) reported other TNP use, including E-cigarettes, moist snuff, nicotine pouches, cigars, cigarillos, or filtered cigars filled with tobacco products while about 30% of ever users (from 19.8% to 32.7%) reported smoking, chewing tobacco, using pipe tobacco, hookah or water pipe tobacco, and aids to help smoking. Of those who reported ever cigarette use (n=914), 32.7% (n=299) smoked over the past 30 days and for those who reported using *General Snus*® over the past 30 days, only 18.1% (n=299) used cigarettes concurrently. Of those who reported ever cigarette use, the majority of participants (67.2%) reported that they did not smoke at all over the past 30 days while 13.1% reported that they smoked every day and 19.6% reported that they smoked on some days.

For these *General Snus*® users, less than a third reported other TNP use and only 18.1% reported smoking concurrently over the past 30 days.

Primary Objective 1: Evaluate baseline intention to quit TNP based on the Motivation to Stop Scale (MTSS) and cigarette quitting behavior

Cigarette quitting behavior and intention to quit TNP based on the MTSS: Among the 299 *General Snus*® users who responded they smoked every day or on some days over the past 30 days, 16.4% reported that they completely quit smoking. Of the 250 that reported they did not completely quit smoking, 44.0% reported that they were currently trying to quit smoking. The average MTSS score for cigarettes was 2.5 suggesting low intentions to quit smoking.

Primary Objective 2: Evaluate baseline average number of days General Snus® pouches and cigarettes were used over the past 30 days.

Reported number of days General Snus® pouches and cigarettes were used over the past 30 days: Over the past 30 days, 82.1% of *General Snus*® users reported using *General Snus*® every day and they used an average of 10.5 pouches per day. The remaining participants reported using *General Snus*® on 49.8% of days and an average of 5.3 pouches on the days they are used.

In addition, 7.3% of *General Snus*® users reported smoking cigarettes every day at an average of 12.3 cigarettes per day.

Secondary Objective 1: Assess perceptions of absolute risk of certain health conditions (mouth cancer, heart disease and lung cancer) among General Snus® users attributed to using only General Snus® daily, smoking only cigarettes daily, dual use of General Snus® and cigarettes daily, and never having used any TNPs.

Perceptions of Absolute Risk: When looking across all absolute risk metrics, a consistent pattern emerged. Respondents perceived that cigarettes presented the greatest risk of harm across different health conditions (mouth cancer, heart disease and lung cancer). Usage of *General Snus*® products alone was associated with some risk of health conditions, although at a lower rate than smoking. Never using TNP was generally deemed to carry the lowest risk.

Secondary Objective 2: Assess baseline understanding of the risk reduction as described in the modified risk claim among General Snus® users, especially new users.

The majority of respondents comprehended that *General Snus*® puts them at lower risk than smoking cigarettes for mouth cancer, heart disease, lung cancer, stoke, emphysema, and chronic

bronchitis. The majority of responders also understood the modified risk claim that smoking zero cigarettes would lower their risk of disease.

Similar response patterns were observed within the new user cohort. Although about 20% responded that they did not understand the claim that *General Snus*® puts them at lower risk than smoking cigarettes for different diseases, this response came from a small sample of 11 respondents.

Strengths and Limitations of the Baseline Study:

This study was conducted following the guidance of the Center for Tobacco Products ([FDA Guidance for Industry, 2011](#)) within the FDA on data for human studies designed to evaluate the risks and benefits to the population, including users and non-users of tobacco products. The study benefitted from the administration of the web-based survey which allowed for improved survey designs and accurate data capture.

Additionally, in virtually all cases survey questions utilized validated scales, or scales directly comparable to studies in literature. In particular, usage of the Motivation to Stop Scale allowed for simple, justifiable interpretation. Scales used in risk perception questions line up with other tobacco-related research, such as HINTS.

There were limitations to the current study, arguably none of which should draw concern regarding data integrity. The data collected were from current users of *General Snus*®. The perceived health risk assessments were intended to evaluate real-world perceptions after exposure to real-world information on *General Snus*®, but obviously they did not have the same contextual, social, and emotional consequences of actual decisions. One could only expect a limited degree of accuracy and extrapolation while capturing behavioral intentions, as unforeseen factors can impact actual behaviors. Thus, differences may arise between stated and actual choices, and stated and actual behaviors. Potential hypothetical bias may be limited by constructing questions that mimic realistic perceptions and behaviors as closely as possible. In addition, since data from this study were dependent on respondent self-reporting, subsequently reported variables may also be subjected to recall bias and the inability to confirm actual tobacco use behavior. Self-reported data collection is a standard approach and any potential problems with recall bias were anticipated to be constant across time points.

Respondents were recruited based on invitation stickers placed directly on *General Snus*® canisters. As a result, recruitment could be considered a convenience sample. Further, due to sample selection during recruitment, respondents who were more interested in research, or perhaps healthy enough to participate, may be over-represented, hence the possibility of

selection bias. Although these issues raised concerns about the external validity of the findings (e.g., our sample may not be fully generalizable to all consumers), the recruitment plan was designed to mirror the underlying populations.

Baseline Study Conclusion:

Baseline study findings support the conclusion that overall, the introduction of *General Snus*[®] does not appear to compromise public health in any way, based on perceptions of risk as assessed in the Baseline study. Specifically, results demonstrated that respondents perceived that cigarettes presented the greatest risk of health conditions which include mouth cancer, heart disease and lung cancer. Moreover, usage of *General Snus*[®] products alone was associated with some risk of health conditions, although at a lower rate than smoking. Never using TNP was generally deemed to carry the lowest risk.

In addition, current *General Snus*[®] users include a significant number of former cigarette smokers (67.2%) suggesting that use of *General Snus*[®] may support a reduction in smoking.

Final Date: October 7, 2020

3. TABLE OF CONTENTS

| | |
|---|----|
| 1. TITLE | 1 |
| 2. SYNOPSIS | 2 |
| 3. TABLE OF CONTENTS | 9 |
| 3.1 LIST OF IN-TEXT TABLES | 11 |
| 3.2 LIST OF IN-TEXT FIGURES..... | 12 |
| 4. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS..... | 13 |
| 5. RESPONSIBLE PARTIES..... | 14 |
| 5.1 Investigator and Contributors | 14 |
| 5.2 Sponsor | 14 |
| 6. ETHICS | 14 |
| 6.1 Institutional Review Board (IRB)..... | 14 |
| 6.2 Ethical Conduct of the Study | 14 |
| 6.3 Respondent Information and Consent..... | 14 |
| 7. INTRODUCTION | 16 |
| 7.1 Background | 16 |
| 7.2 Rationale | 16 |
| 8. STUDY OBJECTIVES | 16 |
| 8.1 Primary Objectives..... | 16 |
| 8.2 Secondary Objectives..... | 17 |
| 9. INVESTIGATIONAL PLAN..... | 17 |
| 9.1 Overall Study Design and Plan: Description | 17 |
| 9.1.1 Study Design..... | 17 |
| 9.2 Study Cohorts..... | 18 |
| 9.2.1 Inclusion Criteria | 18 |
| 9.2.2 Exclusion Criteria | 18 |
| 9.3 Determination of Sample Size | 18 |
| 9.4 Variables of Relevance to the Study | 20 |
| 9.4.1 Outcomes | 20 |
| 9.4.2 Respondent Characteristics..... | 21 |
| 9.4.3 Respondent Characteristics..... | 32 |
| 9.5 Time Points of Importance..... | 32 |
| 10. STATISTICAL ANALYSIS | 32 |
| 10.1 Study Analysis | 32 |
| 10.2 Socio-demographics..... | 33 |
| 10.3 Statistical Analysis by Study Objective..... | 33 |
| 10.3.1 Primary and Secondary Objectives..... | 33 |
| 10.4 Changes in the Conduct of the Study or Planned Analyses..... | 33 |
| 11. STATISTICAL AND ANALYTICAL ISSUES | 34 |
| 11.1 Data Capture and Management..... | 34 |
| 11.1.1 Data Capture | 34 |

| | |
|--|----|
| 11.1.2 Data Management and Analysis QC Process | 34 |
| 11.2 Missing Data | 35 |
| 11.3 Identification of Outliers | 35 |
| 12. STUDY RESPONDENTS | 36 |
| 12.1 Study Fielding Summary | 36 |
| 12.2 Final Sample | 36 |
| 13. WAVE 1 (BASELINE) STUDY RESULTS | 36 |
| 13.1 Descriptive Results | 36 |
| 13.2 Demographics and Respondent Characteristics | 37 |
| 13.3 Baseline Results for Primary Objectives | 38 |
| 13.3.1 Primary Objective 1: Baseline TNP use in the past 30 days. | 38 |
| 13.3.2 Baseline intention to quit TNP based on the Motivation to Stop Scale (MTSS) and cigarette quitting behavior. | 42 |
| 13.3.3 Primary Objective 2: Baseline average number of days <i>General Snus</i> [®] pouches were used over the past 30 days | 44 |
| 13.3.4 Primary Objective 2: Baseline average number of days cigarettes were smoked over the past 30 days | 44 |
| 13.3.5 Primary Objective 3: Characterize <i>General Snus</i> [®] users, especially new users, in terms of prior TNP use and demographics and compare this to new users of smokeless TNP as reported in the Population Assessment of Tobacco and Health (PATH) | 45 |
| 13.4 Baseline Results for Secondary Objectives | 45 |
| 13.4.1 Secondary Objective 1: Baseline Perception of absolute risk to using only <i>General Snus</i> [®] daily, smoking only cigarettes daily, dual use of <i>General Snus</i> [®] and cigarettes daily, and never having used any TNPs | 45 |
| 13.4.2 Secondary Objective 2: Baseline understanding of the risk reduction as described in the modified risk claim among <i>General Snus</i> [®] users, especially new users | 49 |
| 13.5 Results Summary | 51 |
| 14. DISCUSSION AND OVERALL CONCLUSIONS | 52 |
| 14.1 Strengths and Limitations of the Study | 52 |
| 14.2 Overall Baseline Study Conclusions | 53 |
| 15. REFERENCES | 54 |

3.1 LIST OF IN-TEXT TABLES

| | |
|---|----|
| Table 1: Patterns of Use Study Cohorts..... | 18 |
| Table 2: Sample Sizes for Waves 1 to 4 Studies. | 20 |
| Table 3. Outcomes Table for Primary Objective 1 – TNP patterns of use among <i>General Snus</i> [®] users. | 23 |
| Table 4. Outcomes Table for Primary Objective 2 – <i>General Snus</i> [®] and cigarettes pattern of use. | 24 |
| Table 5. Outcomes Table for Primary Objective 3 – TNP patterns of use among <i>General Snus</i> [®] and New <i>General Snus</i> [®] users compared to PATH Study users | 26 |
| Table 6. Outcomes Table for Primary Objective 4 – Quitting cigarettes, incremental use, supplemental use, and completely substituting <i>General Snus</i> [®] in place of cigarettes. | 27 |
| Table 7. Outcomes Table for Secondary Objective 1 – Perceptions of absolute risk..... | 29 |
| Table 8. Outcomes Table for Secondary Objective 1 – Perceptions of absolute risk..... | 29 |
| Table 9. Outcomes Table for Secondary Objective 1 – Perceptions of absolute risk..... | 30 |
| Table 10. Outcomes Table for Secondary Objective 2 – Understanding of the MRTP claim for <i>General Snus</i> [®] | 30 |
| Table 11. Outcomes Table for Secondary Objective 2 – Understanding of the MRTP claim for <i>General Snus</i> [®] | 31 |
| Table 12: Fielding Summary | 36 |
| Table 13: Socio-demographics of <i>General Snus</i> [®] and New <i>General Snus</i> [®] users..... | 37 |
| Table 14. TNP patterns of use for <i>General Snus</i> [®] users. Reported TNP use in the last 30 days .. | 40 |
| Table 15. TNP patterns of use for <i>General Snus</i> [®] users. Intention to quit TNP based on the Motivation to Stop Scale (MTSS) at Baseline..... | 43 |
| Table 16. TNP patterns of use for <i>General Snus</i> [®] users. Quitting cigarettes behavior. | 43 |
| Table 17. <i>General Snus</i> [®] patterns of use. Outcomes include percent of days that <i>General Snus</i> [®] is used and average number of <i>General Snus</i> [®] pouches used. | 44 |
| Table 18. Cigarettes pattern of use among <i>General Snus</i> [®] users. Outcomes include percent of days cigarettes are smoked and average number of cigarettes smoked. | 45 |
| The sample size of new users in PATH could not be established at the time of this report and for Table 19. In addition, Table 20 and 21 will be provided in Wave 2 to Wave 4 reporting follow up data from Month 6 to Year 2..... | 45 |
| Table 22. Perceptions of absolute risk for daily <i>General Snus</i> [®] users and smokers | 46 |
| Table 23. Perceptions of absolute risk for dual <i>General Snus</i> [®] users and smokers and never TNP users | 48 |
| Table 24. Understanding of the MRTP claim for <i>General Snus</i> [®] | 49 |

3.2 LIST OF IN-TEXT FIGURES

| | |
|---|----|
| Figure 1: Summary of Research Phases..... | 17 |
|---|----|

4. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

| Abbreviation or Specialist Term | Definition |
|---------------------------------|---|
| CASRO | Council of American Survey Research Organizations |
| CTP | Center for Tobacco Products |
| FDA | FDA Food and Drug Administration |
| FTP | File Transfer Protocol |
| HCP | Health Care Professional |
| HINTS | Health Information National Trends Survey |
| ICF | Informed Consent Form |
| IRB | IRB Institutional Review Board |
| MRTTP | Modified Risk Tobacco Product |
| MRTPA | Modified Risk Tobacco Product Application |
| PATH | Population Assessment of Tobacco and Health |
| PII | Personally Identifiable Information |
| PMTA | Premarket Tobacco Product Application |
| RDD | Random Digit Dialing |
| SAP | Statistical Analysis Plan |
| SMNA | Swedish Match North America, LLC |
| TNP | Tobacco/Nicotine Product(s) |
| U.S. | United States |

5. RESPONSIBLE PARTIES

5.1 Investigator and Contributors

| | |
|-------------------------|---------|
| Principal Investigator: | (b) (4) |
| (b) (4) Project Team: | |

5.2 Sponsor

| | |
|----------|--|
| Sponsor: | Swedish Match North America, LLC Tryggve Ljung, MD., Ph.D., Vice President Scientific Affairs |
|----------|--|

6. ETHICS

6.1 Institutional Review Board (IRB)

Documented approval from a central IRB in the U.S. was obtained prior to the initiation of the study. (b) (4) approved this study. When necessary, an extension, amendment or renewal of the IRB approval was obtained from (b) (4) and forwarded to SMNA.

6.2 Ethical Conduct of the Study

The study was carried out within an approved indication and in accordance with Center for Tobacco Products (CTP) guidance on data for human studies designed to evaluate the risks and benefits to the population as a whole (CTP Addendum, 2017)¹. Additionally, (b) (4) conducts all our research in accordance with the requirements of our Quality System, which confirms to ISO 20252:2012 the International Standard for Market Research, Certification Number: 1019.

6.3 Respondent Information and Consent

Prior to beginning the survey, potential respondents were provided with a statement of informed consent. The consent informed potential respondents that participation in the study was voluntary,

and that responses remained confidential. It also included information about the goals of the study, the approximate length of the survey, and incentives for participation. Lastly, the statement of informed consent provided potential respondents with the resource references to address any concerns they could have. A link to each panel was given if the respondent had any specific questions about the survey instrument or incentives for participation.

After potential respondents read the statement of informed consent, they were asked, “Do you voluntarily agree to participate in this study?” Respondents who selected “I agree to participate” were able to complete the survey. At any time during survey completion, the respondent could choose to exit the survey should they decided not to participate any further. Data provided by a respondent who exited the survey prematurely were not utilized in any analyses. Respondents who selected “I do not agree to participate” were thanked for their time before exiting. IRB written approval / favorable opinion of the electronic informed consent form and any other written information provided to respondents were obtained prior to the initiation of the study.

7. INTRODUCTION

7.1 Background

In November 2015, Swedish Match North America, (SMNA) received market authorization for *General Snus*[®], a moist tobacco product placed under the upper lip that does not involve spitting or chewing². In its first applications reviewed through the MRTP pathway, the FDA deferred final action on providing *General Snus*[®] a MRTP designation providing some guidance on how SMNA could amend their application to provide greater support for a modified risk designation. SMNA filed its amended MRTPA on September 17, 2018 and the FDA granted the risk modification order on October 22, 2019. This study is being conducted as required for post marketing surveillance following risk modification order.

7.2 Rationale

The protocol and questionnaire were reviewed with FDA and output of this research will be submitted to the agency as part of the surveillance requirement of the MRTP order.

8. STUDY OBJECTIVES

The overarching research questions within this study are as follows: (i) *How do General Snus*[®] users use TNP, and (ii) *how do they perceive health risks associated with cigarettes and General Snus*[®]? These questions will be studied using a self-reported survey examining patterns of use for the previous 30 days (Baseline-Wave 1) and assessment of TNP use among the same General Snus[®] users again at 6 months (Wave 2), 1-year (Wave 3) and 2-year (Wave 4) intervals post Baseline.

8.1 Primary Objectives

Use behavior will be assessed, utilizing data from all 4 waves of the study:

1. Compare TNP patterns of use, between all 4 waves. The study will examine self-reported usage patterns for participants, in aggregate, over time. The study will report on frequency of use of *General Snus*[®] use, as well as other TNP, if multiple TNP use is reported. Of specific interest will be usage patterns of cigarettes. Intent to quit and actual quitting of cigarettes will be assessed at each wave of the study.
2. Among *General Snus*[®] users, compare consumption patterns of cigarettes and *General Snus*[®] over the last 30 days (Baseline) with consumption patterns in Waves 2 through 4.

Of particular interest is whether usage of *General Snus*[®] offsets usage of cigarettes.

3. Characterize *General Snus*[®] users, especially new users, in terms of prior TNP use and demographics and compare this to new users of smokeless TNP as reported in the Population Assessment of Tobacco and Health (PATH)³.
4. Compare the tendencies of General Snus[®] users to quit cigarettes or use *General Snus*[®] in an incremental fashion, in a supplemental fashion, or in complete substitution of cigarettes.

8.2 Secondary Objectives

Risk Perception and understanding of the MRTTP claim will be assessed utilizing data from all 4 Waves of the study:

1. Assess perceptions of risk of certain health conditions (mouth cancer, heart disease and lung cancer, separately) among *General Snus*® users.
 - a. Asses the absolute risk attributed to using only *General Snus*® daily, smoking only cigarettes daily, dual use of *General Snus*® and cigarettes daily, and never having used any TNPs.
2. Assess the extent to which *General Snus*® users, especially new users, understand the risk reduction as described in the modified risk claim

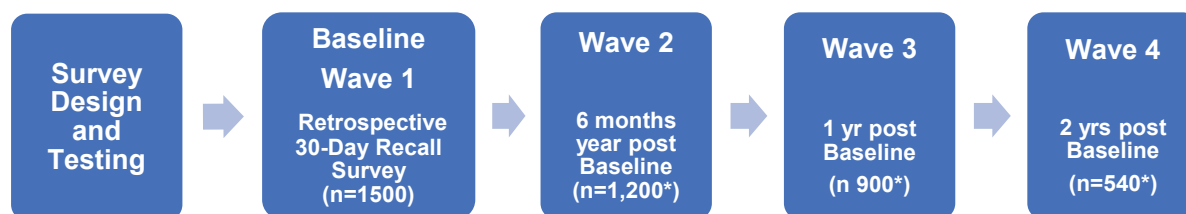
9. INVESTIGATIONAL PLAN

9.1 Overall Study Design and Plan: Description

9.1.1 Study Design

As noted previously, the *General Snus*® Patterns of Use Study seeks to evaluate TNP patterns of use among *General Snus*® users through a Baseline Study focused on 30-day recall of TNP use, accompanied by follow up studies comprised of another 30-day recall period at 6-months, 1- and 2-year intervals after the Baseline study.

Figure 1: Summary of Research Phases



*Study population estimated for Waves 2, 3 and 4, were based on (b) (4) experience in implementing multiple wave longitudinal studies, coupled with enhanced retention strategies.

For the Baseline Study, all participants who qualified and signed the electronic Informed Consent form accessed a web survey online via a computer, smartphone, or tablet. The Baseline Wave was a 15-minute survey where participants were asked to self-report TNP use history within the past 30 days. A 30-day recall period was selected based both upon review of the available tobacco and nicotine peer reviewed literature utilizing 30-day recall for understanding current and recent usage of TNP as well as applying the PATH methodology of asking consumers to recall specific TNP use in a 30-day period.³

Prior to launching the study in full, (b) (4) conducted a quality check of the survey. The primary objective of this quality check was to confirm that all facets of the data collection process function according to protocol; items of specific interest include the length of interview, and the accuracy of the web-based instrument (i.e., survey), all of which worked to ensure the primary objectives of the research were met.

At the completion of the Baseline Wave 1, *General Snus*® users were reminded about the next wave of the study. Interim reminders between each wave will be sent to each participant at 3-month intervals to reduce the attrition rate between surveys.

9.2 Study Cohorts

The study population consisted of U.S. adults ages 21 years or older who were current users of *General Snus*®, where a current user is defined as having reported using *General Snus*® within 30 days prior to receiving the survey invitation. The study included respondents from the cohorts described in [Table 1](#)

Table 1: Patterns of Use Study Cohorts

| | |
|-------------------------------------|--|
| Current <i>General Snus</i> ® users | <p>All <i>General Snus</i>® users were recruited through the canister sticker program. Users were then confirmed through the screener to:</p> <ul style="list-style-type: none"> Have used <i>General Snus</i>® at least once over the past 30 days |
|-------------------------------------|--|

9.2.1 Inclusion Criteria

In addition to the cohorts to be included in this study, respondents had to meet the following criteria to be included:

- Have used *General Snus*® at least once or more within past 30 days prior AND use it every day or some days prior to study initiation
- Minimum age of 21 years
- Agree to participate in four surveys over the two-year period
- Able to read and speak English
- Currently a resident of the United States
- Individuals who provide electronic informed consent and personal contact information

9.2.2 Exclusion Criteria

Respondents who meet any of the following criteria were excluded from the study:

- Respond as “don’t know” or “decline to answer” to specific demographics (gender, geographical region)
- Unwilling or unable to provide electronic informed consent and personal contact information
- Employed in any of the following fields or professions: market research, marketing, advertising, manufacturers of TNP, or physicians
- Have taken part in a consumer research study on tobacco in the past 2 weeks

9.3 Determination of Sample Size

The Wave 1 or Baseline Study targeted a total sample of n=1,500 participants. Each participant who participated in the Baseline study agreed to participate in the subsequent waves.

Additionally, periodic reminders will be sent at 3-month intervals to all participants in the Baseline study in an attempt to retain participants for each subsequent wave. Respondents who completed the Baseline study may participate in any of the subsequent waves.

Using retention strategies, which included increased honoraria, periodic reminders, and allowing a respondent to continue in any subsequent wave, so long as they complete the Baseline wave, (b) (4) anticipates a 40% drop out rate each year, resulting an estimated sample of n=1200 participants in Wave 2, n=900 participants in Wave 3 and n=540 participants in Wave 4⁴. With an estimated population of at least 40,000 *General Snus*® users in the U.S., a sample size of 540 would provide 0.05% margin of error with 95% confidence interval.

Table 2: Sample Sizes for Waves 1 to 4 Studies.

| Cohort Number | Completing Wave 1 (Baseline) Study | Completing Wave 2 Study | Completing Wave 3 Study | Completing Wave 4 Study |
|--|---|--------------------------------|--------------------------------|--------------------------------|
| Current <i>General Snus</i> [®] users | 1655 | TBD | TBD | TBD |

9.4 Variables of Relevance to the Study

9.4.1 Outcomes

9.4.1.1 Outcomes for Primary Objectives

Outcomes that were used to evaluate the primary objectives are as follows:

Reported use in the last 30 days was assessed by using one item observing **frequency** of use for cigarettes, *General Snus*[®] and other TNP used over the last 30 days. The item is based on the approach employed in PATH for observing current TNP use.³ Response options for frequency of use included “Every day,” “Some Days,” “Not at All,” and “Don’t know”.

Self-reported consumption for both cigarettes and *General Snus*[®] was assessed with questions regarding daily use in each wave of the survey. Examples of reported *General Snus*[®] consumption survey questions can be found in the *General Snus*[®] Pattern of Use Study protocol. Similar consumption questions were asked of those who also reported using cigarettes in the previous 30 days.

Average number of *General Snus*[®] pouches used per day for everyday users were assessed using one item asked of participants who report using *General Snus*[®] every day. The item reported the number of *General Snus*[®] pouches used each day. This item was based on the approach employed in PATH for observing TNP use².

Average number of *General Snus*[®] pouches used per day for somedays users was assessed using two items asked of participants who reported using *General Snus*[®] some days. One item reported the number of days *General Snus*[®] pouches was used. The second item reported the number of *General Snus*[®] pouches used on each of those days. These items were based on the approach employed in PATH for observing TNP use².

Average Percent of days *General Snus*[®] is used in aggregate was derived based on the item in the survey assessing *General Snus*[®] usage in everyday users and the items assessing *General Snus*[®] in the some day users.

Intention to quit cigarettes was assessed using the Motivation to Stop Scale (MTSS).⁵ The MTSS consists of one item with seven response options ranging from 1 (lowest) to 7 (highest level of motivation to stop smoking), also including “Don’t know.” Scale developers found that odds of quit attempts increased linearly with increasing levels of motivation. In the current study, we used the MTSS both for assessing intention to quit cigarettes and for other TNPs. Consistent with published research using the MTSS, we reported the mean MTSS score.⁵ The MTSS was

selected for use in the *General Snus*® Patterns of Use Study due to its brevity and validation as a strong and accurate predictor of quit attempts. Low intention to stop was defined as a MTSS score of 1-3, and high intention to stop will be defined as a MTSS score of 4-7.

Quitting behaviors for cigarettes was assessed with items assessing past and current quitting and for those who have not or are not currently trying to quit, by assessing intention to quit. Respondents who have not quit using cigarettes in the past 30 days, were asked if they are currently trying to quit. **Currently trying to quit** was assessed using one item asking “Are you currently trying to quit smoking cigarettes with “yes” or “no” response options.

9.4.1.2 Outcomes for Secondary Objectives

Outcomes that were used to evaluate the secondary objectives were as follows:

Perceptions of absolute risk was assessed using a single-choice scale (5-point Likert scale, fully anchored; from 1= Very low chance to 5= Very high chance, also including “Don’t know” and “Decline to answer”) for each of three health conditions (mouth cancer, heart disease, and lung cancer). This scale was modified from the risk perception scale in HINTS.⁶

Understanding of the MRTP claim was assessed using two items to determine risk perception relative to cigarettes and the elements stated in the claim. The first item was whether there is correct understanding of the claim for using *General Snus*® instead of cigarettes. Response options included *General Snus*® “puts you at lower risk for mouth cancer, heart disease, lung cancer, stoke, emphysema, and chronic bronchitis”, “Does not affect your risk for mouth cancer, heart disease, lung cancer, stoke, emphysema, and chronic bronchitis”, “Puts you at higher risk for mouth cancer, heart disease, lung cancer, stoke, emphysema, and chronic bronchitis”, “None of the above,” “Don’t know” and “Decline to answer.”

The second item is whether there was correct understanding on the number of cigarettes smoked per day to lower the risk of diseases. Response options were zero, up to 5, or up to 20 cigarettes, “As many as you want to smoke”, “Don’t know” and “Decline to answer.”

Summaries of the outcomes for primary and secondary objectives, including measurement domain, subcategories, measurement details, and metrics, are presented in [Tables 3-6](#) and [7-11](#), respectively.

9.4.2 Respondent Characteristics

Sociodemographic Variables

- **New *General Snus*® users** were defined as first time *General Snus*® use less than 30 days ago.
- **US region of residence** was assessed using a single item asking the respondent what state they spend most days of the year in.

- **Age of the respondent** was assessed using a single item asking the respondent how many years old they are. Age of respondent was categorized and reported using the following age groups: 21-24, 25-34, 35-44, 45-54, and 55+ years old. Decline to answer was presented as an option.
- **Gender** was assessed using a single item asking the respondent if they are male or female. Decline to answer was presented as an option.
- **Racial or ethnic background** was assessed using a single item asking the respondent which best describes their racial/ethnic background. Response options included: Caucasian/White, Black/African American, Hispanic (e.g., Latin American, Mexican, Puerto Rican, Cuban), Asian or Pacific Islander, Native American or Alaskan native, mixed racial background, other, don't know, and decline to answer.
- **Highest grade or level of school completed** was assessed using a single item asking the respondent which response corresponded to the highest level of education they have attained. Response options included: Less than high school, some high school – no diploma, General Educational Development (GED), high school graduate – diploma, some college but no degree, Associate degree, Bachelor's degree (e.g., BA, AB, BS), Post-graduate degree (e.g., MBA, PhD, JD, etc.), don't know, and decline to answer.
- **Marital Status** was assessed using a single item asking the respondent their marital status. Response options included: Now married, widowed, divorced, separated, never married, and decline to answer.
- **Household income in the last 12 months** was assessed using a single item asking respondents which category best described their total household income in the last 12 months. Response options included: Less than \$10,000, \$10,000 to \$14,999, \$15,000 to \$24,999, \$25,000 to \$34,999, \$35,000 to \$49,999, \$50,000 to \$74,999, \$75,000 to \$99,999, \$100,000 to \$199,999, \$200,000 or more, don't know, and decline to answer.

Table 3. Outcomes Table for Primary Objective 1 – TNP patterns of use among *General Snus*® users.

| Measurement Domain | Subcategory | Measurement Details | Metric |
|---|---|--|---|
| Patterns of use: Reported use (Baseline, Month 6, Year 1, Year 2) | Cigarettes | One item for each TNP assessing the frequency of use (10 TNPs in total). | Patterns of use over the last 30 days has 3 response options: "Every day," "Some days" and "Not at all." "Don't know" and "Decline to answer" are also available as response options. |
| | E-cigarettes | | |
| | Moist snuff | | |
| | Chewing tobacco | | |
| | <i>General Snus</i> ® | | |
| | Nicotine pouches | | |
| | Cigars, cigarillos or filtered cigars filled with tobacco | | |
| Patterns of use: Intention to quit (Baseline) | Pipe tobacco | Response based on the validated Motivation to Stop Scale (MTSS) ⁵ will be used to measure intent to quit smoking. | The MTSS ⁵ has 7 response options ranging from 1= I don't want to stop smoking to 7= I REALLY want to stop smoking and intend to in the next month. A "Don't know" response is also available. |
| | Hookah or water pipe tobacco | | |
| | Aids to help stop smoking | | |
| | Cigarettes | | |
| Patterns of use: Quitting behavior (Baseline, Month 6, Year 1, Year 2) | Cigarettes | 1) One item assessing quitting behavior for cigarettes over the past 30 days. | 1) Quitting behavior for cigarettes over the past 30 days response options are "yes" and "no" |
| | | 2) One item assessing current quitting behavior for cigarettes if | 2) Respondents who have not quit using cigarettes in the past 30 days, will be |

| | | | |
|--|--|---|--|
| | | response to quitting behavior in the past 30 days is no | asked if they are currently trying to quit. Response options are “yes” and “no” |
|--|--|---|--|

Table 4. Outcomes Table for Primary Objective 2 – *General Snus*® and cigarettes pattern of use.

| Measurement Domain | Subcategory | Measurement Details | Metric |
|---|-----------------------|---|---|
| Patterns of use: Average reported <i>General Snus</i> ® use <u>everyday</u> (Baseline, Month 6, Year 1, Year 2) | <i>General Snus</i> ® | One item assessing the number of <i>General Snus</i> ® pouches used <u>everyday</u> over the past 30 days | Average reported number of <i>General Snus</i> ® pouches <u>everyday</u> at Baseline, Month 6, Year 1, and Year 2 will be derived based on the number of <i>General Snus</i> ® pouches used each day |
| Patterns of use: Average reported <i>General Snus</i> ® use on <u>some days</u> (Baseline, Month 6, Year 1, Year 2) | <i>General Snus</i> ® | One item assessing the number of <i>General Snus</i> ® pouches used on <u>some days</u> One item assessing how many days were <i>General Snus</i> ® pouches used over the past 30 days | Average reported number of <i>General Snus</i> ® pouches on <u>some days</u> at Baseline, Month 6, Year 1, and Year 2 will be derived based on the number of <i>General Snus</i> ® pouches over the number of days used |

| | | | |
|--|--|--|--|
| <p>Patterns of use: Percent of days <i>General Snus</i>[®] is used (Baseline, Month 6, Year 1, Year 2)</p> | <p><i>General Snus</i>[®]</p> | <p>One item assessing the number of <i>General Snus</i>[®] pouches used <u>everyday</u> over the past 30 days.</p> | <p>The percent of days that <i>General Snus</i>[®] pouches were used <u>everyday</u> over a 30 day period at Baseline, Month 6, Year 1, and Year 2 will be derived based on the number of days <i>General Snus</i>[®] pouches were used, divided by the 30 day period.</p> |
| <p>Patterns of use: Average reported cigarettes smoked <u>everyday</u> (Baseline, Month 6, Year 1, Year 2)</p> | <p><i>General Snus</i>[®]</p> | <p>One item assessing the number of cigarettes smoked <u>everyday</u> over the past 30 days</p> | <p>Average reported number of cigarettes smoked <u>everyday</u> at Baseline, Month 6, Year 1, and Year 2 will be derived based on the number of cigarettes smoked each day</p> |
| <p>Patterns of use: Average reported cigarettes smoked on <u>some days</u> (Baseline, Month 6, Year 1, Year 2)</p> | <p><i>General Snus</i>[®]</p> | <p>One item assessing the number of cigarettes smoked on <u>some days</u> over the past 30 days One item assessing how many smoking days were there over the past 30 days</p> | <p>Average reported number of cigarettes smoked on <u>some days</u> at Baseline, Month 6, Year 1, and Year 2 will be derived based on the number of cigarettes smoked over the number of days smoked</p> |

| | | | |
|--|----------------------|---|---|
| Patterns of use: Percent of days cigarettes were smoked (Baseline, Month 6, Year 1, Year 2) | <i>General Snus®</i> | One item assessing the number of cigarettes smoked <u>everyday</u> over the past 30 days. | The percent of days that cigarettes were smoked <u>everyday</u> over a 30 day period at Baseline, Month 6, Year 1, and Year 2 will be derived based on the number of days cigarettes were smoked, divided by the 30 day period. |
|--|----------------------|---|---|

Table 5. Outcomes Table for Primary Objective 3 – TNP patterns of use among *General Snus®* and New *General Snus®* users compared to PATH Study users

| Measurement Domain | Subcategory | Measurement Details | Metric |
|--|---|--|---|
| Patterns of use: Reported use (Baseline, Month 6, Year 1, Year 2, PATH) | Cigarettes | One item for each TNP assessing the frequency of use (10 TNPs in total). | Patterns of use over the last 30 days has 3 response options: "Every day," "Some days" and "Not at all." "Don't know" and "Decline to answer" are also available as response options. |
| | E-cigarettes | | |
| | Moist snuff | | |
| | Chewing tobacco | | |
| | <i>General Snus®</i> | | |
| | Nicotine pouches | | |
| | Cigars, cigarillos or filtered cigars filled with tobacco | | |
| | Pipe tobacco | | |
| | Hookah or water pipe tobacco | | |
| | Aids to help stop smoking | | |

Table 6. Outcomes Table for Primary Objective 4 – Quitting cigarettes, incremental use, supplemental use, and completely substituting *General Snus*® in place of cigarettes.

| Measurement Domain | Subcategory | Measurement Details | Metric |
|---|-------------|--|---|
| Patterns of use: Quitting smoking cigarettes among <i>General Snus</i>® users at Month 6, Year 1, and Year 2 cigarette use | Cigarettes | One item assessing the number of times cigarettes were smoked everyday or on some days over the past 30 days. | Quitting all cigarettes during the Month 6, Year 1 and Year 2 will be derived based on the number of cigarettes smoked. Respondents who smoked everyday or on some days during the Baseline period but none during the Month 6, Year 1 and Year 2 periods will be considered to have quit all cigarette use |
| | | One item assessing whether cigarette smokers have completely quit smoking | Completely quit smoking will be assessed at Month 6, Year 1 and Year 2 with response options of “yes” and “no” |
| Patterns of use: Complete Substitution of <i>General Snus</i>® in place cigarettes at Month 6, Year 1, and Year 2 | Cigarettes | <p>One item assessing the number of times cigarettes were smoked everyday or on some days during the Baseline period.</p> <p>One item assessing the number of times cigarettes were smoked everyday or on some days during the Month 6, Year 1 and Year 2 periods.</p> | Completely substituting of <i>General Snus</i> ® in place of smoking cigarettes during the Month 6, Year 1 and Year 2 will be derived based on the number of cigarettes smoked. <i>General Snus</i> ® users who smoked cigarettes during the Baseline period but use only <i>General Snus</i> ® during the Month 6, Year 1 and Year 2 periods will be considered to have completely substituted <i>General Snus</i> ® in place of smoking cigarettes. |

* Note: Incremental and supplemental use will be evaluated for *General Snus*® users based on the average daily reported use outcome presented in Table 6 above. Incremental *General Snus*® use is defined as number of cigarettes smoked in the Month 6, Year 1, and Year 2 periods be greater

than number of cigarettes smoked at the Baseline period while concurrently using *General Snus*[®]. Supplemental *General Snus*[®] use is defined as number of cigarettes smoked be less than number of cigarettes smoked at the Baseline period, while concurrently using *General Snus*[®].

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

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

Table 8. Outcomes Table for Secondary Objective 1 – Perceptions of absolute risk.

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

Table 9. Outcomes Table for Secondary Objective 1 – Perceptions of absolute risk.

| Measurement Domain | Subcategory | Measurement Details | Metric |
|---|---------------|--|--|
| Absolute risk attributed to never having used any TNP's (Baseline, Month 6, Year 1, Year 2) | Mouth cancer | One item for each health condition (3 health conditions total) will assess the perception of the absolute risk from never having used any TNP. | Absolute risk perception of a person suffering from each health condition will be assessed with "Very low chance," "Low chance," "Moderate chance," "High chance" and "Very high chance." "Don't know" is also available as a response option. |
| | Heart disease | | |
| | Lung cancer | | |

Table 10. Outcomes Table for Secondary Objective 2 – Understanding of the MRTP claim for *General Snus*®

| Measurement Domain | Subcategory | Measurement Details | Metric |
|--|---------------------------------|--|--|
| Understanding of the MRTP claim for risk of disease from using <i>General Snus</i> ® instead of cigarettes (Baseline, Month 6, Year 1, Year 2) | <i>General Snus</i> ® | One item assessing whether the risk for mouth cancer, heart disease, lung cancer, stoke, emphysema, and chronic bronchitis is lower, the same, or higher with <i>General Snus</i> ® vs. smoking cigarettes | Understanding of the MRTP claim will have 6 response options including: "Puts you at lower risk for mouth cancer, heart disease, lung cancer, stoke, emphysema, and chronic bronchitis", "Does not affect your risk for mouth cancer, heart disease, lung cancer, stoke, emphysema, and chronic bronchitis", "Puts you at higher risk for mouth cancer, heart disease, lung cancer, stoke, emphysema, and chronic bronchitis", "None of the above", "Don't know", and "Decline to answer". |
| | New <i>General Snus</i> ® users | | |

Table 11. Outcomes Table for Secondary Objective 2 – Understanding of the MRTP claim for *General Snus*®

| Measurement Domain | Subcategory | Measurement Details | Metric |
|--|---------------------------------|--|---|
| Understanding of the MRTP claim for number of cigarettes smoked to lower risk of disease (Baseline, Month 6, Year 1, Year 2) | <i>General Snus</i> ® | One item assessing the number of cigarettes smoked to lower the risk for mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis | Understanding of the MRTP claim will have 6 response options including: “Zero cigarettes”, “Up to 5 cigarettes”, “Up to 20 cigarettes”, “As many as you want to smoke”, “Don't know” and “Decline to answer”. |
| | New <i>General Snus</i> ® users | | |

9.4.3 Respondent Characteristics

9.4.3.1 Socio-demographic Variables

State of residence, which will be assessed using a single item asking the respondent what state they spend most days of the year in.

Age of the respondent will be assessed using a single item asking the respondent how many years old they are. Age of respondent will be categorized for reporting using the following age groups: 21-24, 25-34, 35-44, 45-54, and 55+ years old.

Gender will be assessed using a single item asking the respondent if they are male or female. Decline to answer is also an option.

9.5 Time Points of Importance

Time points of importance in the Prospective Study included the 30-day period for Baseline (Wave 1), Month 6 (Wave 2), Year 1 (Wave 3) and Year 2 (Wave 4).

10. STATISTICAL ANALYSIS

10.1 Study Analysis

All analyses performed for the *General Snus*[®] Patterns of Use Study included descriptive analysis and inferential statistical testing of changes over time, across waves of the study.

Descriptive Analysis

Descriptive statistics used to understand the distribution of socio-demographic and outcomes variables (see **Sections 9.4.1** and **9.4.2**) were based on the raw data (i.e., prior to any recoding or any aggregation required for the final presentation of results). Respondents with values for variables that are illogical or deemed unreliable, as determined by the underlying distribution, will be considered for removal prior to performing the main analyses. (See **Section 11.2** and **11.4** for details regarding this process). Numeric variables were described using total sample size, number of missing observations (if applicable), means, standard deviations, medians, minimums, and maximums. Categorical variables will be described using frequencies, percentages, and the number of missing observations (if applicable).

Unless otherwise specified in the table, descriptive statistics reported for the main analyses included the number of non-missing observations, means, standard deviations, and 95% confidence intervals (CIs), for numeric variables. For categorical variables, they included the number of non-missing observations, frequencies, percentages, and 95% CIs for the percentage of respondents endorsing each category.

Inferential Statistical Testing (after Wave 1 or Baseline Study)

Inferential statistical testing will be conducted to evaluate change in primary and secondary outcome measures (i.e., patterns of use, risk perception, understanding of claim) from baseline and each follow-up wave of the study. Baseline vs. each follow-up (Waves 2, 3, and 4) will be conducted using paired sample t-tests for continuous variables and McNemar test for categorical variables in order to account for correlated measures. These inferential statistical comparisons will reveal whether changes are occurring across the waves of the study within individuals. For paired sample t-tests, means (baseline and follow-up), standard deviations (baseline and follow-up), t-test statistic, degrees of freedom, and p-value will be reported. For McNemar tests, proportions in percentages (baseline and follow-up) and p-values will be reported. Any two-sided p-values of less than 0.05 will be considered to be statistically significant.

The study team formatted and properly labelled the data sets (including all responses from respondents and the date that the survey was completed) using Statistical Package for the Social Sciences ([IBM SPSS Statistics v23, 2015](#)) and [R software \(version 3.5.2\)](#) so they were suitable for analysis. The data sets contained a subject ID number and did not contain any information that could be used to identify individual respondents.

10.2 Socio-demographics

Descriptive statistics were summarized in this Wave 1 (Baseline) Study report for all socio-demographic variables outlined in **Section 9.4.2**. Specifically, state of residence, age of respondent, gender, racial or ethnic background, highest grade or level of school completed, marital status, and household income in the last 12 months, were reported for the *General Snus*[®] users.

10.3 Statistical Analysis by Study Objective

10.3.1 Primary and Secondary Objectives

Descriptive statistics for accomplishing primary and secondary objectives for patterns of *General Snus*[®] use will be provided after completion of the Wave 2, Wave 3, and Wave 4 accordingly.

10.4 Changes in the Conduct of the Study or Planned Analyses

There were no changes made to the protocol or statistical analysis plan.

11. STATISTICAL AND ANALYTICAL ISSUES

11.1 Data Capture and Management

11.1.1 Data Capture

The web-based survey was created by the (b) (4) programming team using (b) (4) for web-based survey programming (v117, Fresno, CA). After the survey has been programmed and tested, the survey link and content were reviewed by a separate team within (b) (4) fielding operations group from the perspective of the respondent (i.e., the link was reviewed online and not within the (b) (4)).

The data collected for this study was monitored for adherence with the Study Protocol ([Attachment 16.3](#)). All data were collected using a programmed web survey ([Attachment 16.2](#)). Prior to initiating the study, the appropriate edit programming was conducted to assure the final dataset required minimal cleaning of invalid responses. These programming procedures for the web-based survey data entry tool included response ranges, consistency checks, skip patterns, and other special edit procedures where applicable. At every step of data processing, results or creating grouping variables were cross-checked by (b) (4) operations team members who independently replicated the results and/or verified that the data had been handled appropriately and accurately. Any inconsistencies identified during this process were corrected before data were provided to (b) (4) analytical team to begin study analysis.

11.1.2 Data Management and Analysis QC Process

- Until the approval of the *General Snus*® Patterns of Use SAP ([Attachment 16.4](#)) by SMNA, the data remained blinded and locked.
- Once the data were unlocked, the analytical team performed the following checks prior to conducting data analyses specified in the SAP:
 - The classification of participants into the study cohorts based on self-reported use or non-use of TNP was confirmed.
 - Completion of the survey was verified, and any respondent who did not complete the full survey was removed from analysis.
 - It was verified that respondents satisfied the inclusion and exclusion criteria.
 - The actual quota frequencies for each study cohort in the data set was compared against the quota frequencies specified in the Study Protocol. Any discrepancies were documented in the final report.
- All variable coding followed as specified in the SAP (e.g., grouping age by age brackets, grouping the number of adults/children in the household, and total household income in the last 12 months).
- All statistical analyses and results output were validated by another researcher on the analytical team for quality control. Validation covered:

- Correct coding of variables.
- Correct use of statistical methods as specified in the analysis section.
- Correct export of results from [R software \(version 3.5.2\)](#) output to Excel tables.

11.2 Missing Data

The structure of the Study questionnaire did not have “true” missing data. The online survey did not allow respondents to proceed without receiving an answer to the present question. No partially completed surveys will be included in the final Study analyses. For the Study, data points are either missing because the respondent selected “Don’t know” or “Decline to answer,” or they did not qualify to answer the question due to survey skip logic. Thus, these types of missing data were kept as is and will be reported descriptively (percentages and counts). The questionnaire was designed so that instructions were easy to understand and as clear as possible, to help avoid missing data.

The Baseline period questionnaire did not allow respondents to proceed without answering the present question. Hence, missing observations for completed surveys arise because the respondent selected “Don’t know” or “Decline to answer,” or s/he did not qualify to answer the question due to prior answers. No modifications took place in these instances.

The rationale and utilization of “Don’t know” and “Decline to answer” response options were as follows:

- In this study, a “Decline to answer” response option without a “Don’t Know” option was provided for any question where there was personally sensitive information, but the answer would be known to the respondent (e.g., age, gender, etc.).
- “Don’t know” and “Decline to answer” options were provided for all other questions.

11.3 Identification of Outliers

When conducting online research, invariably some respondents will find a way to complete the survey without attempting to provide accurate, relevant responses. To ensure that those respondents did not compromise the integrity of the data, measures were taken to eliminate their data from consideration prior to actual analyses. This process required objectivity and removed respondent data regardless of directionality. The process sought to identify the following respondent types:

- Respondents who are “speeders”, defined as those who complete the survey in under 2 minutes.
- Respondents who were found to be inattentive. Specifically, we included an item at the end of the survey (Section C [demographics]) to serve as an *attention check*, “*For this question, please select number two to demonstrate your attention.*”

Data from these respondents were flagged in the data file. Additionally, the number of respondents flagged and the rationale for their identification as outliers were reported in this Wave 1 (Baseline) report.

12. STUDY RESPONDENTS

12.1 Study Fielding Summary

The fielding summary for number of respondents who entered the Wave 1 Baseline survey, those who did not complete the survey, those who were terminated (and the reasons for termination) are summarized in [Table 12](#) below.

Table 12: Fielding Summary

| | Current <i>General Snus</i> ® users |
|---|-------------------------------------|
| Number of respondents who entered the survey | 4581 |
| Number of respondents who did not complete the survey | 1864 |
| Number of respondents who were terminated based inclusion/exclusion criteria/quota filled/Intellectual Property blocker | 1048 |
| Number of respondents who failed the attention check | 14 |
| Total respondents retained | 1655 |

12.2 Final Sample

There were 1655 participants who met the criteria for the Wave 1 (Baseline) Study and were *General Snus*® users which exceeded the targeted 1,500 participants.

13. WAVE 1 (BASELINE) STUDY RESULTS

13.1 Descriptive Results

All respondents were included in the raw data descriptive results ([Descriptive Tables 1a to 4; Appendix 16.1](#)), and descriptive statistical analyses for overall *General Snus*® users are presented in [Tables 13-24](#).

13.2 Demographics and Respondent Characteristics

The overall demographic results (for *General Snus*® and for New *General Snus*® users) are summarized in [Descriptive Table 2; Attachment 16.1](#) and in [Table 13](#).

Overall *General Snus*® respondents' mean age was 36.1 years (range: 21-79 years) ([Descriptive Table 1b; Attachment 16.1](#)). Among *General Snus*® users, the New *General Snus*® product users were defined as first time *General Snus*® use less than 30 days ago. The New *General Snus*® users were younger with mean ages of 34.2 years (range: 21 to 63 years) ([Descriptive Table 1b; Attachment 16.1](#)). There were more male respondents in the *General Snus*® users (91.7%) than within the New *General Snus*® user cohorts (82.7%) ([Table 13](#)). The majority of respondents (89.9% in the *General Snus*® users and 80.4% within New *General Snus*® users) were Caucasian ([Table 13](#)).

The largest proportion of all *General Snus*® respondents had a Bachelor's degree (34.6%). Within the New *General Snus*® product users, the majority had some college but no degree (30.8%) ([Table 13](#)). A little more than a quarter of all respondents (28.0%) reported a household income of \$100,000.00 or more per year while the same proportion of respondents (28.8%) within the New *General Snus*® product users reported an annual household income between \$25,000 to \$49,999 ([Table 13](#)). Half of all respondents (50.8%) and half of those within the New *General Snus*® (50.0%) were reported to be married at the time of the survey ([Table 13](#)).

Table 13: Socio-demographics of *General Snus*® and New *General Snus*® users.

| | General Snus® users N | New General Snus® users* N |
|-----------------------------|--------------------------|-------------------------------|
| | 1655 | 52 |
| U.S. census region | | |
| Northeast (%) | 199 (12.0%) | 5 (9.6%) |
| Midwest (%) | 467 (28.2%) | 19 (36.5%) |
| South (%) | 567 (34.3%) | 18 (34.6%) |
| West (%) | 422 (25.5%) | 10 (19.2%) |
| Respondent age | | |
| 21-24 (%) | 161 (9.7%) | 12 (23.1%) |
| 25-34 (%) | 704 (42.5%) | 18 (34.6%) |
| 35-44 (%) | 489 (29.5%) | 10 (19.2%) |
| 45-54 (%) | 198 (12.0%) | 9 (17.3%) |
| 55+ (%) | 103 (6.2%) | 3 (5.8%) |
| Gender | | |
| Male (%) | 1517 (91.7%) | 43 (82.7%) |
| Female (%) | 138 (8.3%) | 9 (17.3%) |
| Racial or ethnic background | | |

| | | |
|--|--------------|------------|
| Caucasian/White (%) | 1471 (89.9%) | 41 (80.4%) |
| Black/African American (%) | 24 (1.5%) | 2 (3.9%) |
| Hispanic (e.g. Latin American, Mexican, Puerto Rican, Cuban) (%) | 42 (2.6%) | 1 (2.0%) |
| Asian or Pacific Islander (%) | 19 (1.2%) | 3 (5.9%) |
| Native American or Alaskan Native (%) | 17 (1.0%) | 1 (2.0%) |
| Mixed racial background (%) | 52 (3.2%) | 2 (3.9%) |
| Other (%) | 12 (0.7%) | 1 (2.0%) |
| Highest grade or level of school completed | | |
| Less than high school (%) | 3 (0.2%) | 1 (1.9%) |
| Some high school, no diploma (%) | 23 (1.4%) | 0 (0.0%) |
| General Educational Development (GED) (%) | 60 (3.6%) | 8 (15.4%) |
| High school graduate - diploma (%) | 175 (10.6%) | 10 (19.2%) |
| Some college but no degree (%) | 442 (26.8%) | 16 (30.8%) |
| Associate degree (%) | 179 (10.9%) | 4 (7.7%) |
| Bachelor's degree (ex. BA, AB, BS) (%) | 571 (34.6%) | 9 (17.3%) |
| Post-graduate degree (e.g. MBA, PhD, JD, etc.) (%) | 195 (11.8%) | 4 (7.7%) |
| Marital status | | |
| Now married (%) | 841 (50.8%) | 26 (50.0%) |
| Widowed (%) | 19 (1.1%) | 2 (3.8%) |
| Divorced (%) | 145 (8.8%) | 3 (5.8%) |
| Separated (%) | 36 (2.2%) | 3 (5.8%) |
| Never married (%) | 601 (36.3%) | 18 (34.6%) |
| Decline to answer (%) | 13 (0.8%) | 0 (0.0%) |
| Household income in the last 12 months | | |
| Less than \$25,000 (%) | 142 (8.6%) | 10 (19.2%) |
| \$25,000 to \$49,999 (%) | 366 (22.1%) | 15 (28.8%) |
| \$50,000 to \$74,999 (%) | 339 (20.5%) | 9 (17.3%) |
| \$75,000 to \$99,999 (%) | 282 (17.0%) | 9 (17.3%) |
| \$100,000 or more (%) | 463 (28.0%) | 8 (15.4%) |
| Don't know (%) | 5 (0.3%) | 0 (0.0%) |
| Decline to answer (%) | 58 (3.5%) | 1 (1.9%) |

*Per study protocol, new General Snus® users will be defined as first time General Snus® use less than 30 days ago.

13.3 Baseline Results for Primary Objectives

Descriptive statistical analyses for overall users are presented in [Descriptive Tables 3a-3b \(Attachment 16.1\)](#).

13.3.1 Primary Objective 1: Baseline TNP use in the past 30 days.

Among the respondents that used *General Snus*® in the past 30 days, the highest proportion of respondents reported doing so every day (82.1%), followed by some days (17.9%) ([Table 14](#)). Of

those who reported ever cigarette use (n=914), 32.7% (n=299) smoked over the past 30 days and for those who reported using *General Snus*[®] over the past 30 days, only 18.1% (n=299) used cigarettes concurrently. Of those who reported ever cigarette use, the majority of participants (67.2%) reported that they did not smoke at all over the past 30 days while 13.1% reported that they smoked every day and 19.6% reported that they smoked on some days ([Table 14](#)).

Among respondents who reported ever E-cigarettes use (n=642), 43.3% (n=278) used E-cigarettes over the past 30 days and among those who reported using *General Snus*[®] in the past 30 days, 16.8% (n=278) used E-cigarettes during the same time period. Similar to cigarette use pattern, of those who reported ever E-cigarette use, more than half did not use any E-cigarettes at all over the past 30 days (56.2%), 27.6% used on some days and 15.7% reported E-cigarette use everyday ([Table 14](#)).

Over 60% of respondents reported ever use of moist snuff (n=1069). Of those, 51.4% (n=549) used moist snuff products over the past 30 days and among those who reported using *General Snus*[®] over the past 30 days, 33.2% (n=549) also used moist snuff during the same time period. More users of moist snuff use the product on some days (34.1%) than every day (17.3%) ([Table 14](#)).

Among respondents who reported ever use of nicotine pouches (n=880), 62.3% (n=548) used them over the past 30 days. For those who reported using *General Snus*[®] in the past 30 days, 33.1% (n=548) also used nicotine pouches during the same time period. More users of nicotine pouches use them on some days (51.2%) than every day (11.0%) ([Table 14](#)).

Almost 50% of respondents reported ever use of cigars, cigarillos, or filtered cigars filled with tobacco products (n=771). Of those, 48.5% (n=374) used those products over the past 30 days. Of the 771 who reported using *General Snus*[®] over the past 30 days, 22.5% (n=374) also used cigars, cigarillos, or filtered cigars filled with tobacco products during the same time period. More users of cigars, cigarillos, or filtered cigars filled with tobacco products them on some days (46.8%) than every day (1.7%) ([Table 14](#)).

There were less than 31% of responders who were ever users for the remainder TNPs in the past 30 days including chewing tobacco (n=508, 30.6%), pipe tobacco use (n=328, 19.8%), hookah or water pipe tobacco use (n=402, 24.2%), or use of aids to help smoking (n=389, 23.5%). Details about frequency of use of these TNPs can be found in [Table 14](#).

Of note, participants were asked about snus use which included *General Snus*[®] so data for that TNP was presented in [Table 14](#) but considered to be duplicate results.

(b) (4)

(b) (4)

(b) (4)

(b) (4)

CI: Confidence Interval

*Number of non-missing responses

13.3.2 Baseline intention to quit TNP based on the Motivation to Stop Scale (MTSS) and cigarette quitting behavior.

Baseline quitting cigarettes behavior: Among *General Snus*[®] users who responded they smoked every day or on some days over the past 30 days (n=299), 16.4% reported that they completely quit smoking. Of those that reported they did not completely quit smoking (n=250), 44.0% reported that they were currently trying to quit smoking cigarettes over the past 29 days ([Table 16](#)).

Respondents' intention to quit smoking was assessed among those who reported that they are currently not trying to quit, using the MTSS. The MTSS consisted of one item with seven response options ranging from 1 ("I don't want to stop") to 7 ("I really want to stop and intend to in the next month") ([Table 15](#)). The average MTSS score was 2.50 suggesting low intentions to quit smoking given that a score of 2 was defined as "I think I should stop smoking but don't really want to" and a score of 3 was defined as "I want to stop smoking but haven't thought about when".

Table 15. TNP patterns of use for *General Snus*® users. Intention to quit TNP based on the Motivation to Stop Scale (MTSS) at Baseline.

| | | |
|---------|--|---------|
| | | (b) (4) |
| | | |
| | | |
| (b) (4) | | |

CI: Confidence Interval

*Number of non-missing responses

The MTSS has 7 response options ranging from 1=I don't want to stop smoking to 7=I REALLY want to stop smoking and intend to in the next month. A "Don't know" response is also available.

The MTSS was validated to predict quit attempts for cigarette usage but has been adapted to measure quit intention for other TNP.

Intention to quit cigarettes was asked only among those not currently trying to quit smoking cigarettes.

Table 16. TNP patterns of use for *General Snus*® users. Quitting cigarettes behavior.

| | General Snus® users |
|---------|---------------------|
| | Baseline |
| (b) (4) | |

13.3.3 Primary Objective 2: Baseline average number of days *General Snus*[®] pouches were used over the past 30 days

Over the past 30 days, 1358 (82.1% of *General Snus*[®] users) reported using *General Snus*[®] every day. These 1358 participants reported using an average of 10.5 *General Snus*[®] pouches per day.

The remaining 297 participants reported that they used *General Snus*[®] on 49.8% of days and use an average of 5.3 *General Snus*[®] pouches on the days they are used ([Table 17](#)).

Table 17. *General Snus*[®] patterns of use. Outcomes include percent of days that *General Snus*[®] is used and average number of *General Snus*[®] pouches used.

| | |
|---------|-----|
| (b) (4) | |
| (b) | (4) |

13.3.4 Primary Objective 2: Baseline average number of days cigarettes were smoked over the past 30 days

Over the past 30 days, 120 (7.3% of *General Snus*[®] users) reported smoking cigarettes every day. These 120 participants reported smoking an average of 12.3 cigarettes per day.

The remaining 179 participants reported that they smoked on 31.0% of days and use an average of 4.81 cigarettes on the days they smoked ([Table 18](#)).

Table 18. Cigarettes pattern of use among *General Snus*[®] users. Outcomes include percent of days cigarettes are smoked and average number of cigarettes smoked.

| | |
|---------|--|
| (b) (4) | |
| (b) (4) | |

13.3.5 Primary Objective 3: Characterize *General Snus*[®] users, especially new users, in terms of prior TNP use and demographics and compare this to new users of smokeless TNP as reported in the Population Assessment of Tobacco and Health (PATH)

The sample size of new users in PATH could not be established at the time of this report and for Table 19. In addition, Table 20 and 21 will be provided in Wave 2 to Wave 4 reporting follow up data from Month 6 to Year 2.

13.4 Baseline Results for Secondary Objectives

Descriptive statistical analyses for overall users are presented in [Descriptive Table 4 \(Attachment 16.1\)](#).

13.4.1 Secondary Objective 1: Baseline Perception of absolute risk to using only *General Snus*[®] daily, smoking only cigarettes daily, dual use of *General Snus*[®] and cigarettes daily, and never having used any TNPs

Respondents were asked to assess the absolute risk of developing three health conditions (mouth cancer, heart disease and lung cancer) across four scenarios: using only *General Snus*[®] daily, smoking only cigarettes daily, dual use of *General Snus*[®] and cigarettes daily, and never having

used TNP. For each scenario and condition, response options ranged from a very low to a very high risk of developing these conditions

Considering a person who uses *General Snus*[®] products every day but uses no other TNP, respondents reported a low to moderate risk of developing mouth cancer and heart disease, and a very low to low risk of developing lung cancer (Table 22).

Respondents reported that daily smokers who use no other TNP have a moderate to high chance of developing mouth cancer and a high to very high chance of developing heart disease or lung cancer (Table 22).

Respondents also perceived that daily dual users of *General Snus*[®] products and cigarettes were to have a moderate to high risk of developing mouth cancer and high to very high risk of developing heart disease and lung cancer.

Lastly, respondents reported that those who have never used any TNP have a very low to low risk of developing mouth cancer or lung cancer and a low to moderate risk of developing heart disease (Table 23).

When looking across all absolute risk metrics, a consistent pattern emerged. Respondents perceived that cigarettes presented the greatest risk of harm. Usage of *General Snus*[®] products alone was associated with some risk of health conditions, although at a lower rate than smoking. Never using TNP was generally deemed to carry the lowest risk.

Table 22. Perceptions of absolute risk for daily *General Snus*[®] users and smokers



(b) (4)

Table 23. Perceptions of absolute risk for dual General Snus® users and smokers and never TNP users

(b) (4)

(b) (4)

13.4.2 Secondary Objective 2: Baseline understanding of the risk reduction as described in the modified risk claim among *General Snus*[®] users, especially new users

Almost 70% of all respondents (69.8%) understood the modified risk claim that *General Snus*[®] use puts them at lower risk than smoking cigarettes for mouth cancer, heart disease, lung cancer, stoke, emphysema, and chronic bronchitis. The majority of responders (80.3%) also understood the modified risk claim that smoking zero cigarettes would lower their risk of disease ([Table 24](#)).

Similar response patterns were observed within the New *General Snus*[®] users cohort with 61.5% of respondents reporting that they understood the modified risk claim that *General Snus*[®] use puts them at lower risk than smoking cigarettes for mouth cancer, heart disease, lung cancer, stoke, emphysema, and chronic bronchitis. Although about 20% (21.2%) responded that they did not understand this claim, this response came from a small sample of 11 respondents. The majority of new users (84.4%) did understand the modified risk claim that smoking zero cigarettes would lower their risk of disease ([Table 24](#)).

Table 24. Understanding of the MRTP claim for *General Snus*[®].

(b) (4)

(b) (4)

13.5 Results Summary

Results and Discussion:

Overall, the *General Snus*[®] respondents and New *General Snus*[®] cohorts were comparable, though the new product user cohort was slightly younger, more were female, more had some college but no degree, and reported an annual household income less than \$49,999. However, due the small sample size of the new users (n=52), this data may be difficult to generalize and make conclusions.

Primary Objective 1: Evaluate baseline TNP use in the past 30 days.

Reported TNP use in the past 30 days: Among the 1655 *General Snus*[®] respondents, at least 40% of ever users (from 43.3% to 62.3%) reported other TNP use, including E-cigarettes, moist snuff, nicotine pouches, cigars, cigarillos, or filtered cigars filled with tobacco products while about 30% of ever users (from 19.8% to 32.7%) reported smoking, chewing tobacco, using pipe tobacco, hookah or water pipe tobacco, and aids to help smoking. Of those who reported ever cigarette use (n=914), 32.7% (n=299) smoked over the past 30 days and for those who reported using *General Snus*[®] over the past 30 days, only 18.1% (n=299) used cigarettes concurrently. Of those who reported ever cigarette use, the majority of participants (67.2%) reported that they did not smoke at all over the past 30 days while 13.1% reported that they smoked every day and 19.6% reported that they smoked on some days.

Primary Objective 1: Evaluate baseline intention to quit TNP based on the Motivation to Stop Scale (MTSS) and cigarette quitting behavior

Cigarette quitting behavior and intention to quit TNP based on the MTSS: Among the 299 *General Snus*[®] users who responded they smoked every day or on some days over the past 30 days, 16.4% reported that they completely quit smoking. Of the 250 that reported they did not completely quit smoking, 44.0% reported that they were currently trying to quit smoking. The average MTSS score for cigarettes was 2.5 suggesting low intentions to quit smoking.

Primary Objective 2: Evaluate baseline average number of days General Snus[®] pouches and cigarettes were used over the past 30 days.

Reported number of days General Snus[®] pouches and cigarettes were used over the past 30 days: Over the past 30 days, 82.1% of *General Snus*[®] users reported using *General Snus*[®] every day and they used an average of 10.5 pouches per day. The remaining participants reported using *General Snus*[®] on 49.8% of days and an average of 5.3 pouches on the days they are used.

In addition, 7.3% of *General Snus*[®] users reported smoking cigarettes every day at an average of 12.3 cigarettes per day.

Secondary Objective 1: Assess perceptions of absolute risk of certain health conditions (mouth cancer, heart disease and lung cancer) among General Snus[®] users attributed to using only General Snus[®] daily, smoking only cigarettes daily, dual use of General Snus[®] and cigarettes daily, and never having used any TNPs.

Perceptions of Absolute Risk: When looking across all absolute risk metrics, a consistent pattern emerged. Respondents perceived that cigarettes presented the greatest risk of harm across different health conditions (mouth cancer, heart disease and lung cancer). Usage of *General Snus*[®] products alone was associated with some risk of health conditions, although at a lower rate than smoking. Never using TNP was generally deemed to carry the lowest risk.

Secondary Objective 2: Assess baseline understanding of the risk reduction as described in the modified risk claim among General Snus[®] users, especially new users.

The majority of respondents comprehended that *General Snus*[®] puts them at lower risk than smoking cigarettes for mouth cancer, heart disease, lung cancer, stoke, emphysema, and chronic bronchitis. The majority of responders also understood the modified risk claim that smoking zero cigarettes would lower their risk of disease.

Similar response patterns were observed within the new user cohort. Although about 20% responded that they did not understand the claim that *General Snus*[®] puts them at lower risk than smoking cigarettes for different diseases, this response came from a small sample of 11 respondents.

14. DISCUSSION AND OVERALL CONCLUSIONS

The principal research questions, “*How do General Snus[®] users use TNP, and how do they perceive health risks associated with cigarettes and General Snus[®]?*” These questions were addressed in this observational Pattern of Use Baseline study.

14.1 Strengths and Limitations of the Study

This study was conducted following the guidance of the Center for Tobacco Products ([FDA Guidance for Industry, 2011](#)) within the FDA on data for human studies designed to evaluate the risks and benefits to the population, including users and non-users of tobacco products. The study benefitted from the administration of the web-based survey which allowed for improved survey designs and accurate data capture.

Additionally, in virtually all cases survey questions utilized validated scales, or scales directly comparable to studies in literature. In particular, usage of the Motivation to Stop Scale allowed for simple, justifiable interpretation. Scales used in risk perception questions line up with other tobacco-related research, such as HINTS.

There were limitations to the current study, arguably none of which should draw concern regarding data integrity. The data collected were from current users of *General Snus*®. The perceived health risk assessments were intended to evaluate real-world perceptions after exposure to real-world information on *General Snus*®, but obviously they did not have the same contextual, social, and emotional consequences of actual decisions. One could only expect a limited degree of accuracy and extrapolation while capturing behavioral intentions, as unforeseen factors can impact actual behaviors. Thus, differences may arise between stated and actual choices, and stated and actual behaviors. Potential hypothetical bias may be limited by constructing questions that mimic realistic perceptions and behaviors as closely as possible. In addition, since data from this study were dependent on respondent self-reporting, subsequently reported variables may also be subjected to recall bias and the inability to confirm actual tobacco use behavior. Self-reported data collection is a standard approach and any potential problems with recall bias were anticipated to be constant across time points.

Respondents were recruited based on invitation stickers placed directly on *General Snus*® canisters. As a result, recruitment could be considered a convenience sample. Further, due to sample selection during recruitment, respondents who were more interested in research, or perhaps healthy enough to participate, may be over-represented, hence the possibility of selection bias. Although these issues raised concerns about the external validity of the findings (e.g., our sample may not be fully generalizable to all consumers), the recruitment plan was designed to mirror the underlying populations.

14.2 Overall Baseline Study Conclusions

Baseline study findings support the conclusion that overall, the introduction of *General Snus*® does not appear to compromise public health in any way, based on perceptions of risk as assessed in the Baseline study. Specifically, results demonstrated that respondents perceived that cigarettes presented the greatest risk of health conditions which include mouth cancer, heart disease and lung cancer. Moreover, usage of *General Snus*® products alone was associated with some risk of health conditions, although at a lower rate than smoking. Never using TNP was generally deemed to carry the lowest risk.

In addition, current *General Snus*® users include a significant number of former cigarette smokers (67.2%) suggesting that use of *General Snus*® may support a reduction in smoking.

15. REFERENCES

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General Snus® Patterns of Use Study

Wave 2 Study Report

SMU 19-01GENS

| | |
|----------------------------|--|
| Product Name: | General Snus® |
| First Respondent Enrolled: | February 2, 2021 |
| Last Respondent Completed: | March 6, 2021 |
| Principal Investigators: | (b) (4) |
| Sponsor: | Swedish Match North America Tryggve Ljung, MD., Ph.D., Vice President Scientific Affairs |
| Version: | 2.0 - Final |
| Report Date: | July 13, 2021 |

Confidentiality Statement

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2. SYNOPSIS

Sponsor:

Swedish Match North America (SMNA)

Two James Center
1021 East Cary Street, Suite 1600
Richmond, VA 23219

Name of Finished Product: *General Snus®*
Name of Active Ingredient: Not applicable

Study Title: *General Snus®* Patterns of Use Study

Investigator: (b) (4)

Publication (reference): Not applicable

Studied Period: Wave 1 Baseline

Start of data collection: July 25, 2020

End of data collection: August 17, 2020

Wave 2

Start of data collection: February 2, 2021

End of data collection: March 6, 2021

Objective: The overarching research questions within this study are as follows: (i) *How do General Snus® users use tobacco and nicotine products (TNP), and (ii) how do they perceive health risks associated with cigarettes and General Snus®?* These questions will be studied using a self-reported survey examining patterns of use for the previous 30 days (Baseline-Wave 1) and assessment of TNP use among the same *General Snus®* users again at 6 months (Wave 2), 1-year (Wave 3) and 2-year (Wave 4) intervals post baseline.

Primary Objectives:

Use behavior will be assessed, utilizing data from all 4 waves of the study:

1. Compare TNP patterns of use, between all 4 waves. The study will examine self-reported usage patterns for participants, in aggregate, over time. The study will report on frequency of *General Snus*® use, as well as other TNP, if multiple TNP use is reported. Of specific interest will be usage patterns of cigarettes. Intent to quit and actual quitting of cigarettes will be assessed at each wave of the study.
2. Among *General Snus*® users, compare consumption patterns of cigarettes and *General Snus*® over the last 30 days (Baseline) with consumption patterns in Waves 2 through 4. Of particular interest is whether usage of *General Snus*® offsets usage of cigarettes.
3. Characterize *General Snus*® users in terms of prior TNP use and demographics and compare this to new users of smokeless TNP as reported in the Population Assessment of Tobacco and Health (PATH).
4. Compare the tendencies of *General Snus*® users to quit cigarettes or use *General Snus*® in an incremental fashion, in a supplemental fashion, or in complete substitution of cigarettes.

Secondary Objectives:

Risk Perception and understanding of the MRTP claim will be assessed utilizing data from all 4 Waves of the study:

1. Assess perceptions of risk of certain health conditions (mouth cancer, heart disease, and lung cancer, separately) among *General Snus*® users.
 - a. Assess the absolute risk attributed to using only *General Snus*® daily, smoking only cigarettes daily, dual use of *General Snus*® and cigarettes daily, and never having used any TNPs.
2. Assess the extent to which *General Snus*® users understand the risk reduction as stated in the modified risk claim

Methodology: *General Snus*® user groups were recruited directly from purchasers of *General Snus*® through invitation stickers placed directly on *General Snus*® canisters

A third-party vendor, News America Marketing, was hired to place the study invitation stickers on product packaging (e.g., each individual *General Snus*® canister) for all varieties of *General Snus*® available at retail outlets, from July 25 – August 7, 2020. The sticker initiative targeted approximately 10,600 retail stores carrying *General Snus*® across all locations where *General Snus*® was sold at the time of recruitment. Additionally, the sticker identified a website where users who were interested in participating accessed the survey through a secure and unique survey link. The first set of questions were the survey screener, designed to qualify the participant using the study inclusion and exclusion criteria. Once qualified, all respondents accessed a web survey online via a computer, smartphone, or tablet. The study was a 15-minute survey where participants were asked to self-report TNP use within the past 30 days.

This study will be a longitudinal, prospective study that consists of multiple waves to gain an understanding of how *General Snus*® is used by consumers. Respondents completed surveys at Baseline, and will also be questioned at 6 months, 1 year and 2 years post Baseline period. All participants for the Baseline wave must have reported use of *General Snus*® at least once in the previous 30 days and reported use on some days or every day.

In addition to reporting TNP use, participants will report their perceptions of health risk and their understanding of the modified risk claim.

Number of Patients (Planned and Analyzed):

Planned: The Baseline study was planned to recruit a total sample of 1500 participants but was able to exceed target with 1669 participants. Each participant who participated in the Baseline study agreed to participate in the subsequent waves. Respondents who completed the Baseline study may participate in any of the subsequent waves.

Analyzed: The study retained 1655 participants (*General Snus*® users) at baseline. Fourteen out of the 1669 participants were excluded from baseline analysis because they failed the attention check question in the survey. In Wave 2 (6 months follow-up), the study retained 706 participants but 11 were excluded from analysis due to failing the attention check. Thus, a total of 695 participants were retained for analysis.

Inclusion Criteria:

In addition to the already mentioned cohort definitions, respondents met the following criteria to be included in the study:

- Have used *General Snus*® at least once or more within past 30 days prior AND use it every day or some days prior to study initiation
- Minimum age of 21 years
- Agree to participate in four surveys over the two-year period
- Able to read and speak English
- Currently a resident of the United States
- Individuals who provide electronic informed consent and personal contact information

Exclusion Criteria:

Respondents who met any of the following criteria were excluded from the study:

- Respond as “don’t know” or “decline to answer” to specific demographics (gender, geographical region)
- Unwilling or unable to provide electronic informed consent and personal contact information
- Employed in any of the following fields or professions: market research, marketing, advertising, manufacturers of TNP, or physicians

- Have taken part in a consumer research study on tobacco in the past 2 weeks

Statistical Methods: All analyses performed for the *General Snus®* Patterns of Use Study were descriptive in nature.

Descriptive analyses provide summary statistics for all variables. Summary statistics include counts and proportions for categorical variables and means, standard deviations, medians, minimums, and maximums for ordinal and continuous variables. Descriptive statistics describe the sample as well as verify the quality of the data. Inferential statistical testing will be conducted to evaluate change in primary and secondary outcome measures (i.e., patterns of use, risk perception, understanding of claim) from baseline and each follow-up wave of the study. Baseline vs. each follow-up (waves 2, 3, and 4) will be conducted using paired sample t-tests for continuous variables and McNemar test for categorical variables in order to account for correlated measures.

The study team formatted and properly labelled the data sets (including all responses from respondents and the date that the survey was completed) using Statistical Package for the Social Sciences ([IBM SPSS Statistics v23, 2015](#)) and [R software \(version 3.5.2\)](#) so they were suitable for analysis. The data sets contained a subject ID number and did not contain any information that could be used to identify individual respondents.

Results and Discussion:

Baseline: Overall, the *General Snus®* respondents and New *General Snus®* cohorts were comparable, though the new product user cohort was slightly younger, more were female, more had some college but no degree, and reported an annual household income less than \$49,999. However, due the small sample size of the new users (n=52), this data may be difficult to generalize and make conclusions.

Wave 2: The sociodemographic characteristics of the respondents who returned at Wave 2 of the study were comparable to those observed at Baseline, across both the *General Snus®* users and the New *General Snus®* users cohorts, although the Wave 2 participants were slightly older across cohorts, with females being more prevalent among the returning new users, compared with those enrolled at Baseline.

Primary Objective 1: Evaluate baseline TNP use in the past 30 days.

Baseline: Among the 1655 *General Snus®* respondents, at least 40% of ever users (from 43.3% to 62.3%) reported other TNP use, including E-cigarettes, moist snuff, nicotine pouches, cigars, cigarillos, or filtered cigars filled with tobacco products while about 30% of ever users (from 19.8% to 32.7%) reported smoking, chewing tobacco, using pipe tobacco, hookah or water pipe tobacco, and aids to help smoking. A total of n=914, (55.2%) reported ever cigarette use, and

among these n=299 (18.1%) smoked over the past 30 days. Of those who reported ever cigarette use, the majority of participants (67.2%) reported that they did not smoke at all over the past 30 days while 13.1% reported that they smoked every day and 19.6% reported that they smoked on some days. For these General Snus® users, less than a third reported other TNP use and only 18.1% reported smoking concurrently over the past 30 days.

Wave 2: Among the General Snus® users who returned at Month 6 (n=695), 94.1% of them reported using General Snus® pouches over the past 30 days, with 74.5% (n=518) using every day, 19.6% (n=136) using some days, and 5.9% (n=41) of them reported not using General Snus® product at all. Of all General Snus® users who participated in the second wave of the study (n=695), 12.3% (n=86) of them smoked cigarettes every day (4.0%, n=28) or some days (8.3%, n=58), and 87.2% (n=606) of them reported not using cigarettes at all, over the past 30 days. The most common TNPs used concurrently with the General Snus® product were cigarettes, E-cigarettes, nicotine pouches, moist snuff, and cigars, cigarillos, or filtered cigars filled with tobacco (ranging from 37.6% to 12.4%).

At 6 months follow-up, the reported cigarette smoking in the past 30 days decreased for both everyday users (4.0%) and some days users (8.3%) among all General Snus® users (n=695), compared with the results observed at Baseline (7.3% [everyday use] and 10.8% [some days use], respectively) among overall respondents (n=1655). A similar trend regarding TNP use was observed for the Month 6 respondents across all other reported TNPs used, except for those using nicotine pouches and the General Snus® product. While the reported General Snus® use among all participants decreased for everyday users from 82.1% at Baseline to 74.5% at Month 6, it increased slightly for some days users in the past 30 days, from 17.9% at Baseline to 19.6% at Wave 2.

Primary Objective 1: Evaluate baseline intention to quit TNP based on the Motivation to Stop Scale (MTSS) and cigarette quitting behavior

Baseline: Among the 299 General Snus® users who responded they smoked every day or on some days over the past 30 days, 16.4% reported that they completely quit smoking over the past 29 days. Of the 250 that reported they did not completely quit smoking, 44.0% reported that they were currently trying to quit smoking. The average MTSS score for cigarettes was 2.5 suggesting low intentions to quit smoking.

Wave 2: Among General Snus® users who smoked cigarettes (n=86), at 6 months follow-up, 8.1% (n=7) of them reported that they completely quit smoking cigarettes in the past 29 days. However, 40.5% (n=32) of those who did not report quitting smoking cigarettes in the past 29 days (n=79), were currently trying to quit cigarette smoking. However, given that the overall percentage of regular cigarette use among General Snus® users decreased from 18.1% (n=299)

to 12.3% (n=86) between Baseline and Month 6, these results could indicate that some *General Snus®* users quit cigarette smoking before the reported period of 29 days, at the time of the Wave 2 survey.

Primary Objective 2: Evaluate baseline average number of days General Snus® pouches and cigarettes were used over the past 30 days.

Baseline: Over the past 30 days, 82.1% of *General Snus®* users reported using *General Snus®* every day and they used an average of 10.5 pouches per day. The remaining participants reported using *General Snus®* on 49.8% of days and an average of 5.3 pouches on the days they are used. In addition, 7.3% of *General Snus®* users reported smoking cigarettes every day at an average of 12.3 cigarettes per day. Further, 10.8% of *General Snus®* users reported smoking cigarettes some days day at an average of 4.81 cigarettes per day.

Wave 2: Among the *General Snus®* users who returned for the 6 months follow-up (n=695), 74.5% (n=518) of them reported using *General Snus®* every day and they used an average of 10.2 pouches per day, while 19.6% (n=136) of them reported using on average 6.3 *General Snus®* pouches for a mean percentage of 47.7% of days in the past 30 days. The Wave 2 study results for *General Snus®* users indicate a similar pattern of *General Snus®* use, compared with the results observed at Baseline.

Of the total participants at Wave 2 (n=695), 4.0% (n=28) of them reported smoking on average 11.4 cigarettes every day, while 8.3% (n=58) of them reported smoking on average 3.0 cigarettes for a mean percentage of 25.1% days in the past 30 days days. Compared with the results observed at Baseline, the findings at Month 6 of the study indicate a decrease in the percentage of days cigarettes were smoked among all *General Snus®* users from Baseline (31.0%) to 6 months follow-up (25.0%), although the average number of daily cigarettes used in the past 30 days remained comparable at the first two waves of the study, for both every day and some days cigarette smokers.

Primary Objective 4: Compare the tendencies of General Snus® users to quit cigarettes or use General Snus® in an incremental fashion, in a supplemental fashion, or in complete substitution of cigarettes.

Wave 2: Incremental *General Snus®* use was defined as having greater or the equal cigarette use at Month 6 than at Baseline, while concurrently using *General Snus®*. Supplemental *General Snus®* use was defined as having less cigarette use at Month 6 than at Baseline, while concurrently using *General Snus®*. The participants considered for this analysis were those who did not switch frequency of use from Baseline to Month 6, i.e., everyday users in both waves or some day users in both waves.

For participants who continued to be everyday *General Snus*® users at Month 6 (n=492), their average number of *General Snus*® pouches used daily in the past 30 days decreased from the daily product usage recorded at Baseline by 0.43, and for those who remained some days users at 6 months follow-up (n=47), their usage of *General Snus*® on some days decreased on average by 0.53 pouches, compared with the pattern of use recorded at Baseline.

A similar trend was also observed, at a slightly higher magnitude, among *General Snus*® users who smoked cigarettes. The average number of cigarettes used daily by *General Snus*® users who continued to be everyday cigarette smokers at Month 6 (n=24), decreased by 0.92 from the daily usage recorded at Baseline, and for those who remained some days smokers at 6 months follow-up (n=27), their average number of cigarettes smoked on some days decreased by 0.89, compared with the pattern of use recorded at Baseline. These findings indicate a tendency for supplemental use of *General Snus*® product among those who continued to smoke cigarettes at 6 months follow-up. Among the 299 *General Snus*® users who were identified as cigarette smokers at Baseline, 32 of them reported having quit cigarettes at Month 6, with 29 among those completely substituting *General Snus*® in place of cigarettes at 6 months follow up.

Secondary Objective 1: Assess perceptions of absolute risk of certain health conditions (mouth cancer, heart disease and lung cancer) among General Snus® users attributed to using to using only General Snus® daily, smoking only cigarettes daily, dual use of General Snus® and cigarettes daily, and never having used any TNPs.

Baseline and Wave 2: When looking across all absolute risk metrics at the first two phases of the study, a consistent pattern emerged. Respondents perceived that cigarettes presented the greatest risk of harm across different health conditions (mouth cancer, heart disease and lung cancer). Usage of *General Snus*® products alone was associated with some risk of health conditions, although at a lower rate than smoking. Never using TNP was generally deemed to carry the lowest risk.

Secondary Objective 2: Assess baseline understanding of the risk reduction as described in the modified risk claim among General Snus® users, especially new users.

Baseline: The majority of respondents comprehended that *General Snus*® puts them at lower risk than smoking cigarettes for mouth cancer, heart disease, lung cancer, stoke, emphysema, and chronic bronchitis. The majority of responders also understood the modified risk claim that smoking zero cigarettes would lower their risk of disease. Similar response patterns were observed within the new user cohort. Although about 20% responded that they did not understand the claim that *General Snus*® puts them at lower risk than smoking cigarettes for different diseases, this response came from a small sample of 11 respondents.

Wave 2: The response patterns observed at Month 6 are similar across cohorts with those demonstrated at Baseline, although at Month 6 the New *General Snus*® users cohort was small (n=16).

Strengths and Limitations of the Baseline Study:

This study was conducted following the guidance of the Center for Tobacco Products ([FDA Guidance for Industry, 2011](#)) within the FDA on data for human studies designed to evaluate the risks and benefits to the population, including users and non-users of tobacco products. The study benefitted from the administration of the web-based survey which allowed for improved survey designs and accurate data capture.

Additionally, in virtually all cases survey questions utilized validated scales, or scales directly comparable to studies in literature. In particular, usage of the Motivation to Stop Scale allowed for simple, justifiable interpretation. Scales used in risk perception questions line up with other tobacco-related research, such as HINTS.

There were limitations to the current study, arguably none of which should draw concern regarding data integrity. The data collected were from current users of *General Snus*®. The perceived health risk assessments were intended to evaluate real-world perceptions after exposure to real-world information on *General Snus*®, but obviously they did not have the same contextual, social, and emotional consequences of actual decisions. One could only expect a limited degree of accuracy and extrapolation while capturing behavioral intentions, as unforeseen factors can impact actual behaviors. Thus, differences may arise between stated and actual choices, and stated and actual behaviors. Potential hypothetical bias may be limited by constructing questions that mimic realistic perceptions and behaviors as closely as possible. In addition, since data from this study were dependent on respondent self-reporting, subsequently reported variables may also be subjected to recall bias and the inability to confirm actual tobacco use behavior. Self-reported data collection is a standard approach and any potential problems with recall bias were anticipated to be constant across time points.

Respondents were recruited based on invitation stickers placed directly on *General Snus*® canisters. As a result, recruitment could be considered a convenience sample. Further, due to sample selection during recruitment, respondents who were more interested in research, or perhaps healthy enough to participate, may be over-represented, hence the possibility of selection bias. Although these issues raised concerns about the external validity of the findings (e.g., our sample may not be fully generalizable to all consumers), the recruitment plan was designed to mirror the underlying populations.

Study Conclusion:

Baseline: Baseline study findings support the conclusion that overall, the introduction of *General Snus*® does not appear to compromise public health in any way, based on perceptions of risk as assessed in the Baseline study. Specifically, results demonstrated that respondents perceived that cigarettes presented the greatest risk of health conditions which include mouth cancer, heart disease and lung cancer. Moreover, usage of *General Snus*® products alone was associated with some risk of health conditions, although at a lower rate than smoking. Never using TNP was generally deemed to carry the lowest risk.

In addition, current *General Snus*® users include a significant number of former cigarette smokers (67.5%) suggesting that use of *General Snus*® may support a reduction in smoking.

Wave 2: Study findings at Wave 2 confirm the conclusion based on the perceptions of risk assessed in the Baseline study that overall, the introduction of *General Snus*® does not appear to compromise public health in any way.

Relative to baseline, use of cigarette smoking at Month 6 demonstrated a pattern of:

- Decreased cigarette smoking in the last 30 days for everyday and some day users
- Decrease in percent of days cigarettes are smoked and average number of cigarettes smoked everyday and on some days

Additionally, at Month 6, 4.2% (n=32) of participants reported having quit cigarettes and another 4.2% (n=29) had completely substituted cigarettes with *General Snus*®.

Risk perception results were similar to baseline results. That is, cigarettes posed the greatest risk of developing health conditions, the use of *General Snus*® alone posed some risks (but lower relative to cigarettes), and not using any TNP carried the lowest risk.

Final Date: July 13, 2021

3. TABLE OF CONTENTS

| | |
|--|----|
| 1. TITLE | 1 |
| 2. SYNOPSIS | 2 |
| 3. TABLE OF CONTENTS | 11 |
| 3.1 LIST OF IN-TEXT TABLES | 12 |
| 3.2 LIST OF IN-TEXT FIGURES..... | 12 |
| 4. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS..... | 13 |
| 5. RESPONSIBLE PARTIES..... | 14 |
| 5.1 Investigator and Contributors | 14 |
| 5.2 Sponsor | 14 |
| 6. WAVE 2 STUDY RESPONDENTS..... | 15 |
| 6.1 Study Fielding Summary | 15 |
| 6.2 Final Sample (Wave 2) | 15 |
| 7. WAVE 2 STUDY RESULTS..... | 15 |
| 7.1 Wave 2 Descriptive Results | 16 |
| 7.2 Demographics and Respondent Characteristics..... | 16 |
| 7.3 Wave 2 Results for Primary Objectives..... | 16 |
| 7.3.1 Primary Objective 1: Evaluate TNP use in the past 30 days at Month 6..... | 16 |
| 7.3.2 Primary Objective 1: Evaluate cigarette quitting behavior at Wave 2 | 26 |
| 7.3.3 Primary Objective 2: Evaluate the average number of days <i>General Snus®</i> pouches and cigarettes were used over the past 30 days at Wave 2 | 28 |
| 7.3.4 Primary Objective 3: Characterize <i>General Snus®</i> users, especially new users, in terms of prior TNP use and demographics and compare this to new users of smokeless TNP, as reported in the Population Assessment of Tobacco and Health (PATH) at Wave 2 | 31 |
| 7.3.5 Primary Objective 4: Compare the tendencies of <i>General Snus®</i> users to quit cigarettes or use <i>General Snus®</i> in an incremental fashion, in a supplemental fashion, or in complete substitution of cigarettes at Wave 2..... | 31 |
| 7.4 Wave 2 Results for Secondary Objectives..... | 34 |
| 7.4.1 Secondary Objective 1: Perception of absolute risk to using only <i>General Snus®</i> daily, smoking only cigarettes daily, dual use of <i>General Snus®</i> and cigarettes daily, and never having used any TNPs at Wave 2 | 34 |
| 7.4.2 Secondary Objective 2: Understanding of the risk reduction as described in the modified risk claim among <i>General Snus®</i> users, especially new users | 38 |
| 7.5 Wave 2 Results Summary..... | 40 |
| 8. WAVE 2 DISCUSSION AND OVERALL CONCLUSIONS | 43 |
| 8.1 Overall Wave 2 Study Conclusions | 43 |
| 9. ATTACHMENTS..... | 44 |
| 9.1 Descriptive Tables 1-4 | 44 |
| 9.2 Study Questionnaire..... | 44 |
| 9.3 Protocol..... | 44 |
| 9.4 Statistical Analysis Plan..... | 44 |

3.1 LIST OF IN-TEXT TABLES

| | |
|---|-----------|
| Table 1: Fielding Summary at Wave 2 | 15 |
| Table 2. Primary Objective 1 – TNP patterns of use for <i>General Snus®</i> users at Month 6. Reported TNP use in the last 30 days..... | 18 |
| Table 3. Primary Objective 1 – TNP patterns of use for <i>General Snus®</i> users at Month 6. Quitting cigarettes behavior | 27 |
| Table 4. Primary Objective 2 – Pattern of <i>General Snus®</i> use among <i>General Snus®</i> users at Month 6. Outcomes include percent of days that <i>General Snus®</i> was used and average number of <i>General Snus®</i> pouches used in the past 30 days | 29 |
| Table 5. Primary Objective 2 – Pattern of cigarettes use among <i>General Snus®</i> users at Month 6. Outcomes include percent of days cigarettes were smoked and average number of cigarettes smoked in the past 30 days | 30 |
| Table 6. Primary Objective 4 – <i>General Snus®</i> and cigarettes pattern of use, based on the average daily reported TNP use at Month 6..... | 32 |
| Table 7. Primary Objective 4 – Among <i>General Snus®</i> users, quitting all TNP use, and completely substituting cigarettes for <i>General Snus®</i> at Month 6. | 34 |
| Table 8. Secondary Objective 1 – Perceptions of absolute risk for daily <i>General Snus®</i> users and smokers at the first two waves of study | 35 |
| Table 9. Secondary Objective 1 – Perceptions of absolute risk for dual <i>General Snus®</i> users and smokers and never TNP users at the first two waves of study..... | 37 |
| Table 10. Secondary Objective 2 – Understanding of the MRTP claim for <i>General Snus®</i> at Month 6..... | 38 |

3.2 LIST OF IN-TEXT FIGURES

No table of figures entries found.

4. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

| Abbreviation or Specialist Term | Definition |
|---------------------------------|---|
| CASRO | Council of American Survey Research Organizations |
| CTP | Center for Tobacco Products |
| FDA | FDA Food and Drug Administration |
| FTP | File Transfer Protocol |
| HCP | Health Care Professional |
| HINTS | Health Information National Trends Survey |
| ICF | Informed Consent Form |
| IRB | IRB Institutional Review Board |
| MRTP | Modified Risk Tobacco Product |
| MRTPA | Modified Risk Tobacco Product Application |
| PATH | Population Assessment of Tobacco and Health |
| PII | Personally Identifiable Information |
| PMTA | Premarket Tobacco Product Application |
| RDD | Random Digit Dialing |
| SAP | Statistical Analysis Plan |
| SMNA | Swedish Match North America, LLC |
| TNP | Tobacco/Nicotine Product(s) |
| U.S. | United States |

5. RESPONSIBLE PARTIES

5.1 Investigator and Contributors

| | |
|-------------------------|---------|
| Principal Investigator: | (b) (4) |
| (b) (4) Project Team: | |

5.2 Sponsor

| | |
|----------|--|
| Sponsor: | Swedish Match North America, LLC Tryggve Ljung, MD., Ph.D., Vice President Scientific Affairs |
|----------|--|

6. WAVE 2 STUDY RESPONDENTS

6.1 Study Fielding Summary

The fielding summary for number of respondents who entered the Wave 2 survey, those who did not complete the survey, those who were terminated (and the reasons for termination) are summarized in [Table 1](#) below.

Table 1: Fielding Summary at Wave 2

| | |
|---|-----|
| Number of respondents who entered the Wave 2 survey | 931 |
| Number of respondents who were terminated based inclusion/exclusion criteria/quota filled/Intellectual Property blocker | 159 |
| Number of respondents who did not complete the Wave 2 survey | 66 |
| Number of respondents retained (closed fielding) | 706 |
| Total respondents retained at Wave 2 after data quality check* | 695 |

*Data quality check per SAP included outliers, straightliners, speeders, those who failed the attention check question, and illogical responses.

6.2 Final Sample (Wave 2)

Of the respondents enrolled in the initial phase of the study (n=1655 at Baseline), 706 respondents returned at the 6 months follow up and were considered in the Wave 2 study. Among the 706 respondents, 11 failed the attention check, thus, 695 were retained for study analysis. Among them, 16 participants who were classified as New *General Snus*® users at Baseline returned for the Wave 2 (6 months follow-up) study. Of note, at Baseline, among *General Snus*® users, the New *General Snus*® product users were defined as first time *General Snus*® use less than 30 days ago.”

7. WAVE 2 STUDY RESULTS

Respondents were recruited from 50 U.S. states, including District of Columbia. Participation at Wave 2 ranged from 0.1% of overall respondents from the District of Columbia (n=1), Rhode Island (n=1), and Wyoming (n=1) to 5.5% of them from California (n=38), Illinois (n=38), and Ohio (n=38) ([Descriptive Table 1a](#); [Attachment 8.1](#)). The largest proportion (12.5%) of New *General Snus*® users who returned from Baseline were from Colorado (n=2), Illinois (n=2), and Ohio (n=2). The greatest proportion of overall respondents at the second wave of study were from the Southern region (32.7%, n=227), followed by the Midwestern (29.2%, n=203), Western (26.2%, n=182), and Northeastern (11.9%, n=83) regions of the country. More than a third (37.5%, n=6) of the New *General Snus*® users who returned from Baseline at Month 6 resided in the

Midwest, followed in equal proportions (31.3%, n=5) by residents from the Southern and Western regions of the country.

7.1 Wave 2 Descriptive Results

All respondents were included in the raw data descriptive results (Tables 1a to 4; Attachment 8.1), and the descriptive statistical analyses presented in Tables 2-10.

7.2 Demographics and Respondent Characteristics

The sociodemographic characteristics of *General Snus*® users and New *General Snus*® users participating in Wave 2 study are summarized in Descriptive Tables 1a-b and Table 2; Attachment 8.1.

The mean age of the overall *General Snus*® users who returned from Baseline at Month 6 was 37.6 (range: 21 to 76 years), with the New *General Snus*® users among them being slightly younger (mean age: 35.3 years, ranging from age 21 to 57), including more female respondents (31.3%) than the overall participants (5.9%), and reporting in a considerably larger proportion (50.1%) an annual household income of less than \$50,000, compared with the *General Snus*® users (28.6%) who participated at Wave 2 (Descriptive Tables 1a-b and Table 2; Attachment 8.1). A majority of respondents across both cohorts (55.3% of *General Snus*® users and 50.0% of New *General Snus*® users) self-identified as married at the time of the survey, and a similar proportion of them (32.7% *General Snus*® users and 31.3% New *General Snus*® users) reported never being married (Descriptive Table 2; Attachment 8.1).

Overall, the sociodemographic characteristics of the participants at Month 6 of the study were comparable to those observed at Baseline, across both the *General Snus*® users and the New *General Snus*® users cohorts, although the Wave 2 participants were slightly older (1-1.5 more years of age) across cohorts, with females being more prevalent among the returning new users (31.3%), compared with the new users enrolled at Baseline (17.3%) (Descriptive Tables 1a-b; Attachment 8.1).

7.3 Wave 2 Results for Primary Objectives

7.3.1 Primary Objective 1: Evaluate TNP use in the past 30 days at Month 6

The TNP patterns of use in the last 30 days for overall respondents at Wave 2 are presented in Table 2 below. Note that comparisons with Baseline results are speaking to the column labelled “Baseline (with autofill)”. In the Baseline survey, TNP use in the past 30 days was asked to respondents who indicated ever regularly used or don't know. At follow-up waves, it was asked to everyone. In order to appropriately observe changes in TNP use from baseline to 6 months follow-up, we created “baseline with autofill” whereby those who did not use regularly were coded as “not at all”, with the exception of snus, which was autofilled to include *General Snus*® use (e.g.,

there were 34 respondents who used *General Snus®* in the past 30 days but did not ever use snus regularly. They were autofilled to everyday or someday users of snus).

Among the *General Snus®* users who returned at Month 6 (n=695), 94.1% of them reported using *General Snus®* pouches over the past 30 days, with 74.5% (n=518) using every day, 19.6% (n=136) using some days, and 5.9% (n=41) of them reported not using *General Snus®* product at all. Of note, participants were asked about snus use, which included *General Snus®*, therefore data presented for snus use in [Table 2](#) overlaps with *General Snus®* use results.

Among all *General Snus®* users who participated in the second wave of the study (n=695), 12.3% (n=86) of them smoked cigarettes every day (4.0%, n=28) or some days (8.3%, n=50), 14.1% (n=98) of them used E-cigarettes every day (4.9%, n=34) or some days (9.2%, n=64), 28.2% of them (n=196) used moist snuff every day (10.5%, n=73) or some days (17.7%, n=123), and more than one third (37.6%, n=261) of them were using nicotine pouches every day (9.4%, n=65) or some days (28.2%, n=196), over the past 30 days ([Table 2](#)).

At 6 months follow-up, the reported cigarette smoking in the past 30 days decreased for both everyday users (4.0%) and some days users (8.3%) among all *General Snus®* users (n=695), compared with the results observed at Baseline (7.3% [everyday use] and 10.8% [some days use], respectively) among overall respondents (n=1655). A similar trend regarding TNP use was observed for the Month 6 respondents across all other reported TNPs used, except for those using nicotine pouches and the *General Snus®* product. The Wave 2 study results indicate an increased everyday use of nicotine pouches (9.4%) among all *General Snus®* users (n=695) in the past 30 days, compared with the results observed at Baseline (5.9%), among overall respondents (n=1655). While the reported *General Snus®* use among all participants decreased for everyday users from 82.1% at Baseline to 74.5% at Month 6, it increased slightly for some days users in the past 30 days, from 17.9% at Baseline to 19.6% at Wave 2 ([Table 2](#)).

Among participants who returned at month 6 (n=695), within individual changes in TNP use the past 30 days were examined. Reported everyday use of snus and *General Snus®* pouches decreased significantly (both $p < 0.0001$; [Table 2](#)). Reported everyday use of nicotine pouches and aids to help stop smoking increased significantly ($p = 0.012$ and 0.004 , respectively; [Table 2](#)). No other within individual changes in TNP use were statistically significant. There was a total of 41 respondents who used *General Snus®* at baseline but no longer use *General Snus®* at month 6. Their TNP use in the last 30 days is reported in [Table 2a](#). In general, these individuals tended to decrease their everyday useage of TNPs (except for nicotine pouches and aids to help stop smoking) compared with baseline.

Table 2. Primary Objective 1 – TNP patterns of use for *General Snus*® users at Month 6. Reported TNP use in the last 30 days

| | |
|---------|--|
| (b) (4) | |
|---------|--|

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(b) (4)

7.3.2 Primary Objective 1: Evaluate cigarette quitting behavior at Wave 2

Among *General Snus*® users who smoked cigarettes (n=86), at 6 months follow-up, 8.1% (n=7) of them reported that they completely quit smoking cigarettes in the past 29 days. However, 40.5% (n=32) of those who did not report quitting smoking cigarettes in the past 29 days (n=79), were currently trying to quit cigarette smoking (Table 3). Additionally, among the same individuals who returned at baseline, there was a significant decrease in number of individuals who reported currently trying to quit smoking cigarettes (48.1% vs. 40.5%, p=0.048; Table 3).

The number of *General Snus*® users who smoked cigarettes and quit (n=7) or were trying to quit (n=32) in the past 29 days at Month 6 represent a decrease from the counts observed at Baseline (n=49 and n=110, respectively). However, given that the overall percentage of regular cigarette use among *General Snus*® users decreased from 18.1% (n=299) to 12.3% (n=86) between Baseline and Month 6 (Table 2), these results could indicate that some *General Snus*® users quit cigarette smoking before the reported period of 29 days, at the time of the Wave 2 survey.

(b) (4)

7.3.3 Primary Objective 2: Evaluate the average number of days *General Snus*® pouches and cigarettes were used over the past 30 days at Wave 2

Among the *General Snus*® users who returned for the 6 months follow-up (n=695), 74.5% (n=518) of them reported using *General Snus*® every day and they used an average of 10.2 pouches per day (range: 9.7 to 10.7), while 19.6% (n=136) of them reported using on average 6.3 *General Snus*® pouches (range: 5.5 to 7.0) for a mean percentage of 47.7% of days (range: 43.5% to 51.8%) in the past 30 days (Table 4). The Wave 2 study results for *General Snus*® users indicate a similar pattern regarding the percentage of days *General Snus*® was used and the average number of pouches used every day or on some days in the past 30 days, compared with the results observed at Baseline (p=0.619). Of note, the value of 49.84% of days per month recorded at Baseline is equivalent of 15.0 days, and the value of 47.7% of days per month at Wave 2 represents 14.3 days.

Of the total number of participants at Wave 2 (n=695), 4.0% (n=28) of them reported smoking on average 11.4 cigarettes (range: 8.6 to 14.1) every day, while 8.3% (n=58) of them reported smoking on average 3.0 cigarettes (range: 2.2 to 3.8) for a mean percentage of 25.1% days (range: 19.5% to 30.7%) in the past 30 days days (

Table 5). Compared with the results observed at Baseline, the findings at Month 6 of the study indicate a decrease in the percentage of days cigarettes were smoked among all *General Snus*® users from Baseline (31.0%; range: 27.0% to 35.0%) to 6 months follow-up (25.0%; range: 19.5% to 30.7%). However, among individuals who returned at month 6 (n=695), there was no significant change in percent of days cigarettes were smoked (26.1% vs. 25.1%, p=0.452). Of note, the value of 31.0% of days per month recorded at baseline is equivalent of 9.3 days, and the value of 25.1% of days per month at Wave 2 represents 7.5 days. However, a similar average number of daily cigarettes used in the past 30 days was observed at the first two waves of the study, for both every day and some days cigarette smokers.

(b) (4)

(b) (4)

7.3.4 Primary Objective 3: Characterize *General Snus*® users, especially new users, in terms of prior TNP use and demographics and compare this to new users of smokeless TNP, as reported in the Population Assessment of Tobacco and Health (PATH) at Wave 2

It has been determined that the data available currently cannot address this objective. PATH Wave 5 dataset has not been released yet at the time of the surveys to make comparisons with the current study findings. Although the participants' age group at the time of smokeless tobacco initiation is also provided in PATH for new smokeless users, this categorical variable cannot be solely relied upon to identify new users. Thus, there may not be a way to define new smokeless users between PATH and the current study for them to be comparable.

7.3.5 Primary Objective 4: Compare the tendencies of *General Snus*® users to quit cigarettes or use *General Snus*® in an incremental fashion, in a supplemental fashion, or in complete substitution of cigarettes at Wave 2

Incremental and supplemental use was evaluated for TNP users based on the average daily reported use outcome. Incremental *General Snus*® use was defined as having greater or the equal cigarette use at Month 6 than at Baseline, while concurrently using *General Snus*®. Supplemental *General Snus*® use was defined as having less cigarette use at Month 6 than at Baseline, while concurrently using *General Snus*®. Total participants considered for this analysis were those who did not switch frequency of General Snus use from Baseline to Wave 2 of the study (i.e., everyday General Snus users that continued everyday use, and someday General Snus users that continued some days use).

Findings at the second wave of study revealed that of the 605 everyday *General Snus*® users at Baseline who returned, 492 (81.3%) of them were still using the *General Snus*® product everyday (included in analysis), 89 (14.7%) of them switched to using some days (not included in analysis), and 24 (4.0%) of them switched to not using at all (not included in analysis) at Month 6. Out of the 90 some days *General Snus*® users at baseline who returned, 47 (52.2%) of them were still using the product some days (included in analysis), 26 (28.9%) switched to using everyday (not included in analysis), and 17 (18.9%) of switched to not using at all (not included in analysis) at the 6 months follow-up, as presented in [Table 6a](#) below.

Out of the 36 everyday cigarette users at Baseline who returned, 24 (66.7%) of them were still smoking everyday (included in analysis), 7 (19.4%) of them switched to using some days (not included in analysis), and 5 (13.9%) of them switched to not using at all (not included in analysis) at 6 months follow-up. Out of the 56 someday cigarette users at baseline, 27 (48.2%) were still using some days at 6 months follow-up (included in analysis), 2 (3.6%) of them switched to using everyday (not included in analysis), and 27 (48.2%) of them switched to not using at all (not included in analysis) at Month 6, as summarized in [Table 6b](#) below.

At Wave 2 of the study, a consistent, albeit small, decrease in the average number of daily *General Snus*® pouches was observed across *General Snus*® users, compared with the corresponding

Baseline observations. For participants who continued to be everyday *General Snus*® users at Month 6 (n=492), their average number of *General Snus*® pouches used daily in the past 30 days decreased significantly from the daily product usage recorded at Baseline by 0.43 (p=0.045), and for those who remained some days users at 6 months follow-up (n=47), their usage of *General Snus*® on some days decreased on average by 0.53 pouches (although not significant, p=0.382), compared with the pattern of use recorded at Baseline (Table 6).

A similar trend was also observed, at a slightly higher magnitude, among *General Snus*® users who smoked cigarettes. For instance, the average number of cigarettes used daily by *General Snus*® users who continued to be everyday cigarette smokers at Month 6 (n=24), decreased by 0.92 from the daily usage recorded at Baseline, and for those who remained some days smokers at 6 months follow-up (n=27), their average number of cigarettes smoked on some days decreased by 0.89, compared with the pattern of use recorded at Baseline (Table 6). However, note that these changes were not statistically significant. Nonetheless, these findings suggest a tendency for supplemental use of *General Snus*® product among those who continued to smoke cigarettes at 6 months follow-up.

Among the 299 *General Snus*® users who were identified as cigarette smokers at Baseline, 32 (4.6% of n=695 Wave 2 respondents) of them reported quitting cigarettes at Month 6, with 29 (4.2% of n=695 Wave 2 respondents) among those completely substituting *General Snus*® in place of cigarettes at 6 months follow up, and the remaining 3 users quitting both TNPs (

Table 7). Of note, at Month 6, those who reported quitting cigarettes were either using *General Snus*® pouches or not, unlike those who completely substituted smoking cigarettes with *General Snus*® product use and therefore continued to use *General Snus*® pouches.

(b) (4)

(b) (4)

Table 6b. Dynamic of Cigarette Smokers Cohorts between Baseline and Wave 2

(b) (4)

Table 7. Primary Objective 4 – Among *General Snus*® users, quitting all TNP use, and completely substituting cigarettes for *General Snus*® at Month 6.

(b) (4)

7.4 Wave 2 Results for Secondary Objectives

Descriptive statistical analyses for overall *General Snus*® users enrolled at Baseline (n=1655) and Wave 2 (n=695) of the study are presented in Table 8 and Table 9.

7.4.1 Secondary Objective 1: Perception of absolute risk to using only *General Snus*® daily, smoking only cigarettes daily, dual use of *General Snus*® and cigarettes daily, and never having used any TNPs at Wave 2

Respondents were asked to assess the absolute risk of developing three health conditions (mouth cancer, heart disease, and lung cancer) across four scenarios: using only *General Snus*® daily, smoking only cigarettes daily, dual use of *General Snus*® and cigarettes daily, and never having used any TNP. For each scenario and condition, response options ranged from a very low to a very high risk of developing these health conditions, as summarized in Table 8 and Table 9 below.

More than two thirds of all respondents who returned at Month 6 of the study (n=695) associated the daily use of *General Snus*® product and no other concurrent TNP with a low to moderate risk of developing mouth cancer or heart disease (71.4% and 75.4%, respectively), and a very low to low risk (88.5%) of developing lung cancer (Table 8). Most Wave 2 respondents also perceived that a person who smokes cigarettes every day and uses no other concurrent TNP has a moderate to high chance of developing mouth cancer or heart disease (69.3% and 76%, respectively), and a

high to very high chance (77.2%) of developing lung cancer. These findings are comparable to the results observed at Baseline.

Dual use of *General Snus*® pouches and cigarettes was associated by a majority of participants who returned at Month 6 with a moderate to high risk (65.5%) of developing mouth cancer, and high to very high risk of developing heart disease or lung cancer (69.2% and 72.7%, respectively) (Table 9). Lastly, a vast majority of overall respondents at Month 6 reported that those who have never used any TNP have a very low to low risk of developing mouth cancer or lung cancer (86.4% and 80.3%, respectively), and a low to moderate risk (79.4%) of developing heart disease. A similar pattern of perceived absolute risk for each scenario and health condition was observed among overall *General Snus*® users participating at Baseline.

When looking across all absolute risk metrics at the first two phases of the study, a consistent pattern emerged. Respondents perceived that cigarettes presented the greatest risk of harm across all examined health conditions. Usage of *General Snus*® product alone was associated with some risk regarding those health conditions, although at a lower rate than exclusive or concurrent cigarette smoking. Not surprisingly, never using TNP was generally deemed to carry the lowest health risk.

Table 8. Secondary Objective 1 – Perceptions of absolute risk for daily *General Snus*® users and smokers at the first two waves of study

(b) (4)

(b) (4)

(b) (4)

(b) (4)

7.4.2 Secondary Objective 2: Understanding of the risk reduction as described in the modified risk claim among *General Snus*® users, especially new users

More than two thirds (72.5%) of the *General Snus*® users who returned for the second phase of the study understood the modified risk claim that *General Snus*® use puts them at lower risk than smoking cigarettes for developing mouth cancer, heart disease, lung cancer, stoke, emphysema, and chronic bronchitis, and a vast majority of them (83.5%) also comprehended the modified risk claim that lowering their risk of disease would be achieved when smoking zero cigarettes ([Table 10](#)). Similar response patterns were observed for the New *General Snus*® users at Month 6, with a vast majority of them understanding the modified risk claim that *General Snus*® use puts them at lower risk than smoking cigarettes for developing mouth cancer, heart disease, lung cancer, stoke, emphysema, and chronic bronchitis (81.2%), as well the modified risk claim that smoking zero cigarettes would lower their risk of disease (76.9%).

The response patterns observed at Wave 2 are similar to the Baseline results, although the New *General Snus*® users cohort at Month 6 was small (n=16) ([Table 10](#)).

Table 10. Secondary Objective 2 – Understanding of the MRTP claim for *General Snus*® at Month 6.

(b) (4)

(b) (4)



7.5 Wave 2 Results Summary

Overall, the sociodemographic characteristics of the respondents who returned at Wave 2 of the study were comparable to those observed at Baseline, across both the overall *General Snus*® users and the New *General Snus*® user cohorts. However, participants who returned for Wave 2 were slightly older across cohorts, with females being more prevalent among the returning new users, compared with those enrolled at Baseline.

Primary Objective 1: Evaluate TNP use in the past 30 days at Wave 2

Among the *General Snus*® users who returned at Month 6 (n=695), 94.1% of them reported using *General Snus*® pouches over the past 30 days, with 74.5% (n=518) using every day, 19.6% (n=136) using some days, and 5.9% (n=41) of them reported not using *General Snus*® product at all. Of all *General Snus*® users who participated in the second wave of the study (n=695), 12.3% (n=86) of them smoked cigarettes every day (4.0%, n=28) or some days (8.3%, n=50), and 87.2% (n=606) of them reported not using cigarettes at all, over the past 30 days. The most common TNPs used concurrently with the *General Snus*® product were cigarettes, E-cigarettes, nicotine pouches, moist snuff, and cigars, cigarillos, or filtered cigars filled with tobacco (ranging from 37.6% to 12.4%).

At 6 months follow-up, the reported cigarette smoking in the past 30 days decreased for both everyday users (4.0%) and some days users (8.3%) among all *General Snus*® users (n=695), compared with the results observed at Baseline (7.3% [everyday use] and 10.8% [some days use], respectively) among overall respondents (n=1655). A similar trend regarding TNP use was observed for the Month 6 respondents across all other reported TNPs used, except for those using nicotine pouches and the *General Snus*® product. While the reported *General Snus*® use among all participants decreased for everyday users from 82.1% at Baseline to 74.5% at Month 6, it increased slightly for some days users in the past 30 days, from 17.9% at Baseline to 19.6% at Wave 2.

Primary Objective 1: Evaluate cigarette quitting behavior at Wave 2

Among *General Snus*® users who smoked cigarettes (n=86), at 6 months follow-up, 8.1% (n=7) of them reported that they completely quit smoking cigarettes in the past 29 days. However, 40.5% (n=32) of those who did not report quitting smoking cigarettes in the past 29 days (n=79), were currently trying to quit cigarette smoking. However, given that the overall percentage of regular cigarette use among *General Snus*® users decreased from 18.1% (n=299) to 12.3% (n=86) between Baseline and Month 6, these results could indicate that some *General Snus*® users quit cigarette smoking before the reported period of 29 days, at the time of the Wave 2 survey.

Primary Objective 2: Evaluate average number of days General Snus® pouches and cigarettes were used over the past 30 days at Wave 2

Among the General Snus® users who returned for the 6 months follow-up (n=695), 74.5% (n=518) of them reported using General Snus® every day and they used an average of 10.2 pouches per day, while 19.6% (n=136) of them reported using on average 6.3 General Snus® pouches for a mean percentage of 47.7% of days in the past 30 days. The Wave 2 study results for General Snus® users indicate a similar pattern of General Snus® use, compared with the results observed at Baseline.

Of the total participants at Wave 2 (n=695), 4.0% (n=28) of them reported smoking on average 11.4 cigarettes every day, while 8.3% (n=58) of them reported smoking on average 3.0 cigarettes for a mean percentage of 25.1% days in the past 30 days. Compared with the results observed at Baseline, the findings at Month 6 of the study indicate a decrease in the percentage of days cigarettes were smoked among all General Snus® users from Baseline (31.0%) to 6 months follow-up (25.0%), although the average number of daily cigarettes used in the past 30 days remained comparable at the first two waves of the study, for both every day and some days cigarette smokers.

Primary Objective 4: Compare the tendencies of General Snus® users to quit cigarettes or use General Snus® in an incremental fashion, in a supplemental fashion, or in complete substitution of cigarettes at Wave 2

Incremental General Snus® use was defined as having greater or the equal cigarette use at Month 6 than at Baseline, while concurrently using General Snus®. Supplemental General Snus® use was defined as having less cigarette use at Month 6 than at Baseline, while concurrently using General Snus®. The participants considered for this analysis were those who did not switch frequency of use from Baseline to Month 6, i.e., everyday users in both waves or some day users in both waves.

For participants who continued to be everyday General Snus® users at Month 6 (n=492), their average number of General Snus® pouches used daily in the past 30 days decreased from the daily product usage recorded at Baseline by 0.43, and for those who remained some days users at 6 months follow-up (n=47), their usage of General Snus® on some days decreased on average by 0.53 pouches, compared with the pattern of use recorded at Baseline.

A similar trend was also observed, at a slightly higher magnitude, among General Snus® users who smoked cigarettes. The average number of cigarettes used daily by General Snus® users who continued to be everyday cigarette smokers at Month 6 (n=24), decreased by 0.92 from the daily usage recorded at Baseline, and for those who remained some days smokers at 6 months follow-up (n=27), their average number of cigarettes smoked on some days decreased by 0.89, compared with the pattern of use recorded at Baseline. These findings indicate a tendency for supplemental use of General Snus® product among those who continued to smoke cigarettes at 6 months follow-up. Among the 299 General Snus® users who were identified as cigarette smokers at Baseline, 32 of them reported having quit cigarettes at Month 6, with 29 among those completely substituting General Snus® in place of cigarettes at 6 months follow up.

Secondary Objective 1: Assess perceptions of absolute risk of certain health conditions (mouth cancer, heart disease and lung cancer) among General Snus® users attributed to using only General Snus® daily, smoking only cigarettes daily, dual use of General Snus® and cigarettes daily, and never having used any TNPs at Wave 2.

When looking across all absolute risk metrics at the first two phases of the study, a consistent pattern emerged. Respondents perceived that cigarettes presented the greatest risk of harm across all examined health conditions. Usage of General Snus® product alone was associated with some risk regarding those health conditions, although at a lower rate than exclusive or concurrent cigarette smoking. Not surprisingly, never using TNP was generally deemed to carry the lowest health risk.

Secondary Objective 2: Assess baseline understanding of the risk reduction as described in the modified risk claim among General Snus® users, especially new users at Wave 2.

More than two thirds (72.5%) of the General Snus® users who returned for the second phase of the study understood the modified risk claim that General Snus® use puts them at lower risk than smoking cigarettes for developing mouth cancer, heart disease, lung cancer, stoke, emphysema, and chronic bronchitis, and a vast majority of them (83.5%) also comprehended the modified risk claim that lowering their risk of disease would be achieved when smoking zero cigarettes. Similar response patterns were observed for the New General Snus® users at Month 6, with a vast majority of them understanding the modified risk claim that General Snus® use puts them at lower risk than smoking cigarettes for developing mouth cancer, heart disease, lung cancer, stoke, emphysema, and chronic bronchitis (81.2%), as well the modified risk claim that smoking zero cigarettes would lower their risk of disease (76.9%). The response patterns observed at Wave 2 were similar to the Baseline results, although the New General Snus® users cohort at Month 6 was small (n=16).

8. WAVE 2 DISCUSSION AND OVERALL CONCLUSIONS

The principal research questions, “*How do General Snus® users use TNP, and how do they perceive health risks associated with cigarettes and General Snus®?*” These questions were addressed in this observational Pattern of Use Baseline study.

8.1 Overall Wave 2 Study Conclusions

Study findings at Wave 2 confirm the conclusion based on the perceptions of risk assessed in the Baseline study that overall, the introduction of *General Snus®* does not appear to compromise public health in any way.

Relative to baseline, use of cigarette smoking at Month 6 demonstrated a pattern of:

- Decreased cigarette smoking in the last 30 days for everyday and some day users
- Decrease in percent of days cigarettes are smoked and average number of cigarettes smoked everyday and on some days

Additionally, at Month 6, 4.2% (n=32) of participants reported having quit cigarettes and another 4.2% (n=29) had completely substituted cigarettes with *General Snus®*.

Risk perception results were similar to baseline results. That is, cigarettes posed the greatest risk of developing health conditions, the use of *General Snus®* alone posed some risks (but lower relative to cigarettes), and not using any TNP carried the lowest risk.

9. ATTACHMENTS

9.1 Descriptive Tables 1-4

9.2 Study Questionnaire

9.3 Protocol

9.4 Statistical Analysis Plan



General Snus® Patterns of Use Study

Wave 3 Final Report

SMU 19-01GENS

| | |
|-----------------------------------|---|
| Product Name: | General Snus® |
| First Respondent Enrolled: | 05 August 2021 |
| Last Respondent Completed: | 07 September 2021 |
| Principal Investigator: | (b) (4) |
| Prepared By: | |
| Sponsor: | Tryggve Ljung, MD., Ph.D., Vice President, Swedish Match North America |
| Version: | 2.0—Wave 3 Final Report |
| Finalized Report Date: | 10 February 2022 |

Confidentiality Statement

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1. SYNOPSIS

Sponsor:

Swedish Match North America (SMNA)

Two James Center

1021 East Cary Street, Suite 1600

Richmond, VA 23219

Name of Finished Product: *General Snus®*
Study Title: *General Snus®* Patterns of Use Study

Investigator:

(b) (4)

Prepared By:

(b) (4)

Study Periods:
Wave 1 (Baseline):

Start of data collection: 25 July 2020

End of data collection: 17 August 2020

Wave 2 (6 Months from Baseline):

Start of data collection: 02 February 2021

End of data collection: 06 March 2021

Wave 3 (12 Months from Baseline):

Start of data collection: 05 August 2021

End of data collection: 07 September 2021

Research Questions:

The research questions for this study are the following: (1) how do *General Snus*® users use tobacco and nicotine products (TNP) and (2) how do *General Snus*® users perceive health risks associated with use of *General Snus*® and cigarettes? Data from four study waves—baseline, 6 months from baseline (Wave 2), 12 months from baseline (Wave 3), 24 months from baseline (Wave 4)—will be used to help address these questions.

Primary Objectives:

1. Compare TNP patterns of use between all four study waves. The study will examine self-reported patterns of TNP use for all surveyed respondents over time. The study will report on frequency of *General Snus*® use and use of other TNP use, if reported.
 - a. Of specific interest will be patterns of cigarette use. Intent to quit and actual quitting of cigarettes will be assessed at each wave of the study.
2. Compare consumption patterns of cigarettes and *General Snus*® over the past 30 days (baseline) with consumption patterns at Wave 2 through Wave 4.
 - a. Of specific interest is whether use of *General Snus*® offsets use of cigarettes.
3. Characterize *General Snus*® users in terms of prior TNP use and demographics and compare this to new users of smokeless TNP as reported in the Population Assessment of Tobacco and Health (PATH).
4. Compare the tendencies of *General Snus*® users to quit cigarettes or use *General Snus*® incrementally, supplementally, or in complete substitution of cigarettes.

Secondary Objectives:

1. Assess perceptions of risk of certain health among *General Snus*® users.
 - a. Assess the absolute risk attributed to using only *General Snus*® every day, using only cigarettes every day, using both *General Snus*® and cigarettes every day, and never having used any TNP.
2. Assess the extent to which *General Snus*® users understand the risk reduction as stated in the modified risk claim.

Summary of Results:

- *General Snus*® was used in the P30D among 90.0% of returning respondents (n=527)
 - The pattern of *General Snus*® use **significantly differed** from baseline ($p<0.001$) due to the number of respondents that switched from every day to some day use by Wave 3 (n=94)
- Every day *General Snus*® users used more pouches on days used than some day users (10.5 pouches/day vs. 6.6 pouches/day)
 - Some day users reported using *General Snus*® 12 days in the P30D; this **did not significantly differ** from baseline ($p=0.27$)
- Among the respondents returning for Wave 3 (n=586), 14.1% (n=83) reported P30D cigarette smoking, and most of these respondents smoked only on some days (10.9%, n=64)
 - 37.3% of these respondents had initiated (n=11) or re-initiated (n=20) cigarettes in the 12 months since baseline, but all reported that they now smoked only on some days
- Only 14.3% of respondents that returned for Wave 3 were cigarette smokers at baseline (n=84)
 - Of these respondents, 36.9% had completely quit smoking cigarettes, with 93.5% of those quitting reporting complete substitution of cigarettes with *General Snus*® (n=29)
- Respondents correctly perceived that cigarette smoking contributed significant risks to health, associating it with moderate to very high chances of developing mouth cancer (81.7%, n=479), heart disease (98.3%, n=576), and lung cancer (93.5%, n=548)
 - Use of *General Snus*® was perceived as being less risky to health than cigarette smoking but that use of *General Snus*® was not without risks to health
 - Dual use of *General Snus*® and cigarettes was perceived as equally risky as use of only cigarettes, suggesting that respondents understand that any use of cigarettes is associated with highest risks to health
- Respondents understood the MRTP claim that using *General Snus*® instead of cigarettes puts users at a lower risk for various diseases compared to cigarette smoking
 - 77.8% of respondents correctly endorsed that *General Snus*® was lower risk (n=456)
- Most understood that no cigarettes can be when using *General Snus*® to benefit from it being reduced risk (80.3%, n=366), indicating that they are aware users need to completely substitute cigarettes for *General Snus*®

2. TABLE OF CONTENTS

| | |
|--|----|
| 1. SYNOPSIS | 2 |
| 2. TABLE OF CONTENTS | 5 |
| 3. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS..... | 6 |
| 4. RESPONSIBLE PARTIES..... | 7 |
| 4.1 Investigator and Contributors | 7 |
| 4.2 Sponsor | 7 |
| 5. METHODOLOGY | 8 |
| 6. WAVE 3 STUDY RESPONDENTS..... | 10 |
| 6.1 Study Fielding Summary | 10 |
| 6.2 Final Sample at Wave 3 | 10 |
| 7. WAVE 3 STUDY RESULTS..... | 11 |
| 7.1 Wave 3 Results for Respondent Demographics..... | 11 |
| 7.2 Wave 3 Results for Primary Objectives..... | 12 |
| 7.2.1 TNP Use in the Past 30 Days at 12 Months from Baseline (Wave 3)..... | 12 |
| 7.2.2 TNP Use in the Past 30 Days at 12 Months from Baseline (Wave 3) Among Respondents that Quit Using <i>General Snus</i> ® Between Baseline and Wave 3 | 17 |
| 7.2.3 Cigarette Quitting Behavior at 12 Months from Baseline (Wave 3)..... | 22 |
| 7.2.4 Percent of Days in the Past 30 Days that <i>General Snus</i> ® and Cigarettes Were Used and the Quantity Used on Days Used at 12 Months from Baseline (Wave 3) | 23 |
| 7.2.5 Changes in Patterns of Use of <i>General Snus</i> ® and Cigarettes from Baseline to 12 Months from Baseline (Wave 3)..... | 26 |
| 7.2.6 Incremental, Supplemental, or Complete Substitution of Cigarettes for <i>General Snus</i> ® Among Dual Users of Both Cigarettes and <i>General Snus</i> ® from Baseline to 12 Months from Baseline (Wave 3)..... | 29 |
| 7.3 Wave 3 Results for Secondary Objectives..... | 31 |
| 7.3.1 Perceptions of Absolute Risk for Use of Only <i>General Snus</i> ® Every Day and Use of Only Cigarettes Every Day | 31 |
| 7.3.2 Perceptions of Absolute Risk for Use of Both Both <i>General Snus</i> ® and Cigarettes Every Day and Never Having Used Any TNP | 35 |
| 7.3.3 Understanding of the Modified Risk Claim for <i>General Snus</i> ® | 38 |
| 8. SUMMARY OF WAVE 3 RESULTS | 41 |

3. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

| Abbreviation or Specialist Term | Definition |
|--|---|
| CASRO | Council of American Survey Research Organizations |
| CTP | Center for Tobacco Products |
| FDA | FDA Food and Drug Administration |
| FTP | File Transfer Protocol |
| HCP | Health Care Professional |
| HINTS | Health Information National Trends Survey |
| ICF | Informed Consent Form |
| IRB | IRB Institutional Review Board |
| MRTP | Modified Risk Tobacco Product |
| MRTPA | Modified Risk Tobacco Product Application |
| PATH | Population Assessment of Tobacco and Health |
| PII | Personally Identifiable Information |
| PMTA | Premarket Tobacco Product Application |
| RDD | Random Digit Dialing |
| SAP | Statistical Analysis Plan |
| SMNA | Swedish Match North America, LLC |
| TNP | Tobacco/Nicotine Product(s) |
| U.S. | United States |

4. RESPONSIBLE PARTIES

4.1 Investigator and Contributors

| | | |
|----------------------------------|---------|--|
| Investigator: | (b) (4) | |
| Prepared By: | | |
| (b) (4) Project Team: | | |

4.2 Sponsor

| | |
|-----------------|---|
| Sponsor: | Tryggve Ljung, MD., Ph.D., Vice President Swedish Match North America, LLC |
|-----------------|---|

5. METHODOLOGY

General Snus® users were recruited directly via invitation stickers placed directly on *General Snus*® tins. A third-party vendor, News America Marketing, was hired to place the study invitation stickers on product packaging (e.g., each individual *General Snus*® tins) for all varieties of *General Snus*® available at retail outlets. This took place from 25 July 2020 to 17 August 2020. The sticker initiative targeted approximately 10,600 retail stores carrying *General Snus*® across all locations where *General Snus*® was sold. The sticker presented a website where users that were interested in participating accessed the survey through a secure and unique survey link. The first set of questions were used to screen potential respondents and were designed to qualify the respondent using the study inclusion and exclusion criteria. Once qualified, respondents were directed to the online survey. The survey took approximately 15-minutes. Respondents were asked to self-report TNP use within the past 30 days (P30D) and various questions related to TNP use, risk perceptions, and understanding of the modified risk messaging for *General Snus*® products.

This study is a longitudinal, prospective study consisting of multiple waves to gain an understanding of how *General Snus*® and other TNP are used by the participating respondents. Respondents completed a baseline survey (Wave 1) and will have the opportunity to respond again at 6 months from baseline (Wave 2), 12 months from baseline (Wave 3) and 24 months from baseline (Wave 4). All respondents in the baseline survey must have reported use of *General Snus*® at least once in the P30D and reported use every day or on some days.

Respondents had to meet the following criteria to be included in the study:

- Have used *General Snus*® at least once or more within the P30D and use it every day or on some days
- Minimum age of 21 years
- Agree to participate in four surveys over the 24-month period
- Able to read and speak English
- Currently a resident of the United States
- Agreeing to provide informed consent and personal contact information

Respondents meeting any of the following criteria were excluded from the study:

- Respond “don’t know” or “decline to answer” to questions asking their gender and geographic region
- Unwilling or unable to provide electronic informed consent and personal contact information
- Employed in any of the following fields or professions: market research, marketing, advertising, TNP manufacturing, or employed as a physician
- Participated in a consumer research study on TNP in the 2 weeks prior to the baseline survey

All analyses conducted were either descriptive or inferential. Descriptive analyses provided summary statistics for all variables. These statistics included counts and proportions for categorical variables and means, standard deviations, medians, minimums, and maximums for ordinal and continuous variables. Inferential statistical testing was conducted to evaluate changes in primary and secondary outcome measures (i.e., patterns of use, risk perceptions, understanding of claims) from baseline and each follow-up wave. Results comparing baseline data versus data from each follow-up wave was conducted using paired sample t-tests for continuous variables and McNemar tests for categorical variables.

6. WAVE 3 STUDY RESPONDENTS

6.1 Study Fielding Summary

The fielding summary for number of respondents that entered the Wave 3 survey, those that did not complete the survey, those that were terminated (and the reasons for termination) are summarized in [Table 1](#) below.

Table 1: Fielding Summary for the Wave 3 Survey

| | Wave 2 | Wave 3 |
|--|--------|--------|
| Number of respondents that entered the survey | 931 | 728 |
| Number of respondents that were terminated based inclusion/exclusion criteria/quota filled/intellectual property blocker | 159 | 70 |
| Number of respondents that did not complete the survey | 66 | 65 |
| Number of respondents retained (closed fielding) | 706 | 593 |
| Total respondents retained after data quality check* | 695 | 586 |

*Data quality check per SAP included outliers, straightliners, speeders, those that failed the attention check question, and illogical responses.

6.2 Final Sample at Wave 3

Of the respondents that participated in the baseline survey (N=1,655), only 35.8% returned for Wave 3 (12 months from baseline) and completed the full survey (n=593). However, some respondents failed the attention check (n=7); thus, only a subset of respondents were able to be included in data analyses (n=586). Some respondents that were classified as new *General Snus*® users at baseline returned for Wave 3 (n=15); new *General Snus*® users were defined as first using *General Snus*® in the 30 days prior to the baseline survey.

7. WAVE 3 STUDY RESULTS

7.1 Wave 3 Results for Respondent Demographics

The demographics of *General Snus*® users and new *General Snus*® users at baseline that returned for Wave 3 are summarized in Table 2; these results represent data collected at Wave 3 as respondent demographics may have changed from baseline. Only results for the overall group of *General Snus*® users is discussed here; findings for new *General Snus*® users can be found below in Table 2. Most respondents that returned for Wave 3 lived in the South (33.4%, n=196) while the fewest respondents lived in the Northeast (13.1%, n=77). Nearly all respondents were male (93.5%, n=548). The mean age of *General Snus*® users at baseline that returned for Wave 3 was 37.6 years (range: 21 to 73 years). Similar percentages of respondents were married (56.0%, n=328) or not married (42.6%, n=250). Most respondents had notably high household incomes; 39.1% (n=299) reported that they earned over \$100,000 in the past 12 months.

Table 2: Demographics of *General Snus*® Users and New *General Snus*® Users at 12 Months from Baseline (Wave 3)

| | <i>General Snus</i> ® Users | New <i>General Snus</i> ® Users |
|------------------------------------|-----------------------------|---------------------------------|
| | 586 | 15 |
| Geographic region | | |
| West (%) | 142 (24.2%) | 4 (26.7%) |
| South (%) | 196 (33.4%) | 3 (20.0%) |
| Midwest (%) | 171 (29.2%) | 7 (46.7%) |
| Northeast (%) | 77 (13.1%) | 1 (6.7%) |
| Gender | | |
| Male (%) | 548 (93.5%) | 10 (66.7%) |
| Female (%) | 38 (6.5%) | 5 (33.3%) |
| Decline to answer (%) | 0 (0.0%) | 0 (0.0%) |
| Respondent age | | |
| Age in years \pm SD* | 37.6 \pm 10.0 | 36.9 \pm 9.0 |
| **Marital status | | |
| Married (%) | 328 (56.0%) | 8 (53.3%) |
| Not married (%) | 250 (42.6%) | 6 (40.0%) |
| Decline to answer (%) | 8 (1.4%) | 1 (6.7%) |
| **Household income | | |
| Below \$50,000 (%) | 149 (25.4%) | 5 (33.3%) |
| Between \$50,000 and \$100,000 (%) | 188 (32.1%) | 5 (33.3%) |
| Above \$100,000 (%) | 299 (39.1%) | 5 (33.3%) |
| Don't know (%) | 0 (0.0%) | 0 (0.0%) |
| Decline to answer (%) | 20 (3.4%) | 0 (0.0%) |

*SD: Standard deviation

**Results for marital status and household income were collapsed into the categories presented; in the Wave 3 survey, marital status had six categories and household income had eleven categories. Household income represents earnings in past 12 months.

7.2 Wave 3 Results for Primary Objectives

7.2.1 TNP Use in the Past 30 Days at 12 Months from Baseline (Wave 3)

Patterns of TNP use in the past 30 days (P30D) among all Wave 3 respondents are presented in [Table 3](#) below. In the baseline survey, TNP use in the P30D was asked to respondents that indicated they had ever regularly used any of eleven categories of TNP, including *General Snus*®, and for those TNP to which they responded, “Don't know.” At Wave 3, TNP use in the P30D was asked to all respondents for the same eleven categories of TNP.

Among *General Snus*® users at baseline that returned for Wave 3 (n=586), 90.0% (n=527) reported using *General Snus*® in the P30D, with 67.1% (n=393) using every day and 22.9% (n=134) using on some days. Some respondents that had regularly used *General Snus*® at baseline had quit use of the product by Wave 3 (9.9%, n=58). Additionally, some respondents switched from every day use at baseline to some day use at Wave 3 (18.5%, n=94) and others switched from some day use to every day use (25.6%, n=20) ([Section 7.2.5; Table 7](#)). This change in patterns of use for *General Snus*® from baseline to Wave 3 **was significantly different** (p<0.0001). All respondents at Wave 3 that reported using snus in the P30D reported that they used *General Snus*® specifically; thus, results presented in [Table 3](#) for snus and *General Snus*® are the same.

[Table 3](#) also presents P30D use for other categories of TNP among *General Snus*® users at baseline that returned for Wave 3. Only 14.1% (n=83) of these respondents reported P30D cigarette smoking, with 3.2% (n=19) reporting smoking cigarettes every day and 10.9% (n=64) reporting smoking cigarettes on some days. Prevalence of P30D cigarette smoking among *General Snus*® users at Wave 3 **did not significantly differ** from prevalence of P30D cigarette smoking at baseline (p=0.17). Over a quarter of *General Snus*® users at Wave 3 reported P30D use of moist snuff (27.6%, n=162), with 10.4% (n=61) reporting use every day and 17.2% (n=101) reporting use on some days; prevalence of P30D moist snuff use among *General Snus*® users at Wave 3 **did not significantly differ** from prevalence of P30D moist snuff use at baseline (p=0.71). Prevalence of P30D use of nicotine pouches, however, **significantly increased** among *General Snus*® users between baseline and Wave 3 (p<0.0001); 43.1% of *General Snus*® users reported P30D use of nicotine pouches at Wave 3 (n=253), with 12.6% (n=74) reporting use every day and 30.5% (n=179) reporting use on some days. This represents n=46 new nicotine pouch users at Wave 3 as compared to baseline, and nearly all new nicotine pouch users reported use of nicotine pouches every day. Additionally, the number of *General Snus*® users reporting use of aids to help stop smoking cigarettes also **significantly increased** between baseline and Wave 3 (p=0.0002); 9.4% of *General Snus*® reported P30D use of aids to help stop smoking cigarettes (n=55), with 2.2% (n=13) reporting use every day and 7.2% (n=42) reporting use on some days. This represents n=29 new users of aids to help stop smoking cigarettes at Wave 3 as compared to baseline, suggesting that these dual users (presumably) of cigarettes and *General Snus*® may currently be attempting to quit smoking.

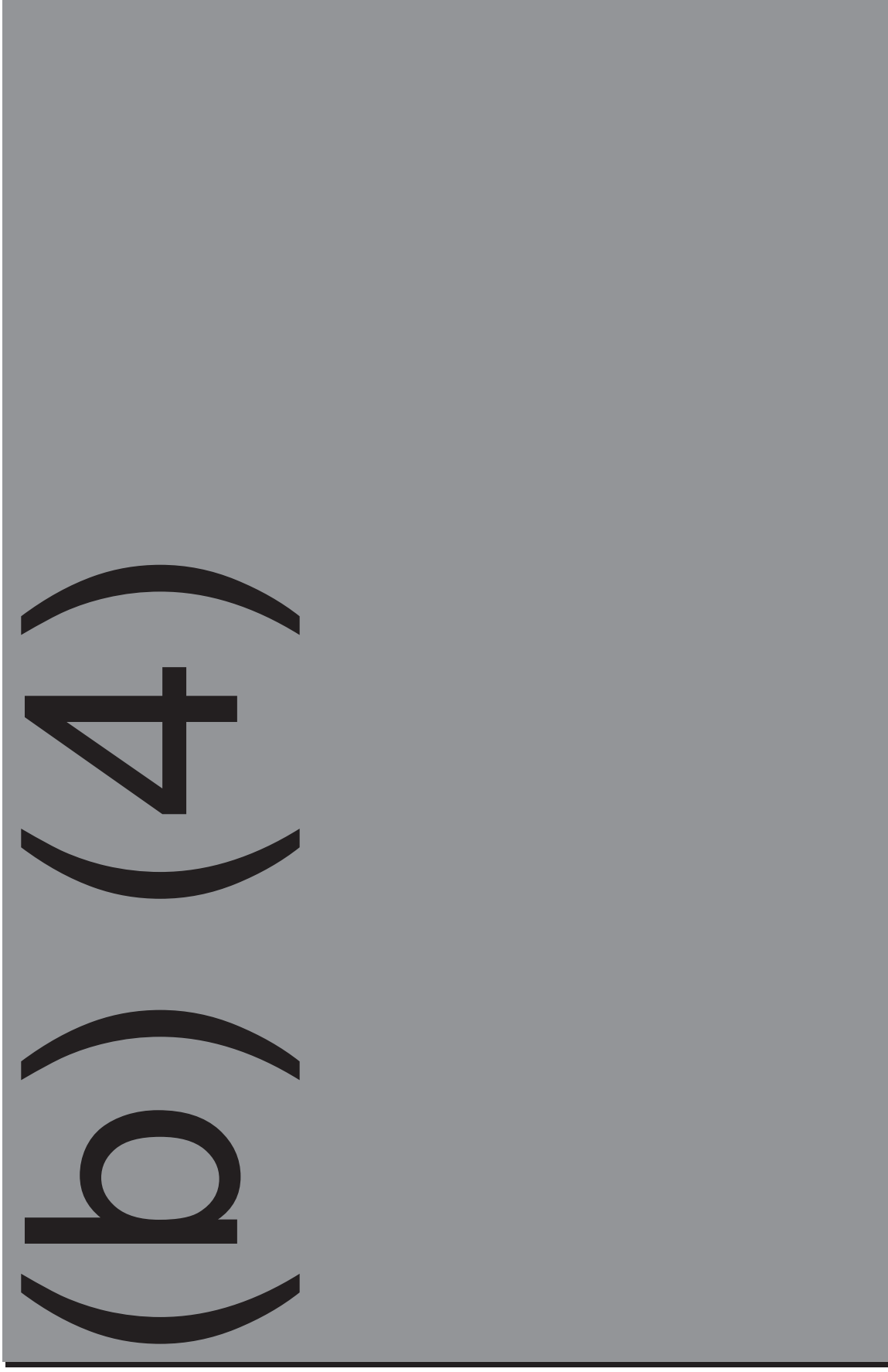
Table 3: TNP Use in the Past 30 Days at 12 Months from Baseline (Wave 3)

(b) (4)



(b) (4)





(b) (4)

7.2.2 TNP Use in the Past 30 Days at 12 Months from Baseline (Wave 3) Among Respondents that Quit Using *General Snus*® Between Baseline and Wave 3

TNP use in the P30D is reported in [Table 4](#) among respondents that initially used *General Snus*® at baseline but had since quit using *General Snus*® by Wave 3. Though no formal statistical testing was conducted for this objective, results generally suggest that respondents that quit using *General Snus*® by Wave 3 did not substantially change their patterns of use for other TNP. The number of respondents reporting P30D use or no use in the P30D, for each category of TNP, only differed between baseline and Wave 3 by few respondents.

More respondents used cigarettes (n=6), e-cigarettes (n=2), and aids to help stop smoking cigarettes (n=6) at Wave 3 as compared to baseline; sample sizes in parentheses represent the *increase* in the number of respondents reporting use of that product at Wave 3 than at baseline. Fewer respondents used moist snuff (n=8), chewing tobacco (n=7), pipe tobacco (n=2), and hookah (n=2) at Wave 3 as compared to baseline; sample sizes in parentheses represent the *decrease* in respondents reporting use of that product at Wave 3 than at baseline. The number of respondents reporting use of cigars and nicotine pouches did not change from baseline to Wave 3.

Table 4: TNP Use in the Past 30 Days at 12 Months from Baseline (Wave 3) Among Respondents that Quit Using *General Snus*® Between Baseline and Wave 3

(b) (4)

(b) (4)

(b) (4)

(b) (4)

7.2.3 Cigarette Quitting Behavior at 12 Months from Baseline (Wave 3)

Among *General Snus*® users at baseline that returned for Wave 3 (n=586), 14.1% (n=83) smoked cigarettes in the P30D. Of these respondents, 18.1% (n=15) reported that they had completely quit smoking cigarettes in the past 29 days (P29D) and another 42.6% reported that they were currently making a quit attempt (n=29). This indicates that over half of *General Snus*® users surveyed at Wave 3 that currently or previously smoked cigarettes had reduced or were trying to reduce the number of cigarettes they smoked (53.0%, n=44). Results for the number of respondents that had quit smoking in the P29D at Wave 3 **did not significantly differ** from that at baseline (p=0.48) nor were results for the number of respondents making a quit attempt at Wave 3 (p=1.00). These results are presented in [Table 5](#) below.

Table 5: Cigarette Quitting Behavior at 12 Months from Baseline (Wave 3)

(b) (4)

7.2.4 Percent of Days in the Past 30 Days that *General Snus*® and Cigarettes Were Used and the Quantity Used on Days Used at 12 Months from Baseline (Wave 3)

Among the *General Snus*® users at baseline that returned for Wave 3 (n=586), 67.1% reported using *General Snus*® every day (n=393), 22.9% reported using *General Snus*® on some days (n=134), and 9.9% reported no P30D use of *General Snus*® (n=58) at Wave 3. Some day *General Snus*® users were asked on how many days out of the P30D that they used the product, while every day *General Snus*® users were assumed to have used the product on each of the P30D. Every day and some day users were also asked how many *General Snus*® pouches they used on the days that they used the product. These results are presented in [Table 6a](#) below.

Some day *General Snus*® users (n=134) reported that they used the product on 40.5% of the P30D, equating to 12.1 days. The percent of days *General Snus*® was used in the P30D among some day *General Snus*® users **did not significantly differ** from that reported at baseline (p=0.27). These respondents used on average 6.6 pouches on the days they used the product. Every day *General Snus*® users reported using a greater number of pouches than did some day users; every day *General Snus*® users reported using an average of 10.5 pouches each day within the P30D. This demonstrates that some day users used approximately 3 cans of *General Snus*® in the P30D (24 pouches per can), while every day users used approximately 13 cans in the P30D.

Among the *General Snus*® users at baseline that returned for Wave 3 (n=586), 3.2% reported smoking cigarettes every day (n=19), 10.9% reported smoking cigarettes on some days (n=64), and 85.2% reported no P30D cigarette smoking (n=499) at Wave 3. Some day cigarette smokers were asked on how many days out of the P30D that they smoked, while every day cigarette users were assumed to have smoked on each of the P30D. Every day and some day cigarette smokers were also asked how many cigarettes they used on the days that they smoked. These results are presented in [Table 6b](#) below.

Some day cigarette smokers (n=64) reported that they smoked on 27.5% of the P30D, equating to 8.3 days. The percent of days smoked in the P30D among some day cigarette smokers **did not significantly differ** from that reported at baseline (p=0.12). These respondents smoked on average 3.0 cigarettes on the days they smoked. Every day cigarette smokers reported smoking a greater number of cigarettes than did some day cigarette smokers; every day cigarette smokers reported smoking an average of 9.9 cigarettes each day within the P30D. This demonstrates that some day cigarette smokers smoked approximately 1 pack of cigarettes in the P30D (20 cigarettes per pack), while every day cigarette smokers smoked approximately 15 packs of cigarettes in the P30D.

Table 6a: Percent of Days *General Snus*® Was Used in the Past 30 Days and Quantity of *General Snus*® Used on Days Used at Wave 3

(b) (4)

Table 6b: Percent of Days Cigarettes Were Smoked in the Past 30 Days and Quantity of Cigarettes Smoked on Days Smoked at Wave 3

(b) (4)

7.2.5 Changes in Patterns of Use of *General Snus*® and Cigarettes from Baseline to 12 Months from Baseline (Wave 3)

Respondent patterns of use were measured by determining whether a given product was used every day, some days, or not at all within the P30D. Patterns of use for *General Snus*® and cigarettes were measured in both the baseline and Wave 3 surveys. Baseline and Wave 3 patterns of use for *General Snus*® and cigarettes were compared to understand changes in patterns of use over time and were measured separately among every day and some day users of the respective products at baseline. Changes in patterns of use from baseline to Wave 3 are presented in [Table 7](#) below.

Among the *General Snus*® users at baseline that returned for Wave 3 (n=586), 86.7% were every day *General Snus*® users at baseline (n=508) and 13.3% were some day *General Snus*® users at baseline (n=78). About a quarter of every day *General Snus*® users at baseline that returned for Wave 3 had either partially or completely reduced the number of days that they used the product in the P30D (26.4%, n=134), reporting that they now used *General Snus*® on some days (18.5%, n=94) or that they had not used *General Snus*® in the P30D (7.9%, n=40). The remaining every day *General Snus*® users at baseline that returned for Wave 3 were still using the product every day (73.4%, n=373). Additionally, about a quarter of some day *General Snus*® users at baseline that returned for Wave 3 had completely reduced the number of days that they used the product by Wave 3, reporting that they had not used *General Snus*® in the P30D (23.1%, n=18). Another quarter of some day *General Snus*® users at baseline that returned for Wave 3 had increased the number of days that they used the product, reporting that they now used *General Snus*® every day (25.6%, n=20). The remaining some day *General Snus*® users at baseline that returned for Wave 3 were still using the product on some days (51.3%, n=40).

Among the *General Snus*® users at baseline that returned for Wave 3 (n=586), 5.6% were every day cigarette smokers at baseline (n=32) and 8.9% were some day cigarette smokers at baseline (n=52); the remaining *General Snus*® users at baseline that returned for Wave 3 were not cigarette smokers at baseline (85.7%, n=502). Exactly one half of every day cigarette smokers at baseline that returned for Wave 3 had either partially or completely reduced the number of days that they smoked (50.0%, n=16), reporting that they now only smoked on some days (28.1%, n=9) or that they had not smoked in the P30D (21.9%, n=7). The remaining every day cigarette smokers at baseline that returned for Wave 3 were still smoking every day (50.0%, n=16).

About half of some day cigarette smokers at baseline that returned for Wave 3 (n=52) had completely reduced the number of days that they smoked, reporting that they had not smoked in the P30D (46.2%, n=24). Few some day cigarette smokers at baseline that returned for Wave 3 had increased the number of days that they smoked, reporting that they now smoked every day (5.8%, n=3). The remaining some day cigarette smokers at baseline that returned for Wave 3 were still smoking on some days (46.2%, n=24).

Results among the baseline cigarette smokers that returned for Wave 3 (n=84) indicate that 36.9% had completely quit smoking cigarettes (n=31) ([Table 7](#)). Of these respondents, 93.5% reported that they completely substituted cigarette smoking for use of *General Snus*® products (n=29) ([Section 7.2.6](#); [Table 8b](#)).

Nearly all non-cigarette smokers at baseline (defined as not having smoked in the P30D prior to baseline) that returned for Wave 3 were still not smoking cigarettes, reporting that they had not smoked cigarettes in the P30D (93.2%, n=468). The remaining non-cigarette smokers at baseline that returned for Wave 3 had initiated (n=11) or re-initiated (n=20) smoking cigarettes, reporting that they now smoked on some days (6.2%, n=31); no non-cigarette smokers at baseline that returned for Wave 3 reported that they now smoked every day (0.0%, n=0).

Table 7: Changes in Patterns of Use of *General Snus*® and Cigarettes from Baseline to Wave 3

(b) (4)

7.2.6 Incremental, Supplemental, or Complete Substitution of Cigarettes for General Snus® Among Dual Users of Both Cigarettes and General Snus® from Baseline to 12 Months from Baseline (Wave 3)

Incremental and supplemental use of cigarettes and General Snus® and complete substitution of cigarettes for General Snus® was evaluated among dual users of both cigarettes and General Snus® at Wave 3. Results were calculated by comparing frequency of use of both cigarettes and General Snus® at baseline and subtracting frequency of use of the respective products at Wave 3. Frequency of use was measured by asking respondents the quantity of cigarettes and General Snus® used on days used. Respondents included in analyses measuring incremental and supplemental use were those that did not switch their pattern of use for either product between baseline and Wave 3—meaning, every day users of either cigarettes or General Snus® at baseline that also reported every day use at Wave 3 and some day users of either cigarettes or General Snus® at baseline that also reported some day use at Wave 3.

Incremental use was defined as using a greater or equal number of cigarettes or General Snus® at Wave 3 than at baseline; a difference in frequency of use between baseline to Wave 3 resulting in a value that is positive or equal to zero was considered incremental use. Supplemental use was defined as using fewer cigarettes or General Snus® at Wave 3 than at baseline; a difference in frequency of use between baseline to Wave 3 that is negative was considered supplemental use. Complete substitution was defined as fully replacing cigarette use and only using General Snus® or completely quitting use of both products. Results for incremental and supplemental use for both cigarettes and General Snus® are presented below in [Table 8a](#) and results for complete substitution are presented in [Table 8b](#).

All changes in frequency of use, regardless of patterns of use, among users of cigarettes or General Snus® were found to be supplemental. Each of the four categories of users presented in [Table 8a](#) reported reductions in use of either cigarettes or General Snus® between baseline to Wave 3. However, all findings for this measure **were not statistically different** (range of p-values: 0.07 to 0.67). Results presented in [Table 8b](#) for complete substitution of cigarettes for General Snus® indicate that 5.3% of General Snus® users at baseline that returned for Wave 3 (n=586) had completely quit smoking cigarettes since baseline (n=31) and that 2.6% (n=15) had quit within the P29D ([Section 7.2.3](#); [Table 5](#)). Among respondents that had completely quitting smoking by Wave 3, 93.5% reported that they exclusively used General Snus® to replace cigarettes (n=29); this indicates that 4.9% (n=29) of all General Snus® users at baseline that returned for Wave 3 (n=586) used General Snus® to replace cigarettes. Less than 1.0% of those returning for Wave 3 reported quitting use of both products (0.34%, n=2).

Table 8a: Incremental or Supplemental Use of Cigarettes and *General Snus*® from Baseline to Wave 3

(b) (4)

Table 8b: Complete Substitution of Cigarettes for *General Snus*® at Wave 3

(b) (4)

7.3 Wave 3 Results for Secondary Objectives

7.3.1 Perceptions of Absolute Risk for Use of Only *General Snus*® Every Day and Use of Only Cigarettes Every Day

All respondents evaluated the absolute risk of developing three diseases—mouth cancer, heart disease, lung cancer—from use of only *General Snus*® every day or from use of only cigarettes every day. Perceptions of absolute risk were measured using a 5-point scale ranging from 1 (“Very low chance”) to 5 (“Very high chance”); “Don’t know” was also an available response option. These results are presented in [Table 9a](#) below.

General Snus® and other snus products contain markedly lower levels of harmful and potentially harmful constituents (HPHCs) compared to traditional smokeless tobacco. Numerous scientific publications have found no associations between use of snus products and development of mouth cancer or heart disease [citations]; this differs from use of traditional smokeless tobacco for which associations with these diseases have been found.¹ Findings among respondents that returned for Wave 3 suggest that *General Snus*® users may be misinformed about the health risks of using the product and may misattribute risks of traditional smokeless tobacco to *General Snus*®—over half perceived use of only *General Snus*® every day to be associated with a moderate to very high chance of developing mouth cancer (55.0%, n=322) and nearly half perceived use of only *General Snus*® every day to be associated with a moderate to very high chance of developing heart disease (47.1%, n=276).

Among *General Snus*® users at baseline that returned for Wave 3 (n=586), respondents correctly perceived that use of only *General Snus*® every day carried lower risks to health than use of only cigarettes every day across the three diseases assessed. This is also evidenced by results for perceived risk of developing lung cancer as 85.3% of respondents at Wave 3 associated use of only *General Snus*® every day to be associated with a low to very low chance of developing lung cancer (n=85), which is also evidenced in scientific literature.²

¹ Smita A, Labani S, Kailash U, *et al.* **Association of smokeless tobacco use and oral cancer: a systematic global review and meta-analysis.** *Nicotine & Tobacco Research*. Volume 21, Issue 9 (2019).

² Clarke E., Thompson K., Weaver S., *et al.* **Snus: a compelling harm reduction alternative to cigarettes.** *Harm Reduction Journal*. Volume 16, Issue 62 (2019).

General Snus® products can be marketed in the U.S. with the following modified risk messaging: “Using *General Snus*® instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.”³ Risk perceptions among *General Snus*® users at Wave 3 provide evidence that respondents understand that *General Snus*® is a reduced risk tobacco product (compared to cigarettes) but that use of *General Snus*® is not without risks to health. Findings also provide evidence that respondents can correctly attribute use of only *General Snus*® to reductions in risk of developing specific diseases stated in the modified risk messaging.

Among *General Snus*® users at baseline that returned for Wave 3 (n=586), use of only cigarettes every day was perceived to carry much higher risks to health than use of only *General Snus*® every day across the three diseases assessed. Large majorities of respondents at Wave 3 perceived use of only cigarettes every day to be associated with a moderate to very high chance of developing each of the three disease states assessed—mouth cancer (81.7%, n=479), heart disease (98.3%, n=576), lung cancer (93.5%, n=548). This suggests these respondents understand that use of cigarettes contributes extreme risks to health and to the development of mouth cancer, heart disease, and lung cancer, specifically.

³ U.S. Food and Drug Administration. **FDA grants first-ever modified risk orders to eight smokeless tobacco products.** Press Release (2019).

Table 9a: Perceptions of Absolute Risk for Use of Only *General Snus*® Every Day and Use of Only Cigarettes Every Day

(b) (4)

(b) (4)

7.3.2 Perceptions of Absolute Risk for Use of Both Both General Snus® and Cigarettes Every Day and Never Having Used Any TNP

All respondents evaluated the absolute risk of developing three diseases—mouth cancer, heart disease, lung cancer—from use of both General Snus® and cigarettes every day or from never having used any TNP. Perceptions of absolute risk were measured using a 5-point scale ranging from 1 (“Very low chance”) to 5 (“Very high chance”); “Don’t know” was also an available response option. These results are presented in [Table 9b](#) below.

Among General Snus® users at baseline that returned for Wave 3 (n=586), large majorities of respondents perceived use of both General Snus® and cigarettes every day (dual use) to be associated with a moderate to very high chance of developing each of the three disease states assessed—mouth cancer (87.7%, n=514), heart disease (94.2%, n=552), lung cancer (93.9%, n=550). As General Snus® is a modified risk tobacco product (MRTP) and carries a modified risk message⁴, this finding provides evidence that respondents do not perceive that supplementing cigarette use with General Snus® (dual use) reduces risks for developing diseases from cigarette use—perceived risks associated with dual use of General Snus® and cigarettes every day were nearly identical to perceived risks associated with use of only cigarettes every day. ([Section 7.3.1](#); [Table 9a](#)). Thus, these results do not provide evidence of a “halo effect” related to use of General Snus® products, a concern that has recently been raised by both public health researchers and FDA.⁵

Among General Snus® users at baseline that returned for Wave 3 (n=586), never having used any TNP was perceived as having minimal risk of developing cancer. Large majorities of respondents at Wave 3 associated never having used any TNP with low or very low chances of developing mouth cancer (85.0%, n=498) and lung cancer (81.7%, n=479). Perceived risk of developing heart disease from never having used any TNP was considerably higher; more than half of respondents associated never having used any TNP with a moderate to very high chance of developing heart disease (62.8%, n=368). This suggests that respondents at Wave 3 may understand that there is a higher incidence of heart disease in the U.S., regardless of whether a person uses TNP, than mouth and lung cancer.⁶

⁴ The modified risk messaging approved for General Snus® states the following: “Using General Snus® instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.” U.S. Food and Drug Administration. **FDA grants first-ever modified risk orders to eight smokeless tobacco products.** Press Release (2019).

⁵ Seidenberg AB, Popova L, Ashley DL, *et al.* **Inferences beyond a claim: a typology of potential halo effects related to modified risk tobacco product claims.** *Tobacco Control*. Volume 30 (2021).

⁶ Incidence of heart disease in the U.S. (2018): 0.27% [870,000 new cases]; incidence of mouth cancer in the U.S. (2018): 0.02% [50,000 new cases]; incidence of lung cancer in the U.S. (2018): 0.07% [220,000 new cases]. U.S. National Center for Health Statistics. **Disease incidence in the United States.** Annual Report (2018).

Table 9b: Perceptions of Absolute Risk for Use of Both *General Snus*® and Cigarettes Every Day and Never Having Used Any TNP

(b) (4)

(b) (4)



7.3.3 Understanding of the Modified Risk Claim for *General Snus*®

Understanding of the modified risk claim for *General Snus*® was assessed among all *General Snus*® users at baseline that returned for Wave 3 (n=586). Two questions were asked to respondents at Wave 3. The first asked them to correctly identify the language used in the modified risk claim. Response options included “lower risk,” “higher risk,” or “the same risk” of developing certain diseases from using *General Snus*® compared to smoking cigarettes. Respondents that correctly answered this question (i.e., endorsed “lower risk”) were presented with a second question asking how many cigarettes you can smoke per day while using *General Snus*® and still benefit from the reduction in risk of developing the diseases stated in the modified risk claim. Response options included “Zero cigarettes,” “Up to 5 cigarettes,” “Up to 20 cigarettes,” and “As many as you want to smoke.” “Don’t know” and “Decline to answer” were also available response options. The correct response option, based on language used in the modified risk claim, is “Zero cigarettes,” as the claim states a user must use *General Snus*® *instead of cigarettes*. Results are presented in [Table 10](#) below and are separated between *General Snus*® users overall and new *General Snus*® users (defined as first using *General Snus*® in the 30 days prior to the baseline survey). Only results for the overall group of *General Snus*® users are described here.

Most respondents correctly reported that use of *General Snus*® instead of cigarettes reduces risk of developing the diseases stated in the modified risk claim (77.8%, n=456). Again, most respondents that correctly responded to the modified risk claim messaging (n=456) then reported that you could not use any cigarettes (i.e., endorsed “Zero cigarettes”) and still benefit from the reduction in risk of developing the diseases stated in the modified risk claim (80.3%, n=366). These findings suggest that *General Snus*® users understand that use of *General Snus*® instead of cigarettes puts them at a lower risk of developing various tobacco-related diseases and that this reduction in risk is predicated on not smoking cigarettes (“Using *General Snus*® instead of cigarette[s]”).

Table 10: Understanding of the MRTP Claim Related to Reduced Risk Among *General Snus*® Users and New *General Snus*® Users

(b) (4)

8. SUMMARY OF WAVE 3 RESULTS

Summary of Results:

- *General Snus*® was used in the P30D among 90.0% of returning respondents (n=527)
 - The pattern of *General Snus*® use **significantly differed** from baseline (p<0.001) due to the number of respondents that switched from every day to some day use by Wave 3 (n=94)
- Every day *General Snus*® users used more pouches on days used than some day users (10.5 pouches/day vs. 6.6 pouches/day)
 - Some day users reported using *General Snus*® 12 days in the P30D; this **did not significantly differ** from baseline (p=0.27)
- Among the respondents returning for Wave 3 (n=586), 14.1% (n=83) reported P30D cigarette smoking, and most of these respondents smoked only on some days (10.9%, n=64)
 - 37.3% of these respondents had initiated cigarettes in the 12 months since baseline (n=31), but all reported that they smoked only on some days
- Only 14.3% of respondents that returned for Wave 3 were cigarette smokers at baseline (n=84)
 - Of these respondents, 36.9% had completely quit smoking cigarettes, with 93.5% of those quitting reporting complete substitution of cigarettes with *General Snus*® (n=29)
- Respondents correctly perceived that cigarette smoking contributed significant risks to health, associating it with moderate to very high chances of developing mouth cancer (81.7%, n=479), heart disease (98.3%, n=576), and lung cancer (93.5%, n=548)
 - Use of *General Snus*® was perceived as being less risky to health than cigarette smoking but that use of *General Snus*® was not without risks to health
 - Dual use of *General Snus*® and cigarettes was perceived as equally risky as use of only cigarettes, suggesting that respondents understand that any use of cigarettes is associated with highest risks to health
- Respondents understood the MRTP claim that using *General Snus*® instead of cigarettes puts users at a lower risk for various diseases compared to cigarette smoking
 - 77.8% of respondents correctly endorsed that *General Snus*® was lower risk (n=456)
 - Most understood that no cigarettes can be when using *General Snus*® to benefit from it being reduced risk (80.3%, n=366), indicating that they are aware users need to completely substitute cigarettes for *General Snus*®

(b) (4)



General Snus® Patterns of Use Study

Wave 4 Technical Report – Final

Swedish Match North America Protocol Number: SMU 19-01 GENS

(b) (4)

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General Snus® Patterns of Use Study – Wave 4 Technical Report
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EXECUTIVE SUMMARY

General Snus® was used in the P30D by 87.3% (n=394) of those returning at Wave 4

- The pattern of General Snus® use **significantly differed** from Baseline ($p<0.0001$) due to the proportion of respondents who had switched from every day to some day use by Wave 4

Every day General Snus® users used more pouches on days used than some day users (10.4 pouches/day vs. 6.7 pouches/day)

- Some day General Snus® users reported using the product an average of 13.1 days in the P30D, which **did not significantly differ** from that reported at Baseline ($p=0.8367$)

Among returning General Snus® users at Wave 4, only 13.9% (n=63) reported smoking at Baseline and 13.5% (n=61) reported at Wave 4, which **did not significantly differ** ($p=0.6232$)

Respondents correctly perceived that cigarette smoking contributed significant risks to health, associating it with moderate to very high chances of developing mouth cancer (78.5%, n=354), heart disease (93.8%, n=423), lung cancer (92.5%, n=417).

- Dual use of General Snus® and cigarettes was generally perceived as being just as risky to health as use of only cigarettes, suggesting that respondents understand that any use of cigarettes is associated with high risks to health
- Use of General Snus® was perceived as being less risky to health than cigarette smoking but that use of General Snus® was not without risks to health.

Respondents understood the MRTP claim that using General Snus® instead of cigarettes puts users at a lower risk for various diseases compared to cigarette smoking

- 77.8% (n=351) of respondents correctly endorsed that use of General Snus® presented less risk to health than cigarette smoking
- Most respondents who correctly endorsed that use of General Snus® presented less risk to health than cigarette smoking understood that no cigarettes can be smoked while using General Snus® to benefit from it being lower risk (79.8%, n=280)
- Results suggest that General Snus® users are aware of the need to completely substitute cigarettes for General Snus®

General Snus® Patterns of Use Study – Wave 4 Technical Report
FINAL – Version 1.0 – Issue Date: 04NOV2022

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TABLE OF CONTENTS

| | |
|--|----|
| SIGNATURES OF RESPONSIBLE PARTIES | 1 |
| Swedish Match North America..... | 1 |
| (b) (4) | 1 |
| EXECUTIVE SUMMARY | 2 |
| (b) (4) | 3 |
| DOCUMENT HISTORY | 4 |
| TABLE OF CONTENTS | 5 |
| LIST OF ABBREVIATIONS | 7 |
| 1. BACKGROUND & RATIONALE | 8 |
| 2. STUDY OBJECTIVES..... | 8 |
| 2.1 Primary Objectives..... | 8 |
| 2.2 Secondary Objectives..... | 9 |
| 3. OVERVIEW OF RESEARCH METHODS | 9 |
| 3.1 Inclusion Criteria | 10 |
| 3.2 Exclusion Criteria | 10 |
| 4. OVERVIEW OF ANALYSIS METHODS | 11 |
| 5. WAVE 4 FIELDING SUMMARY..... | 12 |
| 5.1 Study Fielding Summary | 12 |
| 6. WAVE 4 STUDY RESULTS..... | 13 |
| 6.1 Demographic Characteristics of Respondents at Wave 4 | 13 |
| 6.2 Wave 4 Results for Primary Objectives..... | 15 |
| 6.2.1 TNP Use in the Past 30 Days at Wave 4 | 15 |
| 6.2.2 TNP Use in the Past 30 Days at Wave 4 Among Respondents Who Quit Using <i>General Snus</i> ® | 20 |
| 6.2.3 Cigarette Quitting Behavior at Wave 4 | 24 |
| 6.2.4 Percent of Days in the Past 30 Days that <i>General Snus</i> ® And Cigarettes Were Used and the Quantity Used on Days Used at Wave 4 | 25 |
| 6.2.5 Changes in Patterns of Use of <i>General Snus</i> ® and Cigarettes at Wave 4 | 28 |

6.2.6 Incremental, Supplemental, or Complete Substitution of Cigarettes for *General Snus*® Among Dual Users of Both Cigarettes and *General Snus*® at Wave 430

6.3 Wave 4 Results for Secondary Objectives.....33

6.3.1 Perceptions of Absolute Risk for Use of Only *General Snus*® Every Day and Use of Only Cigarettes Every Day.....33

6.3.2 Perceptions of Absolute Risk for Use of Both *General Snus*® and Cigarettes Every Day and Never Having Used Any TNP.....37

6.3.3 Understanding of the Modified Risk Claim for *General Snus*®40

7. SUMMARY OF WAVE 4 RESULTS.....42

LIST OF ABBREVIATIONS

| Abbreviation | Definition |
|--------------|---|
| FDA | FDA Food and Drug Administration |
| MRTP | Modified Risk Tobacco Product |
| MRTPA | Modified Risk Tobacco Product Application |
| P30D | Past 30 Days |
| PATH | Population Assessment of Tobacco and Health |
| PMTA | Premarket Tobacco Product Application |
| SAP | Statistical Analysis Plan |
| SMNA | Swedish Match North America, LLC |
| TNP | Tobacco/Nicotine Product(s) |
| U.S. | United States |

1. BACKGROUND & RATIONALE

In November 2015, Swedish Match USA, Inc. (SMU) received market authorization for *General Snus*®, a moist tobacco product placed under the upper lip that does not involve spitting or chewing. In its first applications reviewed through the MRTP pathway, the FDA deferred final action on providing *General Snus*® a MRTP designation, providing guidance on how SMU could amend their application to provide greater support for a modified risk designation. SMU filed its amended MRTPA on 17 September 2018, and the FDA granted the risk modification order on 22 October 2019. The *General Snus*® Patterns of Use Study (the study) is for post-marketing surveillance reporting following the granted risk modification order.

2. STUDY OBJECTIVES

The overarching research questions for this study were the following:

1. How do *General Snus*® users use tobacco and nicotine products (TNP)?
2. How do *General Snus*® users perceive health risks associated with cigarettes and *General Snus*®?

These questions were studied using a self-reported survey examining patterns of past-30-day (P30D) TNP use among *General Snus*® users in a Baseline assessment (Wave 1) and again, among the same *General Snus*® users, at 6 months (Wave 2), 1 year (Wave 3) and 2 years (Wave 4) after Baseline.

2.1 PRIMARY OBJECTIVES

The primary objectives of the study were the following:

1. Compare patterns of TNP use between all 4 study waves by examining self-reported TNP use for participants, in aggregate, over time.
 - The study will report on frequency of use of *General Snus*® use, as well as other TNP, if multiple TNP use is reported. Of specific interest were patterns cigarette use.
 - Intent to quit and actual quitting of cigarettes was assessed at each wave of the study.
2. Among *General Snus*® users, compare consumption patterns of cigarettes and *General Snus*® in the P30D at Baseline with consumption patterns for both products at Wave 2 through Wave 4.
 - Of specific interest was whether use of *General Snus*® offsets use of cigarettes.
3. Characterize *General Snus*® users, especially new *General Snus*® users, in terms of prior TNP use and demographic characteristics and compare these findings to new users of smokeless TNP as reported in the Population Assessment of Tobacco and Health Study.
4. Compare the tendencies of *General Snus*® users to quit cigarettes or use *General Snus*® in an incremental fashion, in a supplemental fashion, or in complete substitution of cigarettes.

2.2 SECONDARY OBJECTIVES

The secondary objectives of the study were the following:

1. Assess perceptions of risk of certain health conditions (mouth cancer, heart disease and lung cancer, separately) among *General Snus*® users.
 - Asses the absolute risk attributed to using only *General Snus*® daily, smoking only cigarettes daily, dual use of *General Snus*® and cigarettes daily, and never having used any TNP.
2. Assess the extent to which *General Snus*® users, especially new users, understand the risk reduction as described in the modified risk claim

3. OVERVIEW OF RESEARCH METHODS

General Snus® users were recruited directly via invitation stickers placed directly on *General Snus*® tins. A third-party vendor (News America Marketing) was hired to place the study invitation stickers on product packaging (e.g., each individual *General Snus*® tins) for all varieties of *General Snus*® available at retail outlets. This took place from 25 July 2020 to 17 August 2020. The sticker initiative targeted approximately 10,600 retail stores carrying *General Snus*® across all locations where *General Snus*® was sold. The sticker presented a website where *General Snus*® users that were interested in participating could access the Baseline survey through a secure and unique survey link.

The first set of questions were used to screen potential respondents and were designed to qualify the respondent using the study inclusion and exclusion criteria. Once qualified, respondents were directed to the online survey. Respondents were asked to self-report TNP use within the P30D and various questions related to TNP use, risk perceptions, and understanding of the modified risk messaging for *General Snus*® products.

The study was a longitudinal, prospective assessment consisting of multiple survey waves to gain an understanding of how *General Snus*® and other TNP are used by the participating respondents. Respondents completed an initial survey at Baseline (Wave 1) and had the opportunity to participate again at 6 months (Wave 2), 1 year (Wave 3), and 2 years (Wave 4) from Baseline. All respondents at Baseline must have reported use of *General Snus*® at least once in the P30D and reported use every day (daily) or on some days (non-daily).

Full details of all research methods and study procedures can be found in the *General Snus*® Patterns of Use Study – Study Protocol.

3.1 INCLUSION CRITERIA

Respondents had to meet each of the following criteria to be included in the study:

1. Have used *General Snus*® at least once or more within the P30D and use it every day or on some days
2. Minimum age of 21 years
3. Agree to participate in four surveys over the 24-month period
4. Able to read and speak English
5. Currently a resident of the United States
6. Agreeing to provide informed consent and personal contact information

3.2 EXCLUSION CRITERIA

Respondents who met of the following criteria were excluded from the study:

1. Responded “don’t know” or “decline to answer” to questions asking their gender and geographic region
2. Unwilling or unable to provide electronic informed consent and personal contact information
3. Employed in any of the following fields or professions: market research, marketing, advertising, TNP manufacturing, or employed as a physician
4. Participated in a consumer research study on TNP in the 2 weeks prior to the Baseline survey

4. OVERVIEW OF ANALYSIS METHODS

All analyses conducted were either descriptive or inferential. Descriptive analyses provided summary statistics for all variables. These statistics included counts and proportions for categorical variables and means, standard deviations, medians, minimums, and maximums for ordinal and continuous variables. Inferential statistical testing was conducted to evaluate changes in primary and secondary outcome measures (i.e., patterns of use, risk perceptions, understanding of claims) from baseline and each follow-up wave. Results comparing baseline data versus data from each follow-up wave was conducted using paired sample t-tests for continuous variables and McNemar tests for categorical variables.

5. WAVE 4 FIELDING SUMMARY

5.1 STUDY FIELDING SUMMARY

The fielding summary for number of respondents that entered the Wave 4 survey, those that did not complete the survey, those that were terminated (and the reasons for termination) are summarized below in [Table 1](#).

Table 1: Fielding Summary for the Wave 4 Survey

| | Wave 4 |
|--|--------|
| Number of respondents that entered the survey | 589 |
| Number of respondents that were terminated based inclusion/exclusion criteria/quota filled/intellectual property blocker | 56 |
| Number of respondents that did not complete the survey | 77 |
| Number of respondents retained (closed fielding) | 456 |
| Total respondents retained after data quality check* | N=451 |

*Data quality check per the SAP included outliers, straightliners, speeders, those that failed the attention check question, and illogical responses.

6. WAVE 4 STUDY RESULTS

6.1 DEMOGRAPHIC CHARACTERISTICS OF RESPONDENTS AT WAVE 4

The demographic characteristics of *General Snus*® users and the subset of new *General Snus*® users that returned for Wave 4 are summarized in [Table 2](#). Results represent data collected at Wave 4 as these demographic characteristics may have changed over the course of the study. Only results for the overall group of *General Snus*® users is discussed here given the small sample size. Findings for the subset of new *General Snus*® users can be found below in [Table 2](#).

Most respondents that returned for Wave 4 lived in the South (36.1%; n=163), while the least number of respondents lived in the Northeast (13.1%, n=59). Nearly all respondents were male (93.8%, n=423). The mean age of *General Snus*® users that returned for Wave 4 was 39.4 years (median: 38.0 years; range: 24.0 to 79.0 years). Most respondents were currently married (56.5%, n=255). There was a considerable number of respondents with high household incomes, as 42.8% (n=193) reported that they earned \$100,000 or more in the past 12 months.

Table 2: Demographic Characteristics of General Snus® Users and New General Snus® Users Who Returned for Wave 4

| | <i>General Snus® Users</i> | <i>New General Snus® Users</i> |
|---|----------------------------|--------------------------------|
| | N = 451 | N* = 15 |
| Geographic Region | | |
| West (%) | 99 (22.0%) | 4 (26.7%) |
| South (%) | 163 (36.1%) | 5 (33.3%) |
| Midwest (%) | 130 (28.8%) | 3 (20.0%) |
| Northeast (%) | 59 (13.1%) | 3 (20.0%) |
| Gender | | |
| Male (%) | 423 (93.8%) | 11 (73.3%) |
| Female (%) | 28 (6.2%) | 4 (26.7%) |
| Declined to answer (%) | 0 (0.0%) | 0 (0.0%) |
| Respondent Age | | |
| Age in years \pm SD* | 39.4 \pm 10.5 | 38.5 \pm 13.0 |
| Marital Status** | | |
| Currently married (%) | 255 (56.5%) | 6 (40.0%) |
| Not currently married (%) | 190 (42.1%) | 8 (53.3%) |
| Declined to answer (%) | 6 (1.3%) | 1 (6.7%) |
| Household Income** | | |
| Less than \$50,000 (%) | 90 (20.0%) | 5 (33.3%) |
| \$50,000 to \$99,999 (%) | 149 (33.0%) | 5 (33.3%) |
| \$100,000 or more (%) | 193 (42.8%) | 5 (33.3%) |
| Don't know (%) | 0 (0.0%) | 0 (0.0%) |
| Declined to answer (%) | 19 (4.2%) | 0 (0.0%) |
| <p>N represents all returning General Snus® users at Wave 4. N* represents the subset of new General Snus® users at Wave 4. *SD: Standard deviation. **Results for marital status and household income were collapsed into the categories presented. In the Wave 4 survey, marital status had six categories and household income had eleven categories. Household income represents earnings in past 12 months.</p> | | |

6.2 WAVE 4 RESULTS FOR PRIMARY OBJECTIVES

6.2.1 TNP USE IN THE PAST 30 DAYS AT WAVE 4

Patterns of TNP use in the past 30 days (P30D) among all Wave 4 respondents are presented in [Table 3](#) below. At Baseline, TNP use in the P30D was asked to respondents that indicated they had ever regularly used any of eleven categories of TNP, including *General Snus*®, and for those TNP to which they responded, “Don't know.” At Wave 4, TNP use in the P30D was asked to all respondents for the same eleven categories of TNP.

Among *General Snus*® users who returned for Wave 4, 87.3% (n=394) reported using *General Snus*® in the P30D, with 60.5% (n=273) using every day and 26.8% (n=121) using on some days. Some respondents that had regularly used *General Snus*® at Baseline had quit use of the product by Wave 4 (12.2%, n=55). The change in patterns of use for *General Snus*® from Baseline to Wave 4 **was significantly significant** (p<0.0001) given the differences in proportion of *General Snus*® users who used every day vs. some days at Wave 4 than at Baseline.

[Table 3](#) also presents P30D use for other categories of TNP among *General Snus*® users who returned for Wave 4. Only 13.5% (n=61) reported P30D cigarette smoking, with 4.7% (n=21) reporting smoking cigarettes every day and 8.9% (n=40) reporting smoking cigarettes on some days. Prevalence of P30D cigarette smoking among *General Snus*® users at Wave 4 **did not significantly differ** from prevalence of P30D cigarette smoking at Baseline (p=0.6232).

Prevalence of P30D use of nicotine pouches **significantly increased** among *General Snus*® users between Baseline and Wave 4 (p<0.0001) – 42.7% of *General Snus*® users reported using of nicotine pouches at Wave 4 (n=193), with 18.0% (n=81) reporting use every day and 24.8% (n=112) reporting use on some days. Additionally, the number of *General Snus*® users reporting use of aids to help stop smoking cigarettes also **significantly increased** between Baseline and Wave 4 (p=0.0050) – 6.7% (n=30) of *General Snus*® users reported P30D use of aids to help stop smoking cigarettes, with 2.7% (n=12) reporting use every day and 4.0% (n=18) reporting use on some days.

Table 3: TNP Use in the Past 30 Days at Wave 4

(b) (4)







(b) (4)

Table 4: TNP Use in the Past 30 Days at Wave 4 Among Respondents Who Quit Using General Snus®

(b) (4)

(b) (4)

(b) (4)

6.2.3 CIGARETTE QUITTING BEHAVIOR AT WAVE 4

Among General Snus® users who returned for Wave 4 who had smoked cigarettes, 18.1% (n=15) reported that they had completely quit smoking cigarettes in the P30D. Those who had not quit smoking were asked if they were trying to quit smoking. Among those who had not quit smoking, 39.2% (n=20) reported they had made a quit attempt in the P30D. and another 42.6% reported that they were currently making a quit attempt (n=29). Results for the number of respondents that had quit smoking **did not significantly differ** from that at Baseline (p=0.7728), nor were results for the number of respondents making a quit attempt at Wave 4 (p=1.0000). These results are presented in [Table 5](#) below.

Table 5: Cigarette Quitting Behaviors at Wave 4

(b) (4)

6.2.4 PERCENT OF DAYS IN THE PAST 30 DAYS THAT GENERAL SNUS® AND CIGARETTES WERE USED AND THE QUANTITY USED ON DAYS USED AT WAVE 4

Among the General Snus® users who returned for Wave 4, 60.5% (n=273) reported using General Snus® every day and 26.8% (n=121) reported using General Snus® on some days. Some day General Snus® users were asked on how many days out of the P30D that they used the product, while every day General Snus® users were assumed to have used the product on each of the P30D. Every day and some day users were then asked how many General Snus® pouches they used on the days that they used the product. These results are presented in [Table 6a](#) below.

Some day General Snus® users reported that they used the product 43.58% of days in the P30D (equating to 13.1 days). The percent of days General Snus® was used in the P30D among some day General Snus® users **did not significantly differ** from that reported at Baseline (p=0.8367).

Some day General Snus® users reported they used, on average, 6.7 pouches on the days they used the product. Every day General Snus® users reported using a greater number of pouches than did some day users, reporting they used 10.4 pouches each day, on average, within the P30D.

Among the General Snus® users who returned for Wave 4, 4.7% (n=21) reported smoking cigarettes every day and 8.9% (n=40) reported smoking cigarettes on some days. Some day cigarette smokers were asked on how many days out of the P30D that they smoked, while every day cigarette users were assumed to have smoked on each of the P30D. Every day and some day cigarette smokers were also asked how many cigarettes they used on the days that they smoked. These results are presented in [Table 6b](#) below.

Some day cigarette smokers reported that they smoked 22.83% of days in the P30D (equating to 6.8 days). The percent of days smoked in the P30D among some day cigarette smokers **did not significantly differ** from that reported at Baseline (p=0.2146).

Some day cigarette users reported they smoked, on average, 2.9 cigarettes on the days they smoked. Every day cigarette smokers reported smoking a greater number of cigarettes than did some day cigarette smokers, reporting they smoked 9.9 cigarettes each day, on average, within the P30D.

Table 6a: Percent of Days *General Snus*® Was Used in the Past 30 Days and Quantity of *General Snus*® Used on Days Used at Wave 4

(b) (4)

Table 6b: Percent of Days Cigarettes Were Smoked in the Past 30 Days and Quantity of Cigarettes Smoked on Days Smoked at Wave 4

(b) (4)

6.2.5 CHANGES IN PATTERNS OF USE OF *GENERAL SNUS*® AND CIGARETTES AT WAVE 4

Respondent patterns of use were measured by determining whether a given product was used every day, some days, or not at all within the P30D. Patterns of use for *General Snus*® and cigarettes were measured in both the baseline and Wave 4 surveys. Baseline and Wave 4 patterns of use for *General Snus*® and cigarettes were compared to understand changes in patterns of use over time and were measured separately among every day and some day users of the respective products at Baseline. Changes in patterns of use from Baseline to Wave 4 are presented in [Table 7](#) below.

Among the *General Snus*® users who returned for Wave 4, 65.0% (n=260) were every day *General Snus*® users at both Baseline and Wave 4, while 22.8% (n=91) had gone from every day use at Baseline to some day use at Wave 4. Others who were every day users at Baseline had quit use of *General Snus*® by Wave 4 (11.8%; n=47). Similarly, 58.8% (n=30) of some day *General Snus*® users at Baseline remained some day users at Wave 4, while 25.5% (n=13) had gone from some day use at Baseline to every day use at Wave 4. Others who were some day users at Baseline had quit use of *General Snus*® by Wave 4 (15.7%; n=8).

Most *General Snus*® users who returned for Wave 4 who had not smoked in the P30D at Baseline had also not smoked at Wave 4 (89.9%; n=160). Half of those who smoked every day at Baseline also smoked every day at Wave 4 (50.0%; n=12), while the other half either became some day smokers (33.3%; n=8) or had quit smoking (16.7%; n=4). Over half of those who were some day smokers at Baseline had quit smoking at Wave 4 (59.0%; n=23).

Table 7: Changes in Patterns of Use of *General Snus*® and Cigarettes from Baseline to Wave 4

(b) (4)

6.2.6 INCREMENTAL, SUPPLEMENTAL, OR COMPLETE SUBSTITUTION OF CIGARETTES FOR GENERAL SNUS® AMONG DUAL USERS OF BOTH CIGARETTES AND GENERAL SNUS® AT WAVE 4

Incremental and supplemental use of cigarettes and *General Snus*® and complete substitution of cigarettes for *General Snus*® was evaluated among dual users of both cigarettes and *General Snus*® at Wave 4. Results were calculated by comparing frequency of use of both cigarettes and *General Snus*® at Baseline and subtracting frequency of use of the respective products at Wave 4. Frequency of use was measured by asking respondents the quantity of cigarettes and *General Snus*® used on days used. Respondents included in analyses measuring incremental and supplemental use were those that did not switch their pattern of use for either product between Baseline and Wave 4 – meaning, every day users of either cigarettes or *General Snus*® at Baseline who also reported every day use at Wave 4 and some day users of either cigarettes or *General Snus*® at Baseline who also reported some day use at Wave 4.

Incremental use was defined as using a greater or equal number of cigarettes or *General Snus*® at Wave 4 than at Baseline; a difference in frequency of use between baseline to Wave 4 resulting in a value that is positive or equal to zero was considered incremental use. Supplemental use was defined as using fewer cigarettes or *General Snus*® at Wave 4 than at Baseline; a difference in frequency of use between baseline to Wave 4 that is negative was considered supplemental use. Complete substitution was defined as fully replacing cigarette use and only using *General Snus*® or completely quitting use of both products. Results for incremental and supplemental use for both cigarettes and *General Snus*® are presented below in [Table 8a](#) and results for complete substitution are presented in [Table 8b](#).

There were no statistically significant changes in use behavior among dual users of cigarettes or *General Snus*® – either incremental or supplemental – at Wave 4 (range in p-values: 0.4144 – 0.6291). Additionally, there were only slight changes in use of either product among these respondents, as the change in magnitude of *General Snus*® pouches used was less than 1.0 pouch on for both every day (n=260) and some day (n=30) *General Snus*® users. and the change in magnitude for cigarettes used was 1.25 cigarettes among every day smokers (n=12) and 0.33 cigarettes among some day smokers (n=12). Results presented in [Table 8b](#) for complete substitution of cigarettes for *General Snus*® indicate that 6.0% (n=27) of *General Snus*® users who returned for Wave 4 had completely quit smoking cigarettes since Baseline. Among these respondents, 92.6% (n=25) reported that they exclusively used *General Snus*® to replace cigarettes.

Table 8a: Incremental or Supplemental Use of Cigarettes and General Snus® from Baseline to Wave 4

(b) (4)

Table 8b: Complete Substitution of Cigarettes for *General Snus*® at Wave 4

(b) (4)

6.3 WAVE 4 RESULTS FOR SECONDARY OBJECTIVES

6.3.1 PERCEPTIONS OF ABSOLUTE RISK FOR USE OF ONLY GENERAL SNUS® EVERY DAY AND USE OF ONLY CIGARETTES EVERY DAY

All respondents evaluated the absolute risk of developing three diseases—mouth cancer, heart disease, lung cancer—from use of only *General Snus*® every day or from use of only cigarettes every day. Perceptions of absolute risk were measured using a 5-point scale ranging from 1 (“Very low chance”) to 5 (“Very high chance”); “Don’t know” was also an available response option. These results are presented in [Table 9a](#) below.

General Snus® and other snus products contain markedly lower levels of harmful and potentially harmful constituents (HPHCs) compared to traditional smokeless tobacco. Numerous scientific publications have found no associations between use of snus products and development of mouth cancer^{1,2,3} or heart disease^{4,5,6}; this differs from use of traditional smokeless tobacco for which associations with these diseases have been found.

Findings at Wave 4 suggest that some *General Snus*® users may be misinformed about the health risks of using the product and may misattribute risks of traditional smokeless tobacco to *General Snus*®—about half perceived use of only *General Snus*® every day to be associated with a moderate to very high chance of developing mouth cancer (48.6%, n=219) and nearly half perceived use of only *General Snus*® every day to be associated with a moderate to very high chance of developing heart disease (44.8%, n=202).

¹ Luo J, Ye W, Zendehdel K, *et al.* Oral use of Swedish moist snuff (snus) and risk for cancer of the mouth, lung, and pancreas in male construction workers: a retrospective cohort study. *The Lancet*. Volume 369 (2007).

² Smita A, Labani S, Kailash U, *et al.* Association of smokeless tobacco use and oral cancer: a systematic global review and meta-analysis. *Nicotine & Tobacco Research*. Volume 21, Issue 9 (2019).

³ Araghi M, Galanti MR, Lundberg M, *et al.* No association between moist oral snuff (snus) use and oral cancer: pooled analysis of nine prospective observational studies. *Scandinavian Journal of Public Health*. Volume 28, Issue 8 (2021).

⁴ Lee P. Summary of the epidemiological evidence relating snus to health: an updated review based on recent publications. *Harm Reduction Journal*. Volume 10, Issue 36 (2013).

⁵ Hansson J, Galanti MR, Hergens MP, *et al.* Use of snus and acute myocardial infarction: pooled analysis of eight prospective observational studies. *European Journal of Epidemiology*. Volume 27 (2012).

⁶ Wennberg P, Eliasson M, Hallmans G, *et al.* The risk of myocardial infarction and sudden cardiac death amongst snuff users with or without a previous history of smoking. *Journal of Internal Medicine*. Volume 262, Issue 3 (2007).

General Snus® users who returned for Wave 4 (n=451) correctly perceived that use of only *General Snus*® every day carried lower risks to health than use of only cigarettes every day across the three diseases assessed. This is also evidenced by results for perceived risk of developing lung cancer, as 88.5% (n=399) of respondents at Wave 4 associated use of only *General Snus*® every day to be associated with a low to very low chance of developing lung cancer, which is also evidenced in scientific literature.⁷

General Snus® products can be marketed in the U.S. with the following modified risk messaging: “Using *General Snus*® instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.”⁸ Risk perceptions among *General Snus*® users at Wave 4 provide evidence that respondents understand that *General Snus*® is a reduced risk tobacco product (compared to cigarettes) but that use of *General Snus*® is not without risks to health. Findings also provide evidence that respondents can correctly attribute use of only *General Snus*® to reductions in risk of developing specific diseases stated in the modified risk messaging.

Among *General Snus*® users who returned for Wave 4 (n=451), use of only cigarettes every day was perceived to carry much higher risks to health than use of only *General Snus*® every day across the three diseases assessed. Large majorities of respondents at Wave 4 perceived use of only cigarettes every day to be associated with a moderate to very high chance of developing each of the three disease states assessed—mouth cancer (78.5%, n=354), heart disease (93.8%, n=423), lung cancer (92.5%, n=417). This suggests these respondents understand that use of cigarettes contributes very high risks to health and to the development of mouth cancer, heart disease, and lung cancer, specifically.

⁷ Clarke E., Thompson K., Weaver S., *et al.* **Snus: a compelling harm reduction alternative to cigarettes.** *Harm Reduction Journal*. Volume 16, Issue 62 (2019).

⁸ U.S. Food and Drug Administration. **FDA grants first-ever modified risk orders to eight smokeless tobacco products.** Press Release (2019).

Table 9a: Perceptions of Absolute Risk for Use of Only General Snus® Every Day and Use of Only Cigarettes Every Day

(b) (4)

(b) (4)

6.3.2 PERCEPTIONS OF ABSOLUTE RISK FOR USE OF BOTH GENERAL SNUS® AND CIGARETTES EVERY DAY AND NEVER HAVING USED ANY TNP

All respondents evaluated the absolute risk of developing three diseases—mouth cancer, heart disease, lung cancer—from use of both *General Snus*® and cigarettes every day or from never having used any TNP. Perceptions of absolute risk were measured using a 5-point scale ranging from 1 (“Very low chance”) to 5 (“Very high chance”); “Don’t know” was also an available response option. These results are presented in [Table 9b](#).

Among *General Snus*® users who returned for Wave 4 (n=451), large majorities of respondents perceived use of both *General Snus*® and cigarettes every day (dual use) to be associated with a moderate to very high chance of developing each of the three disease states assessed—mouth cancer (85.4%, n=385), heart disease (91.6%, n=413), lung cancer (92.5%, n=417). As *General Snus*® is a modified risk tobacco product (MRTP) and carries a modified risk message⁹, this finding provides evidence that respondents do not perceive that supplementing cigarette use with *General Snus*® (dual use) reduces risks for developing diseases from cigarette use—perceived risks associated with dual use of *General Snus*® and cigarettes every day were similar in magnitude to perceived risks associated with use of only cigarettes every day ([Table 9a](#)). Thus, these results do not provide evidence of a “halo effect” related to use of *General Snus*®, a concern that has recently been raised by both public health researchers and FDA.¹⁰

Among *General Snus*® users at baseline that returned for Wave 4 (n=451), never having used any TNP was perceived as having minimal risk of developing cancer. Large majorities of respondents at Wave 4 associated never having used any TNP with low or very low chances of developing mouth cancer (89.6%, n=404) and lung cancer (84.9%, n=383). Perceived risk of developing heart disease from never having used any TNP was considerably higher, as more than half of respondents associated never having used any TNP with a moderate to very high chance of developing heart disease (57.2%, n=258).

⁹ The modified risk messaging approved for *General Snus*® states the following: “Using *General Snus*® instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.” U.S. Food and Drug Administration. **FDA grants first-ever modified risk orders to eight smokeless tobacco products**. Press Release (2019).

¹⁰ Seidenberg AB, Popova L, Ashley DL, *et al*. **Inferences beyond a claim: a typology of potential halo effects related to modified risk tobacco product claims**. *Tobacco Control*. Volume 30 (2021).

Table 9b: Perceptions of Absolute Risk for Use of Both *General Snus®* and Cigarettes Every Day and Never Having Used Any TNP

(b) (4)

(b) (4)

6.3.3 UNDERSTANDING OF THE MODIFIED RISK CLAIM FOR *GENERAL* SNUS®

Understanding of the modified risk claim for *General Snus*® was assessed among all *General Snus*® users at Baseline who returned for Wave 4 (N=451). Two questions were asked. The first asked respondents to correctly identify the language used in the modified risk claim. Response options included “lower risk,” “higher risk,” or “the same risk” of developing certain diseases from using *General Snus*® compared to smoking cigarettes.¹¹

Respondents who correctly answered this question (i.e., endorsed “lower risk”) were presented with a second question asking how many cigarettes that can be smoked per day while using *General Snus*® and still benefit from the reduction in risk of developing the diseases stated in the modified risk claim. Response options included “Zero cigarettes,” “Up to 5 cigarettes,” “Up to 20 cigarettes,” and “As many as you want to smoke.” “Don’t know” and “Decline to answer” were also available response options. The correct response option, based on language used in the modified risk claim, is “Zero cigarettes,” as the claim states a user must use *General Snus*® *instead of cigarettes*.

Results are presented in [Table 10](#) below and are separated between *General Snus*® users overall and new *General Snus*® users (defined as first using *General Snus*® in the 30 days prior to the Baseline survey). Only results for the overall group of *General Snus*® users are described here given the small sample size of new *General Snus*® users.

Most respondents correctly reported that use of *General Snus*® instead of cigarettes presents a lower risk of developing the diseases stated in the modified risk claim (77.8%, n=351). Also, most respondents who correctly responded to the modified risk claim messaging (n=351) then correctly reported that cigarettes could not be smoked (i.e., endorsed “Zero cigarettes”) and still benefit from the reduction in risk of developing the diseases stated in the modified risk claim (79.8%, n=280). These findings suggest that *General Snus*® users understand that use of *General Snus*® instead of cigarettes puts them at a lower risk of developing various tobacco-related diseases and that this reduction in risk is predicated on not smoking cigarettes (“Using *General Snus*® instead of cigarette[s]”).

¹¹ Diseases included on the modified risk claim are the following: mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.

Table 10: Understanding of the MRTP Claim Related to Reduced Risk Among General Snus® Users and New General Snus® Users

(b) (4)

7. SUMMARY OF WAVE 4 RESULTS

General Snus® was used in the P30D by 87.3% (n=394) of those returning at Wave 4

- The pattern of *General Snus*® use **significantly differed** from Baseline ($p < 0.0001$) due to the proportion of respondents who had switched from every day to some day use by Wave 4

Every day *General Snus*® users used more pouches on days used than some day users (10.4 pouches/day vs. 6.7 pouches/day)

- Some day *General Snus*® users reported using the product an average of 13.1 days in the P30D, which **did not significantly differ** from that reported at Baseline ($p = 0.8367$)

Among returning *General Snus*® users at Wave 4, only 13.9% (n=63) reported smoking at Baseline and 13.5% (n=61) reported at Wave 4, which **did not significantly differ** ($p = 0.6232$)

Respondents correctly perceived that cigarette smoking contributed significant risks to health, associating it with moderate to very high chances of developing mouth cancer (78.5%, n=354), heart disease (93.8%, n=423), lung cancer (92.5%, n=417).

- Dual use of *General Snus*® and cigarettes was generally perceived as being just as risky to health as use of only cigarettes, suggesting that respondents understand that any use of cigarettes is associated with high risks to health
- Use of *General Snus*® was perceived as being less risky to health than cigarette smoking but that use of *General Snus*® was not without risks to health.

Respondents understood the MRTP claim that using *General Snus*® instead of cigarettes puts users at a lower risk for various diseases compared to cigarette smoking

- 77.8% (n=351) of respondents correctly endorsed that use of *General Snus*® presented less risk to health than cigarette smoking
- Most respondents who correctly endorsed that use of *General Snus*® presented less risk to health than cigarette smoking understood that no cigarettes can be smoked while using *General Snus*® to benefit from it being lower risk (79.8%, n=280)
- Results suggest that *General Snus*® users are aware of the need to completely substitute cigarettes for *General Snus*®

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General Snus[®] Patterns of Use Study

Longitudinal Technical Report – Final

Swedish Match North America Protocol Number: SMU 19-01 GENS

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EXECUTIVE SUMMARY

STUDY OVERVIEW

The *General Snus*® Patterns of Use Study (the study) was conducted to support post-marketing surveillance requirements following marketing and modified risk orders granted for *General Snus*® by the Food and Drug Administration ([Section 1](#)).

- The study consisted of **four waves** conducted at Baseline (Wave 1), Month 6 (Wave 2), Year 1 (Wave 3), and Year 2 (Wave 4).
- To recruit respondents, cans of *General Snus*® were sold at retail with a sticker directing the purchaser or user to a website where they could opt into participating in the study ([Section 3](#)) and, if so, were screened for pre-defined inclusion criteria ([Section 3.1](#)), of which past-30-day (P30D) use of any *General Snus*® product(s) and a minimum age of 21 years were key requirements.
- Patterns of tobacco and nicotine product (TNP) use in the P30D, absolute and relative risk perceptions associated with use of *General Snus*® and cigarettes, and understanding of the modified risk claim on *General Snus*® packaging were assessed at each wave of the study ([Section 2](#)).

LONGITUDINAL RESULTS AMONG RESPONDENTS COMPLETING ALL WAVES

The results summarized here compare TNP use in the P30D, risk perceptions, and understanding of the modified risk claim reported at Waves 2 – 4 to that reported at Wave 1 among respondents completing all study waves ([Section 6](#)).

Fielding Summary and Respondent Demographic Characteristics

There were 281 respondents who completed all four study waves among the 1,655 respondents at Wave 1, representing a **17.0% full-study retention rate**.

Nearly all respondents who completed all four waves were male (93.6%) and White (89.7%), with a mean age of 37 years.

Just over half of all respondents had obtained a Bachelor's degree (36.1%) or a post-graduate degree (15.0%), and about one-third had an annual income of \$100,000 or more (35.9%).

General Snus® Patterns of Use Study – Longitudinal Technical Report
Final – Version 1.0 – Issue Date: 10APR2023

Protocol Number: SMU 19-01 GENS

Patterns of Tobacco and Nicotine Product Use

Patterns of General Snus® use at each follow-up wave were **significantly different** than Wave 1.

- The proportion of every day users decreased from 89.0% at Wave 1 to 58.7% at Wave 4, and the proportion of some day users increased from 11.0% at Wave 1 to 27.4% at Wave 4.
- The number of days in the P30D that some day users reported they used General Snus® **did not significantly differ** from Wave 1 at any follow-up wave.
- Every day and some day users reported they used, on average, about 10 and about 6 General Snus® pouches/day, respectively, at each follow-up wave, which **did not significantly differ** from Wave 1.

Patterns of cigarette smoking at Waves 3 and 4 **did not significantly differ** from Wave 1 among the overall group of respondents who completed all four waves.

- There were also **no significant differences** in patterns of cigarette smoking at any follow-up wave among the subset of respondents who had quit use of General Snus® during the study.

Compared to Wave 1, use of nicotine pouches **significantly increased** at Waves 3 and 4; use of aids to help stop smoking¹ also **significantly increased** from Wave 1 at each follow-up wave.

Overall, these results suggest that, while there were fewer General Snus® users at each follow-up wave, use of General Snus® was **not replaced with more harmful products**, such as cigarettes.

- Instead, respondents who quit use of General Snus® during the study **transitioned to potentially lower risk products**, such as nicotine pouches and/or aids to help stop smoking.

¹ Aids to help stop smoking asked in the survey were all non-prescription, nicotine-containing commercial products, such as NicoDerm® CQ and Nicorette® Gum or Lozenge.

Risk Perceptions of General Snus® and Cigarette Use

Overall findings suggest that some respondents are **misinformed about risks from using General Snus®** for development of certain diseases.

- About half of respondents at each study wave perceived using General Snus® is associated with a **moderate to very high chance** of developing mouth cancer and heart disease.
- However, nearly 90% of respondents at each study wave correctly perceived using General Snus® is associated with a **low to very low chance** of developing lung cancer.

At each study wave, respondents correctly perceived cigarette smoking is associated with **significant health risks**, as nearly all reported smoking contributes a **high to very high chance** of developing mouth cancer, lung cancer, and heart disease.

Dual use of General Snus® and cigarettes was perceived to be associated with **about the same health risks as using only cigarettes**, suggesting respondents understand that any amount of cigarette smoking is associated with significant disease risk.

- This result does not provide evidence of a “halo effect”² related to using General Snus® products, given they carry a modified risk claim.

Understanding of the General Snus® Modified Risk Tobacco Product Claim

Respondents generally understood the claim that using General Snus® instead of smoking cigarettes puts users at a lower risk of developing certain diseases.

- About 80% of respondents at each study wave correctly responded that using General Snus® instead of cigarettes presents a **lower risk** of developing the diseases stated in the modified risk claim.³
- About 85% of those who understood the modified risk messaging also correctly responded that **cigarette smokers must switch completely** to General Snus® (answered “zero cigarettes”) in order to reduce risks of developing certain diseases.

² Seidenberg AB, Popova L, Ashley DL, *et al.* **Inferences beyond a claim: a typology of potential halo effects related to modified risk tobacco product claims.** *Tobacco Control*. Volume 30 (2021).

³ Diseases included on the modified risk claim are the following: mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.

General Snus® Patterns of Use Study – Longitudinal Technical Report

Protocol Number: SMU 19-01 GENS

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TABLE OF CONTENTS

| | |
|---|----|
| SIGNATURES OF RESPONSIBLE PARTIES | 1 |
| Swedish Match North America..... | 1 |
| (b) (4) | 1 |
| EXECUTIVE SUMMARY | 2 |
| Study Overview | 2 |
| Longitudinal Results Among Respondents Completing All Waves | 2 |
| (b) (4) | 5 |
| DOCUMENT HISTORY | 6 |
| TABLE OF CONTENTS | 7 |
| LIST OF ABBREVIATIONS | 9 |
| 1. BACKGROUND & RATIONALE | 10 |
| 2. STUDY OBJECTIVES..... | 10 |
| 2.1 Primary Objectives..... | 11 |
| 2.2 Secondary Objectives..... | 11 |
| 3. OVERVIEW OF RESEARCH METHODS | 12 |
| 3.1 Inclusion Criteria | 13 |
| 3.2 Exclusion Criteria | 13 |
| 4. OVERVIEW OF ANALYSIS METHODS | 14 |
| 5. FIELDING SUMMARY ACROSS ALL WAVES..... | 15 |
| 5.1 Fielding Summary..... | 15 |
| 6. LONGITUDINAL RESULTS AMONG RESPONDENTS COMPLETING ALL WAVES | 16 |
| 6.1 Demographic Characteristics of Respondents Completing All Waves | 16 |
| 6.2 Longitudinal Results for Primary Objectives..... | 18 |
| 6.2.1 Tobacco and Nicotine Product Use in the Past 30 Days at Each Wave | 18 |
| 6.2.2 Tobacco and Nicotine Product Use in the Past 30 Days Among Respondents Who Had Quit Use of General Snus® at Each Wave | 25 |
| 6.2.3 Cigarette Quitting Behaviors at Each Wave..... | 31 |

General Snus® Patterns of Use Study – Longitudinal Technical Report

Protocol Number: SMU 19-01 GENS

Final – Version 1.0 – Issue Date: 10APR2023

| | | |
|-------|---|----|
| 6.2.4 | Percent of Days in the Past 30 Days that <i>General Snus</i> ® And Cigarettes Were Used and the Quantity Used on Days Used at Each Wave | 32 |
| 6.2.5 | Changes in Patterns of Use of <i>General Snus</i> ® and Cigarettes From Wave 1 to Wave 4 | 35 |
| 6.2.6 | Incremental, Supplemental, or Complete Substitution of Cigarettes for <i>General Snus</i> ® Among Dual Users of Both Cigarettes and <i>General Snus</i> ® at Each Follow-Up Wave..... | 37 |
| 6.3 | Longitudinal Results for Secondary Objectives..... | 40 |
| 6.3.1 | Perceptions of Absolute Risk for Use of Only <i>General Snus</i> ® Every Day and Use of Only Cigarettes Every Day at Each Wave | 40 |
| 6.3.2 | Perceptions of Absolute Risk for Use of Both <i>General Snus</i> ® and Cigarettes Every Day and Never Having Used Any Tobacco and Nicotine Products at Each Wave..... | 46 |
| 6.3.3 | Understanding of the Modified Risk Claim for <i>General Snus</i> ® | 51 |
| 7. | SUMMARY OF LONGITUDINAL RESULTS | 54 |
| 7.1 | Patterns of Tobacco and Nicotine Product Use | 54 |
| 7.2 | Risk Perceptions of <i>General Snus</i> ® and Cigarette Use | 55 |
| 7.3 | Understanding of the <i>General Snus</i> ® Modified Risk Tobacco Product Claim..... | 56 |

LIST OF ABBREVIATIONS

| Abbreviation | Definition |
|--------------|---|
| FDA | United States Food & Drug Administration |
| MRTP | Modified Risk Tobacco Product |
| MRTPA | Modified Risk Tobacco Product Application |
| P30D | Past 30 Days |
| PATH | Population Assessment of Tobacco and Health |
| PMTA | Premarket Tobacco Product Application |
| SAP | Statistical Analysis Plan |
| SMNA | Swedish Match North America |
| SMU | Swedish Match USA |
| TNP | Tobacco and Nicotine Product |
| U.S. | United States |

1. BACKGROUND & RATIONALE

In November 2015, Swedish Match USA, Inc. (SMU) received market authorization for *General Snus*®, a moist tobacco product placed under the upper lip that does not involve spitting or chewing. In its first applications reviewed through the MRTP pathway, the FDA deferred final action on providing *General Snus*® a MRTP designation, providing guidance on how SMU could amend their application to provide greater support for a modified risk designation. SMU filed its amended MRTPA on 17 September 2018, and the FDA granted the risk modification order on 22 October 2019. The *General Snus*® Patterns of Use Study (the study) is for post-marketing surveillance reporting following the granted risk modification order.

2. STUDY OBJECTIVES

The overarching research questions for the study were the following:

1. How do *General Snus*® users use tobacco and nicotine products (TNP)?
2. How do *General Snus*® users perceive health risks associated with cigarettes and *General Snus*®?

These questions were studied using a self-reported survey examining patterns of past-30-day (P30D) TNP use among *General Snus*® users in a Baseline assessment (Wave 1) and again, among the same *General Snus*® users, at 6 months (Wave 2), 1 year (Wave 3) and 2 years (Wave 4) after Baseline.

2.1 PRIMARY OBJECTIVES

The primary objectives of the study were the following:

1. Compare patterns of TNP use between all four study waves by examining self-reported TNP use for participants, in aggregate, over time.
 - The study will report on frequency of use of *General Snus*® use, as well as other TNP, if multiple TNP use is reported. Of specific interest were patterns of cigarette use.
 - Intent to quit and actual quitting of cigarettes was assessed at each wave of the study.
2. Among *General Snus*® users, compare consumption patterns of cigarettes and *General Snus*® in the P30D at Baseline with consumption patterns for both products at Wave 2 through Wave 4.
 - Of specific interest was whether use of *General Snus*® offsets use of cigarettes.
3. Characterize *General Snus*® users, especially new *General Snus*® users, in terms of prior TNP use and demographic characteristics and compare these findings to new users of smokeless TNP as reported in the Population Assessment of Tobacco and Health Study.
4. Compare the tendencies of *General Snus*® users to quit cigarettes or use *General Snus*® in an incremental fashion, in a supplemental fashion, or in complete substitution of cigarettes.

2.2 SECONDARY OBJECTIVES

The secondary objectives of the study were the following:

1. Assess perceptions of risk of certain health conditions (mouth cancer, heart disease and lung cancer, separately) among *General Snus*® users.
 - Assess the absolute risk attributed to using only *General Snus*® daily, smoking only cigarettes daily, dual use of *General Snus*® and cigarettes daily, and never having used any TNP.
2. Assess the extent to which *General Snus*® users, especially new users, understand the risk reduction as described in the modified risk claim

3. OVERVIEW OF RESEARCH METHODS

General Snus® users were recruited directly via invitation stickers placed directly on *General Snus*® tins. A third-party vendor (News America Marketing) was hired to place the study invitation stickers on product packaging (e.g., each individual *General Snus*® tin) for all varieties of *General Snus*® available at retail outlets. This took place from 25 July 2020 to 17 August 2020. The sticker initiative targeted approximately 10,600 retail stores carrying *General Snus*® across all locations where *General Snus*® was sold. The sticker presented a website where *General Snus*® users that were interested in participating could access the Baseline survey through a secure and unique survey link.

The first set of questions were used to screen potential respondents and were designed to qualify the respondent using the study inclusion and exclusion criteria. Once qualified, respondents were directed to the online survey. Respondents were asked to self-report TNP use within the P30D and various questions related to TNP use, risk perceptions, and understanding of the modified risk messaging for *General Snus*® products.

The study was a longitudinal, prospective assessment consisting of multiple survey waves to gain an understanding of how *General Snus*® and other TNP are used by the participating respondents. Respondents completed an initial survey at Baseline (Wave 1) and had the opportunity to participate again at 6 months (Wave 2), 1 year (Wave 3), and 2 years (Wave 4) from Baseline. All respondents at Baseline must have reported use of *General Snus*® at least once in the P30D and reported use every day (daily) or on some days (non-daily).

Full details of all research methods and study procedures can be found in the *General Snus*® Patterns of Use Study – Study Protocol.

3.1 INCLUSION CRITERIA

Respondents had to meet each of the following criteria to be included in the study:

1. Have used *General Snus*® at least once or more within the P30D and use it every day or on some days.
2. Minimum age of 21 years.
3. Agree to participate in four surveys over the 2-year (24-month) period.
4. Able to read and speak English.
5. Currently a resident of the United States.
6. Agreeing to provide informed consent and personal contact information.

3.2 EXCLUSION CRITERIA

Respondents who met of the following criteria were excluded from the study:

1. Responded “don’t know” or “decline to answer” to questions asking their gender and geographic region.
2. Unwilling or unable to provide electronic informed consent and personal contact information.
3. Employed in any of the following fields or professions: market research, marketing, advertising, TNP manufacturing, or employed as a physician.
4. Participated in a consumer research study on TNP in the 2 weeks prior to the Baseline survey.

4. OVERVIEW OF ANALYSIS METHODS

All analyses conducted were either descriptive or inferential. Descriptive analyses provided summary statistics for all variables. These statistics included counts and proportions for categorical variables and means, standard deviations, medians, minimums, and maximums for ordinal and continuous variables. Inferential statistical testing was conducted to evaluate changes in primary and secondary outcome measures (i.e., patterns of use, risk perceptions, understanding of claims) from baseline and each follow-up wave. Results comparing baseline data versus data from each follow-up wave was conducted using paired sample t-tests for continuous variables and McNemar tests or Wilcoxon sum-rank tests (where applicable per sample size restrictions) for categorical variables.

5. FIELDING SUMMARY ACROSS ALL WAVES

5.1 FIELDING SUMMARY

The fielding summary for number of respondents that entered the survey for each wave of the study, that were terminated, and included in analyses are summarized below in [Table 1](#). The number of respondents completing all study waves was n=281, resulting in a 17.0% full-study retention rate (based on the N=1,655 respondents participating at Wave 1). All n=281 respondents completing all study waves were included in the analyses described in this report.

Table 1: Fielding Summary Across All Waves

| Fielding Event | Number of Respondents | Percent of Respondents ¹ |
|---|-----------------------|-------------------------------------|
| Entered Wave 1 Survey | 4,581 | --- |
| <i>Terminated/Excluded from Analyses²</i> | <i>2,926</i> | <i>---</i> |
| Included in Wave 1 Analyses | 1,655 | 100.0% |
| Entered Wave 2 Survey | 931 | 56.3% |
| <i>Terminated/Excluded from Analyses²</i> | <i>236</i> | <i>14.3%</i> |
| Included in Wave 2 Analyses | 695 | 42.0% |
| Entered Wave 3 Survey | 728 | 44.0% |
| <i>Terminated/Excluded from Analyses²</i> | <i>142</i> | <i>8.6%</i> |
| Included in Wave 3 Analyses | 586 | 35.4% |
| Entered Wave 4 Survey | 589 | 35.6% |
| <i>Terminated/Excluded from Analyses²</i> | <i>138</i> | <i>8.3%</i> |
| Included in Wave 4 Analyses | 451 | 27.3% |
| Completed All Waves and Included in Analyses³ | 281 | 17.0% |
| ¹ Percent of respondents based on the number included in Wave 1 analyses (N=1,655). ² Terminated/excluded from analyses represents respondents who were terminated from the survey or were not included in analyses. Reasons for termination included the following: failed to meet inclusion criteria or exiting the survey prematurely. Reasons for not being included in analyses included the following: identified as a straightliner, speeder, failed an attention check question, or provided illogical responses based on definitions outlined in the statistical analysis plan (SAP). ³ Represents the full-study retention rate. | | |

6. LONGITUDINAL RESULTS AMONG RESPONDENTS COMPLETING ALL WAVES

6.1 DEMOGRAPHIC CHARACTERISTICS OF RESPONDENTS COMPLETING ALL WAVES

Demographic characteristics of *General Snus*® users and the subset of new *General Snus*® users (i.e., respondents who had initiated use of *General Snus*® in the past 30 days [P30D] at Wave 1 [Baseline]) who completed all four study waves are summarized in [Table 2](#). Each demographic characteristic listed in [Table 2](#) was assessed at Wave 1. Geographic region, respondent age, marital status, and household income were reassessed at each follow-up wave as they may have changed over the course of the study period – results in [Table 2](#) for those characteristics represent responses collected at Wave 4 (Year 2). Only results for the overall group of *General Snus*® users is discussed here given the small sample size of new *General Snus*® users (n=7).

Most respondents who completed all waves lived either in the South (31.7%; n=89) or in the Midwest (31.0%, n=87). Nearly all respondents were male (93.6%, n=263) and White (89.7%, n=252). The mean age of all respondents was 37 years. Over half of respondents were currently married (56.2%, n=158). There was a considerable number of respondents with high household incomes, as 35.9% (n=101) reported that their household earned \$100,000 or more in the past 12 months. Just over half of all respondents had obtained a Bachelor's degree (36.1%, n=101) or a post-graduate degree (15.0%, n=42) as of Wave 1.

Table 2: Demographic Characteristics of Respondents Completing All Waves

| | General Snus® Users | New General Snus® Users* |
|---|---------------------|--------------------------|
| | N=281 | N=7 |
| Geographic Region | | |
| Northeast (%) | 39 (13.9%) | 0 (0.0%) |
| Midwest (%) | 87 (31.0%) | 3 (42.9%) |
| South (%) | 89 (31.7%) | 2 (28.6%) |
| West (%) | 66 (23.5%) | 2 (28.6%) |
| Respondent Age | | |
| Mean age (years) + Std Dev | 37 ± 10 | 34 ± 13 |
| 21-24 (%) | 21 (7.5%) | 2 (28.6%) |
| 25-34 (%) | 105 (37.4%) | 2 (28.6%) |
| 35-44 (%) | 103 (36.7%) | 1 (14.3%) |
| 45-54 (%) | 35 (12.5%) | 1 (14.3%) |
| 55+ (%) | 17 (6.0%) | 1 (14.3%) |
| Gender | | |
| Male (%) | 263 (93.6%) | 4 (57.1%) |
| Female (%) | 18 (6.4%) | 3 (42.9%) |
| Racial or Ethnic Background | | |
| Caucasian/White (%) | 252 (89.7%) | 5 (71.4%) |
| Black/African American (%) | 2 (0.7%) | 0 (0.0%) |
| Hispanic (e.g., Latin American, Mexican, Puerto Rican, Cuban) (%) | 7 (2.5%) | 0 (0.0%) |
| Asian or Pacific Islander (%) | 5 (1.8%) | 1 (14.3%) |
| Native American or Alaskan native (%) | 3 (1.1%) | 0 (0.0%) |
| Mixed racial background (%) | 11 (3.9%) | 1 (14.3%) |
| Other (%) | 1 (0.4%) | 0 (0.0%) |
| Highest Grade or Level of School Completed | | |
| Less than high school (%) | 0 (0.0%) | 0 (0.0%) |
| Some high school, no diploma (%) | 0 (0.0%) | 0 (0.0%) |
| General Educational Development (GED) (%) | 13 (4.6%) | 1 (14.3%) |
| High school graduate - diploma (%) | 14 (5.0%) | 2 (28.6%) |
| Some college but no degree (%) | 72 (25.7%) | 2 (28.6%) |
| Associate degree (%) | 38 (13.6%) | 0 (0.0%) |
| Bachelor's degree (e.g., BA, AB, BS) (%) | 101 (36.1%) | 1 (14.3%) |
| Post-graduate degree (e.g., MBA, PhD, JD, etc.) (%) | 42 (15.0%) | 1 (14.3%) |
| Marital Status | | |
| Now married (%) | 158 (56.2%) | 3 (42.9%) |
| Widowed (%) | 4 (1.4%) | 1 (14.3%) |
| Divorced (%) | 25 (8.9%) | 0 (0.0%) |
| Separated (%) | 3 (1.1%) | 0 (0.0%) |
| Never married (%) | 90 (32.0%) | 3 (42.9%) |
| Decline to answer (%) | 1 (0.4%) | 0 (0.0%) |
| Household Income in the Past 12 Months | | |
| Less than \$24,999 (%) | 20 (7.1%) | 2 (28.6%) |
| \$25,000 to \$49,999 (%) | 49 (17.4%) | 1 (14.3%) |
| \$50,000 to \$74,999 (%) | 51 (18.1%) | 1 (14.3%) |
| \$75,000 to \$99,999 (%) | 49 (17.4%) | 1 (14.3%) |
| \$100,000 or more (%) | 101 (35.9%) | 2 (28.6%) |
| Don't know (%) | 2 (0.7%) | 0 (0.0%) |
| Decline to answer (%) | 9 (3.2%) | 0 (0.0%) |
| New General Snus® users were defined as respondents who had initiated using General Snus® in the P30D at Wave 1 (Baseline). | | |

6.2 LONGITUDINAL RESULTS FOR PRIMARY OBJECTIVES

6.2.1 TOBACCO AND NICOTINE PRODUCT USE IN THE PAST 30 DAYS AT EACH WAVE

Patterns of TNP use in the P30D were assessed at each wave. At Wave 1 (Baseline), TNP use in the P30D was asked to respondents who indicated they had ever regularly used any of eleven categories of TNP in their lifetime, including *General Snus*® products. TNP use in the P30D was asked to all returning respondents for the same eleven categories of TNP at each follow-up wave (Waves 2, 3, and 4). TNP use at each follow-up wave was compared to Wave 1 to understand potential changes in patterns of use over the course of the study. These results are presented in [Table 3](#) below.

Patterns of *General Snus*® use at each follow-up wave were **significantly different** than Wave 1 among the N=281 respondents who completed all four waves ($p < 0.001$ at Waves 2, 3, and 4). The number of every day *General Snus*® users decreased from 89.0% (n=250) at Wave 1 to 58.7% (n=165) at Wave 4. Respondents throughout the study who moved away from every day use mostly switched to some day use versus not using *General Snus*® at all (quitting) – the number of some day users increased from 11.0% (n=31) at Wave 1 to 27.4% (n=77) at Wave 4, and 13.2% (n=37) reported they had not used the product at all at Wave 4 ([Table 3](#)).

At Wave 1, 13.2% (n=37) of respondents who completed all four waves reported they currently smoked cigarettes, with 6.4% (n=18) smoking every day and 6.8% (n=19) smoking on some days. Patterns of cigarette smoking at Wave 2 **did not significantly differ** from Wave 1 ($p = 0.379$). There were slightly more respondents who reported they currently smoked cigarettes at Wave 3 (15.3%, n=43), with fewer every day smokers (3.2%, n=9) and more some day smokers (12.1%, n=34), which was **significantly different** than Wave 1 ($p = 0.015$). Patterns of cigarette smoking at Wave 4 **did not significantly differ** from Wave 1 ($p = 0.179$) ([Table 3](#)).

Only n=1 additional respondent reported using moist snuff at Wave 2 (28.4%, n=80) than at Wave 1 (28.1%, n=79), but the overall pattern of use was **significantly different** ($p = 0.046$) because the proportion of every day users was higher (Wave 2: 13.5%, n=38 | Wave 1: 10.7%, n=30) and some day users was lower (Wave 2: 14.9%, n=42 | Wave 1: 17.4%, n=49). Patterns of moist snuff use at Wave 3 and Wave 4, however, **did not significantly differ** from Wave 1 ($p = 0.399$ and $p = 0.791$, respectively) ([Table 3](#)).

Use of nicotine pouches **significantly increased** at Wave 3 ($p < 0.001$) and Wave 4 ($p < 0.001$), as 41.6% ($n=117$) and 43.8% ($n=123$) of respondents used nicotine pouches at these waves, respectively, compared to 36.3% ($n=102$) at Wave 1. Additionally, the number of respondents who reported use of aids to help stop smoking **significantly increased** from Wave 1 at each follow-up wave ($p < 0.05$ at Waves 2, 3, and 4). At Wave 1, 3.2% ($n=9$) respondents reported using aids to help stop smoking versus 7.2% ($n=20$), 8.2% ($n=23$), and 6.4% ($n=18$) at Waves 2, 3, and 4, respectively ([Table 3](#)).

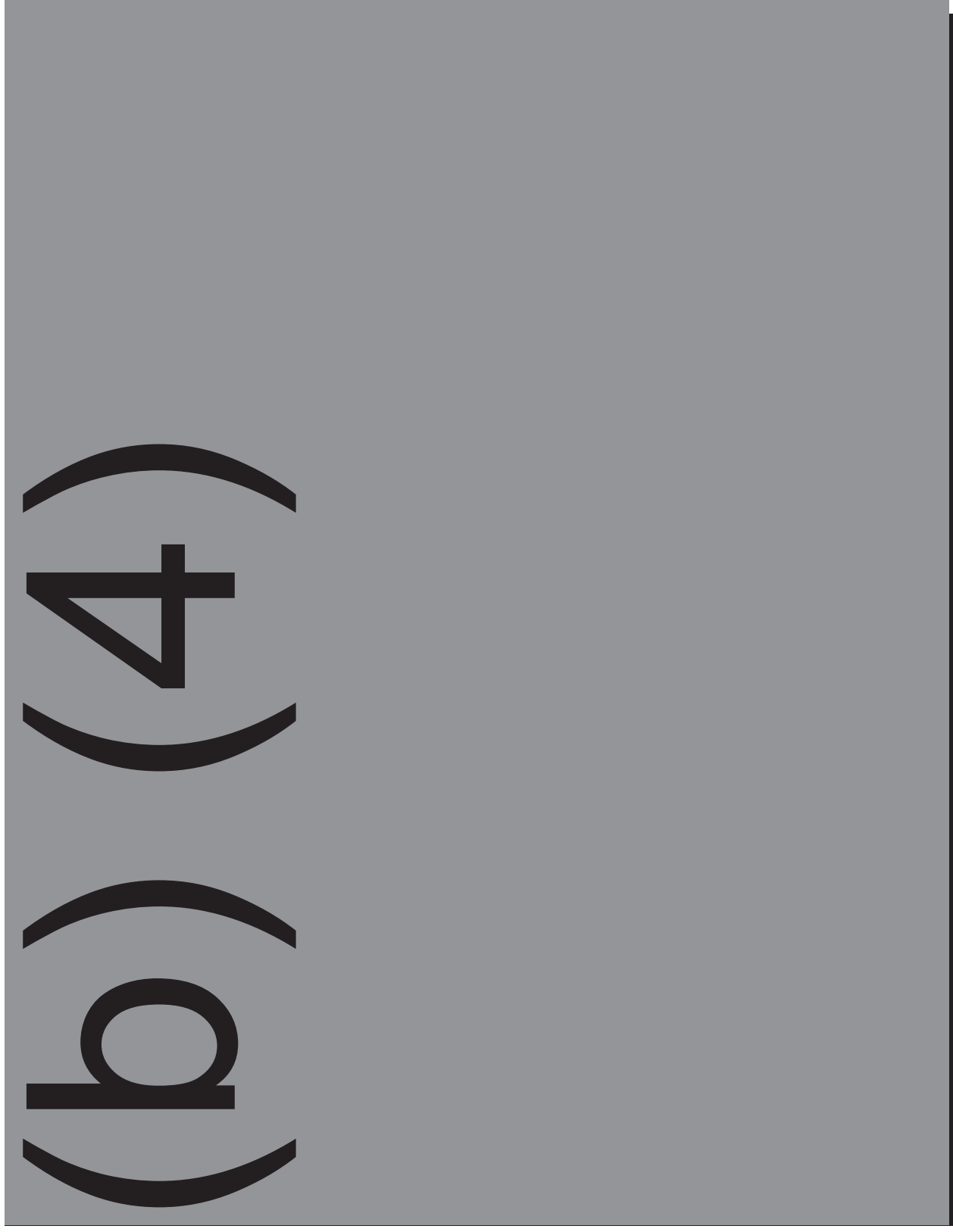
Overall, these results suggest that while there were fewer *General Snus*® users at each follow-up wave, use of *General Snus*® was not replaced with use of more harmful products, such as cigarettes and traditional smokeless tobacco (i.e., moist snuff and chewing tobacco). Instead, respondents who quit use of *General Snus*® throughout the course of the study transitioned to use of nicotine pouches and/or aids to help stop smoking.⁴

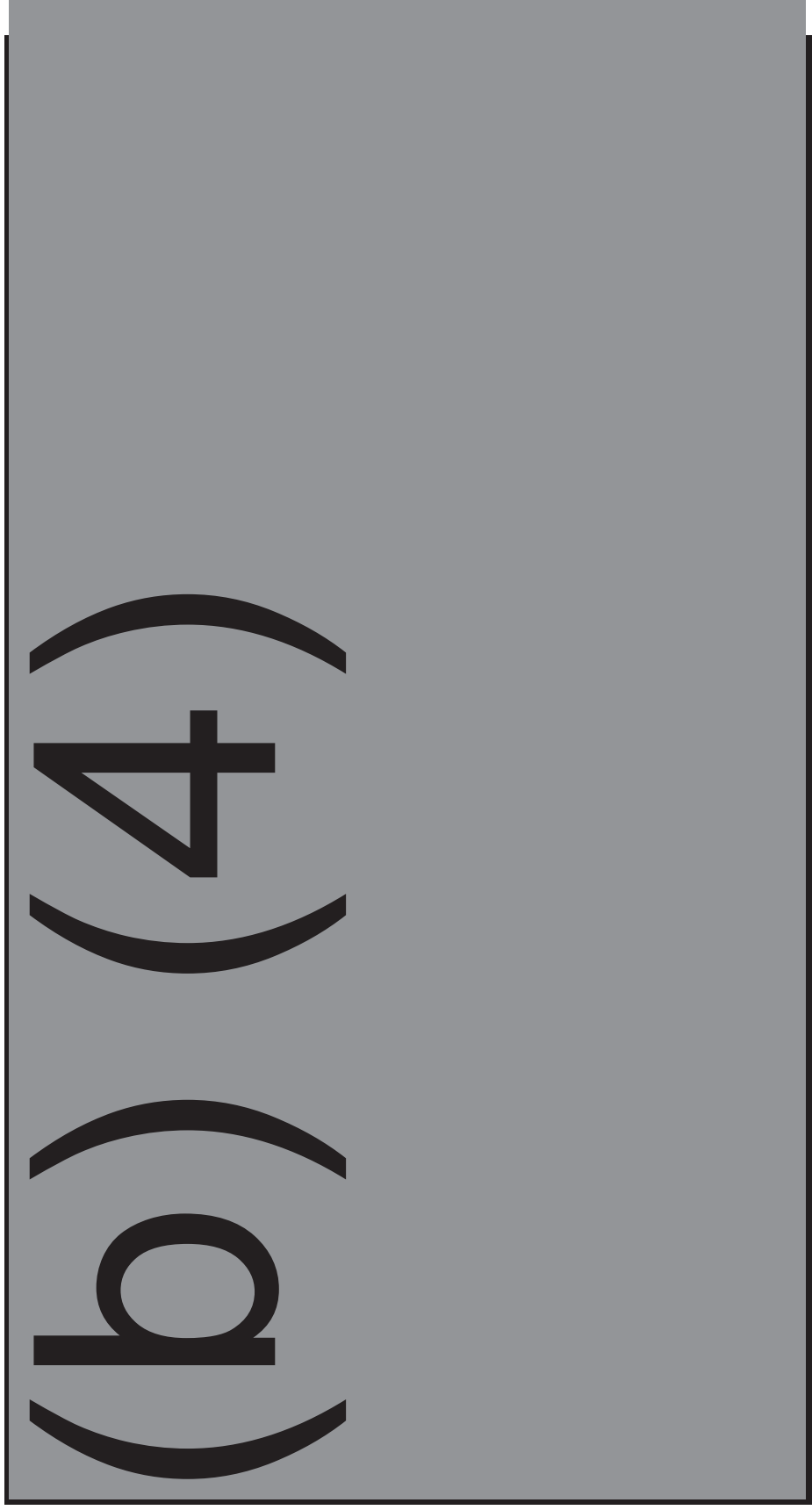
⁴ Aids to help stop smoking asked in the survey were all non-prescription, nicotine-containing commercial products, such as NicoDerm® CQ and Nicorette® products.

Table 3: Tobacco and Nicotine Product Use in the Past 30 Days at Each Wave

(b) (4)

(b) (4)





(b) (4)

6.2.2 TOBACCO AND NICOTINE PRODUCT USE IN THE PAST 30 DAYS AMONG RESPONDENTS WHO HAD QUIT USE OF *GENERAL SNUS*® AT EACH WAVE

TNP use in the P30D is reported in [Table 4](#) among respondents that initially used *General Snus*® at Wave 1 but had quit use of *General Snus*® at a given follow-up wave. Because different numbers of respondents reported not using *General Snus*® at each follow-up wave, statistical tests were conducted within-subject to ensure follow-up TNP use was comparable to Wave 1. It should be noted that the same respondent can be represented in one or multiple follow-up waves – for example, respondents who quit use of *General Snus*® at Wave 2 and never re-initiated use are represented in Wave 3 and Wave 4 analyses. Any comparison that had too little variation to be modeled is reported as an undefined p-value.

Patterns of *General Snus*® use at each follow-up wave were **significantly different** than Wave 1 because all respondents represented had quit use of the product ($p < 0.001$ at Waves 2, 3, and 4 vs. Wave 1).

There were **no significant differences** in patterns of cigarette smoking among those who had quit use of *General Snus*® throughout the course of the study ($p > 0.05$ at Waves 2, 3, and 4 vs. Wave 1). There were also **significantly fewer** respondents who used moist snuff at Wave 3 and Wave 4 than at Wave 1 among those who had quit use of *General Snus*® ($p = 0.024$ and $p = 0.009$, respectively).

Patterns of nicotine pouch use were **significantly different** at Wave 4 than at Wave 1 ($p = 0.002$); there were more every day nicotine pouch users at Wave 4 ($n = 15$) than at Wave 1 ($n = 5$), though the total number of respondents using nicotine pouches at both waves was the same ($n = 16$) among these respondents. There were also **significantly more** respondents who used aids to help stop smoking at Wave 4 ($n = 5$) than at Wave 1 ($n = 0$) among those who had quit use of *General Snus*® at Wave 4 ($p = 0.048$).

These results suggest that – like the overall cohort of *General Snus*® users – those who had quit use of *General Snus*® at a given follow-up wave did not replace *General Snus*® use with more harmful products, such as cigarettes or traditional smokeless tobacco (i.e., moist snuff and chewing tobacco). Instead, respondents who quit use of *General Snus*® throughout the course of the study transitioned to use of nicotine pouches and/or aids to help stop smoking.⁵

⁵ Aids to help stop smoking asked in the survey were all non-prescription, nicotine-containing commercial products, such as NicoDerm® CQ and Nicorette® products.

Table 4: Tobacco and Nicotine Product Use in the Past 30 Days Among Respondents Who Had Quit use of *General Snus*® at Each Wave

(b) (4)

(b) (4)

(b) (4)

(b) (4)

Attachment D - Response to CTP Correspondence dated December 14, 2023 (Page 222 of 253)

General Snus® Patterns of Use Study – Longitudinal Technical Report

Final – Version 1.0 – Issue Date: 10APR2023

Protocol Number: SMU 19-01 GENS

(b) (4)

6.2.3 CIGARETTE QUITTING BEHAVIORS AT EACH WAVE

Respondents were asked at each wave whether they had smoked cigarettes every day, on some days, or not at all in the P30D. Those who reported they had not smoked in the P30D were then asked whether they had quit smoking in the P30D, while those who reported smoking every day or some days were asked if they were currently trying to quit smoking.

The number of respondents who had quit smoking in the P30D at a given follow-up wave **did not significantly differ** from Wave 1 ($p>0.99$ at Waves 2, 3, and 4 vs. Wave 1). Additionally, the number of respondents who reported they were currently trying to quit smoking at a given follow-up wave **did not significantly differ** from Wave 1 ($p>0.05$ at Wave 2, 3, and 4 vs. Wave 1) ([Table 5](#)).

Table 5: Cigarette Quitting Behaviors at Each Wave

(b) (4)

6.2.4 PERCENT OF DAYS IN THE PAST 30 DAYS THAT *GENERAL SNUS*® AND CIGARETTES WERE USED AND THE QUANTITY USED ON DAYS USED AT EACH WAVE

Respondents who returned for a given follow-up wave were asked whether they used had used *General Snus*® every day, on some days, or not at all in the P30D. Some day users were asked how many days they used the product in the P30D. Every day users were assumed to have used the product on all 30 days. Every day and some day users were then asked how many *General Snus*® pouches they used on the days they used the product. These results are presented in [Table 6a](#) below.

The number of some day *General Snus*® users **significantly increased** from Wave 1 at each follow-up wave, ranging from 11.2% (n=31) at Wave 1 to 27.4% (n=77) at Wave 4 (see [Section 6.2.1](#)). However, the percentage of days that some day users reported they used the *General Snus*® **did not significantly differ** from Wave 1 for any follow-up wave ($p>0.05$ at Wave 2, 3, and 4 vs. Wave 1) ([Table 6a](#)).

The number of every day *General Snus*® users **significantly decreased** from Wave 1 at each follow-up wave, ranging from 89.0% (n=250) at Wave 1 to 58.7% (n=165) at Wave 4 (see [Section 6.2.1](#)). Every day users reported they used, on average, about 10 pouches/day at each wave. The average number of pouches/day among every day users **did not significantly differ** from Wave 1 for any follow-up wave ($p>0.05$ at Wave 2, 3, and 4 vs. Wave 1). At each wave, some day users reported they used, on average, fewer pouches/day than every day users. The average number of pouches/day among some day users **did not significantly differ** from Wave 1 for any follow-up wave ($p>0.05$ at Wave 2, 3, and 4 vs. Wave 1) ([Table 6a](#)).

Table 6a: Percent of Days *General Snus*® Was Used in the Past 30 Days and Quantity of *General Snus*® Used on Days Used at Each Wave

(b) (4)

Table 6b: Percent of Days Cigarettes Were Smoked in the Past 30 Days and Quantity of Cigarettes Smoked on Days Smoked at Each Wave

(b) (4)

6.2.5 CHANGES IN PATTERNS OF USE OF *GENERAL* SNUS® AND CIGARETTES FROM WAVE 1 TO WAVE 4

Patterns of use for *General* Snus® and cigarettes were measured at each wave by asking respondents whether they had used the products every day, some days, or not at all in the P30D. Wave 1 (Baseline) and Wave 4 (Year 2) patterns of use for *General* Snus® and cigarettes were compared to understand changes over the course of the study. Changes in patterns of use from Wave 1 to Wave 4 are presented in [Table 7](#) below.

All N=281 respondents – among those who completed all four waves – used *General* Snus® at Wave 1 because using *General* Snus® was an inclusion criterion to participate in the study.⁶ Most respondents who used the product every day at Wave 1 also used the product every day at Wave 4 (56.2%, n=158), while some had switched from every day use to some day use (22.4%, n=63). Others who were every day users at Wave 1 had quit use of *General* Snus® by Wave 4 (11.4%; n=32). Fewer respondents were some day users at both Wave 1 and Wave 4 (5.0%, n=14), while some had switched from some day use to every day use (2.5%, n=7). Some respondents who were some day users at Wave 1 had quit use of *General* Snus® by Wave 4 (1.8%; n=5) ([Table 7](#)).

There were n=37 respondents – among those who completed all four waves – who smoked cigarettes at Wave 1.⁷ Most respondents who smoked every day at Wave 1 also smoked every day at Wave 4 (62.2%, n=23), while some had switched from smoking every day to smoking some days (18.9%, n=7). Others who were every day smokers at Wave 1 had quit smoking by Wave 4 (5.4%, n=2). Fewer respondents were some day smokers at both Wave 1 and Wave 4 (8.1%, n=3), while some had switched from smoking some days to smoking every day (5.4%, n=2). No respondents who were some day smokers at Wave 1 had quit smoking by Wave 4 (0.0%, n=0) ([Table 7](#)).

⁶ Percentages in this section are calculated based on the N=281 *General* Snus® users at Wave 1 (Baseline). There were n=242 respondents – among those who completed all four waves – who used *General* Snus® at Wave 4 (Year 2).

⁷ Percentages in this section are calculated based on the n=37 cigarette smokers at Wave 1 (Baseline). There were n=40 respondents – among those who completed all four waves – who smoked cigarettes at Wave 4 (Year 2).

Table 7: Changes in Patterns of Use of *General Snus*® and Cigarettes from Wave 1 to Wave 4

(b) (4)

6.2.6 INCREMENTAL, SUPPLEMENTAL, OR COMPLETE SUBSTITUTION OF CIGARETTES FOR GENERAL SNUS® AMONG DUAL USERS OF BOTH CIGARETTES AND GENERAL SNUS® AT EACH FOLLOW-UP WAVE

Incremental and supplemental use of cigarettes and *General Snus*® and complete substitution of cigarettes for *General Snus*® was evaluated among dual users of both cigarettes and *General Snus*® at follow-up. Results were calculated by comparing frequency of use of both cigarettes and *General Snus*® at Wave 1 (Baseline) and subtracting frequency of use of the respective products at follow-up. Frequency of use was measured by asking respondents the quantity of cigarettes and *General Snus*® used on days used. Respondents included in analyses measuring incremental and supplemental use were those that did not switch their pattern of use for either product between Wave 1 and a given follow-up – meaning, every day users of either cigarettes or *General Snus*® at Wave 1 who also reported every day use at follow-up and some day users of either cigarettes or *General Snus*® at Wave 1 who also reported some day use at follow-up.

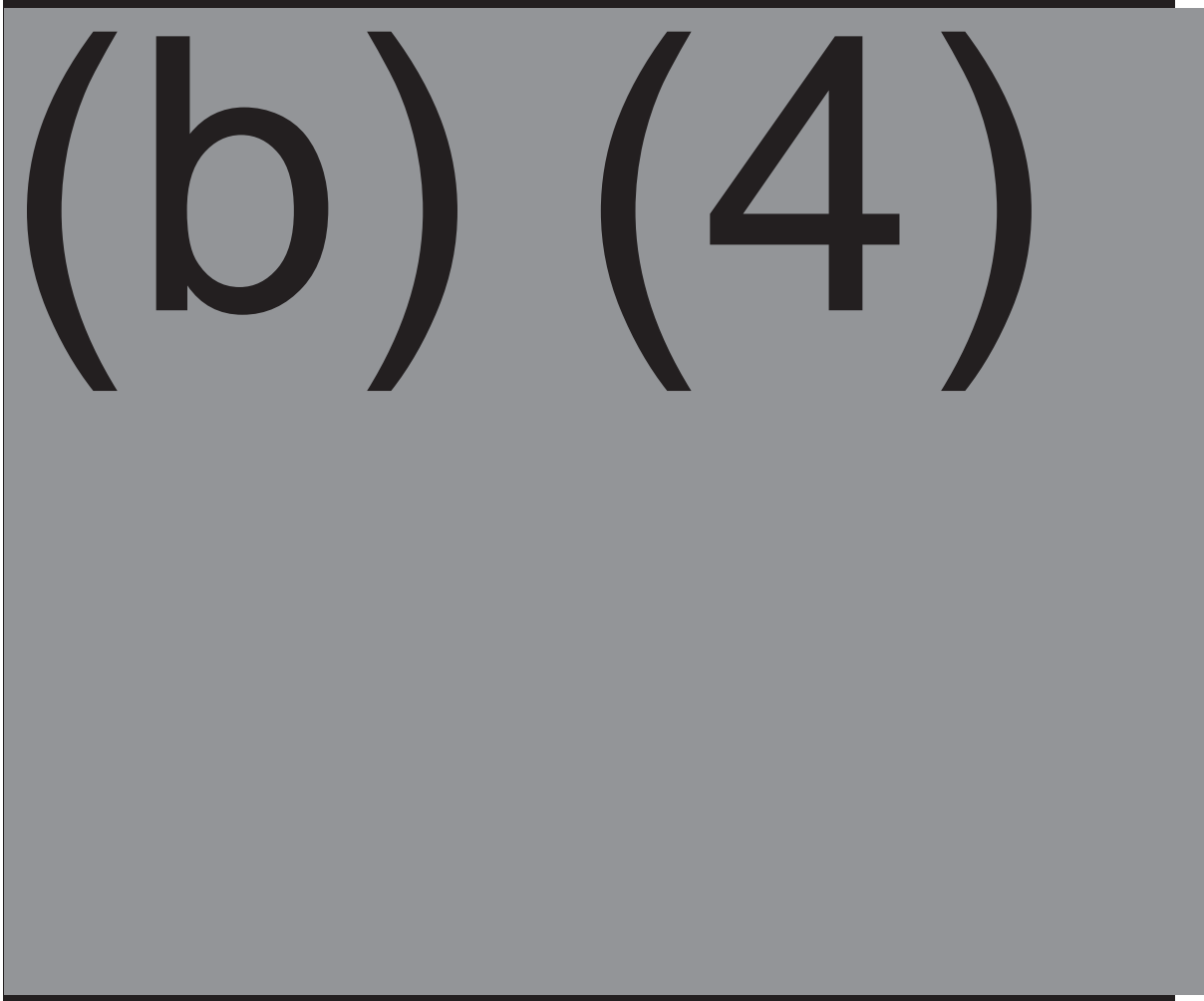
Incremental use was defined as using a greater or equal number of cigarettes or *General Snus*® at follow-up than at Wave 1; a difference in frequency of use between Wave 1 and follow-up resulting in a value that is positive or equal to zero was considered incremental use. Supplemental use was defined as using fewer cigarettes or *General Snus*® at follow-up than at Wave 1; a difference in frequency of use between Wave 1 and follow-up that is negative was considered supplemental use. Complete substitution was defined as fully replacing cigarette use and only using *General Snus*® or completely quitting use of both products. Results for incremental and supplemental use for both cigarettes and *General Snus*® are presented below in [Table 8a](#) and results for complete substitution are presented in [Table 8b](#).

There were **no significant differences** in use behavior among dual users of cigarettes or *General Snus*® – either incremental or supplemental – at any follow-up wave ($p > 0.05$ at Waves 2, 3, and 4 vs. Wave 1). Additionally, there were only slight changes in use of either product among these respondents, as the change in magnitude of *General Snus*® pouches used from Wave 1 to any follow-up wave was less than 1.0 pouch on for both every day and some day users, while the change in magnitude for cigarettes used was less than 3 cigarettes among every day smokers and less than 1 cigarette among some day smokers.

Results presented in [Table 8b](#) for complete substitution of cigarettes for *General Snus*® indicate that nearly all respondents who had quit smoking at any follow-up wave reported that they completely substituted cigarette use with *General Snus*® products. For example, at Wave 2, $n=9$ respondents had quit smoking and $n=8$ of those respondents reported exclusively using *General Snus*® instead.

Table 8a: Incremental or Supplemental Use of Cigarettes and *General Snus*® at Each Follow-Up Wave

(b) (4)

Table 8b: Complete Substitution of Cigarettes for *General Snus*® at Each Follow-Up Wave

6.3 LONGITUDINAL RESULTS FOR SECONDARY OBJECTIVES

6.3.1 PERCEPTIONS OF ABSOLUTE RISK FOR USE OF ONLY *GENERAL SNUS*® EVERY DAY AND USE OF ONLY CIGARETTES EVERY DAY AT EACH WAVE

All respondents evaluated the absolute risk of developing three diseases – mouth cancer, heart disease, lung cancer – from use of only *General Snus*® every day or from use of only cigarettes every day. This assessment was completed for each study wave. Perceptions of absolute risk were measured using a 5-point scale ranging from 1 (“Very low chance”) to 5 (“Very high chance”); “Don’t know” was also an available response option. These results are presented in [Table 9a](#) below.

General Snus® and other snus products contain markedly lower levels of harmful and potentially harmful constituents (HPHCs) compared to traditional smokeless tobacco. Numerous scientific publications have found no associations between use of snus products and development of mouth cancer^{8,9,10} or heart disease^{11,12,13}; this differs from use of traditional smokeless tobacco (e.g., moist snuff and chewing tobacco) for which associations with these diseases have been found.

⁸ Luo J, Ye W, Zendehdel K, *et al.* Oral use of Swedish moist snuff (snus) and risk for cancer of the mouth, lung, and pancreas in male construction workers: a retrospective cohort study. *The Lancet*. Volume 369 (2007).

⁹ Smita A, Labani S, Kailash U, *et al.* Association of smokeless tobacco use and oral cancer: a systematic global review and meta-analysis. *Nicotine & Tobacco Research*. Volume 21, Issue 9 (2019).

¹⁰ Araghi M, Galanti MR, Lundberg M, *et al.* No association between moist oral snuff (snus) use and oral cancer: pooled analysis of nine prospective observational studies. *Scandinavian Journal of Public Health*. Volume 28, Issue 8 (2021).

¹¹ Lee P. Summary of the epidemiological evidence relating snus to health: an updated review based on recent publications. *Harm Reduction Journal*. Volume 10, Issue 36 (2013).

¹² Hansson J, Galanti MR, Hergens MP, *et al.* Use of snus and acute myocardial infarction: pooled analysis of eight prospective observational studies. *European Journal of Epidemiology*. Volume 27 (2012).

¹³ Wennberg P, Eliasson M, Hallmans G, *et al.* The risk of myocardial infarction and sudden cardiac death amongst snuff users with or without a previous history of smoking. *Journal of Internal Medicine*. Volume 262, Issue 3 (2007).

Findings at all four study waves suggest that some *General Snus*® users are misinformed about the risk of developing mouth cancer from using the product. Just over half of the respondents who completed all four waves perceived use of *General Snus*® every day (and using no other TNP) to be associated with a moderate to very high chance of developing mouth cancer (50.2%, 50.2%, 52.7%, and 51.6% at Waves 1 – 4, respectively). Perceived risk of developing mouth cancer **did not significantly differ** from Wave 1 for any follow-up wave ($p>0.05$ at Wave 2, 3, and 4 vs. Wave 1).

Comparatively, respondents correctly perceived smoking cigarettes every day (and using no other TNP) to be associated with a higher risk of mouth cancer than using only *General Snus*® every day – higher proportions of respondents perceived smoking cigarettes every day with a moderate to very high chance of developing mouth cancer (77.2%, 78.6%, 81.9%, and 79.0% at Waves 1 – 4, respectively). Perceived risk of developing mouth cancer from smoking cigarettes every day **did not significantly differ** from Wave 1 for any follow-up wave ($p>0.05$ at Wave 2, 3, and 4 vs. Wave 1).

Findings at all four study waves also suggest that some *General Snus*® users are misinformed about the risk of developing heart disease from using the product. Less than half of the respondents who completed all four waves perceived use of only *General Snus*® every day to be associated with a moderate to very high chance of developing heart disease (40.6%, 42.0%, 48.0%, 47.0% at Waves 1 – 4, respectively). Perceived risk of developing heart disease was **significantly higher** than Wave 1 at Wave 3 ($p=0.017$) and Wave 4 ($p=0.019$).

Again, respondents correctly perceived smoking cigarettes every day (and using no other TNP) to be associated with a higher risk of developing heart disease than using only *General Snus*® every day – nearly all respondents perceived smoking cigarettes every day with a moderate to very high chance of developing heart disease (95.3%, 96.4%, 94.6%, 93.2% at Waves 1 – 4, respectively). Perceived risk of developing heart disease was **significantly lower** than Wave 1 at Wave 4, ($p=0.005$), but nearly all respondents still perceived cigarette smoking with significant risk of heart disease (93.2%, $n=262$). Thus, this finding is likely not meaningful.

Most respondents who completed all four waves correctly perceived use of only *General Snus*® every day to be associated with a low to very low chance of developing lung cancer (91.1%, 89.7%, 86.8%, 89.7% at Waves 1 – 4, respectively).¹⁴ The opposite was true for smoking cigarettes every day, as nearly all respondents reported smoking cigarettes was associated with a moderate to very high chance of developing lung cancer (96.8%, 93.2%, 93.9%, 92.2% at Waves 1 – 4, respectively).

General Snus® products can be marketed in the U.S. with the following modified risk messaging: “Using *General Snus*® instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.”¹⁵ Risk perceptions among respondents who completed all four waves provide evidence that current and former *General Snus*® users generally understood the product is reduced risk compared to cigarettes, but that use of *General Snus*® is not without risks to health. Findings also provide evidence that respondents correctly attribute use of only *General Snus*® to reductions in risk of developing the specific diseases stated in the modified risk messaging and that cigarette smoking contributes very high risks to health and to the development of mouth cancer, heart disease, and lung cancer.

¹⁴ Clarke E., Thompson K., Weaver S., *et al.* **Snus: a compelling harm reduction alternative to cigarettes.** *Harm Reduction Journal*. Volume 16, Issue 62 (2019).

¹⁵ U.S. Food and Drug Administration. **FDA grants first-ever modified risk orders to eight smokeless tobacco products.** Press Release (2019).

Table 9a: Perceptions of Absolute Risk for Use of Only General Snus® Every Day and Use of Only Cigarettes Every Day at Each Wave

(b) (4)

(b) (4)

(b) (4)

6.3.2 PERCEPTIONS OF ABSOLUTE RISK FOR USE OF BOTH *GENERAL SNUS*® AND CIGARETTES EVERY DAY AND NEVER HAVING USED ANY TOBACCO AND NICOTINE PRODUCTS AT EACH WAVE

All respondents evaluated the absolute risk of developing three diseases—mouth cancer, heart disease, lung cancer—from use of both *General Snus*® and cigarettes every day or from never having used any TNP. Perceptions of absolute risk were measured using a 5-point scale ranging from 1 (“Very low chance”) to 5 (“Very high chance”); “Don’t know” was also an available response option. These results are presented in [Table 9b](#).

Findings at all four study waves suggest that *General Snus*® users correctly understand that any cigarette smoking – regardless of whether the tobacco users also uses *General Snus*® – is of significant risks to health. High proportions of the respondents who completed all four waves perceived use of both cigarettes and *General Snus*® every day to be associated with a moderate to very high chance of developing mouth cancer (86.5%, 87.5%, 86.1%, and 86.5% at Waves 1 – 4, respectively). Perceived risk of developing mouth cancer **significantly higher** from Wave 1 at Wave 4 ($p=0.042$), but not at Wave 2 and Wave 3. Though the same proportion of respondents reported moderate to very high chances of developing mouth cancer at Wave 1 and Wave 4, the number reporting high and very high chances was higher at Wave 4 than at Wave 1.

Comparatively, respondents correctly perceived using no TNP at all to be associated with a lower risk of mouth cancer than using cigarettes or *General Snus*® alone or in combination – high proportions of respondents perceived using no TNP at all with low or very low chances of developing mouth cancer (87.2%, 87.9%, 87.2%, and 91.1% at Waves 1 – 4, respectively). Perceived risk of developing mouth cancer from using no TNP at all **did not significantly differ** from Wave 1 for any follow-up wave ($p>0.05$ at Wave 2, 3, and 4 vs. Wave 1).

Findings at all four study waves also suggest that *General Snus*® users correctly understand that any cigarette smoking – regardless of whether the tobacco users also uses *General Snus*® – is of significant risk to developing heart disease. Nearly all respondents who completed all four waves perceived use of both cigarettes and *General Snus*® every day to be associated with a moderate to very high chance of developing heart disease (94.0%, 95.0%, 94.0%, 92.5% at Waves 1 – 4, respectively). Perceived risk of developing heart disease **did not significantly differ** from Wave 1 at any follow-up wave ($p>0.05$ at Waves 2, 3, and 4 vs. Wave 1).

Respondents perceived using no TNP at all to be associated with a lower risk of developing heart disease than using cigarettes or *General Snus*® alone or in combination, but that using no TNP at all was still associated with significant risk of developing heart disease – over half of respondents perceived using no TNP at all with a moderate to very high chance of developing heart disease (67.6%, 64.8%, 59.7%, 54.1% at Waves 1 – 4, respectively). Perceived risk of developing heart disease was **significantly lower** than Wave 1 at Wave 3 ($p=0.003$) and Wave 4 ($p<0.001$).

Nearly all respondents who completed all four waves correctly perceived use of both cigarettes and *General Snus*® every day to be associated with a moderate to very high chance of developing lung cancer (93.6%, 94.7%, 94.3%, 93.6% at Waves 1 – 4, respectively).¹⁶ The opposite was true for using no TNP at all, as high proportions of respondents perceived using no TNP at all with a low to very low chance of developing lung cancer (78.6%, 80.4%, 85.4%, 86.8% at Waves 1 – 4, respectively). Perceived risk of developing lung cancer from using no TNP at all was **significantly lower** than Wave 1 at Wave 3 ($p=0.26$) and Wave 4 ($p=0.013$).

As *General Snus*® is a modified risk tobacco product (MRTP) and carries a modified risk message¹⁷, this finding provides evidence that respondents do not perceive that supplementing cigarette use with *General Snus*® (dual use) reduces risks for developing diseases from cigarette use – perceived risks associated with dual use of *General Snus*® and cigarettes every day were similar in magnitude to perceived risks associated with use of only cigarettes every day ([Table 9a](#)). Thus, these results do not provide evidence of a “halo effect” related to use of *General Snus*®, a concern that has recently been raised by both public health researchers and FDA.¹⁸

¹⁶ Clarke E., Thompson K., Weaver S., *et al.* **Snus: a compelling harm reduction alternative to cigarettes.** *Harm Reduction Journal*. Volume 16, Issue 62 (2019).

¹⁷ The modified risk messaging approved for *General Snus*® states the following: “Using *General Snus*® instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.” U.S. Food and Drug Administration. **FDA grants first-ever modified risk orders to eight smokeless tobacco products.** Press Release (2019).

¹⁸ Seidenberg AB, Popova L, Ashley DL, *et al.* **Inferences beyond a claim: a typology of potential halo effects related to modified risk tobacco product claims.** *Tobacco Control*. Volume 30 (2021).

Table 9b: Perceptions of Absolute Risk for Use of Both *General Snus*® and Cigarettes Every Day and Never Having Used Any Tobacco and Nicotine Products at Each Wave

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6.3.3 UNDERSTANDING OF THE MODIFIED RISK CLAIM FOR *GENERAL SNUS*®

Understanding of the modified risk claim for *General Snus*® was assessed at all four study waves. Two questions were asked. The first asked respondents to correctly identify the language used in the modified risk claim. Response options included “lower risk,” “higher risk,” or “the same risk” of developing certain diseases from using *General Snus*® compared to smoking cigarettes.¹⁹

Respondents who correctly answered this question (i.e., endorsed “lower risk”) were presented with a second question asking how many cigarettes that can be smoked per day while using *General Snus*® and still benefit from the reduction in risk of developing the diseases stated in the modified risk claim. Response options included “Zero cigarettes,” “Up to 5 cigarettes,” “Up to 20 cigarettes,” and “As many as you want to smoke.” “Don’t know” and “Decline to answer” were also available response options. The correct response option, based on language used in the modified risk claim, is “Zero cigarettes,” as the claim states a user must use *General Snus*® instead of cigarettes.

Results are presented in [Table 10](#) below and are separated between *General Snus*® users overall and new *General Snus*® users (defined as first using *General Snus*® in the 30 days prior to the Baseline survey). Only results for the overall group of *General Snus*® users are described here given the small sample size of new *General Snus*® users.

Most respondents correctly reported that use of *General Snus*® instead of cigarettes presents a lower risk of developing the diseases stated in the modified risk claim (77.2%, 72.6%, 79.0%, and 79.4% at Waves 1 – 4, respectively). Also, most respondents who correctly responded to the modified risk claim messaging then correctly reported that cigarettes could not be smoked (i.e., endorsed “Zero cigarettes”) and still benefit from the reduction in risk of developing the diseases stated in the modified risk claim (84.3%, 85.8%, 84.2%, 81.2% at Waves 1 – 4, respectively).

These findings suggest that respondents understood that use of *General Snus*® instead of cigarettes puts them at a lower risk of developing various tobacco-related diseases and that this reduction in risk is predicated on not smoking cigarettes (“Using *General Snus*® instead of cigarette[s]”).

¹⁹ Diseases included on the modified risk claim are the following: mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.

Table 10: Understanding of the MRTP Claim Related to Reduced Risk Among General Snus® Users and New General Snus® Users at Each Wave

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7. SUMMARY OF LONGITUDINAL RESULTS

7.1 PATTERNS OF TOBACCO AND NICOTINE PRODUCT USE

Patterns of *General Snus*® use at each follow-up wave were **significantly different** than Wave 1.

- The proportion of every day users decreased from 89.0% at Wave 1 to 58.7% at Wave 4, and the proportion of some day users increased from 11.0% at Wave 1 to 27.4% at Wave 4.
- The number of days in the P30D that some day users reported they used *General Snus*® **did not significantly differ** from Wave 1 at any follow-up wave.
- Every day and some day users reported they used, on average, about 10 and about 6 *General Snus*® pouches/day, respectively, at each follow-up wave, which **did not significantly differ** from Wave 1.

Patterns of cigarette smoking at Waves 3 and 4 **did not significantly differ** from Wave 1 among the overall group of respondents who completed all four waves.

- There were also **no significant differences** in patterns of cigarette smoking at any follow-up wave among the subset of respondents who had quit use of *General Snus*® during the study.

Compared to Wave 1, use of nicotine pouches **significantly increased** at Waves 3 and 4; use of aids to help stop smoking²⁰ also **significantly increased** from Wave 1 at each follow-up wave.

Overall, these results suggest that, while there were fewer *General Snus*® users at each follow-up wave, use of *General Snus*® was **not replaced with more harmful products**, such as cigarettes.

- Instead, respondents who quit use of *General Snus*® during the study **transitioned to potentially lower risk products**, such as nicotine pouches and/or aids to help stop smoking.

²⁰ Aids to help stop smoking asked in the survey were all non-prescription, nicotine-containing commercial products, such as NicoDerm® CQ and Nicorette® Gum or Lozenge.

7.2 RISK PERCEPTIONS OF GENERAL SNUS® AND CIGARETTE USE

Overall findings suggest that some respondents are **misinformed about risks from using General Snus®** for development of certain diseases.

- About half of respondents at each study wave perceived using General Snus® is associated with a **moderate to very high chance** of developing mouth cancer and heart disease.
- However, nearly 90% of respondents at each study wave correctly perceived using General Snus® is associated with a **low to very low chance** of developing lung cancer.

At each study wave, respondents correctly perceived cigarette smoking is associated with **significant health risks**, as nearly all reported smoking contributes a **high to very high chance** of developing mouth cancer, lung cancer, and heart disease.

Dual use of General Snus® and cigarettes was perceived to be associated with **about the same health risks as using only cigarettes**, suggesting respondents understand that any amount of cigarette smoking is associated with significant disease risk.

- This result does not provide evidence of a “halo effect”²¹ related to using General Snus® products, given they carry a modified risk claim.

²¹ Seidenberg AB, Popova L, Ashley DL, *et al.* **Inferences beyond a claim: a typology of potential halo effects related to modified risk tobacco product claims.** *Tobacco Control*. Volume 30 (2021).

7.3 UNDERSTANDING OF THE GENERAL SNUS® MODIFIED RISK TOBACCO PRODUCT CLAIM

Respondents generally understood the claim that using *General Snus*® instead of smoking cigarettes puts users at a lower risk of developing certain diseases.

- About 80% of respondents at each study wave correctly responded that using *General Snus*® instead of cigarettes presents a **lower risk** of developing the diseases stated in the modified risk claim.²²
- About 85% of those who understood the modified risk messaging also correctly responded that **cigarette smokers must switch completely** to *General Snus*® (answered “zero cigarettes”) in order to reduce risks of developing certain diseases.

²² Diseases included on the modified risk claim are the following: mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.

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GENERAL PROGRAMMING NOTES:

RANDOMIZE ALL LISTS, EXCEPT WHERE NOTED, THEN SHOW SAME ORDER OF THESE LISTS FOR EACH RESPONDENT

PROVIDE A PROGRESS BAR AT KEY POINTS

Draft copy of landing page and text; updated will be inserted once finalized.

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BASELINE AND FOLLOW-UP QUESTIONNAIRES

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BASELINE AND FOLLOW-UP QUESTIONNAIRES

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Job Number: 161103844-7 / CE: 10494415

Final v4.0 - Updated: June 28, 2022

BASELINE AND FOLLOW-UP QUESTIONNAIRES

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Job Number: 161103844-7 / CE: 10494415

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Job Number: 161103844-7 / CE: 10494415

Final v4.0 - Updated: June 28, 2022

BASELINE AND FOLLOW-UP QUESTIONNAIRES

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General Snus MRTTP
Post-Market Surveillance

Consumer Facing Materials

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TYPE OF REVIEW – EXEMPTION FROM IRB REVIEW DETERMINATION

Determination

Date: June 17, 2020

IRB ID: (b) (4)

Protocol: General Snus® Patterns of Use Study

Sponsor: (b) (4)

Principal
Investigator: (b) (4)

(b) (4) is in receipt of submission materials for the above-referenced study.

Items Reviewed:

- Exemption or Non-Human Subjects Research Determination Request
- Protocol (Date: 15 June 2020)
- Baseline Questionnaire (June 16, 2020)
- Consumer Facing Materials
- Perks Login Process

Based on the information available to the (b) (4) (or designee) has determined that:

The above-listed study is exempt from IRB review pursuant to the terms of the U.S. Department of Health and Human Service's Policy for Protection of Human Research Subjects at 45 C.F.R. §46.104(d).

(b) (4) has determined that the following exemption category(ies) applies:

- Category 2 Exemption (DHHS)

(b) (4) exemption determination is based on the study-related information available to (b) (4) as of the determination date listed above. Should any changes be made to the study subsequent to (b) (4), this determination is no longer applicable.

As the project applicant you are responsible for following all policies of (b) (4) as described in the Exemption or Non-Human Subjects Research Determination Request Submission Agreement which you accepted with project submission. It is your responsibility to ensure this project is conducted in accordance with applicable regulations (local, state and federal) as well as any requirements established by the IRB at the time of the review determination. Refer to the Investigator Handbook at (b) (4) details of these responsibilities.

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus[®] Patterns of Use
Protocol No. SMU 19-01GENS



Swedish Match USA, Inc.

Statistical Analysis Plan

General Snus[®] Patterns of Use Study

SMU 19-01GENS

Status: Approved
Date: 24 March 2020
Prepared by: (b) (4)

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Swedish Match USA, its parent and affiliate companies

(b) (4)**STATISTICAL ANALYSIS PLAN**General Snus® Patterns of Use
Protocol No. SMU 19-01GENS**TABLE OF CONTENTS**

| | |
|---|-----------|
| 1. LIST OF ABBREVIATIONS AND DEFINITIONS | 3 |
| 2. RESPONSIBLE PARTIES | 4 |
| 2.1 Investigator and Contributors | 4 |
| 2.1 Sponsor: Swedish Match USA, Inc. | 4 |
| 3. STATISTICAL ANALYSIS PLAN (SAP) AMENDMENTS AND UPDATES..... | 4 |
| 4. BACKGROUND AND RATIONALE | 5 |
| 5. OBJECTIVES | 5 |
| 5.1 Primary Objectives..... | 6 |
| 5.2 Secondary Objectives..... | 6 |
| 6. OVERALL STUDY DESIGN | 6 |
| 6.1 Study Design..... | 6 |
| 6.2 Study Cohorts..... | 8 |
| 6.2.1 Subject Selection: Inclusion Criteria..... | 8 |
| 6.2.2 Subject Selection: Exclusion Criteria..... | 8 |
| 6.3 Study Sample Size | 9 |
| 6.4 Variables of Relevance to the Study | 9 |
| 6.4.1 Outcomes..... | 9 |
| 6.4.2 Respondent Characteristics | 17 |
| 6.5 Time Points of Importance..... | 17 |
| 7. STATISTICAL ANALYSIS | 18 |
| 7.1 Presentation of Analysis Results..... | 18 |
| 7.2 Study Analysis | 18 |
| 7.3 Socio-demographic Characteristics | 19 |
| 7.4 Primary Objectives..... | 19 |
| 7.5 Secondary Objectives..... | 19 |
| 8. STATISTICAL AND ANALYTICAL ISSUES | 27 |
| 8.1 Data Capture and Management..... | 27 |
| 8.1.1 Data Capture..... | 27 |
| 8.1.2 Data Management and Analysis QC Process | 27 |
| 8.2 Handling of Missing Data..... | 28 |
| 8.3 Identification of Outliers..... | 29 |
| 9. REFERENCES..... | 30 |
| 10.TABLE SHELLS | 31 |

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

1. LIST OF ABBREVIATIONS AND DEFINITIONS

| Abbreviations | Definition |
|----------------------|---|
| CTP | Center for Tobacco Products |
| FDA | Food and Drug Administration |
| FTP | File Transfer Protocol |
| HINTS | Health Information National Trends Survey |
| MRTP | Modified Risk Tobacco Product |
| MRTPA | Modified Risk Tobacco Product Application |
| MTSS | Motivation To Stop Scale |
| PATH | Population Assessment of Tobacco and Health |
| PMTA | Premarket Tobacco Product Application |
| SAP | Statistical Analysis Plan |
| SAS® | Statistical Analysis System |
| SMNA | Swedish Match North America |
| SMU | Swedish Match USA, Inc. |
| TNP | Tobacco/Nicotine Product |
| U.S. | United States |

(b) (4)

STATISTICAL ANALYSIS PLAN
 General Snus® Patterns of Use
 Protocol No. SMU 19-01GENS

2. RESPONSIBLE PARTIES

2.1 Investigator and Contributors

Investigator: (b) (4)

(b) (4)

2.1 Sponsor: **Swedish Match USA, Inc.**
 Tryggve Ljung, PhD, Vice President, Scientific Affairs
 (b) (6)

3. STATISTICAL ANALYSIS PLAN (SAP) AMENDMENTS AND UPDATES

| Number | Date | Section of SAP | Amendment or Update | Reason |
|--------|------|----------------|---------------------|--------|
| | | | | |
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STATISTICAL ANALYSIS PLAN
General Snus[®] Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

^a “Tobacco/nicotine products” (TNP) refers to any combination of the following products: cigarettes, e-cigarettes, moist snuff, chewing tobacco, snus, nicotine pouches, cigars, cigarillos, and filtered cigars filled with tobacco, pipe tobacco, hookah and water pipe tobacco, and aids to help stop smoking. This list of tobacco/nicotine products defining TNP is based on the Population Assessment of Tobacco and Health.

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus[®] Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus[®] Patterns of Use

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus[®] Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus[®] Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus[®] Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

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STATISTICAL ANALYSIS PLAN[®]

(b) (4)

(b) (4)

Confidential

Page 15 of 59

Swedish Match 13024 Response to FDA 11724 Deficiency Letter for General Snus MRTP Renewal (Page 343 of 427)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use

(b) (4)

Confidential

Page 16 of 59

Swedish Match 13024 Response to FDA 11724 Deficiency Letter for General Snus MRTP Renewal (Page 344 of 427)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus[®] Patterns of Use
Protocol No. SMU 19-01GENS

6.4.2 Respondent Characteristics

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(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

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STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

Confidential

Page 20 of 59

Swedish Match 13024 Response to FDA 11724 Deficiency Letter for General Snus MRTP Renewal (Page 348 of 427)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus[®] Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus[®] Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

Confidential

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use

(b) (4)

(b) (4)

Confidential

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
SMU 19-01GENS

(b) (4)

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(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus[®] Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

Confidential

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
 General Snus® Patterns of Use
 Protocol No. SMU 19-01GENS

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(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

10. TABLE SHELLS

(b) (4)



(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
GENS

(b) (4)

Confidential

Page 33 of 59

Swedish Match 13024 Response to FDA 11724 Deficiency Letter for General Snus MRTP Renewal (Page 361 of 427)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

Confidential

Page 34 of 59

Swedish Match 13024 Response to FDA 11724 Deficiency Letter for General Snus MRTP Renewal (Page 362 of 427)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

Confidential

Page 35 of 59

Swedish Match 13024 Response to FDA 11724 Deficiency Letter for General Snus MRTP Renewal (Page 363 of 427)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

Confidential

Page 36 of 59

Swedish Match 13024 Response to FDA 11724 Deficiency Letter for General Snus MRTP Renewal (Page 364 of 427)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

Confidential

Page 37 of 59

Swedish Match 13024 Response to FDA 11724 Deficiency Letter for General Snus MRTP Renewal (Page 365 of 427)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

Confidential

Page 38 of 59

Swedish Match 13024 Response to FDA 11724 Deficiency Letter for General Snus MRTP Renewal (Page 366 of 427)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
GENS

(b) (4)

Confidential

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
GENS

(b) (4)

Confidential

(b) (4)

STATISTICAL ANALYSIS PLAN

General Snus® Patterns of Use

NS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

Confidential

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
ENS

(b) (4)

Confidential

Page 44 of 59

Swedish Match 13024 Response to FDA 11724 Deficiency Letter for General Snus MRTP Renewal (Page 372 of 427)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

Confidential

Page 45 of 59

Swedish Match 13024 Response to FDA 11724 Deficiency Letter for General Snus MRTP Renewal (Page 373 of 427)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus[®] Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

Confidential

Page 47 of 59

Swedish Match 13024 Response to FDA 11724 Deficiency Letter for General Snus MRTP Renewal (Page 375 of 427)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

Confidential

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

Confidential

Page 49 of 59

Swedish Match 13024 Response to FDA 11724 Deficiency Letter for General Snus MRTP Renewal (Page 377 of 427)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
SMU 19-01GENS

(b) (4)

Confidential

Page 50 of 59

Swedish Match 13024 Response to FDA 11724 Deficiency Letter for General Snus MRTP Renewal (Page 378 of 427)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus[®] Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

Confidential

Page 53 of 59

Swedish Match 13024 Response to FDA 11724 Deficiency Letter for General Snus MRTP Renewal (Page 381 of 427)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus[®] Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus[®] Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

Confidential

Page 56 of 59

Swedish Match 13024 Response to FDA 11724 Deficiency Letter for General Snus MRTP Renewal (Page 384 of 427)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus® Patterns of Use
Protocol No. SMU 19-01GENS

(b) (4)

(b) (4)

STATISTICAL ANALYSIS PLAN
General Snus[®] Patterns of Use
Protocol No. SMU 19-01GENS

-LAST PAGE-



General Snus® Patterns of Use Study – Version 4.0

Protocol **SMU 19-01GENS**

Swedish Match USA, Inc.

Protocol for General Snus® Patterns of Use Study

Protocol SMU 19-01GENS

Status: Approved

Date: 15 June 2020

Prepared by: (b) (4)

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General Snus® Patterns of Use Study – Version 4.0
Protocol SMU 19-01GENS

TABLE OF CONTENTS

| | |
|-------------------------|---|
| TABLE OF CONTENTS | 2 |
|-------------------------|---|

(b) (4)

General Snus® Patterns of Use Study – Version 4.0
Protocol *SMU 19-01GENS*

(b) (4)

General Snus® Patterns of Use Study – Version 4.0
Protocol *SMU 19-01GENS*

1. ABBREVIATIONS

| | |
|--------------------|---|
| CASRO | Council of American Survey Research Organizations |
| CTP | Center for Tobacco Products |
| FDA | Food and Drug Administration |
| FTP | File Transfer Protocol |
| HINTS | Health Information National Trends Survey |
| IRB | Institutional Review Board |
| MRTP | Modified Risk Tobacco Product |
| MRTPA | Modified Risk Tobacco Product Application |
| PATH | Population Assessment of Tobacco and Health |
| PII | Personally Identifiable Information |
| RESPONDENTS | Users of General Snus at Baseline survey |
| SAP | Statistical Analysis Plan |
| SAS | Statistical Analysis System |
| SMU | Swedish Match USA, Inc. |
| TNP | Tobacco/Nicotine Product(s) |
| U.S. | United States |

General Snus® Patterns of Use Study – Version 4.0
Protocol *SMU 19-01GENS*

(b) (4)

General Snus® Patterns of Use Study – Version 4.0
Protocol SMU 19-01GENS

(b) (4)

(b) (4)

(b) (4)

General Snus® Patterns of Use Study – Version 4.0
Protocol SMU 19-01GENS

(b) (4)

General Snus® Patterns of Use Study – Version 4.0
Protocol *SMU 19-01GENS*

(b) (4)

General Snus® Patterns of Use Study – Version 4.0
Protocol SMU 19-01GENS

(b) (4)

General Snus® Patterns of Use Study – Version 4.0
Protocol *SMU 19-01GENS*

(b) (4)

General Snus® Patterns of Use Study – Version 4.0
Protocol *SMU 19-01GENS*

(b) (4)

General Snus® Patterns of Use Study – Version 4.0
Protocol SMU 19-01GENS

(b) (4)

General Snus® Patterns of Use Study – Version 4.0
Protocol SMU 19-01GENS

(b) (4)

General Snus® Patterns of Use Study – Version 4.0
Protocol SMU 19-01GENS

(b) (4)

General Snus® Patterns of Use Study – Version 4.0
Protocol SMU 19-01GENS

(b) (4)

General Snus® Patterns of Use Study – Version 4.0
Protocol SMU 19-01GENS

(b) (4)

General Snus® Patterns of Use Study – Version 4.0
Protocol SMU 19-01GENS

(b) (4)

General Snus® Patterns of Use Study – Version 4.0
Protocol SMU 19-01GENS

(b) (4)

General Snus® Patterns of Use Study – Version 4.0

(b) (4)

General Snus® Patterns of Use Study – Version 4.0
Protocol *SMU 19-01GENS*

(b) (4)

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General Snus® Patterns of Use Study – Version 4.0
Protocol *SMU 19-01GENS*

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General Snus® Patterns of Use Study – Version 4.0
Protocol SMU 19-01GENS

INVESTIGATOR SIGNATURE

I have read this protocol and agree that it contains all necessary details for carrying out this study. I will conduct the study as outlined herein and will complete the study within the time designated.

I will provide copies of the protocol and all pertinent information to all individuals responsible to me who assist in the conduct of this study. I will discuss this material with them to ensure that they are fully informed regarding the conduct of the study and the obligations of confidentiality.

(b) (4), (b) (6)

Sponsor:

Name (typed or printed):

Tryggve Ljung

Company:

Swedish Match

Signature:

Date:

(Day Month Year)

General Snus® Patterns of Use Study – Version 4.0
Protocol SMU 19-01GENS

(b) (4), (b) (6)



Premarket Tobacco Product Application Amendment and General Correspondence Submission

The Applicant Identification section is comprised of three parts: Current Applicant Information; Request to Change Ownership; and the Addition, Update, Replacement, or Removal of information. Please provide the Applicant information most recently provided to the FDA under the heading: Subsection A: Current Applicant Information. Please provide the proposed new Applicant information under the heading: Subsection B: Request for Change in Ownership. The addition of other new information should be provided under the heading: Subsection C: Addition, Update, Replacement, or Removal of Applicant Identification Information or Point of Contact.

SECTION I – APPLICANT IDENTIFICATION

Subsection A.

Current Applicant Information (The person or organization (manufacturer/importer) seeking a marketing granted order for a new tobacco product)

Date of Submission

1/30/2024

Name of Applicant (Provide only either a person's name or an organization's name)

| | | | |
|--------------------------------------|---------------------------------------|------|----------------|
| Prefix (e.g., Mr., Mrs., Dr.) | First Name | M.I. | Last Name |
| Generational Suffix (e.g., Jr., III) | Professional Suffix (e.g., MD, Ph.D.) | | Position Title |

Organization Name

Swedish Match USA Inc.

Company Headquarters' FDA-Assigned Facility Establishment ID (FEI) Number

(b) (4)

Company Headquarters' D&B DUNS® Number

(b) (4)

Applicant Address and Contact Information

Primary Address (Street Address, P.O. Box)

1021 E., Cary Street

| | | |
|--------------------------------------|---------|--------------------|
| Address 2 (Apt., Suite, Bldg., etc.) | | City |
| Suite 1600 | | Richmond |
| State, Province, or Territory | Country | ZIP or Postal Code |
| VA | USA | 23219 |

Current Contact Name (Optional, for use only if Applicant is an organization)

| | | | |
|--|---------------------------------------|------|-------------------------------|
| Prefix (e.g., Mr., Mrs., Dr.) | First Name | M.I. | Last Name |
| Mr. | Geard | J. | Roerty |
| Generational Suffix (e.g., Jr., III) | Professional Suffix (e.g., MD, Ph.D.) | | Position Title |
| Jr. | Esg. | | VP, Gen Counsel & Sec |
| Telephone (Include Country Code if applicable) | | FAX | Email Address |
| 804-787-5100 | | | gerry.roerty@swedishmatch.com |

Organization Name and Address Information *(Optional, for use only if Applicant is an individual)*

Organization Name

Primary Address (Street Address, P.O. Box)

☐ Select for same address as New Applicant

Address 2 (Apt., Suite, Bldg., etc.)

City

State, Province, or Territory

Country

ZIP or Postal Code

Subsection B.**Request for Change in Ownership****Proposed New Applicant Information** *(Complete this section to change the current Applicant Information, the owner of the PMTA)*

Effective Date of Ownership Change

Name of Applicant *(Provide only either a person's name or an organization's name)*

Prefix (e.g., Mr., Mrs., Dr.)

First Name

M.I.

Last Name

Generational Suffix (e.g., Jr., III)

Professional Suffix (e.g., MD, Ph.D.)

Position Title

Organization Name

Company Headquarters' FDA-Assigned Facility Establishment ID (FEI) Number

Company Headquarters' D&B Duns® Number

Applicant Address and Contact Information

Primary Address (Street Address, P.O. Box)

Address 2 (Apt., Suite, Bldg., etc.)

City

State, Province, or Territory

Country

ZIP or Postal Code

Telephone *(Include Country Code if applicable)*

FAX

Email Address

New Contact Name *(Optional, for use only if Applicant is an organization)*

Prefix (e.g., Mr., Mrs., Dr.)

First Name

M.I.

Last Name

Generational Suffix (e.g., Jr., III)

Professional Suffix (e.g., MD, Ph.D.)

Position Title

Telephone *(Include Country Code if applicable)*

FAX

Email Address

Organization Name and Address Information *(Optional, for use only if Applicant is an individual)*

Organization Name

Primary Address (Street Address, P.O. Box)

☐ Select for same address as New Applicant

Address 2 (Apt., Suite, Bldg., etc.)

City

State, Province, or Territory

Country

ZIP or Postal Code

- ☐ A notice is included stating that all of the former applicant's rights and responsibilities relating to the PMTA have been transferred to the new applicant.
- ☐ A notice is included stating the new applicant's commitment to agreements, promises, and conditions made by the former applicant and contained in the PMTA.

Transfer Requests

- ☐ Request to transfer all related submissions for the named product(s) to the new owner

Tobacco Product Name (Brand/Sub-brand)

Related Submissions: List the FDA Submission Tracking Numbers (STNs) for all your previous submissions for the tobacco product.

| Related Submission Type | Related Submission STN | Submission Date |
|-------------------------|------------------------|-----------------|
| | | |

Subsection C.**Addition, Update, Replacement, or Removal of Applicant Identification Information or Point of Contact (Optional)****Addition, Update, Replacement, or Removal of Applicant Identification Information**

If "Add" or "Replace" (not allowed for Current Applicant Information; use Subsection B.) is selected, provide all demographic information for the new party.

If "Update" is selected, provide only Person's Name and/or Organization's Name and the information which will replace previously submitted information.

If "Remove" is selected, provide only the Person's Name and/or Organization's Name of the party to be removed.

Select type of Applicant Identification Information (Select only one)

- ☐ Applicant (Address and Contact information only) ☐ Authorized Representative ☐ U.S. Agent
- ☐ Manufacturer

Effective Date of Change

Select one *(If "Update" is selected, FDA will update the Applicant Identification address or contact information that was previously submitted):*

- ☐ Add ☐ Update ☐ Replace ☐ Remove

Person's Name *(Provide a person's name for Authorized Representative or U.S. Agent; optional for the Manufacturer)*

| | | | |
|--------------------------------------|---------------------------------------|------|----------------|
| Prefix (e.g., Mr., Mrs., Dr.) | First Name | M.I. | Last Name |
| Generational Suffix (e.g., Jr., III) | Professional Suffix (e.g., MD, Ph.D.) | | Position Title |

Organization Name (Provide an organization name for the Manufacturer)

Address and Contact Information

Primary Address (Street Address, P.O. Box; Provide the postal address for the Authorized Representative; optional for the Manufacturer or the U.S. Agent)

Street Address (Provide the physical location for the Manufacturer or the U.S. Agent; optional for the Authorized Representative)

| | | |
|--|---------|--------------------|
| Address 2 (Apt., Suite, Bldg., etc.) | | City |
| State, Province, or Territory | Country | ZIP or Postal Code |
| Telephone (Include Country Code if applicable) | FAX | Email Address |

New Contact Name *(Optional, for use only if Applicant is an organization; do not use in conjunction with Subsection B)*

| | | | |
|--|---------------------------------------|---------------|----------------|
| Prefix (e.g., Mr., Mrs., Dr.) | First Name | M.I. | Last Name |
| Generational Suffix (e.g., Jr., III) | Professional Suffix (e.g., MD, Ph.D.) | | Position Title |
| Telephone (Include Country Code if applicable) | FAX | Email Address | |

Organization Name and Address Information *(Optional, use for the Applicant only if a person (do not use in conjunction with Subsection B); also may be used for Authorized Representative, or U.S. Agent)*

Organization Name

Primary Address (Street Address, P.O. Box) ☐ Select for same address as New Applicant

| | | |
|--------------------------------------|---------|--------------------|
| Address 2 (Apt., Suite, Bldg., etc.) | | City |
| State, Province, or Territory | Country | ZIP or Postal Code |

Addition, Update, or Removal of Point of Contact

If "Add" is selected, provide all demographic information for the new party.

If "Update" is selected, provide only Company/Institution Name and the information which will replace previously submitted information.

If "Remove" is selected, provide only the Company/Institution Name of the party to be removed.

Select type of Point of Contact Information (Select only one)

- ☐ Applicant ☐ Manufacturer (Other than Applicant) ☐ Authorized Representative
☐ U.S. Agent ☐ Other, Regulatory ☐ Other, Technical

Select one (If "Update" is selected, FDA will update the Point of Contact address or contact information that was previously submitted):

- ☐ Add ☐ Update ☐ Remove

Alternate Point of Contact Name

Company Name

| | | | |
|--------------------------------------|---------------------------------------|------|----------------|
| Prefix (e.g., Mr., Mrs., Dr.) | First Name | M.I. | Last Name |
| Generational Suffix (e.g., Jr., III) | Professional Suffix (e.g., MD, Ph.D.) | | Position Title |

Alternate Point of Contact Address and Contact Information

Primary Address (Street Address, P.O. Box)

| | | |
|--|---------|--------------------|
| Address 2 (Apt., Suite, Bldg., etc.) | | City |
| State, Province, or Territory | Country | ZIP or Postal Code |
| Telephone (Include Country Code if applicable) | FAX | Email Address |

SECTION II – TOBACCO PRODUCT INFORMATION

(Note: Use this section to correct previously submitted information. This section is not intended to be used in place of submissions required for modifications for new tobacco products)

Unique Identification of Previously Submitted New Tobacco Product

(This Subsection is optional and to be used only to change previously submitted information)

For individual tobacco products, fill in the Individual Tobacco Product sub-section below.

For a co-packaged tobacco product, complete Section II for each new tobacco product included within the co-package.

For grouped submissions complete a separate Section II for each tobacco product.)

Individual Tobacco Product

(Only the Previously Submitted New Tobacco Product Name is required. Provide other information only for updates to previously submitted information. Refer to Form 4057, Section VIII, Appendix B to select the appropriate Product Category and Subcategory or Tobacco Product Properties.)

Select to Update or Withdraw New Tobacco Product ☐ Update ☐ Withdraw

Previously Submitted New Tobacco Product Name (Brand/Sub-Brand)

Updated New Tobacco Product Name (Brand/Sub-Brand) (if applicable)

Update New Tobacco Product Category or Subcategory or Update New Tobacco Product Subcategory
(Complete only if Category or Subcategory is different than previously submitted)

Previously Submitted New Tobacco Product:

Category:

Subcategory:

Updated New Tobacco Product:

Category:

Subcategory:

Tobacco Product Properties Needed to Uniquely Identify the Product

(Update previously submitted Tobacco Product Properties Needed to Uniquely Identify Product by selecting Add, Update, or Remove and providing the Property Name. When updating properties provide both the previously submitted target value and the updated target value for the previously submitted new tobacco product.)

| | | New Tobacco Product Name (as provided above) | |
|------------------------------|---------------|--|----------------------|
| Action (Add, Update, Remove) | Property Name | Previously Submitted Target Value | Updated Target Value |
| | | | |

To submit information on additional tobacco product(s), use one or more copies of Section II as appropriate.

SECTION III – SUBMISSION INFORMATION**Type of Submission (Select only one)**

- ☒ Amendment (If selected, provide Date of FDA Letter, if applicable; select Amendment Response Type; and indicate the Scientific Content in Section IV - Amendment Contents)
- ☐ General Correspondence (if selected, provide Subject of Correspondence)

FDA Submission Tracking Number (STN) to be amended: MROOO256.PD1-PD5, PD7-PD9

Date of FDA Letter (if applicable mm/dd/yy): 01/17/24

Amendment Response Type (Select one)

- ☒ Deficiency Letter
- ☐ Unsolicited (Describe in Submission Summary)
- ☐ Other (Describe in Submission Summary)

Subject of Correspondence (Select all that apply)

- ☐ Request for Change in Ownership (Section I)
- ☐ Change in Authorized Representative, U.S. Agent, or Manufacturer Address or Contact Information (Section I)
- ☐ Addition or Removal of a Point of Contact (Section I)
- ☐ Update to Unique Identification Information (Section II)
- ☒ Change in Cross-referenced Content or Related Submissions (Section III)
- ☐ Change in Submission Contents (Section IV)
- ☐ Change in Manufacturing/Packaging/Sterilization Site Information (Section V)
- ☐ Adverse Experience Report (Describe in Submission Summary)
- ☒ Periodic Report (e.g., Annual Report) (Describe in Submission Summary)
- ☐ Request to Withdraw the PMTA

☐ Select to indicate if the withdrawal is due to a health or safety concern related to the tobacco product
- ☐ Other (Describe in Submission Summary)

Submission Summary (Required if instructed to "Describe" by a previous selection)

Solicited response to Deficiency Letter received January 17, 2024 for: General Snus FDA STNs: MR0000256.PD1-MR0000256.PD5, MR0000256.PD7-MR0000256.PD9.

Purpose of Application (Check only one)

- ☐ This PMTA Amendment is for a single new tobacco product
- ☐ This PMTA Amendment is for a group of PMTA Amendments containing multiple new tobacco products with similar modifications in comparison to one predicate tobacco product

Cross-referenced Content
(Optional, use this subsection to add new cross-referenced content, or update or remove previously submitted information)

Select to Add, Update, or Remove Cross-referenced Content

- ☐ Add
- ☒ Update
- ☐ Remove

New Tobacco Product Name (either previously submitted or updated name)

- ☒ Select if this update to Cross-referenced Content is relevant to all amended products in this submission

Identify Cross-referenced Submission Types as one of the following: PMTA, Tobacco Product Master File, or Modified Risk Tobacco Product (MRTPA)

| Cross-referenced Submission Type | Cross-referenced Submission STN |
|----------------------------------|---------------------------------|
| MRTP | MR0000256 |
| | |
| | |

Related Submissions

(List the FDA Submission Tracking Numbers (STNs) for all your previous requests for the new tobacco products (e.g., ITP, SE, MRTPA) where applicable)

Select to Add, Update, or Remove Related Submissions

☐ Add ☒ Update ☐ Remove

New Tobacco Product Name (either previously submitted or updated name)

☒ Select if this update to Related Submission(s) is relevant to all amended products in this submission

| Related Submission Type | Related Submission STN |
|-------------------------|------------------------|
| MRTP | MR0000256 |
| | |
| | |

Formal Meetings Held with FDA pertaining to this tobacco product

(For each meeting, as needed, enter the submission STN and meeting held date.)

Select to Add, Update, or Remove Formal Meetings Held with FDA

☐ Add ☐ Update ☐ Remove

New Tobacco Product Name (either previously submitted or updated name)

☐ Select if this update to Meeting(s) is relevant to all amended products in this submission

| Submission STN | Meeting Held Date |
|----------------|-------------------|
| | |
| | |
| | |

To submit information on additional tobacco product(s), use one or more copies of Section III as appropriate.

SECTION IV – AMENDMENT AND GENERAL CORRESPONDENCE CONTENTS

List all documents included in the PMTA Amendment, according to their respective subject area.

(Refer to Form 4057, Section IV - Application Contents for a representative list of content categories by subject area.)

Administrative

(List the categories of Administrative content provided by this Amendment)

Labeling and Marketing Plans

(List the categories of Labeling and Marketing Plans content provided by this Amendment)

Inspections

(List the categories of Inspections content provided by this Amendment)

Scientific Content*(Select the categories of Scientific Content provided by this Amendment)*

Description of Scientific Content:

Check all that apply

- | | |
|--|---|
| <input type="checkbox"/> General Information | <input type="checkbox"/> Literature Search |
| <input type="checkbox"/> Descriptive Information | <input type="checkbox"/> Organized References |
| <input type="checkbox"/> Product Samples | <input type="checkbox"/> Health Risk Investigations |
| <input type="checkbox"/> Statement of Compliance with 21 CFR part 25 | <input type="checkbox"/> Study Report(s) |
| <input type="checkbox"/> Summary | <input type="checkbox"/> Case Report Form(s) |
| <input type="checkbox"/> Product Formulation | <input type="checkbox"/> Analyzable Data Set(s) |
| <input type="checkbox"/> Manufacturing | |
| <input type="checkbox"/> Other (Specify below) | |

Other Content *(Describe the other content provided by this Amendment)*

Solicited cross-referencing, including 2023 MRTP/PMTA Annual Report, post-market surveillance, environmental assessments

SECTION V – MANUFACTURING/PACKAGING/STERILIZATION SITE RELATING TO A SUBMISSION*(This section is optional.)**If "Add" is selected, provide all demographic information for the new site.**If "Update" is selected, provide only Company/Institution Name and the information which will replace previously submitted information.**If "Remove" is selected, provide only the Company/Institution Name of the site to be removed.)*

Select to Add, Update, or Remove Manufacturing/Packaging/Sterilization Site

☐ Add ☐ Update ☐ Remove

Company/Institution Name

Specify type of Manufacturing/Packaging/Sterilization site

☐ Manufacturer ☐ Contract Manufacturer ☐ Contract Sterilizer ☐ Re-packer/Relabeler

Company Headquarters' FDA-Assigned Facility Establishment ID (FEI) Number

Company Headquarters' D&B DUNS® Number

Division Name (if applicable)

Street Address (Physical location)

Address 2 (Apt., Suite, Bldg., etc.)

City

State, Province, or Territory

Country

ZIP or Postal Code

Telephone *(Include Country Code if applicable)*

FAX

Email Address

| Contact Name | | | |
|---|------------|---------------------------------------|----------------|
| Prefix (e.g., Mr., Mrs., Dr.) | First Name | M.I. | Last Name |
| Generational Suffix (e.g., Jr., III) | | Professional Suffix (e.g., MD, Ph.D.) | Position Title |
| The Manufacturing/Packaging/Sterilization Site is ready for inspection <input type="checkbox"/> Yes <input type="checkbox"/> No | | | |

SECTION VI – CERTIFICATION STATEMENT


Select one of the following, then enter Name of Applicant (or person signing on behalf of the Applicant if Applicant is an organization), Authorized Representative, or U.S. Agent, and the name of the Applicant in the body of the statement.

I am signing as a/an: ☐ Applicant ☒ Authorized Representative ☐ U.S. Agent

| | | | | |
|----|----------------------|------------|---------------------|---|
| I, | First Name Gerard | M.I. J. | Last Name Roerty | Generational Suffix (e.g., Jr., III) Jr. |
|----|----------------------|------------|---------------------|---|

on behalf of the applicant, Swedish Match USA Inc.

hereby certify that the applicant will maintain all records to substantiate the accuracy of this application for the period of time required in 21 CFR 1114.45 and ensure that records remain readily available to the FDA upon request. I certify that this information and the accompanying submission are true and correct, that no material fact has been omitted, and that I am authorized to submit this on the applicant's behalf. I understand that under section 1001 of title 18 of the United States Code, anyone who knowingly and willfully makes a materially false, fictitious, or fraudulent statement or representation in any matter within the jurisdiction of the executive, legislative, or judicial branch of the Government of the United States is subject to criminal penalties.

| | | | |
|-----------|--|------|-----------|
| Signature | Gerard J. Roerty, Jr.  Digitally signed by Gerard J. Roerty, Jr. Date: 2024.01.30 13:44:02 -05'00' | Date | 1-30-2024 |
|-----------|--|------|-----------|

**APPENDIX
INSTRUCTIONS FOR USE**

This form and the instructions for use are solely intended to provide the applicant an organized format to supply information required for a Premarket Tobacco Product Application (PMTA) Amendment and General Correspondence Submission.

Section I – Applicant Identification

Subsection A – Current Applicant Information

- Complete the Date of Submission
- Complete Name of Applicant name and optionally other identifying information. Provide only either a person's name, if the Applicant is an individual, or an Organization Name.
- Complete Applicant address information as previously submitted, and optionally provide contact name, telephone, and email address. (Changes to the current Applicant information should be made only in Subsection C.)
- If the Applicant is an individual, the Organization Name and Address associated with the individual may be provided.

Subsection B – Request for Change in Ownership 21 CFR 1114.13

- Provide the effective date of the change in ownership.
- Complete the Name of the New Applicant and optionally other identifying information. Provide only either a person's name, if the Applicant is an individual, or an Organization Name.
- Provide the Applicant address information, and optionally provide contact name, telephone, and email address.
- If the Applicant is an individual, the Organization Name and Address associated with the individual may be provided.
- Indicate if any notices are included in the submission regarding the transfer of ownership. (List the notice(s) in Section IV under Administrative contents.)
- Indicate if you are transferring all related submissions related to a brand or brands. If so, provide the tobacco product names and corresponding STNs subject to the change in ownership

**Subsection C – Addition, Update, or Removal of Applicant Identification Information or Point of Contact
21 CFR 1114.9**

- Optionally select the type of Applicant information (e.g., Applicant, Authorized Representative, etc.) being provided.
- Optionally select to add, update, replace, or remove Applicant Information.
- To add a new party, complete all information. An Authorized Representative or U.S. Agent must be a person. Provide the person's name, address, and contact information.
- To update or remove party information, the Person's Name or Organization Name must match previously submitted information. For updates, the Address and Contact information provided will be used to update previously provided information.
- To replace a party, the Person's Name or Organization Name must match previously submitted information. It is not necessary to provide address information.
- To provide additional Applicant Identification Information, select "Update Additional Applicant Identification Information" on the form.
- Optionally select the type of Point of Contact information (e.g., Applicant, Authorized Representative, etc.) being provided.
- Optionally select to add, update, or remove Point of Contact information.
- Provide the Company Name associated with the Point of Contact
- To add a new Point of Contact, complete all information. Provide the contact's name, address, and contact information.
- To update or remove information for a Point of Contact, the Person's Name must match previously submitted information.
- To provide information for an addition Point of Contact, the Person's Name must match previously submitted information

Section II – Tobacco Product Identification 21 CFR 1114.7(c)

- For an individual tobacco product, provide the previously submitted new tobacco product's names.
 - Product category, sub-category, and product properties should be provided only if they are changing. When updating product category, sub-category, or properties always give the both previously submitted and the updated information.
- For a co-packaged tobacco product, provide the new tobacco products' names for all products in the co-packaged tobacco product.
 - Product category, sub-category, and product properties should be provided only if they are changing. When updating product category, sub-category, or properties always give the both previously submitted and the updated information.
- For a grouped submission, add an individual or co-packaged tobacco product by selecting "Add Section II" on the form.

Section III – Submission Information

- Indicate whether the submission is an Amendment or General Correspondence.
 - For Amendments, provide the Date of FDA Letter, if applicable, and select the Amendment Response Type. If the type of response, is "Unsolicited" or "Other", describe the purpose of the submission in the Submission Summary. Also indicate the subject of the amendment provided in Section IV – Amendment and General Correspondence Contents.
 - For General Correspondence, select Subject(s) of Correspondence and provide the appropriate information in the Section indicated. If "Other", describe the subject of the correspondence in the Submission Summary. Also describe the subject of the correspondence in Section IV - Amendment and General Correspondence Contents
 - Provide the FDA STN being amended. The Premarket Tobacco Application Amendment and General Correspondence Submission should be used to update only one STN.
 - If instructed to do so, based on the selection of either Amendment Response Type or Subject of Correspondence, or otherwise optionally, complete the Submission Summary.
 - Indicate whether the Amendment submission is for a single individual tobacco product or for a group of tobacco products previously submitted as a grouped PMTA submission.
 - Optionally add, update, or remove cross-referenced content, including Tobacco Product Master Files
 - Provide the New Tobacco Product Name for which the cross-referenced content is relevant. Optionally, indicate if the content is relevant to all tobacco products which are the subject of this amendment submission. By selecting this checkbox, multiple products can be updated with one Section III. However, a Section II must be completed for each product updated by this amendment submission.
 - Provide metadata for each document to identify the cross-referenced content.
 - Select "Update Cross-Referenced Content Information" to add metadata for an additional document.
 - Optionally add, update, or remove related submissions, (e.g., ITP, SE Report, MRTPA).
 - Provide the New Tobacco Name for which the related submission is relevant. Optionally, indicate if the submission is relevant to all tobacco products which are the subject of this amendment submission. By selecting this checkbox, multiple products can be updated with one Section III. However, a Section II must be completed for each product updated by this amendment submission.
-

Section IV – Amendment and General Correspondence Contents

- Select the categories of document submitted from among Administrative, Labeling and Marketing Plans, Inspections, Scientific Content, or Other. For each category (except Scientific Content), list the sub-categories that describe the submission contents. For Scientific Content, select the all the content categories that apply to content provided in this amendment submission. For Scientific Content that does not fit into one of the listed categories, select "Other" and describe the content in the space provided.
- Submission Table of Contents: Optionally, select to add, replace, or suspend (i.e., remove from the active documents for review) submission documents. Provide metadata for each submission document: Action (Add, Replace, or Suspend), Date Document was Submitted if replacing or suspending, Document Filename, Document or Study Title, Table of Contents Category, and all applicable Document Keywords.
- To provide metadata for additional documents select "Update Submission Document". (A Sample of Table of Contents can be found in CTP's "Electronic Submission File Formats and Specifications", Appendix A. The technical specification is posted on CTP's public website page at the very bottom of the "Manufacturing" page under "Resources for Electronic Submissions": <https://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/Manufacturing>)

Section V – Manufacturing/Packaging Sites Relating to a Submission

- Optionally select to add, update, or remove Manufacturing/Packaging Site information. To update or remove information for a Manufacturing/Packaging Site, the "Company/Institution Name" must match previously submitted information.
- If "Add" is selected, provide all demographic information for the new site. If "Update" is selected, provide only "Company/ Institution Name" and the information which will replace previously submitted information. If "Remove" is selected, provide only the "Company/ Institution Name" of the site to be removed.

Section VI – Certification Statement 21 CFR 1114.7(m)

- Select if the signer is acting as an Authorized Representative or U.S. Agent.
- Insert the name of the signer, and sign and date the form where indicated.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 10 minutes per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services Food and Drug
Administration
Office of Operations
Paperwork Reduction Act (PRA) Staff
PRASStaff@fda.hhs.gov

*"An agency may not conduct or sponsor, and a person
is not required to respond to, a collection of
information unless it displays a currently valid OMB
number."*