SWEDISH MATCH USA, INC. RENEWAL MODIFIED RISK TOBACCO PRODUCT APPLICATIONS

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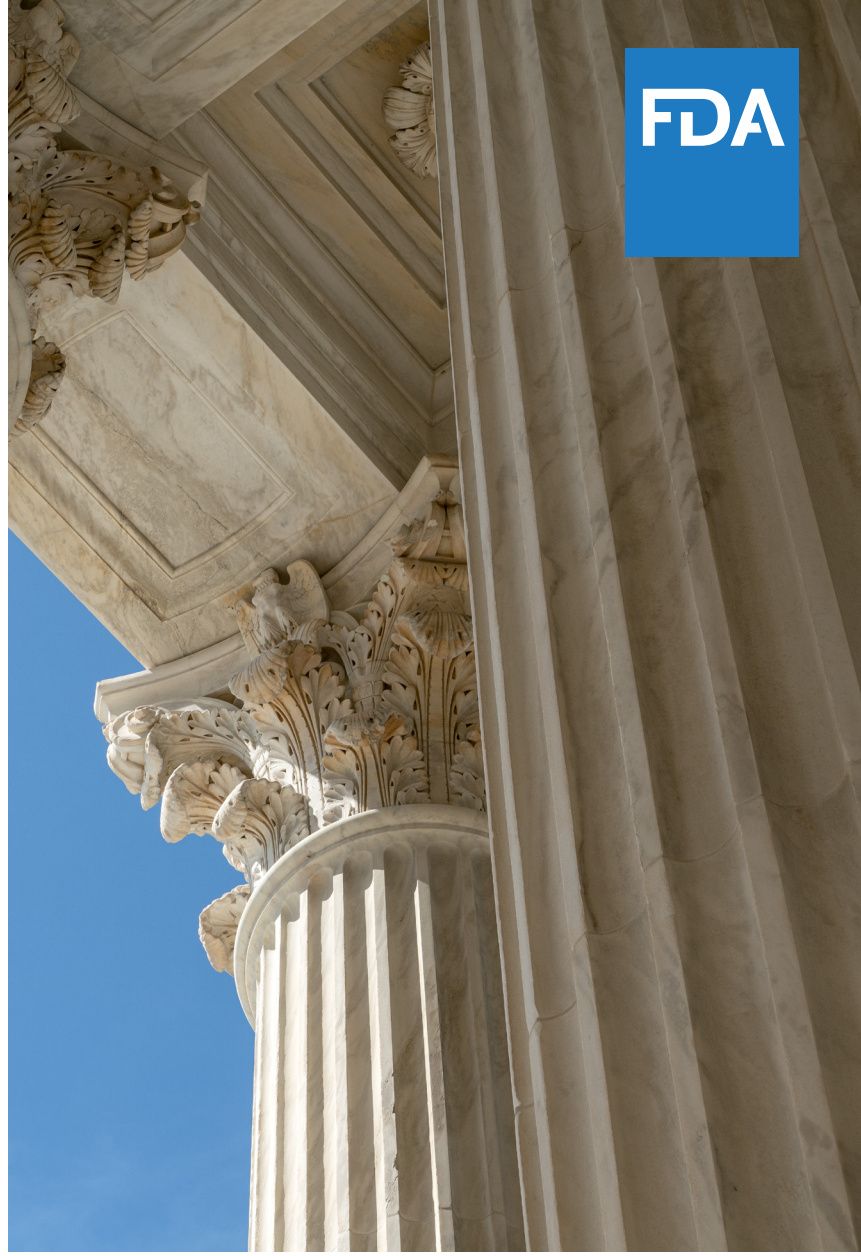

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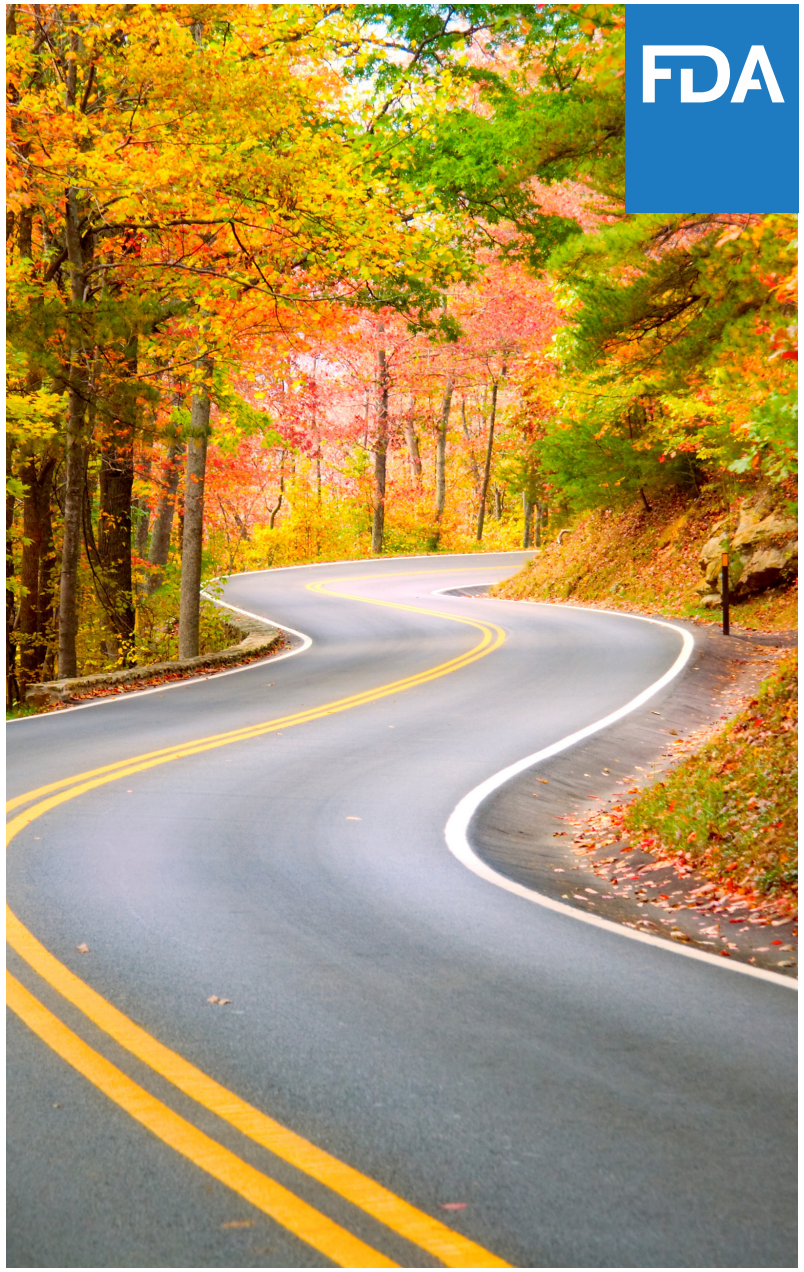
AGENDA

- History of Swedish Match USA, Inc. risk modification order
- Summary of Swedish Match USA, Inc. renewal modified risk tobacco application (MRTPA) under review
- Lines of evidence
- Questions for the committee



HISTORY: RISK MODIFICATION ORDER STANDARD - 911(g)(1)

The Federal Food, Drug, and Cosmetic Act (FD&C Act) requires FDA to determine if an applicant has demonstrated that a proposed modified risk tobacco product (MRTP), as it is actually used by consumers, will:

(1) significantly reduce harm and the risk of tobacco-related disease to people who use tobacco, and

(2) benefit the health of the population as a whole, taking into account both people who use tobacco products and people who do not currently use tobacco products

HISTORY: QUESTIONS RELEVANT TO THE MRTP EVALUATION

These questions are relevant to the evaluation of whether the applicant has met the applicable 911 standard:

1. Is the proposed modified risk claim scientifically accurate?
2. What are the health risks of the MRTP to people who use tobacco?
3. How do consumers perceive and understand the modified risk claim?
4. What are the potential benefits and harms to the health of the population as a whole?

In Swedish Match's previous MRTPA, FDA conducted thorough scientific review of all the available scientific evidence, including but not limited to long-term epidemiological studies and perceptions and intentions data.

HISTORY: SWEDISH MATCH RISK MODIFICATION ORDER

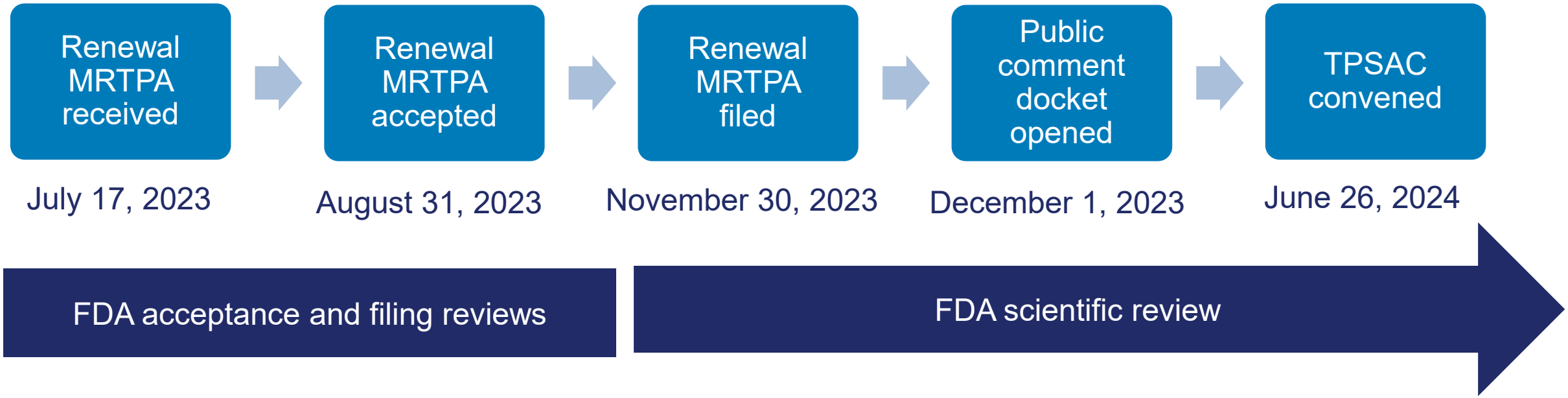
On October 22, 2019, FDA issued Swedish Match a modified risk granted order (MRGO) under Section 911(g)(1) of the FD&C Act for eight General Snus smokeless tobacco products: **General Loose, General Dry Mint Portion Original Mini, General Portion Original Large, General Classic Blend Portion White Large – 12ct., General Mint Portion White Large, General Nordic Mint Portion White Large – 12ct., General Portion White Large, and General Wintergreen Portion White Large.**

FDA authorized the marketing of the eight General Snus products with the following claim:

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

RENEWAL: SWEDISH MATCH RENEWAL SUBMISSION

The risk modification order expires October 22, 2024. Swedish Match is requesting renewal of its risk modification order to continue to market its products with the same modified risk claim.



RENEWAL: POSTMARKET SURVEILLANCE & STUDIES

- Postmarket Surveillance and Studies (PMSS) are required for all products receiving a risk modification order under 911(g)(1). Swedish Match's PMSS requirements included the following:
  - Monitoring use of the eight General Snus products that were authorized to be marketed with the modified risk claim in terms of uptake, dual use, and complete switching
  - An assessment of consumer perceptions of the products and understanding of the claim, particularly that to reduce their risk of disease relative to smoking, they must use General Snus exclusively
  - Surveillance of MRTP sales and distribution, adverse experiences, and new research findings

RENEWAL: MARKETING & SALES (2019 – 2023)

- The applicant's marketing is limited in scope, budget, and impressions.
  - Branded website, trade print advertisements, social media posts on Facebook, paid digital advertising, earned media, and point-of-sale advertisements
- Sales of General Snus products are declining.
  - Wholesale units (by cans) decreased from 4.94M cans to 3.47M cans between Q4 2019 - Q3 2020 and Q4 2022 – Q3 2023.
  - Wholesale dollar sales decreased from 17.52M to 14.96M during the same period.
  - Sales of General Snus products in NielsenIQ Retail Measurement Service (RMS) data have fallen from $6.6M in Q4 of 2019 to $4.9M in Q4 of 2023.

Sample Print Advertisement

Disclaimer: The author's own analyses, calculations and conclusions informed in part by the NielsenIQ Retail Measurement Service (RMS) data through NielsenIQ's RMS for the tobacco product category smokeless tobacco for the time period 2019 through 2023 for Total US Expanded All Outlets Combined (xAOC) and convenience stores are those of the FDA and do not reflect the views of NielsenIQ. NielsenIQ is not responsible for, had no role in, and was not involved in analyzing and preparing the results reported herein, or in developing, reviewing, or confirming the research approaches used in connection with this report. NielsenIQ RMS data consist of weekly purchase and pricing data generated from participating retail store point-of-sale systems in all U.S. markets. See https://NielsenIQ.com/global/en/ for more information.

LINES OF EVIDENCE: FOCUS OF TPSAC DISCUSSION & RECOMMENDATIONS (1 OF 2)

GENERAL SNUS USE AND IMPACTS TO THE POPULATION

FDA will present data from several studies, including nationally representative estimates of snus use, as well as data from the applicant's General Snus Patterns of Use Study, to describe characteristics of people who use snus, patterns of tobacco use among people who use General Snus, and transitions from CC smoking to exclusive use of General Snus.

TPSAC will be asked to discuss the use behaviors with respect to the modified risk tobacco products.

LINES OF EVIDENCE: FOCUS OF TPSAC DISCUSSION & RECOMMENDATIONS (2 OF 2)

FDA

CONSUMER UNDERSTANDING & PERCEPTIONS

FDA will present results from the applicant's General Snus Patterns of Use Study.

TPSAC will be asked to discuss the evidence related to consumer understanding and perceptions of the modified risk claim.

QUESTIONS FOR THE COMMITTEE

QUESTION 1

FDA reviewed the literature and the applicant's data and conducted internal analyses of the applicant's data to describe characteristics of people who use snus, patterns of tobacco use among people who use General Snus, and transitions from CC smoking to exclusive use of General Snus.

Discuss the use behaviors of these modified risk tobacco products and any implications.

QUESTION 2

FDA reviewed the applicant's data on consumer understanding and perception of the modified risk information.

Discuss the evidence related to consumer understanding and perceptions of the modified risk claim and any implications.

GENERAL SNUS USE AND IMPACTS TO THE POPULATION

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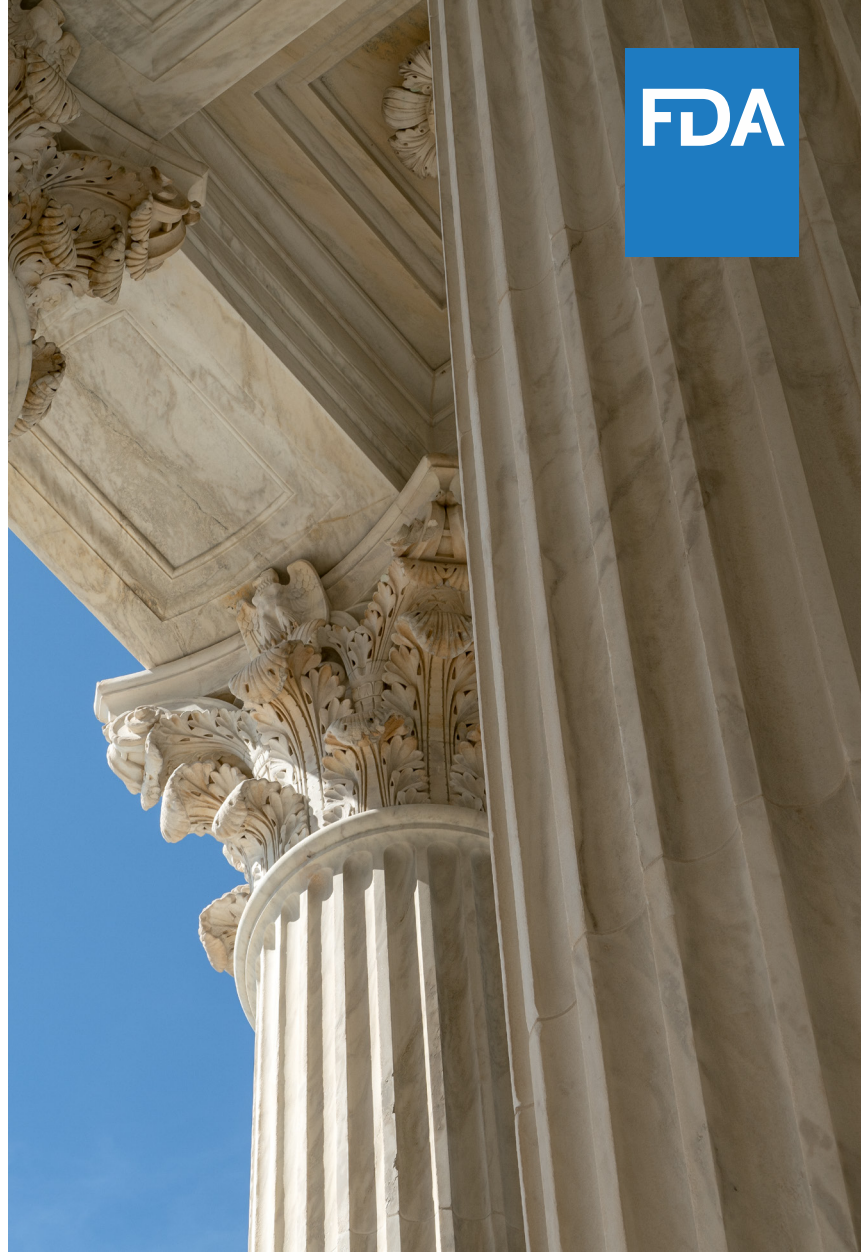

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ORIGINAL MRTPA: INDIVIDUAL HEALTH RISKS EVALUATION

Table 1. Results from published studies[1] of health effects for oral cancers, heart disease, stroke, lung cancer, and emphysema and chronic bronchitis associated with Swedish snus use or smoking compared to non-users of tobacco (Data Source: MRTPAs, Appendix 6A 2013 Environ Snus Monograph; Rostron et al. 2018)

Reference	Tobacco Product Used	Mouth Cancer	Heart Disease	Stroke	Lung Cancer	Emphysema and Chronic Bronchitis
		RR (95% CI), n	RR (95% CI), n	RR (95% CI), n	RR (95% CI), n	RR (95% CI)
Boffetta et al. 2008	Swedish snus	1.0 (0.7-1.3), n=4	n/a	n/a	0.8 (0.6-1.0), n=2	n/a
Lee & Hamling 2009; Lee 2011	Swedish snus	1.01 (0.71-1.45)†, n=4	n/a	n/a	0.82 (0.52-1.28)†, n=2	n/a
Rostron et al. 2018	Swedish snus	n/a	1.04 (0.93-1.16)†§, n=3	1.04 (0.92-1.17)†‖, n=1	n/a	n/a
Boffetta & Straif 2009	Swedish snus	n/a	Any MI: 0.87 (0.75-1.02), n=6 Fatal MI: 1.27 (1.07-1.52), n=5	Any stroke: 1.02 (0.93-1.13), n=3 Fatal stroke: 1.25 (0.91-1.70), n=2	n/a	n/a
Lee 2011	Swedish snus	n/a	0.99 (0.85-1.14)†, n=9	1.06 (0.96-1.17)†, n=6	n/a	n/a
Roosaar et al. 2008	Swedish snus	n/a	n/a	n/a	n/a	0.8 (0.2-3.0)†‡ (<80 years old) 2.0 (1.2-3.4)†‡ (80+ years old)
CPS II Population 1982-1988*	Smoking	10.89	2.80 (35-64 years old) 1.51 (64+ years old)	3.27 (35-64 years old) 1.63 (64+ years old)	23.26	Bronchitis, Emphysema: 17.1 Chronic Airway Obstruction: 10.58

Abbreviations: RR=relative risk; CI=confidence interval; n=number of risk estimates for meta-analysis; n/a=not applicable; MI=myocardial infarction

[1]All but one study (Roosaar et al. 2008) are meta-analyses

*Male current smokers

†RR estimate is for never smokers

‡Nonmalignant respiratory disease death (which includes chronic obstructive pulmonary disease (COPD), bronchitis, emphysema, pneumonia, and influenza)

§RR estimate includes a pooled study of 8 cohorts from Hansson et al. 2012

‖RR estimate includes a pooled study of 8 cohorts from Hansson et al. 2014

INDIVIDUAL HEALTH RISKS RELATIVE TO SMOKING

The scientific evidence published since the original MRGO continues to support the modified risk claim as scientifically accurate.

Mouth Cancer, Lung Cancer, Emphysema, & Chronic Bronchitis	• Mouth Cancer: No association with current snus use (v. never snus use) observed (Araghi et al., 2021). • Lung cancer, emphysema, and chronic bronchitis: No new studies identified since the MRGO
Stroke	• People who currently use snus and have never used CC have a significant increased risk of total stroke (aHR 1.53, CI: 1.02-2.32) and ischemic stroke (aHR 1.65, 95% CI: 1.06-2.57) compared to people who never used tobacco (Titova et al., 2021). • These associations are lower than the risk of stroke among people who smoke CCs (RR 1.92, 95% CI: 1.66-2.21) (Thun et al., 2013).
Heart Disease	• No association between current snus use and ischemic heart disease or acute myocardial infarction and peripheral heart disease (Lee et al., 2022, Yuan et al., 2022). • People who exclusively use snus and have never used CCs have a significant increased risk of CVD mortality (aHR 1.27, 95% CI: 1.15-1.41) compared to people who never used tobacco (Byhamre et al., 2021). • These associations are lower than the risk of CVD mortality among people who smoke combusted cigarettes (CC) (RR 2.50, 95% CI: 2.34-2.66) (Thun et al., 2013).

OBSERVATIONAL STUDIES ASSESSING CHARACTERISTICS AND USE OF SNUS PRODUCTS

Population Assessment of Tobacco and Health (PATH) Study (adult data)	• PATH is a nationally representative longitudinal study of tobacco use and health among adults and youth in the United States. • Literature cited by the applicant presents data from PATH Wave 1 (fielded 2013–2014), which found that **0.4% of adult respondents** identified as people who currently use pouched snus. • Population estimates from FDA analysis of PATH Wave 7 data (fielded 2022–2023) indicate that **0.7% of adults** reported using snus in the past 30 days.
National Youth Tobacco Survey (NYTS) (youth data)	• NYTS is a nationally representative, cross-sectional survey of middle and high school students in the United States. • The applicant provided results from the 2022 NYTS indicating that **1% of students** reported ever use of snus and **0.5%** indicated use of snus at least once in the past 30 days. • Results from an internal analysis of the 2023 NYTS indicate that **0.8% of middle and high school students** report current snus use.

GENERAL SNUS PATTERNS OF USE STUDY: METHODS

DESIGN

- Prospective study
- Conducted online (July 2020 – September 2022) over 4 waves
- Waves launched at baseline, 6 months, 1 year, and 2 years

SAMPLE

- Recruited via invitation stickers placed on General Snus canisters from July 25 - August 7, 2020 and by direct email
- Used General Snus in the past 30 days and used it every day or some days
- U.S. adults aged 21+
- Able to read and speak English
- Agreed to participate in four surveys over a 24-month period
- Provided consent and personal contact information

Source: MRTPA Appendix 4.1-8, 4.1-9

GENERAL SNUS PATTERNS OF USE STUDY: OBJECTIVES

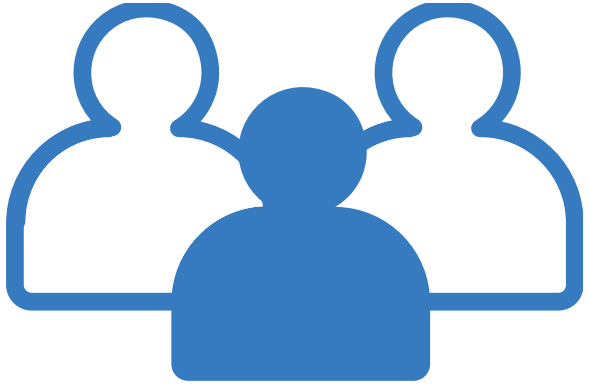
Primary Objectives:

1. Compare tobacco and nicotine product (TNP) patterns of use, across all 4 waves
2. Compare consumption patterns (# of days per month used, number of pouches/CC used) of CCs and General Snus at baseline with consumption patterns in Waves 2 through 4
3. Assess complete substitution and cessation behaviors among people who dual use CC and General Snus

GENERAL SNUS PATTERNS OF USE STUDY: PARTICIPATION BY WAVE

GENERAL SNUS PATTERNS OF USE STUDY: BASELINE DEMOGRAPHICS

- Respondents were predominately male (92%), non-Hispanic White (89%), and resided in the South (28%) or Midwest (34%).
- The mean age was 36 years.
- Most had some college or Associate's degrees (38%) or Bachelor's degrees (35%) and annual household incomes of <$50,000 (31%) or $50,000-$99,999 (38%).



GENERAL SNUS PATTERNS OF USE STUDY: BASELINE TOBACCO USE

- All participants used General Snus.
- Most respondents (75%) had used more than 200 General Snus pouches in their lifetime.
- Approximately 18% of baseline participants reported currently smoking CC, 37% reported formerly smoking CC, and 45% reported never smoking CC.
- Among people who used CC at baseline (n=299), more than 60% reported a readiness to quit by a quit attempt in the past 29 days (16.4%), currently trying to quit (36.8%), or having high intention to quit in the future (8.4%).

GENERAL SNUS PATTERNS OF USE STUDY: GENERAL SNUS AND CC USE*

General Snus Use	W1 (Baseline) n=1,655 n	W1 (Baseline) n=1,655 % (95% CI)	W4 n=451 n	W4 n=451 % (95% CI)
Any General Snus Use: Every day	1,358	82.1 (80.1, 83.9)	273	60.5 (55.9, 65.1)
Any General Snus Use: Some days	297	17.9 (16.1, 19.9)	121	26.8 (22.8, 31.2)
Exclusive General Snus use	428	25.9 (23.8, 28.0)	100	22.2 (18.4, 26.3)
Dual use with CC overall: Every day	120	7.3 (6.0, 8.6)	16	3.5 (2.0, 5.7)
Dual use with CC overall: Some days	179	10.8 (9.4, 12.4)	37	8.2 (5.8, 11.1)
Dual use with CC only	70	4.2 (3.3, 5.3)	11	2.4 (1.2, 4.3)

* Values from FDA internal analysis of data

GENERAL SNUS PATTERNS OF USE STUDY: COMPLETE SUBSTITUTION AND CESSATION*

Evidence from published literature suggests about 5% of people who dual use CC and smokeless tobacco report completely switching to a smokeless tobacco product over time.

Complete Substitution/ Cessation	Participants who completed Wave 2 n	Participants who completed Wave 2 % (95% CI)	Participants who completed Wave 3 n	Participants who completed Wave 3 % (95% CI)	Participants who completed Wave 4 n	Participants who completed Wave 4 % (95% CI)
Complete Substitution	29	9.7 (6.6, 13.6)	29	9.7 (6.6, 13.6)	25	8.4 (5.5, 12.1)
Cessation	32	10.7 (7.4, 14.8)	31	10.4 (7.2, 14.4)	27	9.0 (6.0, 12.9)

* Values from FDA internal analysis of applicant data. Estimates are generated assuming that people who use CC, who did not complete follow-up waves, remained people who use CC.

LIMITATIONS: DIFFERENTIAL ATTRITION

- At Wave 4, attrition was higher among participants who were:
  - Younger, had a lower household income, used General Snus non-daily, and used less than 200 General Snus pouches in their lifetime ($p < 0.05$)
- Among those who smoked CC:
  - Greater proportion of those who reported trying to quit CC returned for Wave 4 (39.7% at Wave 4 versus 36.8% at baseline)
  - Among those not currently trying to quit, those who reported high intention to quit CC at baseline were more likely to return for Wave 4 (9.5% at Wave 4 versus 8.4% at baseline)
- These findings suggest that observed tobacco use transitions may not accurately represent the actual likelihood of transition.
  - Conservatively, FDA calculated complete substitution and cessation using people who report CC use at baseline (n=299) as the denominator

SUMMARY & CONCLUSIONS

- Based on health risk literature, the original MRTPA review conclusions regarding claim substantiation hold.
- U.S.-based tobacco surveillance systems (NYTS and PATH) suggest a low prevalence of reported snus use among youth and adults.
- The General Snus Patterns of Use Study, which was composed entirely of people who use General Snus at baseline, suggests 8.5% or more of people who dual-use General Snus and CC at baseline transition to exclusive General Snus use two years later.
- Study findings add to the body of evidence that some people who use General Snus use the product to help them quit CC.

CONSUMER UNDERSTANDING AND PERCEPTIONS

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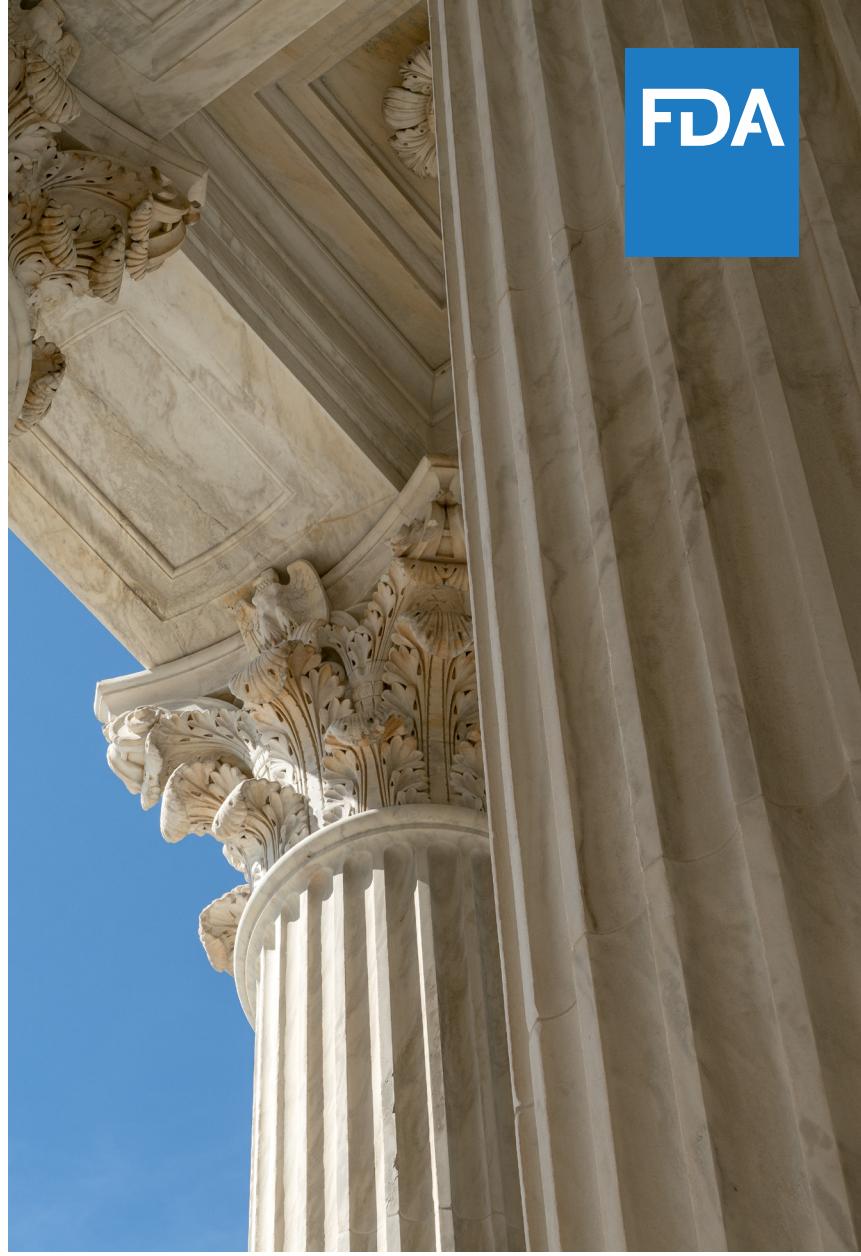

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ADDITIONAL CONDITIONS FOR MARKETING - 911(h)(1)

The FD&C Act requires that any advertising or labeling concerning an MRTP enables the public:

(1) to comprehend the information concerning modified risk, and

(2) to understand the relative significance of such information in the context of total health and in relation to all of the diseases and health-related conditions associated with the use of tobacco products

CONSUMER UNDERSTANDING AND PERCEPTIONS GENERAL SNUS PATTERNS OF USE STUDY: OBJECTIVES

Among people who use General Snus, assess:

1. Absolute risk perceptions of developing mouth cancer, heart disease, and lung cancer from:
   - Using only General Snus daily
   - Smoking only CCs daily
   - Dual-using General Snus and CCs daily
   - Never having used any TNPs
2. Understanding of the risk reduction as stated in the modified risk claim

GENERAL SNUS PATTERNS OF USE STUDY: PROCEDURE

- Participants were not shown the modified risk claim at any time during the study
- Participants answered the same questions at each wave
- All items specifically assessed General Snus

PATTERNS OF USE STUDY: SELECTED OUTCOMES (1 OF 2)

RISK PERCEPTIONS

In your opinion, what is the chance that a person who **only uses General Snus every day** would suffer from the following health conditions during his/her lifetime?

		Very Low Chance	Low Chance	Moderate Chance	High Chance	Very High Chance	Don't Know
1	Heart disease	1	2	3	4	5	99
2	Lung cancer	1	2	3	4	5	99
3	Mouth cancer	1	2	3	4	5	99

Also assessed for a person who:

- Never used tobacco or nicotine products
- Only smokes CCs every day
- Uses both CCs and General Snus every day

PATTERNS OF USE STUDY: SELECTED OUTCOMES (2 OF 2)

UNDERSTANDING

Using General Snus instead of CCs…

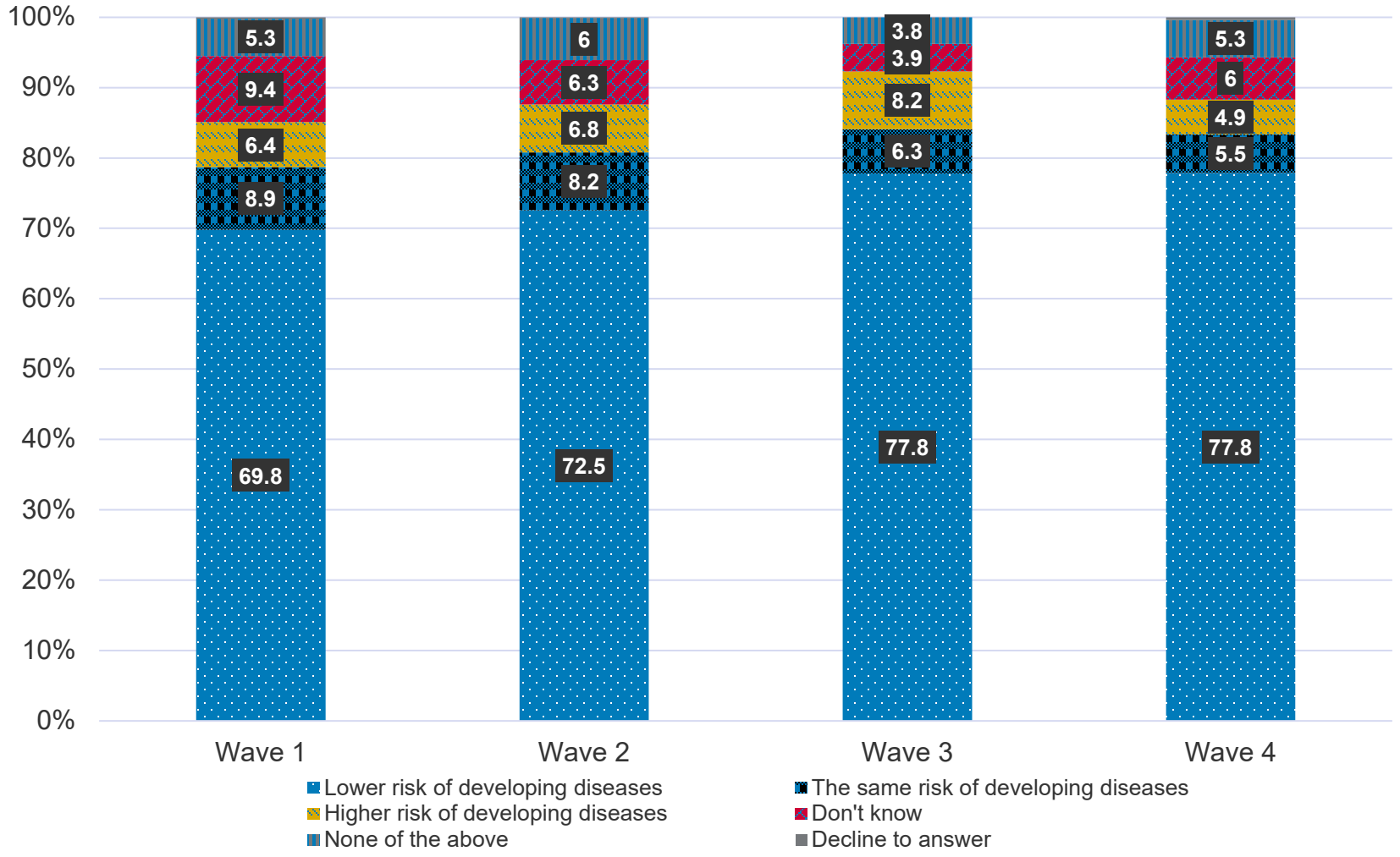
- Puts you at lower risk for mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.
- Does not affect your risk for mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.
- Puts you at higher risk for mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.
- None of the above
- Don't know
- Decline to answer

You said that using General Snus instead of CCs puts you at lower risk of diseases. If you are going to use General Snus instead of CCs to lower your risk of diseases, how many CCs, if any, can you smoke per day?

- Zero (0) CCs
- Up to 5 CCs
- Up to 20 CCs
- As many as you want to smoke
- Don't know
- Decline to answer

UNDERSTANDING THAT USING GENERAL SNUS PRESENTS LESS RISK OF VARIOUS DISEASES THAN SMOKING CCS

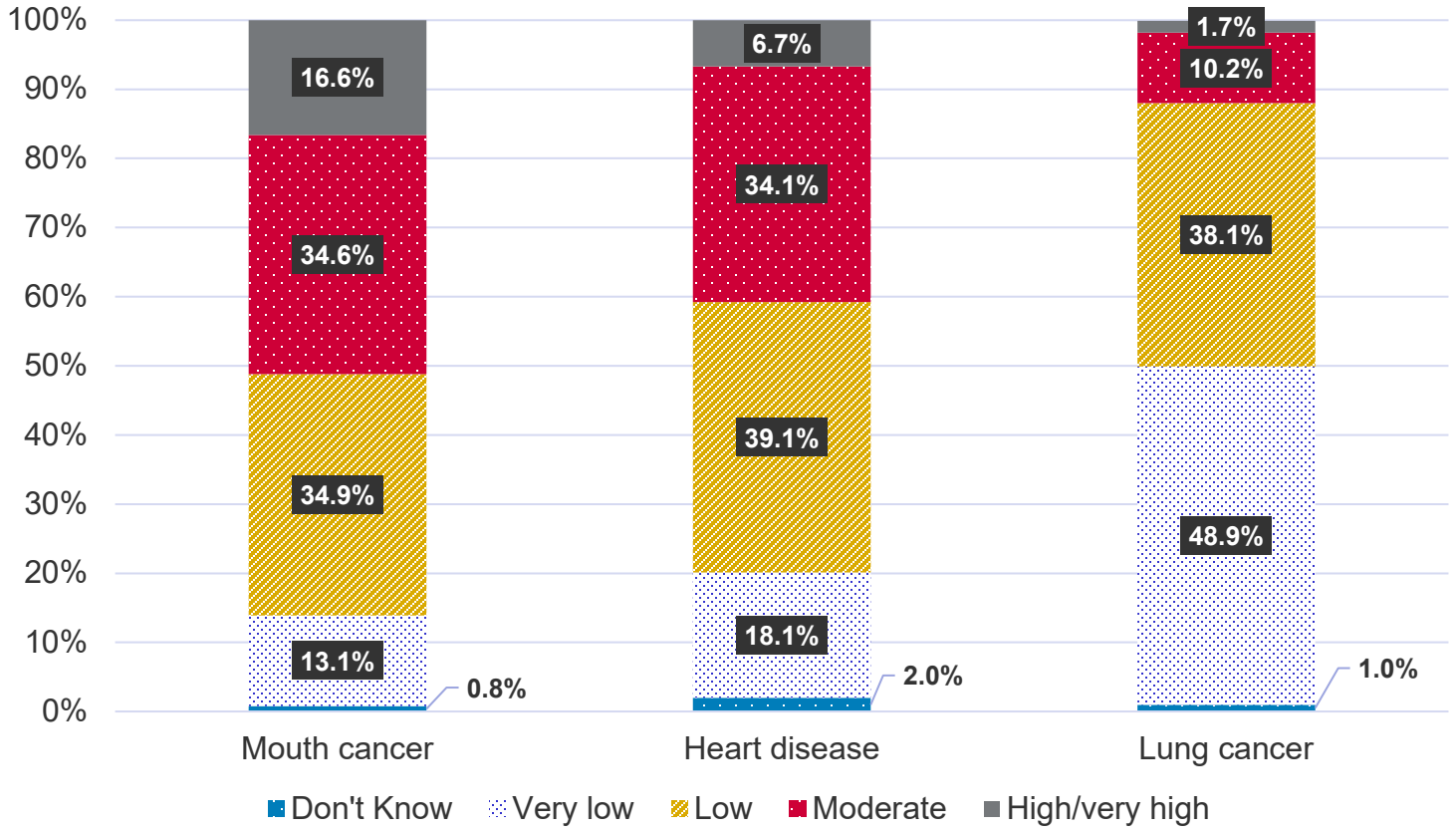
Question: *Using General Snus instead of CCs…*



Most General Snus users correctly answered a multiple-choice question assessing understanding of the modified risk claim for using General Snus instead of CCs.

BASELINE UNDERSTANDING THAT USING GENERAL SNUS STILL PRESENTS SOME RISK

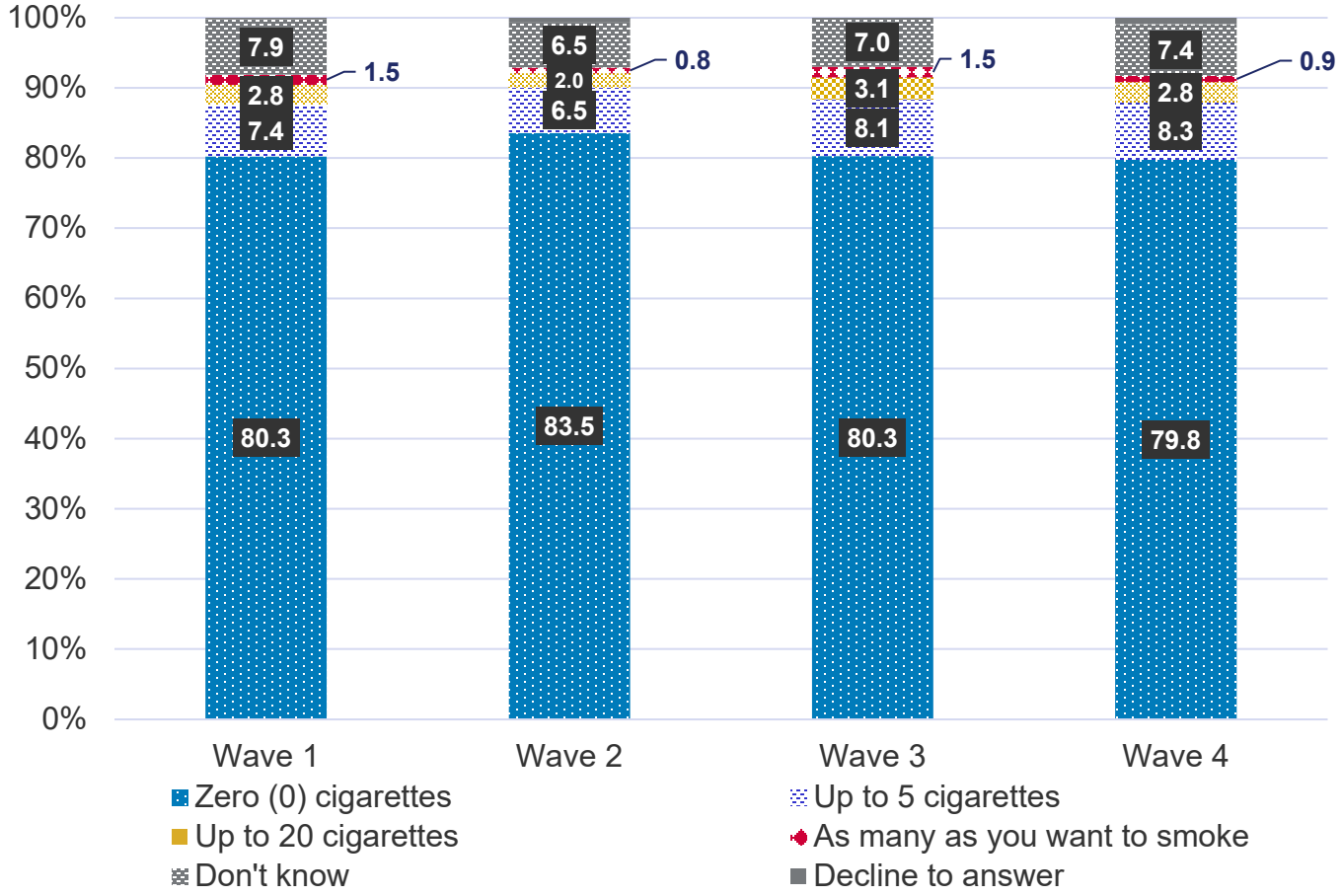
Question: In your opinion, what is the chance that a person who **only uses General Snus every day** would suffer from the following health conditions during his/her lifetime***?***



At baseline, consumers generally view using General Snus as having some risk. This has not changed between study waves.

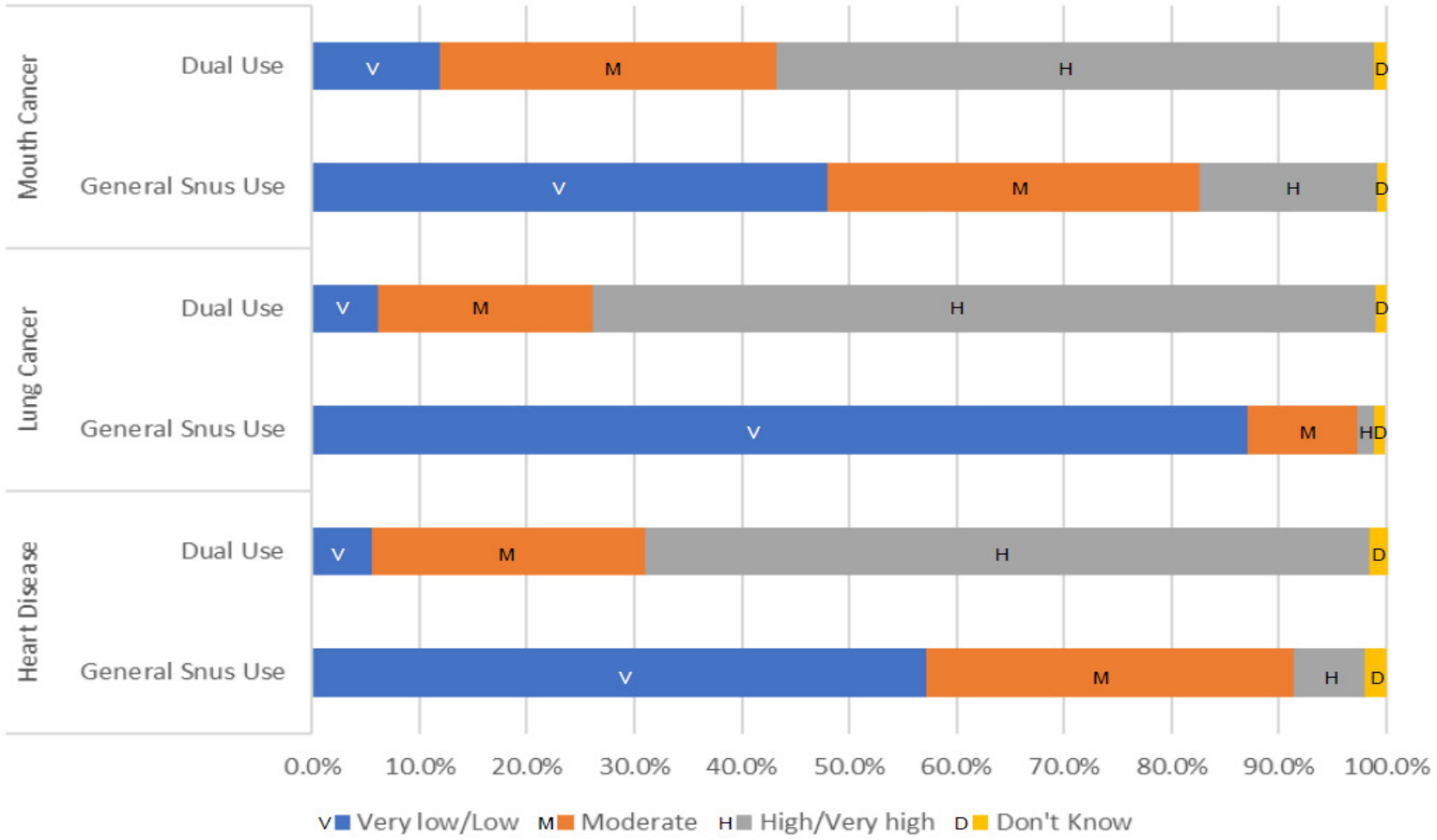
UNDERSTANDING HOW TO USE GENERAL SNUS TO REDUCE RISK

Question: ***If you are going to use General Snus instead of CCs to lower your risk of diseases, how many CCs, if any, can you smoke per day?***



Most General Snus users correctly answered a multiple-choice question assessing understanding of how to use General Snus to reduce risk.

PERCEIVED RISK OF EXCLUSIVE DAILY GENERAL SNUS USE AND DAILY DUAL USE OF GENERAL SNUS WITH CCs AT BASELINE



Adult consumers correctly perceive dual use of CCs and General Snus as more harmful than exclusive use of General Snus.

CONSUMER UNDERSTANDING AND PERCEPTIONS SUMMARY & CONCLUSIONS

- Most study participants accurately understood that using General Snus instead of CCs puts them at lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.
- Most study participants perceived that using General Snus every day carries some risk for some diseases.
- Most participants accurately understood that partial switching would not reduce risk.
- Most participants accurately perceived dual use of CCs and General Snus as more harmful than exclusive use of General Snus.

CLARIFYING QUESTIONS?

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