The Harm Reduction Potential of Oral Tobacco Derived Nicotine Products

Elizabeth Becker
Senior Director, Population Science

Altria
FAMILY OF COMPANIES
Altria’s Approach to Harm Reduction

Harm Reduction Potential of OTDNs

- Reduced Harm
- Adult Tobacco Consumer Interest & Use
- Accurate Communications
## Altria’s Approach to Harm Reduction

### Harm Reduction Potential of OTDNs

<table>
<thead>
<tr>
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Elizabeth Becker | Altria Client Services LLC | Regulatory Affairs | Next Generation Nicotine Delivery | June 22, 2022 |
**Tobacco Harm Reduction Framework**

**Traditional Strategies**
- Decrease Initiation
- Increase Cessation

**Complement to Existing Approach**
- Switching ATC to Less Harmful Products
- Accelerate Smoking-Related Harm Reduction

ATC=Adult Tobacco Consumers
Tobacco Harm Reduction Framework

Traditional Strategies

Decrease Initiation + Increase Cessation

Complement to Existing Approach

Switching ATC to Less Harmful Products = Accelerate Smoking-Related Harm Reduction

ATC=Adult Tobacco Consumers

Sources: Tobacco Product Use Among Middle and High School Students — United States, 2011–2018; Tobacco Product Use and Associated Factors Among Middle and High School Students — United States, 2019; Tobacco Product Use Among Middle and High School Students — United States, 2020; and Tobacco Product Use and Associated Factors Among Middle and High School Students — United States, 2021.

Note: Any tobacco use is past 30-day use of cigarettes, cigars, smokeless tobacco, electronic cigarettes, hookahs, pipe tobacco, and/or bidis, in addition to heated tobacco products (2020–2021) and nicotine pouches (2021) on ≥ 1 day in the past 30 days.

Note: In 2014 and 2015, modifications were made to the e-cigarette measure to enhance its accuracy, which may limit the comparability of these estimates to those collected in previous years. In 2019, modifications were made to the survey, as well as the e-cigarette measure through inclusion of a brand example (JUUL); authors caution against comparisons to prior years. For smokeless tobacco, 2015 and prior years data are not comparable due to methodological changes into 2015. In 2015 smokeless tobacco includes chewing tobacco/snuff/dip, snus, and dissolvable tobacco because of limited sample sizes. Prior to 2015, smokeless tobacco included only chewing tobacco/snuff/dip. In 2021, the survey was conducted online during the COVID-19 pandemic with an overall lower participation rate than during previous years. Due to differences in data collections procedures, any comparison of the 2021 NYTS estimates to previous NYTS survey years that were primarily conducted on school campuses should be interpreted with caution. Dashed lines from 2020-2021 represent these differences.
Tobacco Harm Reduction Framework

Traditional Strategies

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Complement to Existing Approach

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ATC=Adult Tobacco Consumers
Responsibly lead
the transition of adult smokers to a
SMOKE-FREE FUTURE
The Problem: Harm Caused from Cigarette Smoking

COMBUSTIBLE TOBACCO – MOST HAZARDOUS FORM OF TOBACCO

30.8 MILLION US adult smokers¹

OVERWHELMING EVIDENCE

Cigarette smoking is addictive and causes serious diseases including:

- Lung cancer
- Emphysema
- Cardiovascular disease

~443,000 U.S. Deaths Attributable Each Year to Cigarette Smoking*

<table>
<thead>
<tr>
<th>Disease</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung Cancer</td>
<td>128,900</td>
</tr>
<tr>
<td>Ischemic Heart Disease</td>
<td>126,000</td>
</tr>
<tr>
<td>Chronic Obstructive Pulmonary Disease</td>
<td>92,900</td>
</tr>
<tr>
<td>Other Diagnoses</td>
<td>44,000</td>
</tr>
<tr>
<td>Stroke</td>
<td>15,900</td>
</tr>
<tr>
<td>Other Cancers</td>
<td>35,300</td>
</tr>
</tbody>
</table>

*Average annual number of deaths, 2000-2004.
Risk Cliff Between Combustible & Smoke-Free Tobacco

The vast majority of ATCs, believe that non-combustibles are **about the same or more harmful** than smoking.
Harm Misperceptions of E-Vapor

Is using e-cigarettes or other electronic nicotine products less harmful, about the same, or more harmful than smoking cigarettes?*

Based on ALCS analysis of PATH data December 2016 - January 2018; Responses based on Wave 1 and Wave 2 question: “Is using e-cigarettes less harmful, about the same, or more harmful than smoking cigarettes?” At Wave 3 and 4 the question was changed to: “Is using e-cigarettes or other electronic nicotine products less harmful, about the same, or more harmful than smoking cigarettes?”
Percent of Smokers Who Switched to E-Vapor or Smokeless Tobacco the Following Year

Analysis includes adult smokers who stopped smoking and used either e-vapor or smokeless tobacco from PATH Wave 3 to Wave 4.

KEY TAKEAWAY
Smokers with an accurate perception of risk are 2-3x MORE LIKELY TO SWITCH
Altria’s Approach to Harm Reduction

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on!® Harm Reduction Opportunity

on!® nicotine pouches have the most variety of any nicotine pouches currently in the U.S. Market

SEVEN FLAVORS

1. ORIGINAL
2. MINT
3. WINTERGREEN
4. CITRUS
5. CINNAMON
6. BERRY
7. COFFEE

5 NICOTINE STRENGTHS

1.5 MG
2.0 MG
3.5 MG
4.0 MG
8.0 MG

NO TOBACCO LEAF

All flavors are available for purchase through e-commerce. Select SKUs are available in retail.

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Scientific Framework

**CONSTITUENT REDUCTION**
- Product Design and Control
- Chemical and Physical Characterization

**THE PRODUCT**
- Chemistry Manufacturing and Controls
- Product Stability
- Harmful or Potentially Harmful Constituents (HPHC)

**INDIVIDUAL RISK REDUCTION**
- Toxicology and Risk Assessment
- Studies in Adult Human Subjects

**EXPOSURE and HEALTH RISK**
- Health risk assessment (absolute and relative)
- Chemical Analyses
- Human Studies
- Human Factors Assessment
- Risk Assessment

**POPULATION HARM REDUCTION**
- Perception and Behavior Assessment
- Risks and Benefits to Health of the Population

**IMPACT on the POPULATION**
- Risk perceptions (absolute and relative)
- Impact of product on users
- Impact on non-users
- Overall impact on the population
- Environmental Assessment
Scientific Framework

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TOXICOLOGY and Risk Assessment

Studied in Adult Human Subjects

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POPULATION HARM REDUCTION

Perception and Behavior Assessment

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Percent Reduction in HPHC Levels in on!® Nicotine Pouches Compared to Cigarettes

Data source: Percent reductions based on average HPHC levels in 4 mg on!® Mint product compared to cigarette mainstream smoke levels measured under ISO conditions.
HPHCs in on!® Nicotine Pouches are Absent or Substantially Reduced Compared to General® Snus

As = Arsenic; B[a]P = Benzo[a]pyrene; BLOQ = Below Limit of Quantitation; Cd = Cadmium; NNK = 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NNN = N-nitrosonornicotine.

Source: Percent reductions based on average HPHC levels in 4 mg on! Mint product compared to the average HPHC levels for the eight MRTP authorized General® Snus products.
Scientific Framework

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Chemical and Physical Characterization

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Risk Assessment of Non-Tobacco Ingredients Demonstrates Levels Below Acceptable Daily Intake

Our Risk Assessment of Non-Tobacco Ingredients indicates

Exposure is Below Acceptable Daily Intake Values as Established by Authoritative Bodies*

on1® Nicotine Pouches contain tobacco derived nicotine which meets European Pharmacopeia standards

Most ingredients are designated as “Generally Recognized as Safe” (GRAS) for use in food, beverages or chewing gum and are present at levels that result in human exposure deemed acceptable for use in foods

Toxicological risk assessment of non-tobacco ingredients is based on published clinical and nonclinical literature

*e.g., JECFA (Joint Economic Committee of the WHO/FAO on Food Additives), EFSA (European Food Safety Authority), US FDA
The on!® Portfolio Delivers a Wide Range of Nicotine

![Graph showing plasma nicotine concentration over time for different nicotine strengths.]

- Mint 8 mg
- Mint 4 mg
- Mint 3.5 mg
- Mint 2 mg
- Mint 1.5 mg

Time (minutes)

Plasma Nicotine Conc. (ng/ml)
Abuse Potential is Lower Than or Similar to That of Cigarettes or ST Products and Not Impacted by Flavor

The plasma pharmacokinetic profiles from the published literature (dotted lines) are repotted from estimated values based on figures in the publications. For consistency, all data has been baseline adjusted. Results from this study (solid lines) are presented; only the 8 mg NP nicotine PK profile is presented because the 8 mg NP exhibited the higher nicotine PK relative to the lower nicotine level NPs. NP=nicotine pouch; OBC=own brand cigarette; OBMST=own brand moist smokeless tobacco; ST=Smokeless tobacco.

Plasma Nicotine Values Over Time During Use of the 8mg NP and Representative Published data

Cigarettes

Smokeless Tobacco Products

The plasma pharmacokinetic profiles from the published literature (dotted lines) are repotted from estimated values based on figures in the publications. For consistency, all data has been baseline adjusted. Results from this study (solid lines) are presented; only the 8 mg NP nicotine PK profile is presented because the 8 mg NP exhibited the higher nicotine PK relative to the lower nicotine level NPs. NP=nicotine pouch; OBC=own brand cigarette; OBMST=own brand moist smokeless tobacco; ST=Smokeless tobacco.
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Perception & Behavioral Intentions Study Among Users and Nonusers

Participants

Tobacco Users

Tobacco Nonusers

Exposure to Promotional Materials

Measures

Intentions to Use

Purchase Interest

Likelihood to Use
Moderate to Large Proportion of Adult Tobacco Users Classified as Likely to Use on!® Nicotine Pouches

Results shown in the chart are from participants assigned to Reduced Exposure condition. Similar results were observed among tobacco user groups assigned to Full Exposure Condition. Likelihood to use the on!® product was based on an intention composite score >3.5 and answered Yes to the purchase intent question.

ASPQ=adult smokers planning to quit; ASNPQ=adult smokers not planning to quit; LA=Legal age to purchase tobacco; ST=smokeless tobacco.

Source: Section 9A.6, PBI Study Report, Appendix 9A.6-34, Table 11 and 88.
Small Proportions of Adult Tobacco Nonusers Classified as Likely to Use on® Nicotine Pouches

Results shown in the chart are from participants assigned to Reduced Exposure condition. Similar results were observed among tobacco user groups assigned to Full Exposure Condition.

Likelihood to use the on® product was based on an intention composite score >3.5 and answered Yes to the purchase intent question.

ASNPQ=adult smokers planning to quit; ASNPQ=adult smokers not planning to quit; ST=smokeless tobacco; DU=dual user of cigarettes and smokeless tobacco; LA=Legal age to purchase tobacco. Source: Section 9A.6, PBI Study Report, Appendix 9A.6-34, Table 11 and 88.
Actual Use Study of on!® Nicotine Pouches

Participants

Tobacco Users Interested in Using on!® Nicotine Pouches and not planning to quit

Free Selection of Product

Outcomes

Complete Switching

Reduction in Cigarette or Smokeless Tobacco Use

Daily and Weekly Diaries
Large Proportions of Adult Tobacco Users Switched or Reduced Traditional Tobacco Usage

**Switched Completely**

to on!® Nicotine Pouches

<table>
<thead>
<tr>
<th>Population</th>
<th>Reduced cigarette consumption by 50% or more</th>
<th>Reduced ST use by 50% or more</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Smokers</td>
<td>39%</td>
<td>14%</td>
</tr>
<tr>
<td>Adult Dippers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adult Smokers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adult Dippers</td>
<td></td>
<td></td>
</tr>
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ST: Smokeless Tobacco.

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Interest and Use of All Flavor Varieties

Product Likeability, Prevalence, and Purchase Interest by Variety Among Adult Smokers

- Top 2 box likeability week 1
- Prevalence over 6-weeks
- Prevalence week 6
- Purchase Interest

Categories: Original, Berry, Cinnamon, Citrus, Coffee, Mint, Wintergreen
Reasons for Future Use of on!® Nicotine Pouches
Among Adult Smokers Likely to Use on!® Nicotine Pouches

<table>
<thead>
<tr>
<th>Reason</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>To help prevent relapse to smoking</td>
<td>22%</td>
</tr>
<tr>
<td>To help cut back or quit smoking</td>
<td>49%</td>
</tr>
<tr>
<td>Comes in a variety of flavors</td>
<td>47%</td>
</tr>
<tr>
<td>Enjoy the taste</td>
<td>50%</td>
</tr>
<tr>
<td>Has a flavor I like</td>
<td>56%</td>
</tr>
<tr>
<td>Comes in a variety of nicotine strengths</td>
<td>36%</td>
</tr>
<tr>
<td>To satisfy nicotine cravings</td>
<td>52%</td>
</tr>
<tr>
<td>It has a nicotine strength that works for me</td>
<td>40%</td>
</tr>
</tbody>
</table>

Percentage of adult smokers who endorsed each reason why they would use on!® in the future

Switching
Flavors
Nicotine Levels
Altria’s Approach to Harm Reduction

Harm Reduction Potential of OTDNs

Reduced Harm  Adult Tobacco Consumer Interest & Use  Accurate Communications
Evidence for Modified Risk Tobacco Product Application

on!® Nicotine Pouches, as they are actually used by consumers, **WILL SIGNIFICANTLY REDUCE HARM** and the risk of tobacco-related disease to individual tobacco users.

**WILL BENEFIT THE HEALTH** of the population as a whole taking into account both tobacco product users and nonusers.
MRTPA Path Forward

- Overcome Misperceptions and Barriers to Transition
- Optimize Claim Communications
- Submit MRTPAS to Accelerate Transition
Advancing Tobacco Harm Reduction

CHOICES
A variety of FDA authorized reduced risk products for adult tobacco consumers

COMMUNICATION
Accurate, non-misleading information about reduced risk products, authorized by FDA, directed to adult tobacco consumers

CONSISTENCY
A consistent message from public health authorities in addition to FDA-authorized claims from manufacturers
Any Questions?