U.S. SMOKELESS TOBACCO COMPANY LLC (USSTC) MODIFIED RISK TOBACCO PRODUCT APPLICATION

Presented by:
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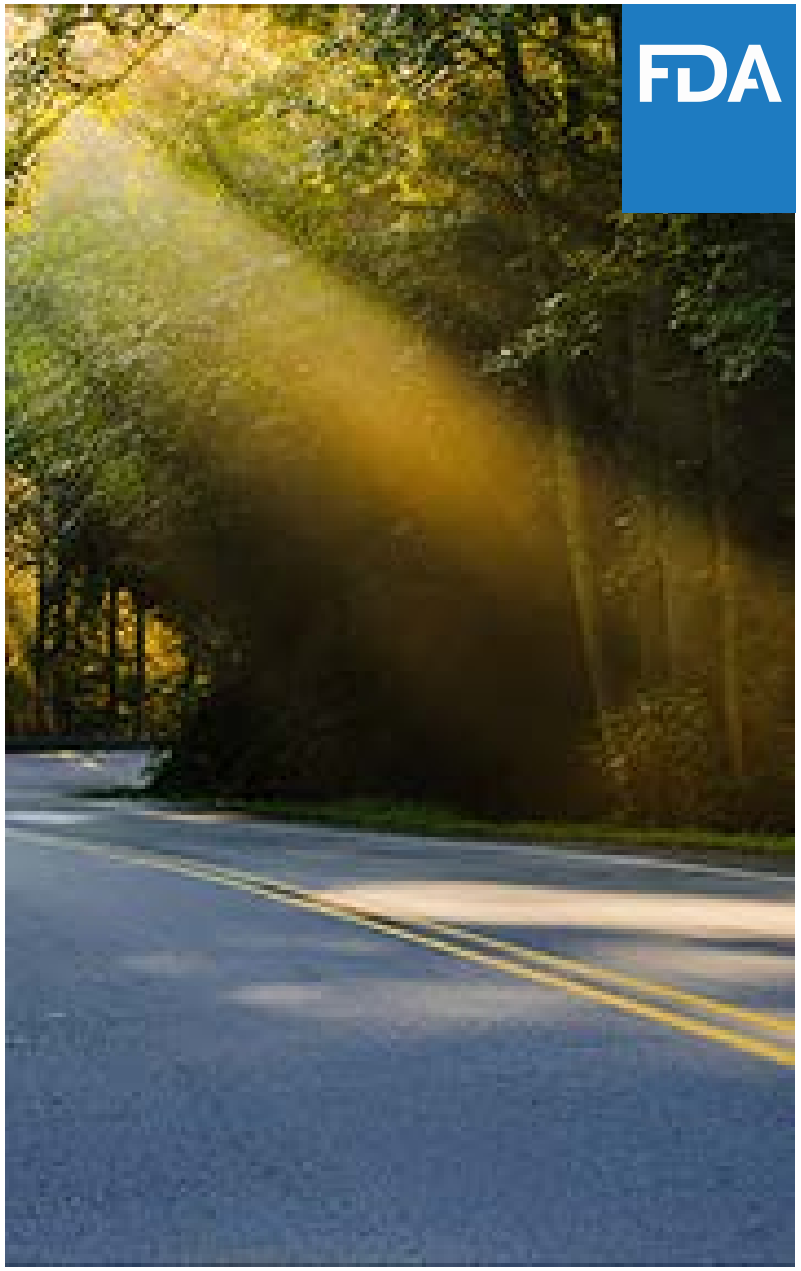
- Summary of USSTC application under review
- Lines of evidence
- Questions for the committee



USSTC MRTPA SUBMISSION

The applicant is seeking an order under Section 911(g)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for:

Copenhagen® Snuff Fine Cut

MRTPA received	MRTPA accepted	MRTPA filed	Public comment docket opened	TPSAC convened
March 20, 2018	April 12, 2018	September 14, 2018	September 21, 2018	February 6-7, 2019

FDA acceptance and filing reviews

FDA scientific review

PROPOSED MODIFIED RISK CLAIM

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

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

The FD&C Act requires FDA to determine if 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 individual tobacco users and

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

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 individual tobacco users?
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?

FOCUS OF TPSAC DISCUSSION & RECOMMENDATIONS

EVIDENCE RELATED TO INDIVIDUAL HEALTH RISKS AND MODIFIED RISK CLAIM

FDA will present the product chemistry, nonclinical and clinical studies, and epidemiological evidence used to assess relative health risks and the proposed modified risk claim.

TPSAC will be asked to discuss the evidence and scientific accuracy of the proposed claim.

FOCUS OF TPSAC DISCUSSION & RECOMMENDATIONS

CONSUMER UNDERSTANDING & PERCEPTIONS

FDA will present sample label and advertising executions submitted by the applicant and the results of the consumer perception study.

TPSAC will be asked to discuss consumer perceptions and understanding of the modified risk information.

FOCUS OF TPSAC DISCUSSION & RECOMMENDATIONS

LIKELIHOOD OF USE OF PROPOSED MRTP AND IMPACTS TO THE POPULATION

FDA will present data from observational studies to describe characteristics of Copenhagen Snuff Fine Cut users, patterns of use, and transitions from cigarettes to smokeless tobacco, as well as USSTC's clinical study, likelihood of use study, and population modeling.

TPSAC will be asked to discuss potential use behaviors with respect to the proposed MRTP, including the likelihood that cigarette smokers will switch completely to Copenhagen Snuff Fine Cut.

QUESTIONS FOR THE COMMITTEE

QUESTIONS FOR TPSAC: MODIFIED RISK CLAIM

Q1: The applicant proposed the following modified risk claim:

“IF YOU SMOKE, CONSIDER THIS: Switching completely to this product from cigarettes reduces risk of lung cancer.”

DISCUSS the available scientific evidence and VOTE on the whether the proposed modified risk claim is scientifically accurate (yes/no/abstain).

QUESTIONS FOR TPSAC: CONSUMER UNDERSTANDING & PERCEPTIONS

Q2: In addition to evaluating the proposed modified risk claim for scientific accuracy, FDA also evaluates consumer understanding and perception of the modified risk information.

DISCUSS the potential implications of the proposed modified risk information on consumer understanding and perceptions.

QUESTIONS FOR TPSAC:
LIKELIHOOD OF USE OF PROPOSED MRTP & POPULATION IMPACT

Q3: DISCUSS the potential users of the proposed MRTP.

a. What is the likelihood that cigarette smokers will switch completely to Copenhagen Snuff Fine Cut?

b. Considering the health risks from the use of Copenhagen Snuff Fine Cut and those who may be likely to use the product, what are the groups of potential concern (e.g., users of smokeless tobacco products with lower HPHC levels, youth)?

U.S. SMOKELESS TOBACCO COMPANY LLC (USSTC) MODIFIED RISK TOBACCO PRODUCT APPLICATION: FDA SCIENTIFIC PRESENTATION

Presented by:
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EVIDENCE RELATED TO HEALTH RISKS & MODIFIED RISK CLAIM

HARMFUL AND POTENTIALLY HARMFUL CONSTITUENTS (HPHCs)

- In 2012, FDA published a list of 93 HPHCs in tobacco and tobacco smoke and a draft guidance that identified an abbreviated list of 20 HPHCs
- 9 HPHCs on the abbreviated list are present in smokeless tobacco
- USSTC reported levels of these 9 HPHCs in Copenhagen Snuff Fine Cut
  - FDA compared the levels of HPHCs between Copenhagen Snuff Fine Cut and cigarettes based on potential daily intake
  - Based on HPHC concentrations and typical consumption patterns, there were relative increases in potential daily intake levels of some HPHCs (arsenic, B[a]P, cadmium, NNK, NNN, and total nicotine) and lower levels of other HPHCs (acetaldehyde and formaldehyde) compared to cigarette smoke
  - It is unclear how relative differences in HPHC intake levels between Copenhagen Snuff Fine Cut and cigarette smoke translate into differences in exposure levels and, ultimately, disease risk

HPHCs IN COPENHAGEN SNUFF FINE CUT COMPARED TO OTHER SMOKELESS TOBACCO PRODUCTS

- Moist snuff comprises the vast majority of the smokeless tobacco market share (>80%)
- Copenhagen Snuff Fine Cut has higher levels of arsenic, B[a]P, cadmium, and total nicotine than other moist snuff products
- Most notable differences in HPHC levels are between Copenhagen Snuff Fine Cut and Swedish snus
- Differences in tobacco growing conditions, tobacco type, curing conditions, and moisture can lead to differences in HPHC levels across different smokeless tobacco products

Constituent (unit)	Copenhagen Snuff Fine Cut Mean Quantity	Moist Snuff Mean Quantity	General Snus Mean Quantity
Acetaldehyde (µg/g)	6.3	35.7	21.62
Arsenic (ng/g)	233	214	BLOQ
Benzo[a]pyrene (ng/g)	117	61.6	BLOQ
Cadmium (ng/g)	1537	1052	579.44
Crotonaldehyde (µg/g)	BLOQ**	2.98	BLOQ
Formaldehyde (µg/g)	1.58	8.43	15.68
NNN (ng/g)	3825	4058	726
NNK (ng/g)	1034	1394	230
Total Nicotine* (mg/g)	12.5	12	8.71
Free Nicotine* (mg/g)	3.92	4.2	5.65

Data Sources: Ammann et al.[1]; Borgerding, et al.[2]; Stepanov et al.[3]; Swedish Match 2014 MRTPAs

*"Total and free nicotine reported "as-is" weight; all other data reported as "dry weight basis"
**BLOQ: Below Limit of Quantitation

EVIDENCE SUBMITTED

- Applicant submitted nonclinical, clinical, and epidemiological evidence to describe the potential health risks of Copenhagen Snuff Fine Cut and to support the proposed modified risk claim
- Some of the evidence submitted is product-specific (i.e., Copenhagen Snuff Fine Cut), but most relies on data from the product category of moist snuff or smokeless tobacco

Nonclinical	• Published literature used to assess long-term exposure, genotoxicity, carcinogenicity, modulating carcinogenicity, immunotoxicology, inflammation, oral toxicity, cardiovascular effects, and reproductive/developmental toxicities • Few studies included Copenhagen Snuff Fine Cut; most used variety of commercial brand smokeless products or research tobacco products
Clinical	• No long-term studies assessing biomarkers among users of Copenhagen Snuff Fine Cut were submitted • Published studies compared biomarkers of exposure and potential harm in smokeless tobacco users to those in cigarette smokers and non-tobacco users
Epidemiological	• No long-term data are available pertaining to the use of Copenhagen Snuff Fine Cut • Published literature on health risks associated with smokeless tobacco used to examine smokeless tobacco use, cigarette smoking, and risk for tobacco-related diseases • Analyses of linked mortality data from the National Health Interview Survey and National Longitudinal Mortality Study

NONCLINICAL EVIDENCE

- No nonclinical studies were conducted to test potential of Copenhagen Snuff Fine Cut to induce toxicities that may then be compared to never use, other smokeless tobacco products, or cigarettes
- Nonclinical studies have found an association between arsenic, B[a]P, NNN, NNK and lung cancer[4-27]
- Assuming 100% extraction, there is an increase in potential daily intake of lung carcinogens with Copenhagen Snuff Fine Cut compared to combustible cigarette products
- Due to variables such as route of exposure, extraction profiles of HPHCs, and portal of entry effects (including toxicant absorption, distribution, metabolism, and excretion), the net exposure, and subsequent potential lung cancer risk, from HPHCs due to exposure to Copenhagen Snuff Fine Cut may be lower than that of exposure to the same HPHCs from cigarette smoking
- In addition to lung cancer, oral exposure to HPHCs found in Copenhagen Snuff Fine Cut is associated with other types of cancer, developmental and reproductive effects, cardiovascular effects, and immunological effects[28-47]

CLINICAL EVIDENCE

Applicant did not assess biomarkers among users of Copenhagen Snuff Fine Cut, but the published literature submitted suggests…

Biomarkers of Exposure

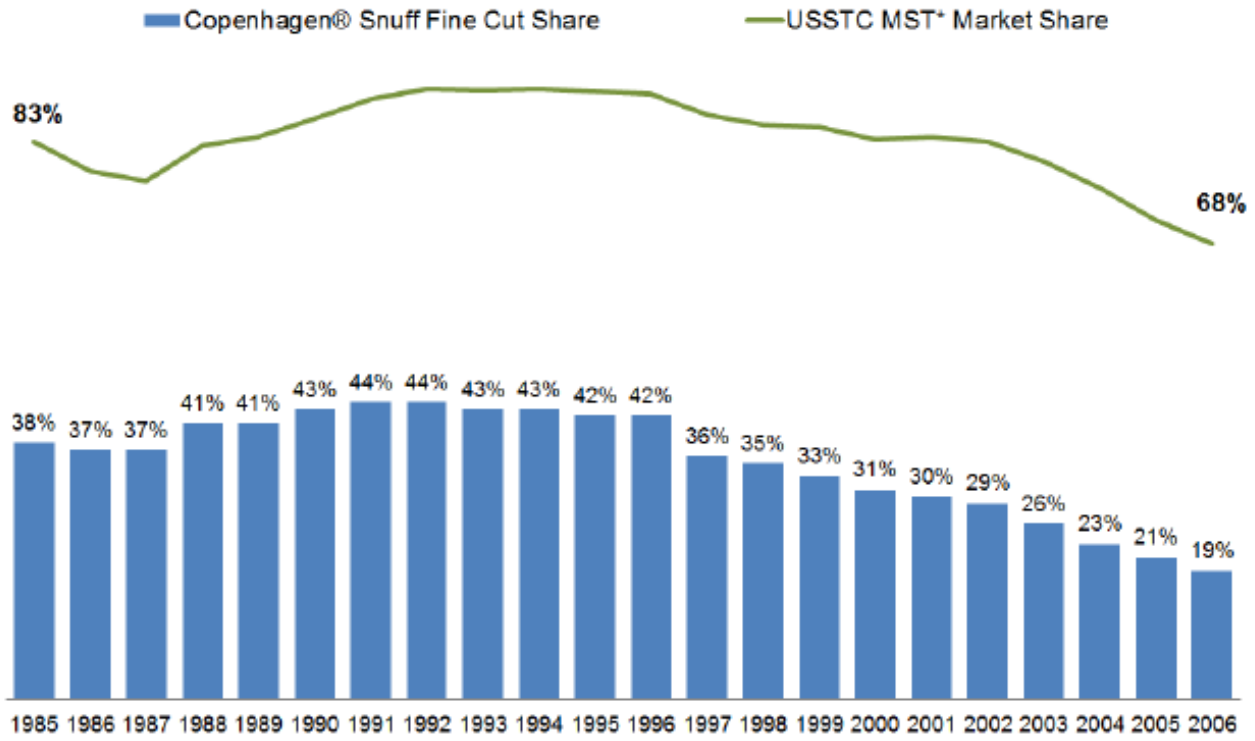
- Smokeless tobacco users may have exposure to nicotine and TSNAs comparable to or higher than smokers[48-50]
- Plasma mercury, cadmium, and urinary arsenic are not elevated in smokeless tobacco users compared to non-tobacco users[50,51]

Biomarkers of Potential Harm

- Significantly higher levels of biomarkers suggest smokers have elevated inflammation and immune response compared to smokeless tobacco users[51,52]
- No significant differences in inflammatory response observed between smokeless tobacco users and non-tobacco users[51,52]

RELEVANCE OF EPIDEMIOLOGICAL DATA TO COPENHAGEN SNUFF FINE CUT

- Applicant states published literature is relevant to the product under review because:
  - Moist smokeless tobacco was the primary form of smokeless tobacco used in U.S. at the time of these studies
  - Copenhagen Snuff Fine Cut held large market share at the time of the studies
  - Production process "essentially unchanged" except for refinements, such as improved process controls and reduced TSNAs



Source: Copenhagen® Fine Cut Natural and USSTC Shipments 1985-2006 based on USSTC historical shipment data and USSTC RAD SVT projected volume and share. 1985-2000 share estimated using USSTC's growth rate during that period and total industry total volume as of 2002.
*Moist Smokeless Tobacco (MST). Yearly data shown until Feb. 2007 (grandfathered product date).

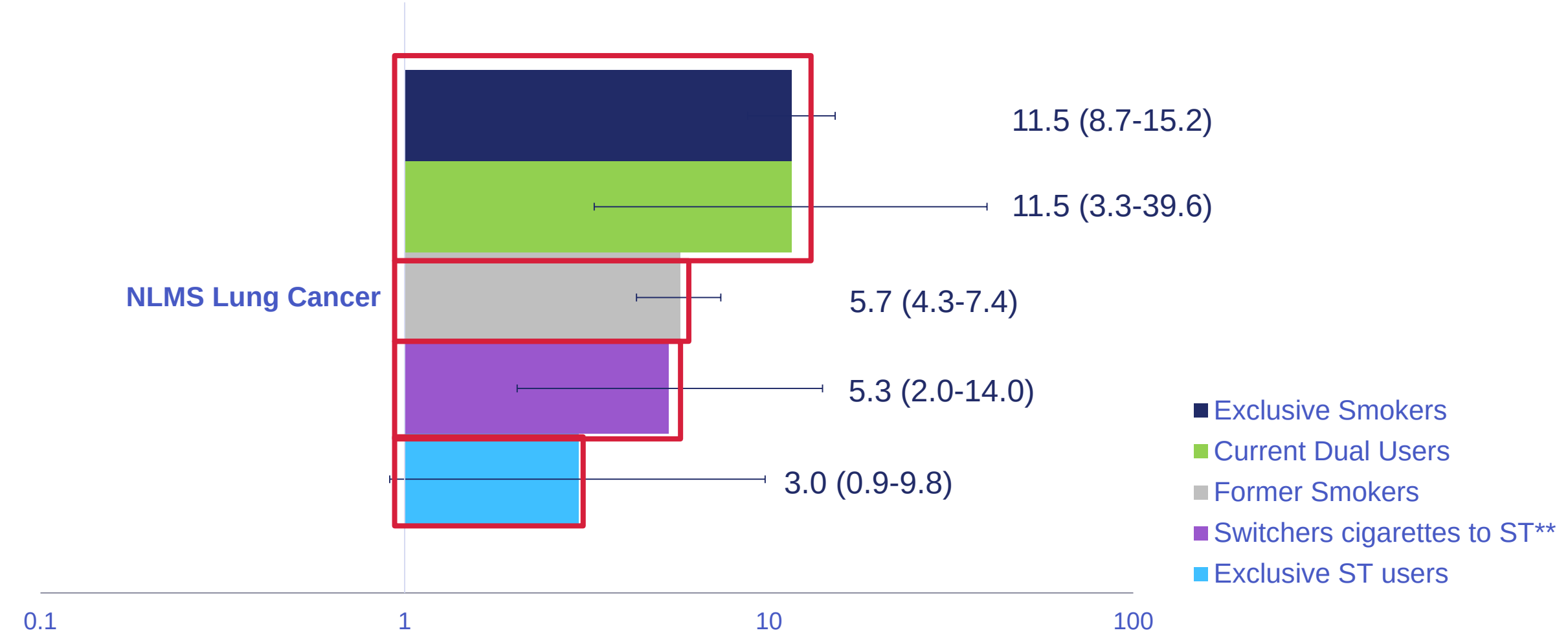
PUBLISHED LITERATURE ON SMOKELESS TOBACCO AND LUNG CANCER

- Current smokeless tobacco use compared to cigarettes
  - No direct comparison between mortality risks for current smokeless tobacco to current cigarette smokers
  - Literature presents ratio measures (hazard ratio (HR)/relative risk (RR)) among smokeless tobacco users, cigarette users, and dual users with a common reference group (never users)
    - Findings from CPS-II presented in the 2014 Surgeon General's Report compared cigarette smokers to never users and found an RR of 12.7 for females and 23.3 for males[53]
    - Individual studies comparing smokeless tobacco to never users are mixed, but two systematic reviews found an HR=1.8[54,63]
- Switching compared to quitting all tobacco
  - Henley et al. 2007: after 20 years of follow-up, men who switched completely from cigarettes to smokeless tobacco had a significantly greater risk of dying from lung cancer compared to those who quit all tobacco[55]

LINKED MORTALITY ANALYSIS DATA SOURCES

National Longitudinal Mortality Study (NLMS)	• NLMS public use file, which is based on the 1993-2005 Current Population Survey Tobacco Use Supplements (CPS-TUS) • Five years of follow-up for each respondent • Outcome: Lung Cancer Mortality ICD-10 codes C33-C34 (malignant neoplasms of trachea, bronchus, and lung)
National Health Interview Survey Linked Mortality File (NHIS-LMF)	• Nationally representative, cross-sectional household interview survey • Analyses of NHIS data from 1986-2009 that NCHS linked to death record certificates from the National Death Index with vital status follow-up through December 31, 2011 • Outcome: Lung Cancer Mortality ICD-10 codes C33-C34 (malignant neoplasms of trachea, bronchus, and lung)

NLMS LINKED MORTALITY ANALYSIS: LUNG CANCER MORTALITY HAZARD RATIOS



Data Source: MRTPA Section 6.1

OTHER HEALTH RISKS ASSOCIATED WITH SMOKELESS TOBACCO

- 2012 IARC monograph: Sufficient evidence in humans for carcinogenicity of smokeless tobacco; smokeless tobacco causes oral cancer, esophageal cancer, and pancreatic cancer[56]
- A meta-analysis reported an association between U.S. smokeless tobacco use and fatal myocardial infarction and stroke[64]
- Data on all-cause mortality from individual studies is mixed[57-59]
- Several studies from Sweden have found an association between smokeless tobacco use and adverse pregnancy outcomes[60-62]
- Relative risks for cancers other than lung cancer are often higher in U.S. studies than Scandinavian studies, possibly due to the lower level of nitrosamines and other HPHCs in Swedish snus than in U.S. smokeless tobacco products[63-65]

CONSUMER UNDERSTANDING AND PERCEPTIONS

LABELS AND ADVERTISING

USSTC provided sample labels and advertising with the proposed modified risk claim.

- Print advertisement
- Direct mail advertisement
- Email advertisement
- Website pop-up screen
- Promotional card
- Can label
- Point-of-sale materials

Sample Bottom of Can Label

Sample Point-of-Sale Advertisement

Source: MRTPA Appendix 4.1-8, 4.1-9

USSTC CONSUMER COMPREHENSION AND INTENTIONS STUDY (CCI): METHODS

OBJECTIVE

To assess participants' (1) comprehension of the modified risk claim; (2) behavioral intentions; and (3) risk perceptions of "Copenhagen Snuff"

DESIGN

- Pre-test/post-test where consumers were assigned to view an advertisement either with the claim (test) or without the claim (control)
- Conducted online (May – July 2017)

SAMPLE

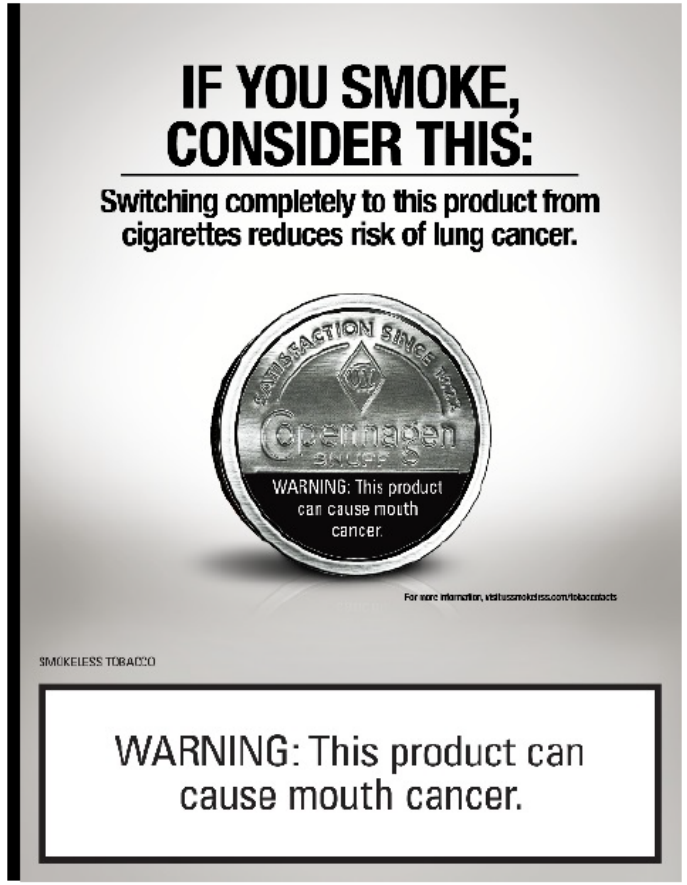
- Recruited via mall intercept, telephone, or email
- Quota sampling approach
- N=5,871 adult participants (including oversample of 944 young adults)
- Main sample categorized to tobacco user subgroups: smokers, moist smokeless tobacco users, dual users, former users, and never users
- Young adult oversample categorized to one of two subgroups: tobacco users and tobacco non-users

PROCEDURE

- Participants completed pre-test, viewed the advertisement, and completed post-test
- Advertisement could be viewed at any time during post-test
- No manipulation check or minimum amount of time to view stimuli

CCI STUDY STIMULI: ADVERTISEMENTS WITH AND WITHOUT MODIFIED RISK CLAIM

Test Condition



Control Condition

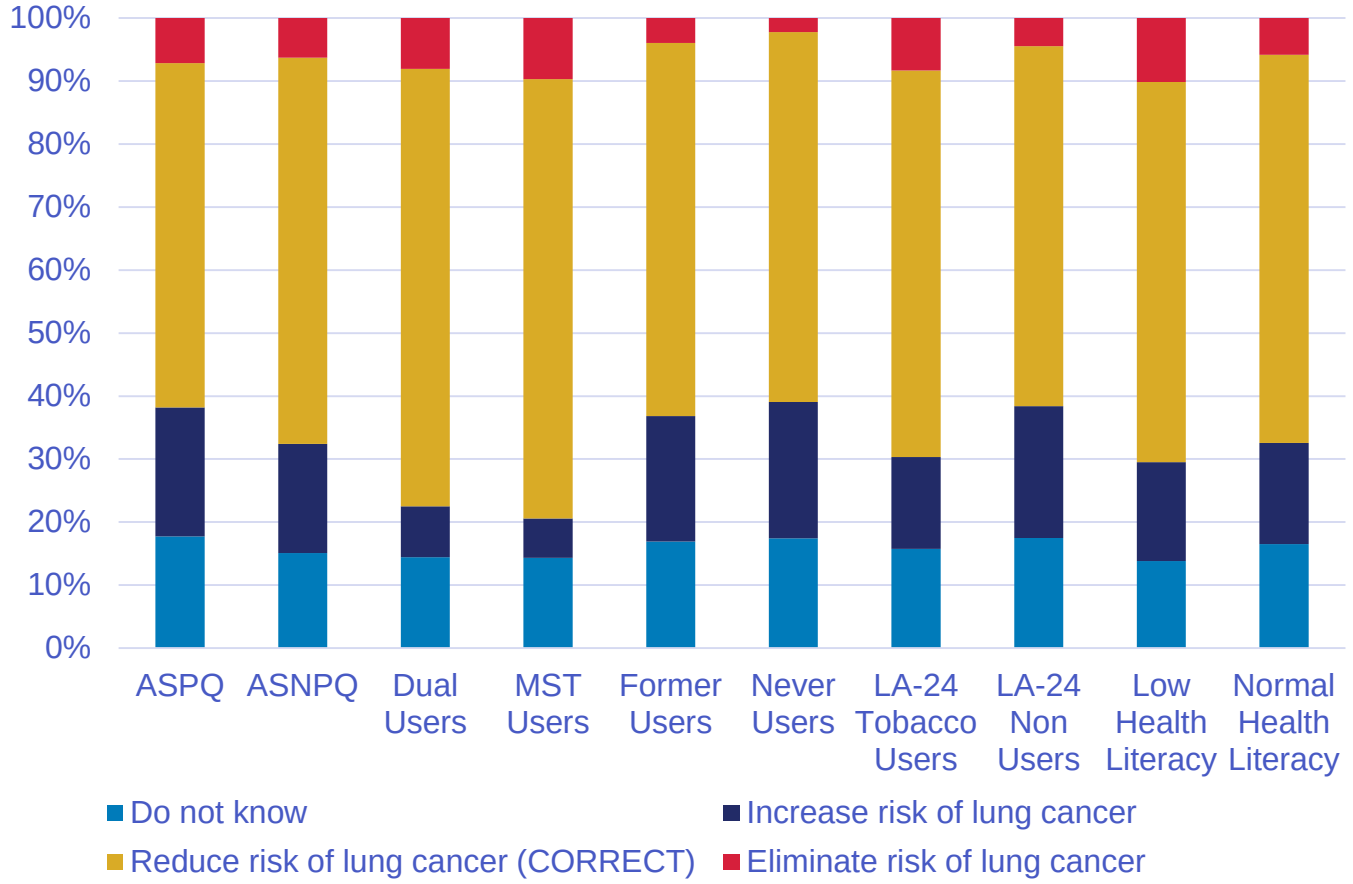
Source: MRTPA Section 7.3.2.1

CCI STUDY: SELECTED OUTCOMES

CLAIM COMPREHENSION **(Test Condition, Post-test)**	**Q: "**Please look at this ad again. Regardless of what you believe to be true, please answer the question based on the information shown in this ad. Based only on the information shown in this ad, smokers who switch completely from cigarettes to Copenhagen Snuff:" **R:** Increase the risk of lung cancer, Reduce the risk of lung cancer, Eliminate the risk of lung cancer, Do not know
SPECIFIC RISK PERCEPTIONS **(Test Condition, Pre-test and Post-test)**	**Qs (6): "**Looking at the same list, how likely is it that these things will happen to a person who only [uses Copenhagen Snuff daily/smokes cigarettes daily]?" • *Negatively impacts health* • *Mouth cancer* • *Nicotine addiction* • *Discolored teeth or decay* • *Heart disease/heart attack* • *Lung cancer* **R:** 0%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%
GENERAL RISK PERCEPTIONS **(Pre-test and Post-test)**	**Qs (5): "**Please rate each item for the risk you feel it could pose to a person's health:" • *Using half a can of Copenhagen Snuff daily* • *Using half a can of other dip/snuff daily* • *Smoking 15 cigarettes daily* • *Using NRT as directed* • *Completely quitting all tobacco* **R:** Not at all risky, Slightly risky, Somewhat risky, Moderately risky, Risky, Very risky, Extremely risky

COMPREHENSION OF PROPOSED MODIFIED RISK CLAIM

Question: ***Based only on the information shown in this ad, smokers who switch completely from cigarettes to Copenhagen Snuff…***



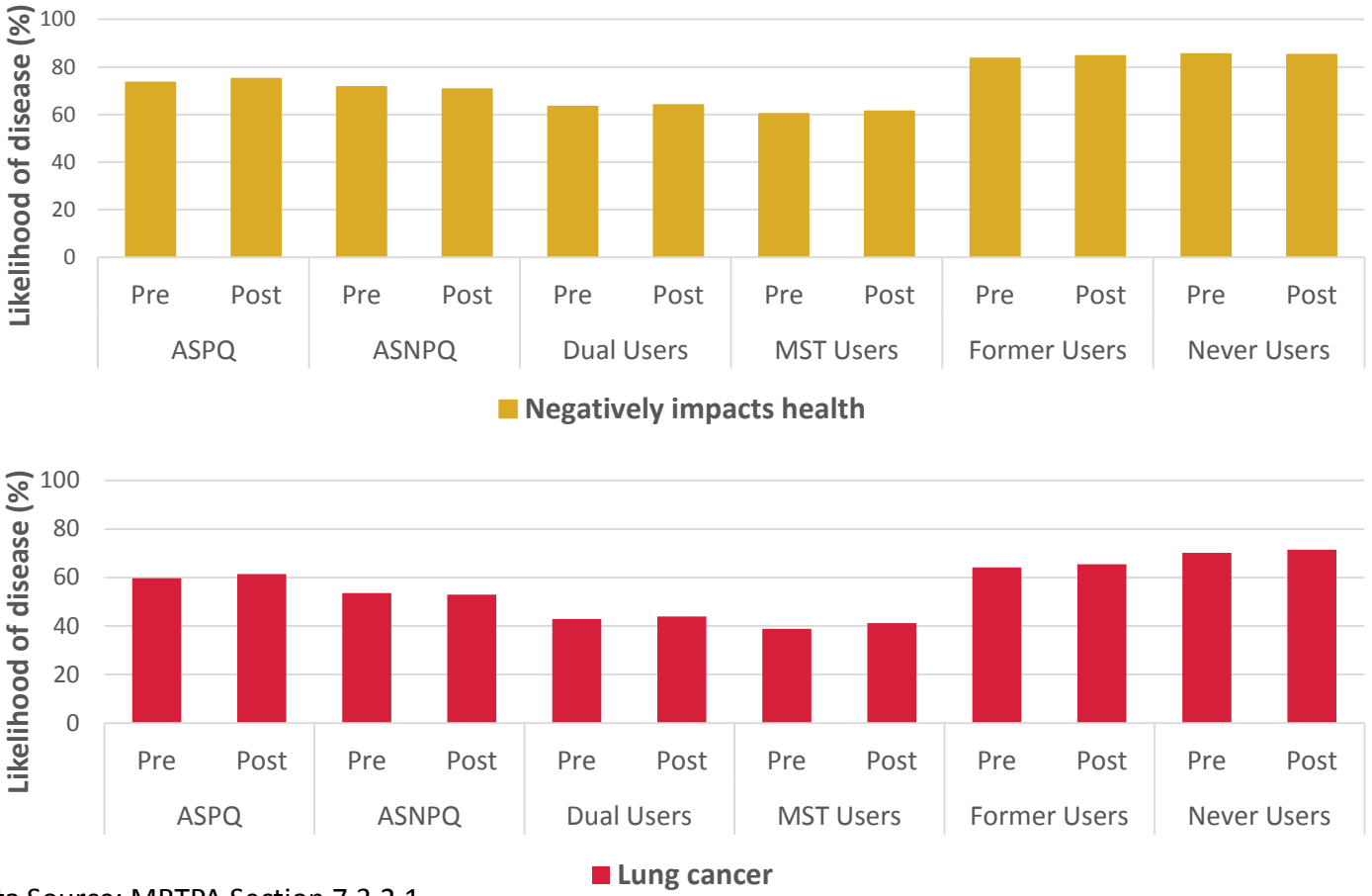
A majority of consumers who viewed the proposed modified risk claim were able to correctly answer a multiple-choice question assessing comprehension of its meaning.

ASPQ: Adult smokers planning to quit
ASNPQ: Adult smokers not planning to quit
MST: Moist smokeless tobacco
LA: Legal age to purchase

Data Source: MRTPA Section 2.3

EFFECT OF PROPOSED MODIFIED RISK CLAIM ON SPECIFIC RISK PERCEPTIONS

Question: ***How likely is it that these things will happen to a person who uses only Copenhagen Snuff daily?***



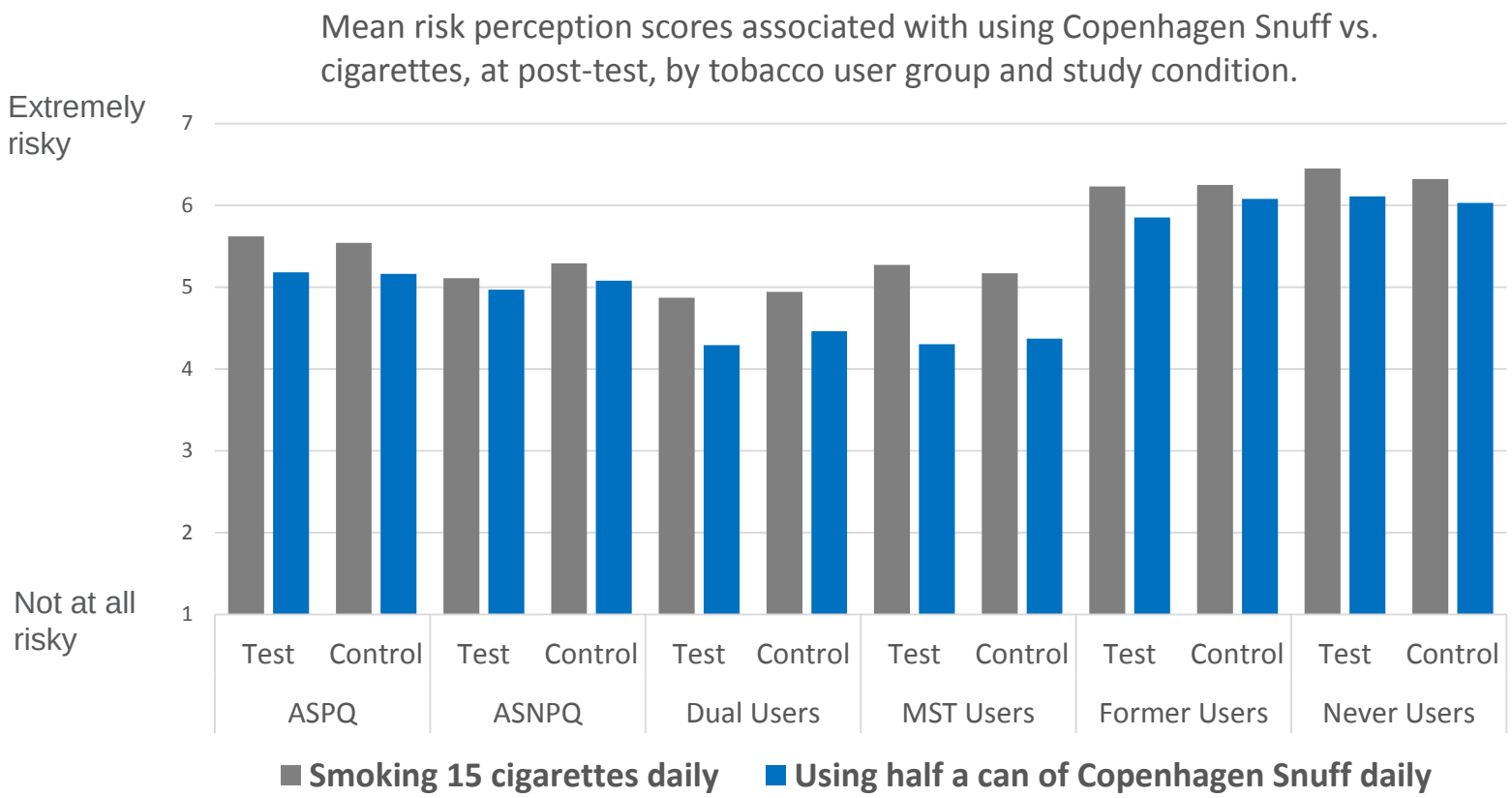
The modified risk claim did not have a significant effect on absolute risk perceptions for specific health outcomes, including lung cancer, among consumers assigned to the test condition.

ASPQ: Adult smokers planning to quit
ASNPQ: Adult smokers not planning to quit
MST: Moist smokeless tobacco

Data Source: MRTPA Section 7.3.2.1

EFFECT OF PROPOSED MODIFIED RISK CLAIM ON GENERAL RELATIVE RISK PERCEPTIONS

Question: ***Please rate each item for the risk you feel it could pose to a person's health***



Consumers perceived using Copenhagen Snuff as less risky than smoking cigarettes and more risky than using NRT or quitting all tobacco.* The modified risk claim does not appear to affect general relative risk perceptions.

***Applicant did not perform statistical testing; it is unknown whether apparent differences in consumers' relative risk perceptions are statistically significant.**

ASPQ: Adult smokers planning to quit
ASNPQ: Adult smokers not planning to quit
MST: Moist smokeless tobacco

Data Source: MRTPA Section 7.3.2.1

CLAIM COMPREHENSION AND RISK PERCEPTIONS AMONG YOUNG ADULTS

Approximately 61% of tobacco users and 57% of tobacco non-users answered the claim comprehension question correctly

Non-users who saw the claim had lower risk perceptions that Copenhagen Snuff negatively impacts health, compared to those who saw the control ad*

There were no significant differences for any of the other five specific risk perception items

*While statistically significant, magnitude of decrease was small (decrease of 1.1 points on 100-point scale (t = -3.96; p <0.001, d = 0.28)). Risk perceptions among young adult non-users of tobacco assigned to the control condition increased 3.67 points on a 100-point scale.

LIKELIHOOD OF USE AND IMPACTS TO THE POPULATION

OBSERVATIONAL STUDIES ASSESSING CHARACTERISTICS AND USE OF COPENHAGEN PRODUCTS

Population Assessment of Tobacco and Health (PATH) Study	• Nationally representative longitudinal study of tobacco use and health among adults and youth in the U.S. • Approximately 49,000 participants ages 12 and older • Wave 1: September 12, 2013-December 14, 2014; Wave 2: October 23, 2014-October 30, 2015 • Brand data were collected about smokeless tobacco products, including brand (“Copenhagen”) and sub-brand (“Copenhagen Snuff”) • Data collected in the absence of modified risk claim
Altria Client Services LLC (ALCS) Tracking Study	• Nationally representative, mixed mode survey used to measure tobacco use prevalence among adults • Enrolls approximately 2,400 adults per month • Data in application relies on 24 months of data prior to August 2017 • Includes form and brand information (e.g., “Copenhagen Fine Cut”) • Data collected in the absence of modified risk claim

USSTC STUDIES ASSESSING LIKELIHOOD OF USE OF COPENHAGEN PRODUCTS

Altria Client Services (ACS) Clinical Study	• Within-subject laboratory study comparing nicotine pharmacokinetics and subjective effects of a test moist snuff tobacco product "produced to the identical specifications as for the Copenhagen Original Fine Cut product marketed on or before February 2007" with participants' usual brand of cigarettes and Nicorette Fresh mint gum • N=24 (aged 21-65 years, ≥ 10 menthol or non-menthol cigarettes per day for at least 1 year; non-daily users of original or flavored moist snuff tobacco products, no use of Nicorette Fresh Mint gum in previous 3 months) • Data collected in the absence of modified risk claim
Claim Comprehension and Intentions Study (CCI)	• Quasi-experimental study examining effects of the modified risk claim on behavioral intentions to use "Copenhagen Snuff" • Pre-test and post-test survey instruments • Behavioral intentions assessed: intentions to try, use, dual use, and switch to Copenhagen Snuff; intentions to purchase Copenhagen Snuff; intentions to quit smoking; intentions to quit all tobacco • Behavioral intentions used as proxies for likelihood of use

CURRENT USE OF SMOKELESS TOBACCO AND COPENHAGEN SNUFF FINE CUT IN THE U.S.

Smokeless tobacco use (excluding pouched snus) is more common among those who are…[66]

- male
- non-Hispanic white
- living in nonurban areas
- aged 25-49

9.4% of adult established users (aged 25+) and 1.5% of 12-17 year old past 30-day non-light smokeless tobacco users reported “Copenhagen Snuff” as last brand used or usual brand

Source: MRTPA Section 6.4

Copenhagen Snuff users report using moist smokeless tobacco on 25+ days in the past month

Source: MRTPA Section 3.2

DUAL USE AND SWITCHING

Switching behavior from exclusive smoking to exclusive smokeless tobacco use among adults is low[67-69]

Approximately 20% of Copenhagen Snuff users reported past 30-day use of cigarettes

Source: MRTPA Section 3.2

PHARMACOKINETIC AND SUBJECTIVE EFFECTS: ACS CLINICAL STUDY FINDINGS

Findings from the ACS Clinical Study suggest that the abuse potential of the test moist snuff product may be lower than usual brand cigarettes and similar to or higher than that of Nicorette gum

Study limitations include:

- Participants were exposed to the study tobacco products under controlled conditions for a very brief duration
- Measures of dependence were not evaluated
- Participants were cigarette smokers (≥ 10 cigarettes per day) with previous experience using moist snuff tobacco products (≥ 20 uses during lifetime, but not used every day in past 30 days)

Plasma nicotine and subjective effects data suggest exclusive cigarette smokers may be unlikely to switch to exclusive use of Copenhagen Snuff Fine Cut

MEASURES OF LIKELIHOOD OF USE: CCI STUDY

INTENT TO TRY (3 items averaged)	**Q:** "I am open to trying Copenhagen Snuff in the next 30 days." **Q:** "Based on what you know about Copenhagen Snuff, how likely or unlikely are you to try Copenhagen Snuff?" **Q:** "Based on what you know about Copenhagen Snuff, how likely or unlikely are you to try Copenhagen Snuff if one of your best friends were to offer Copenhagen Snuff to you?" **R:** 6 point scale of agreement
INTENT TO USE (4 items averaged)	**Q:** "I would consider using Copenhagen Snuff more than once." **Q:** "I expect to use Copenhagen Snuff." **Q:** "It is likely that I will regularly use Copenhagen Snuff in the next 6 months." **Q:** "Copenhagen Snuff will be my regular brand of snuff/dip/smokeless tobacco in the next 30 days." **R:** 6 point scale of agreement
INTENT TO SWITCH (3 items averaged)	**Q:** "I plan to gradually switch from regular cigarettes to a Copenhagen Snuff." **Q:** "I plan on using Copenhagen Snuff as a complete replacement for cigarettes." **Q:** "I intend on switching from cigarettes to Copenhagen Snuff in the next six months." **R:** 6 point scale of agreement

POTENTIAL IMPACT OF MODIFIED RISK CLAIM ON INTENTIONS TO USE AMONG CURRENT USERS: CCI STUDY

Unadjusted mean composite scores for intentions to try, use, switch, and dual use Copenhagen Snuff among adult tobacco users

Group	Condition	Intentions to Try		Intentions to Use		Intentions to Switch		Intentions to Dual Use	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post
ASPQ	Control	2.43	2.30	2.31	2.20	2.19	2.11	2.19	2.06
	Test	2.40	2.36	2.29	2.25	2.16	2.11	2.15	2.05
ASNPQ	Control	2.54	2.46	2.41	2.31	2.08	2.06	2.33	2.22
	Test	2.49	2.48	2.32	**2.34***	2.02	2.09	2.24	2.23
MST Users	Control	4.36	4.35	4.27	4.18	Not asked			
	Test	4.49	4.37	4.22	4.16				
Dual Users	Control	4.51	4.38	4.22	4.13	3.33	3.27	4.19	3.97
	Test	4.59	4.54	4.43	4.32	3.51	3.51	4.32	4.15

*After Bonferroni adjustment, p-values < 0.008 were considered statistically significant.

Modified risk claim had minimal effects on adult tobacco users' behavioral intentions

ASPQ: Adult smokers planning to quit
ASNPQ: Adult smokers not planning to quit
MST: Moist smokeless tobacco

Data Source: MRTPA Section 7.3.2.1

POTENTIAL IMPACT OF MODIFIED RISK CLAIM ON INTENTIONS TO USE AMONG CURRENT NON-USERS: CCI STUDY

Unadjusted mean composite scores for intentions to try and intentions to use Copenhagen Snuff among adult non-users of tobacco

Group	Condition	Intentions to Try		Intentions to Use	
		Pre	Post	Pre	Post
Never users	Test	1.3	1.2	1.3	1.2
	Control	1.4	1.3	1.3	1.3
Former Users	Test	1.4	1.3	1.3	1.3
	Control	1.3	1.3	1.3	1.2
Non-users LA-24*	Test	1.5	1.4	1.4	1.4
	Control	1.4	1.4	1.3	1.3

***Non-users LA-24:** Non-users of tobacco of the minimum legal age to purchase tobacco in their jurisdiction of residence up to age 24

Modified risk claim had no effects on behavioral intentions among adult non-users of tobacco

Data Source: MRTPA Section 7.3.2.1

POPULATION IMPACT: ALCS COHORT MODEL INPUT SOURCES

Excess Relative Risk (ERR)	National Health Interview Survey - Linked Mortality Files data (NHIS public use data from 1987,1991,1992, 1998, 2000, and 2005 linked to the National Death Index for mortality follow-up through the end of 2011)
Transition probabilities between tobacco use states	Three of the six studies (Wetter et al.,[70] Tomar,[71] and Zhu et al.[72]) included in the systematic review of transitions between smokeless tobacco and cigarette use by Tam et al.[67]
Effect of MRTP authorization on transition probabilities	Altria Client Services (ALCS) Claim Comprehension and Intentions (CCI) Study

POPULATION IMPACT: ALCS COHORT MODEL FINDINGS

Single Cohort Approach

Differences of 1,120 (95% Credible Interval = 958,1301) survivors at age 73 years between the Master Case scenario (behaviors for cigarettes and moist smokeless tobacco with proposed claim) and the Base Case scenario (existing tobacco product use behaviors for cigarettes and moist smokeless tobacco)

Time Staggered, Multiple Cohort Approach

93,323 more survivors between the ages of 0 and 84 years in this population in the Master Case scenario compared to the Base Case scenario in 2075, 60 years after authorization of the modified risk claim

Effect of Modified Risk Claim

- **Scaled to Copenhagen Snuff Fine Cut's current market share (8%)**
- **Estimated that an MRTP authorization for Copenhagen Snuff Fine Cut would result in 7,500 additional survivors in the U.S. native-born male population after a follow-up period of 60 years**

Data Source: MRTPA Section 6.5

SUMMARY AND CONCLUSIONS

- Copenhagen Snuff Fine Cut has higher levels of certain HPHCs than other smokeless tobacco products, particularly Swedish snus.
- There are higher potential daily intake levels of certain HPHCs in Copenhagen Snuff Fine Cut than cigarettes, although differences in route of exposure, HPHC extraction rates, and portal of entry effects (including toxicant absorption, distribution, metabolism, and excretion) make it difficult to determine the effect of these relative differences on health risk.
- Despite higher levels of certain HPHCs in Copenhagen Snuff Fine Cut compared to cigarette smoke, epidemiological evidence demonstrates that risk of lung cancer is lower among cigarette smokers who switch to exclusive use of smokeless tobacco than those who continue smoking.

SUMMARY AND CONCLUSIONS

- Although most consumers responded correctly to the claim comprehension item, there is little evidence that the claim affects perceptions of risk.
- Clinical and epidemiological evidence suggests it is likely few cigarette smokers will switch to exclusive use of smokeless tobacco, with dual use more likely.
- Exposure to the proposed modified risk claim does not appear to increase behavioral intentions to try, use, or switch to “Copenhagen Snuff” among tobacco users (i.e., smokers, moist smokeless tobacco users, dual users) or non-users.
- Computational modeling estimated a relatively small net population health benefit from market authorization of Copenhagen Snuff Fine Cut with the proposed modified risk claim.

CLARIFYING QUESTIONS?