



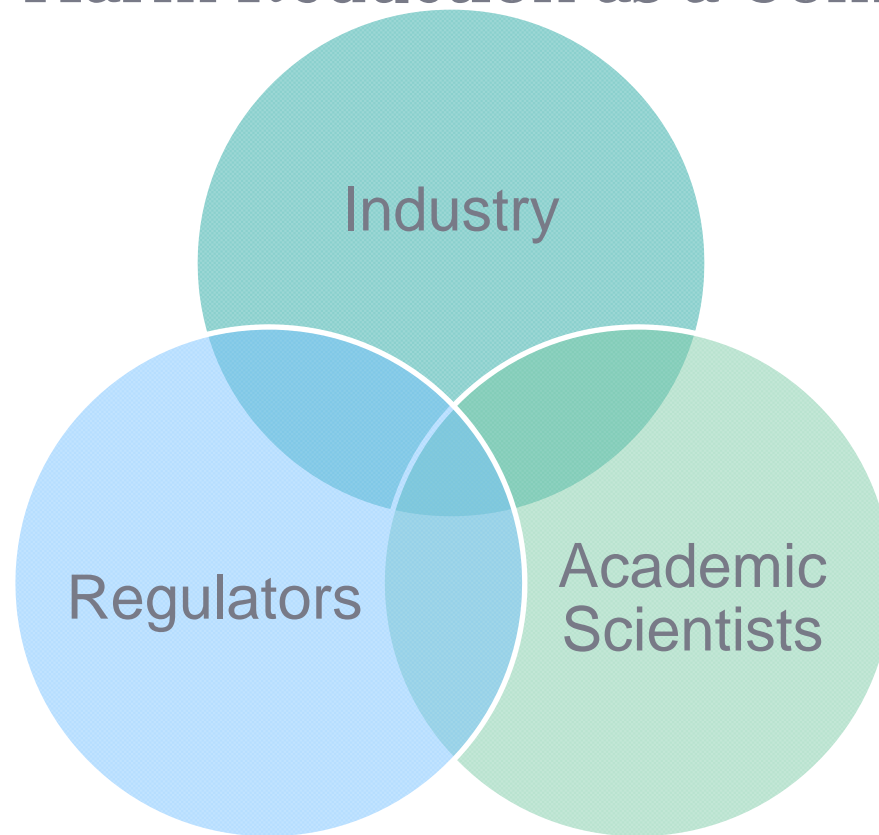
Industry Engagement with the Scientific Community

Willie J. McKinney, PhD, DABT
June 6, 2018



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Tobacco Harm Reduction as a Common Goal?



Science & Evidence





Barriers to Collaboration & Engagement within the Tobacco Industry

“As editors of the *BMJ*, *Heart*, *Thorax* and *BMJ Open*, we have decided that the journals will no longer consider for publication any study that is partly or wholly funded by the tobacco industry. Our new policy is consistent with those of other journals including *PLoS Medicine*, *PLoS One*, *PLoS Biology*;¹ *Journal of Health Psychology*;² journals published by the American Thoracic Society;³ and the *BMJ*'s own *Tobacco Control*.⁴”

Source: <http://thorax.bmj.com/content/68/12/1090> on 5/9/2018

“Editor: We recognise the **tobacco industry is a controversial subject** for many readers. However, many chemists work in this field and we are committed to providing an accurate representation of career paths. This article aims to provide an insight into a chemist's working life and **should not be interpreted as an endorsement of the tobacco industry.**”

Source: chemistryworld.com/careers/working-in-the-tobacco-industry/3007194.article

A World Without an



FDA Recognizes Continuum of Risk

“We must recognize the potential for innovation to lead to less harmful products, which, under FDA’s oversight, could be part of a solution. While there’s still much research to be done on these products and the risks that they may pose, they may also present benefits that we must consider.”

Dr. Scott Gottlieb
FDA Commissioner

Continuum of Risk

Combusted Tobacco Products

Non-combusted Tobacco Products

**MOST
HARMFUL**

**LEAST
HARMFUL**

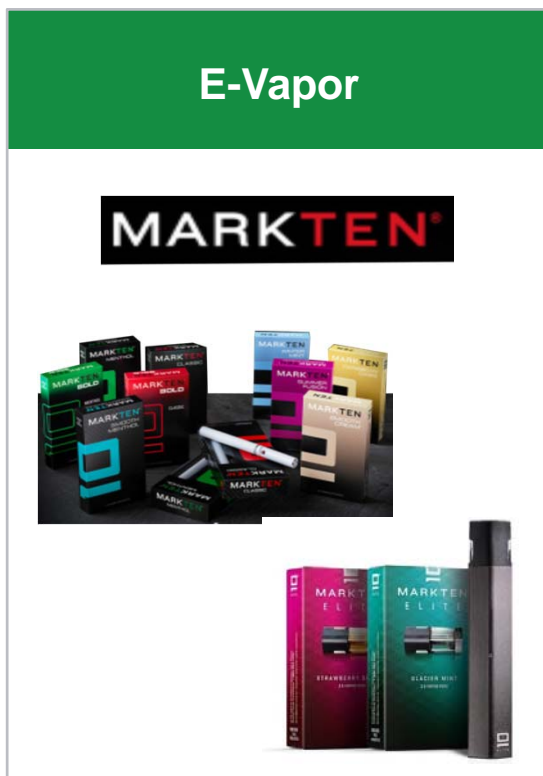
July 28, 2017: Protecting American Families: Comprehensive Approach to Nicotine and Tobacco
<https://www.fda.gov/NewsEvents/Speeches/ucm569024.htm>



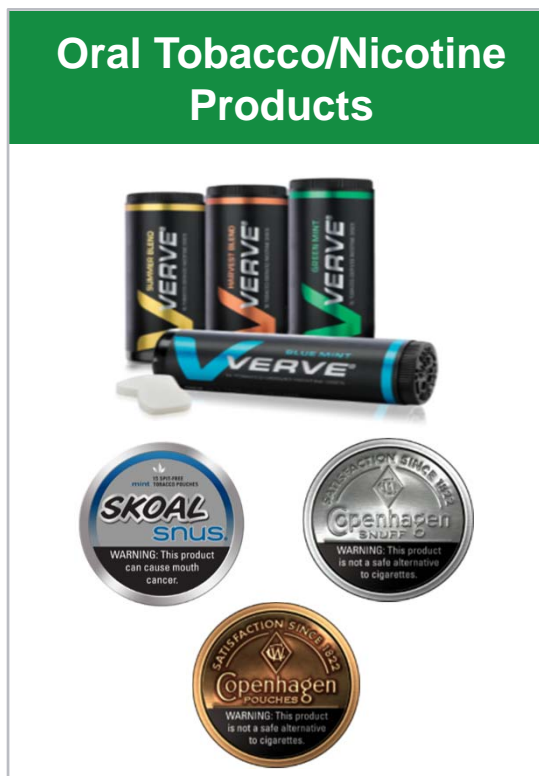
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Noncombustible Tobacco Product Platforms

E-Vapor



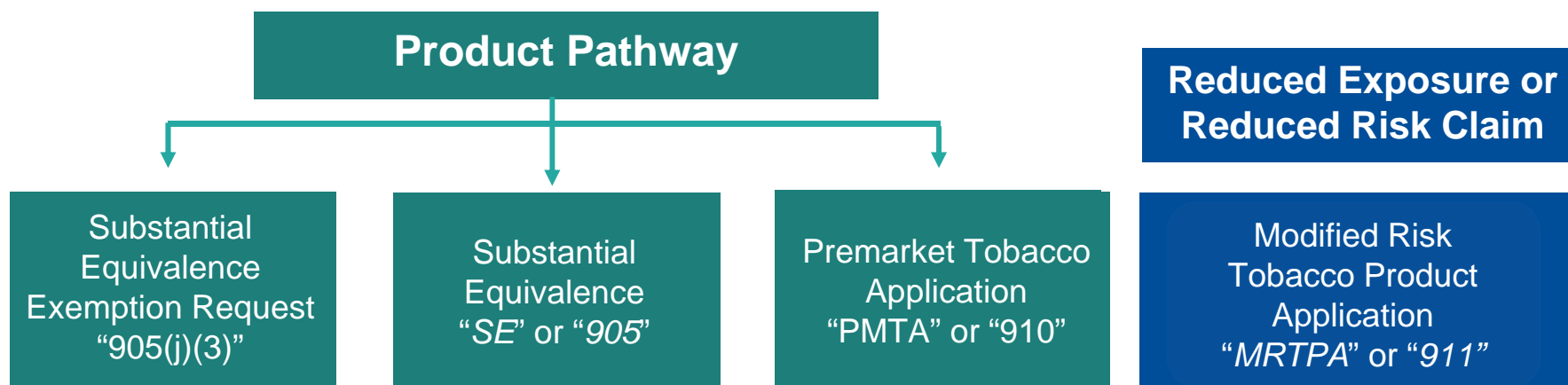
Oral Tobacco/Nicotine Products



Heated Tobacco Products



FDA Market Pathways



ALCS Framework for Reduced Harm Tobacco Products



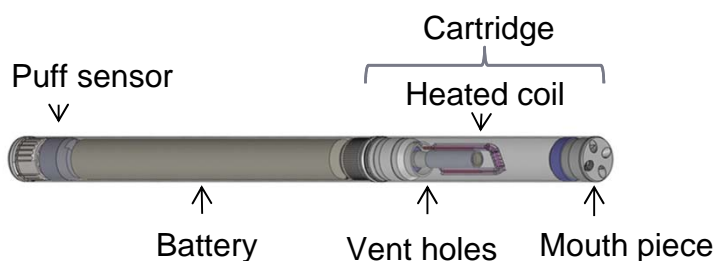
ALCS Framework for Reduced Harm Tobacco Products



MarkTen[®] Product was Designed to Eliminate or Significantly Reduce HPHC¹ Generation

Product Design
and Control

Chemical
and Physical
Characterization



1 Product Design and Controls

2 Chemical and Physical Characterization

- Selection and evaluation of individual components and ingredients
- Manufacturing standards and quality controls
- Product stability
- Battery safety

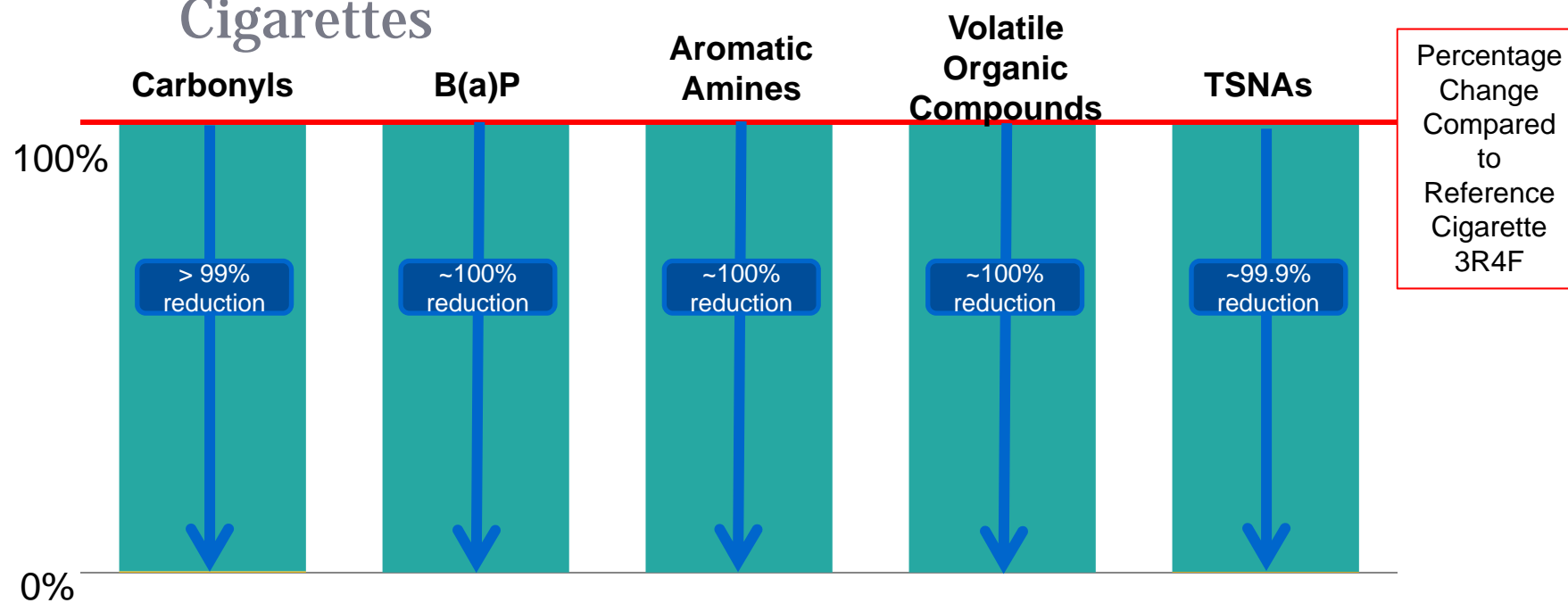
Elimination or reduced formation

- Selected HPHC
- Other targeted constituents (e.g., metals)

¹ HPHC = Harmful or Potentially Harmful Constituents

Harmful and Potentially Harmful Constituents in MarkTen[®] Aerosol Are Substantially Lower Than Reference Cigarettes

Chemical
and Physical
Characterization



ALCS Internal Report LIQUID 16241 – MarkTen[®] XL Classic 3.5% nicotine, Official Stability Study – PMT1, 3, 6 and 9 months.
Average of 140 intense puffs (55mL, 5 second duration, 30 second inter-puff interval).

ALCS Framework for Reduced Harm Tobacco Products



Reduced Risk Assessment: Pre-Clinical Studies

Toxicology
and Risk
Assessment

1 Ingredients risk assessment

Toxicological literature review
Individual flavors and carriers are:

- Generally recognized as safe (GRAS) for use in foods (not appropriate for inhalation)
- Food or pharmaceutical grade

2 Carrier assessment

3 Flavor assessment

Flavor Mixtures:

- 90 day *in vivo* studies

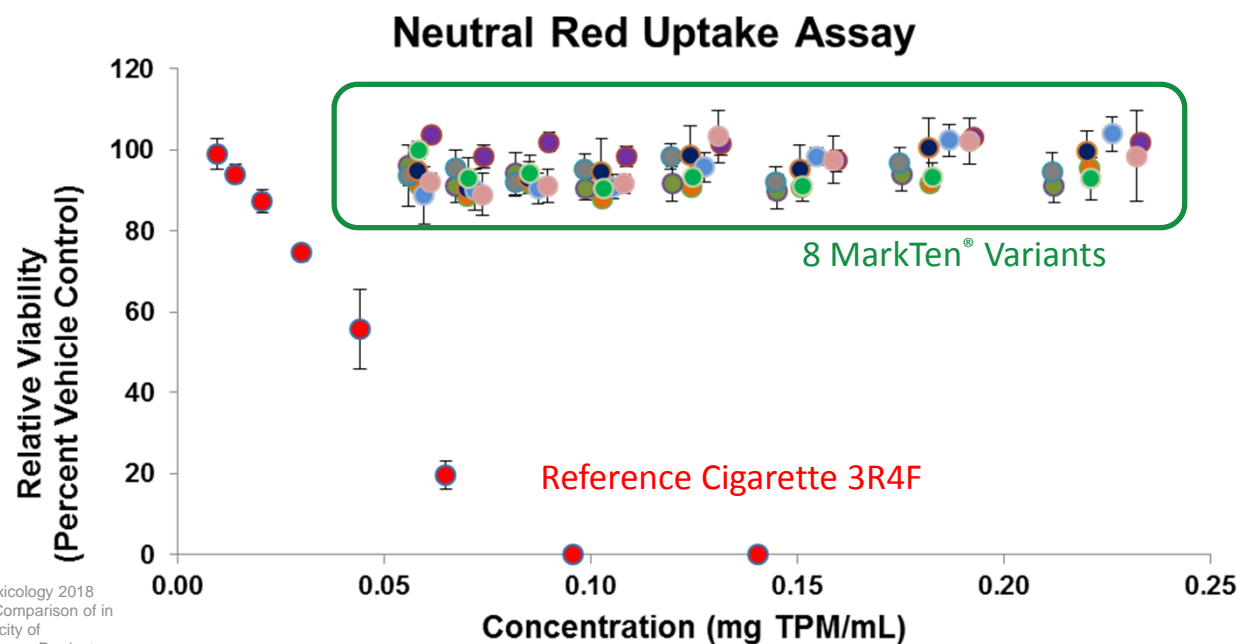
4 E-liquid and aerosol condensate

Product Specific:

- *In vitro* toxicology studies (OECD)
- Cytotoxicity and genotoxicity

No Cytotoxicity Observed from MarkTen[®] Aerosol Condensates in Neutral Red Uptake Assays¹

Toxicology
and Risk
Assessment



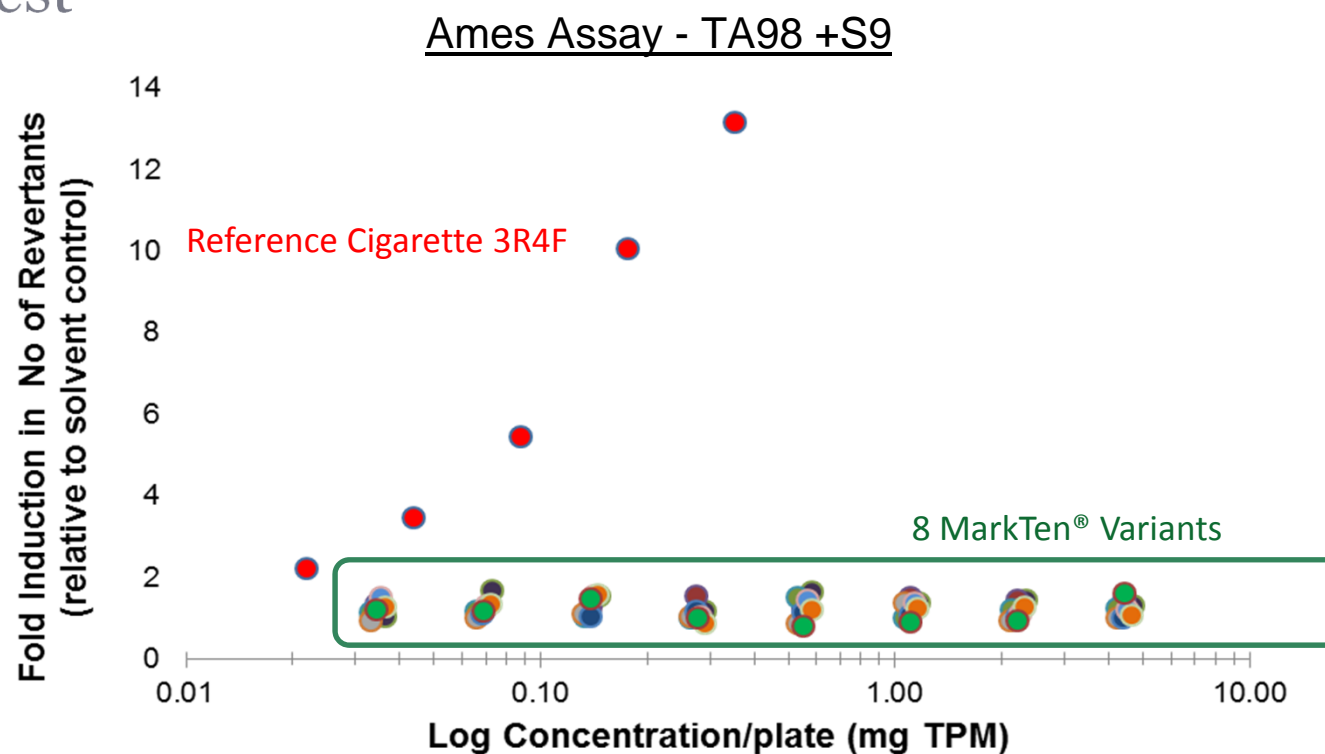
¹ Data shared at Society of Toxicology 2018 Annual Meeting. Doshi et al., Comparison of in vitro Cytotoxicity and Genotoxicity of Condensates Derived from E-vapor Products and Combustible Cigarettes.



- The 3R4F condensate: Positive response (IC₅₀ of 0.048 ± 0.004 mg/mL TPM)
- E-vapor condensates: Viability > 80% (IC₅₀ could not be estimated)

No Mutagenicity Response Observed from MarkTen[®] Aerosol Condensates in Ames Test¹

Toxicology
and Risk
Assessment



Reduced Risk Assessment: Pre-Clinical Studies

Toxicology
and Risk
Assessment

Key Takeaways:

1 Ingredients risk assessment

2 Carrier assessment

3 Flavor assessment

No difference compared to carrier/air control:

- Survival & body weight
- Clinical chemistry & hematology
- Histopathology

4 E-liquid and aerosol condensate

No cytotoxicity or genotoxicity

ALCS Framework for Reduced Harm Tobacco Products



MarkTen[®] Users Have Lower Levels of Biomarkers of Exposure and Potential Harm

Studies in Adult Human Subjects

- 1 Pharmacokinetics/
Pharmacodynamics Nicotine delivery and satisfaction
- 2 Reduced Exposure 3-months Exposure reduction assessment (in progress)
- 3 Reduced Risk 6-months Biomarkers of potential harm (in progress)
- 4 Cross-sectional category study Exposure and risk assessment
- 5 Second hand vapor Impact on non-users

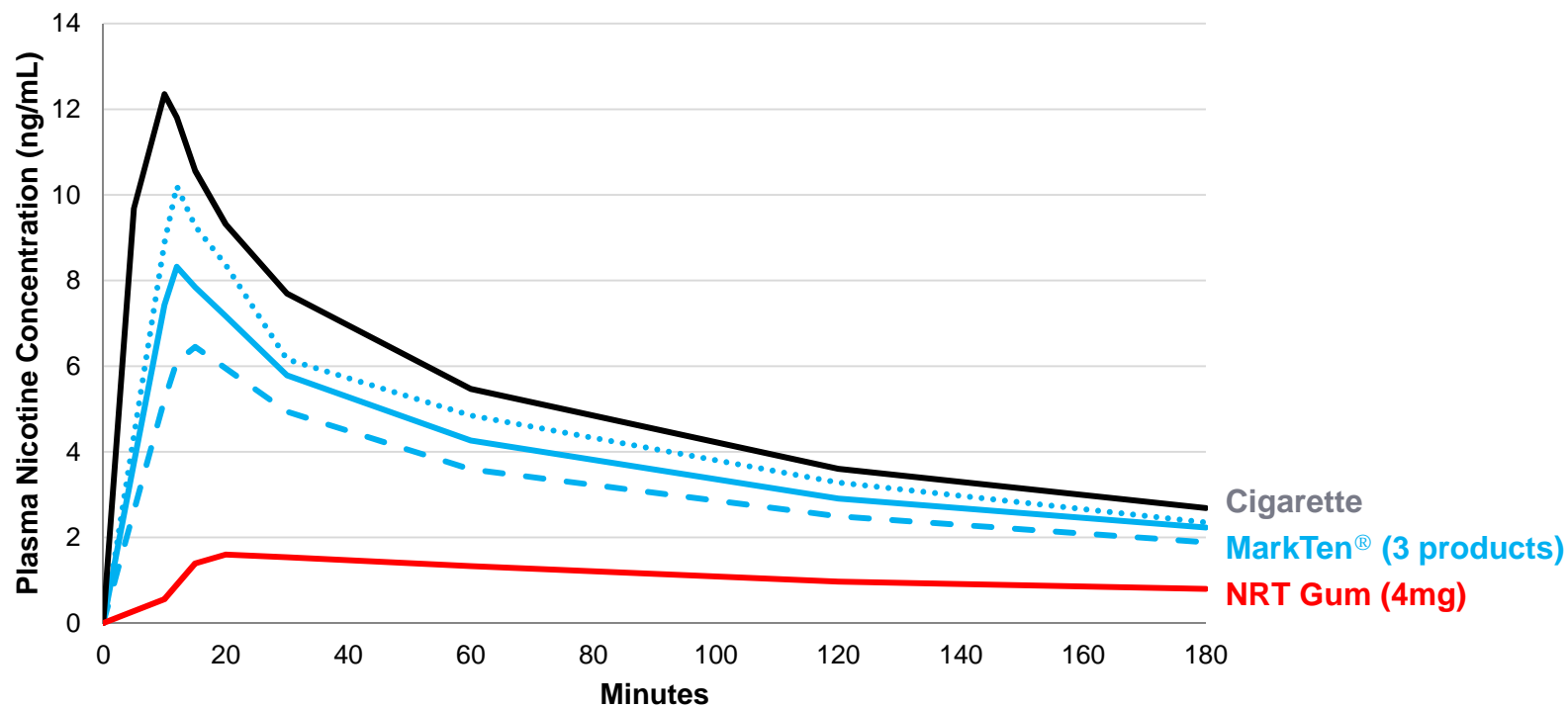


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Results have been shared at the Global Forum on Nicotine, Society for Research on Nicotine and Tobacco, Tobacco Science Research Conference and other scientific meetings. Abstracts and presentations of these data can be found on our science website www.altria.com/alcs-science.

MarkTen[®] Nicotine Pharmacokinetic Studies Demonstrate a Range of Nicotine Deliveries¹

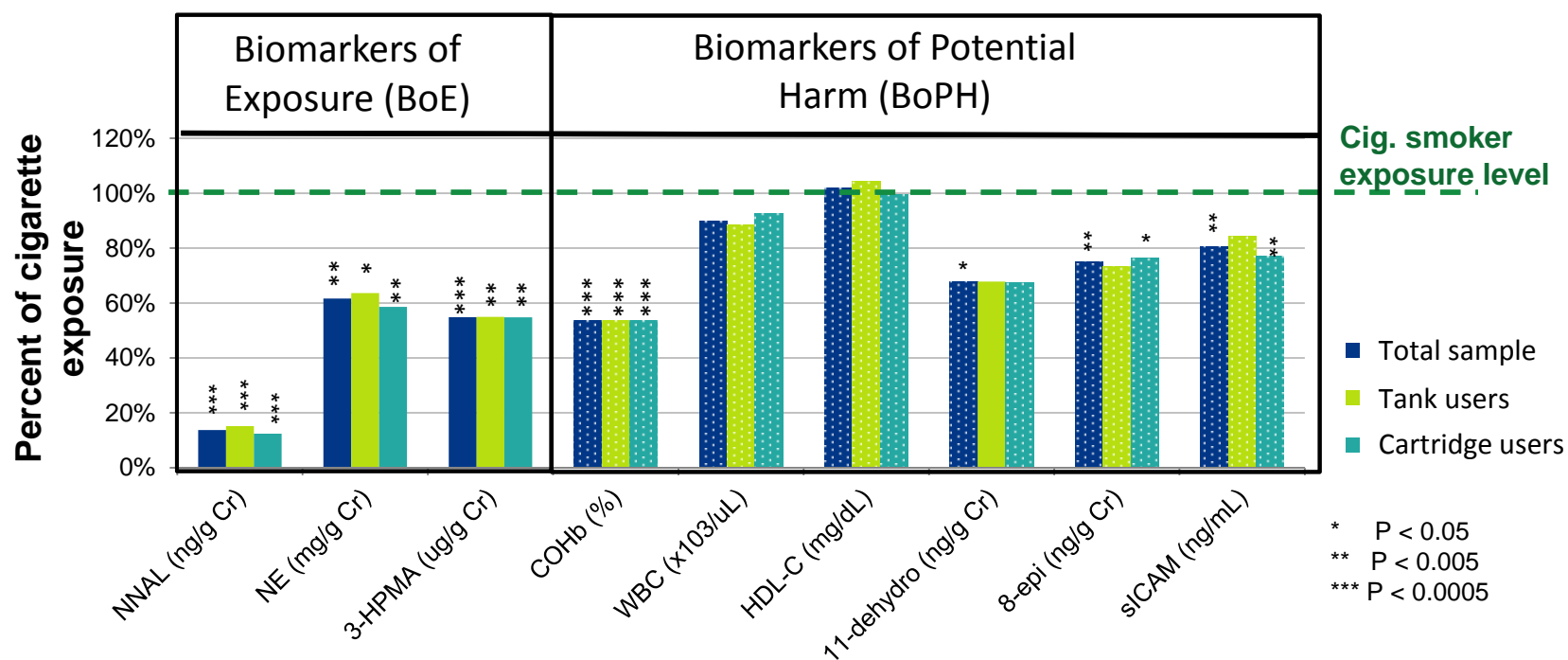
Studies in Adult Human Subjects



¹ Data shared at Society for Research on Nicotine and Tobacco 2018 Annual Meeting. Oliveri et al., Characterization of Nicotine Exposure Profiles and Subjective Measures of e-Vapor Products in Adult Smokers Relative to Conventional Cigarettes.

Significant Differences in BOE and BOPH Between E-vapor Users and Cigarette Smokers¹

Studies in Adult Human Subjects



¹ Data shared at Society for Research on Nicotine and Tobacco 2018 Annual Meeting. Oliveri et al., Cross-Sectional Study Comparing Biomarkers of Exposure to Select Harmful and Potentially Harmful Constituents and Biomarkers of Inflammation and Oxidative Stress Between Adult E-vapor Users and Conventional Cigarette Smokers.

Clinical Studies Support MarkTen® Users Have Lower Levels of Biomarkers of Exposure and Potential Harm

Studies in Adult Human Subjects

Key Takeaways:

1 Pharmacokinetics/
Pharmacodynamics

MarkTen® portfolio offers a range of nicotine deliveries

2 Reduced Exposure 3-months

Reduced exposure and risk biomarker studies for MarkTen® are in progress

3 Reduced Risk 6-months

4 Cross-sectional category study

Significant difference in biomarkers of exposure and potential harm in exclusive users of e-vapor products compared to cigarette smokers

ALCS Framework for Reduced Harm Tobacco Products



Consumer Perception and Behavioral Assessment

Perception
and Behavior
Assessment

1 Perception and behavioral intentions

Risk perceptions and likelihood of use

2 Actual use studies

Use patterns, likelihood of switching

3 In market study

Market data on use behavior, likelihood of initiation and quitting

4 Product instruction comprehension

Ability to comprehend the instructions and assembly of the product

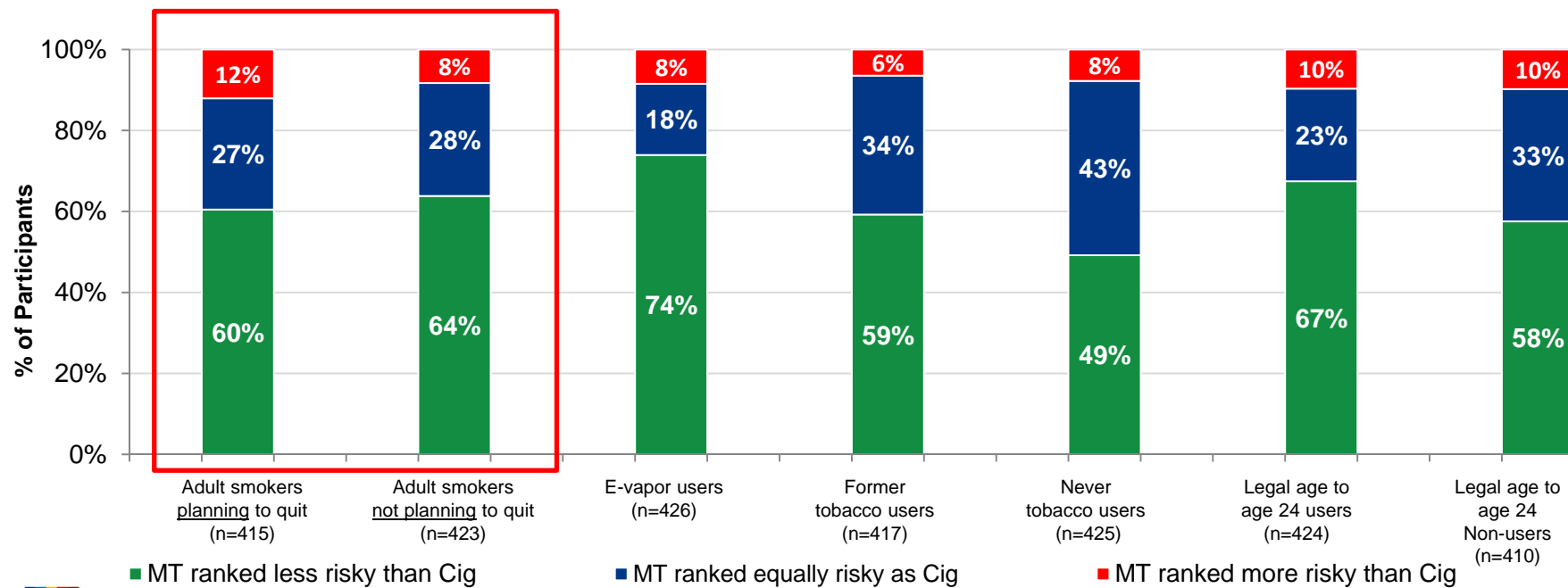


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Risk Perceptions of MarkTen® E-vapor Products Compared to Cigarettes

Perception and Behavior Assessment

Risk perception of MarkTen® relative to smoking cigarettes:
Based on participant exposure to MarkTen® promotional materials



Flavor Portfolio Maximizes Appeal of MarkTen® Products Among Adult Smokers and Vapers

Perception
and Behavior
Assessment

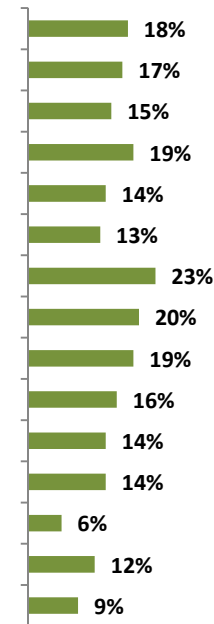
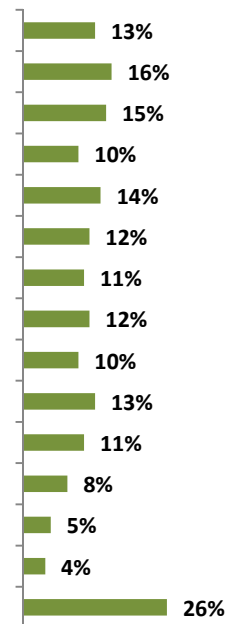
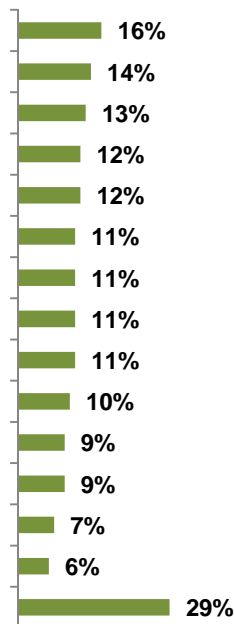
Which of the following products
are most appealing to you?
(select up to 3)

Adult smokers
planning to quit
(N = 415)

Adult smokers NOT
planning to quit
(N = 423)

E-vapor users
(N = 426)

Smooth Menthol
Bold Menthol
Smooth Classic
Smooth Cream
Menthol
Classic
Oasis
Winter Mint
Fusion
Classic
Blend
Mardis Gras
Harvest Blend
Vineyard Blend
None



- No statistical significance testing
- Not all participants rated a product as appealing

Adult Non-tobacco Users Do Not Find MarkTen® Flavors Appealing

Perception
and Behavior
Assessment

Which of the following products
are most appealing to you?
(select up to 3)

Former users
(N = 417)

Never users
(N = 425)

LA-24 Non-users
(N = 410)

Smooth Menthol

8%

5%

5%

Bold Menthol

5%

2%

3%

Smooth Classic

5%

2%

4%

Smooth Cream

6%

7%

7%

Menthol

5%

2%

3%

Classic

4%

2%

2%

Oasis

8%

3%

8%

Winter Mint

4%

3%

7%

Fusion

7%

4%

7%

Classic

4%

1%

2%

Blend

6%

2%

3%

Mardi Gras

5%

4%

3%

Harvest Blend

3%

3%

3%

Vineyard Blend

5%

1%

3%

None

63%

81%

73%

- No statistical significance testing
- Not all participants rated a product as appealing



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Source: Perceptions and Behavioral Intentions Study for Products
Currently Marketed as MarkTen® E-vapor (ALCS-CMI-16-13-EV)

Flavor Varieties Play an Important Role in Switching

Perception
and Behavior
Assessment

Proportion of participants using one or more flavor varieties by cigarette consumption at Week 6

# Flavor varieties used	Total Sample n=526	Switched (0 CPD*) n=208	Decreased CPD n=257	No Change in CPD n=61
1	1.8	0.5	2.7	0
2	7.1	4.8	7	14.8
3	11.2	10.1	10.9	9.8
4	19.3	18.8	19.1	18.0
5	13.0	10.6	16.3	8.2
6	12.9	14.9	10.9	19.7
7 or more	34.7	40.4	33.1	29.5

*CPD: Cigarettes per day

Source: A Longitudinal Study to Assess the Actual Use Of E-Vapor Products
Currently Marketed as MarkTen®: MarkTen® Actual Use Study (M10-AUS)



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Every Day MarkTen[®] Users are More Likely to be Exclusive Users¹

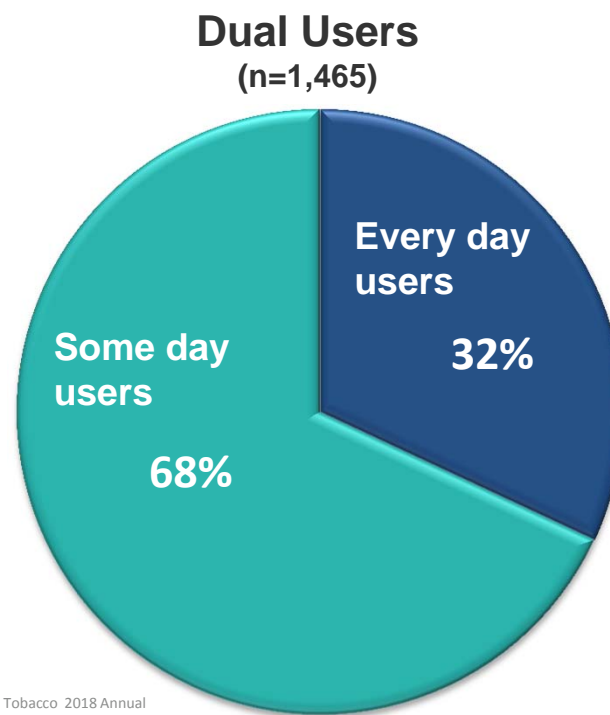
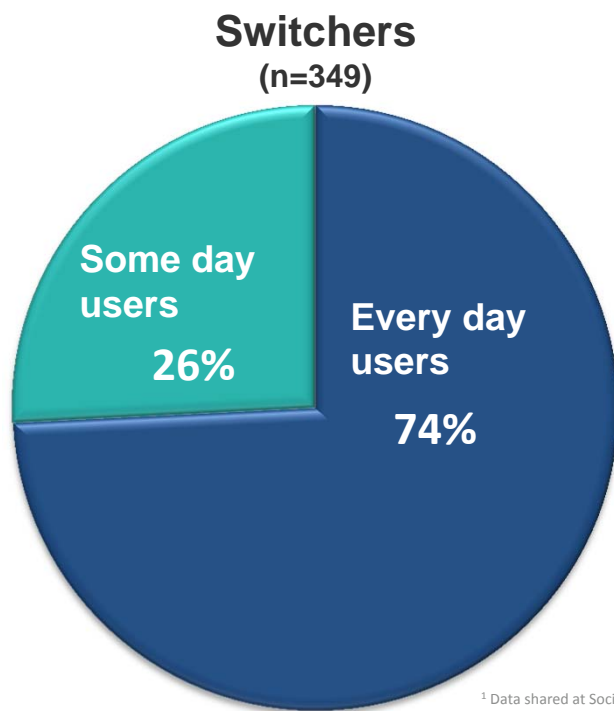
Perception
and Behavior
Assessment

	Current Users	Every day	Some days
E-cigarettes only	25%	42%	12%
E-cigarettes + 1 other tobacco product	45%	36%	52%
E-cigarettes + 2 or more other tobacco products	31%	22%	37%

¹ Data shared at Society for Research on Nicotine and Tobacco 2018 Annual Meeting. Largo et al., USE PATTERNS ASSOCIATED WITH SWITCHING AND DUAL USE AMONG CURRENT CONSUMERS OF MARKTEN[®]XL E-VAPOR PRODUCTS

Larger Proportion of Switchers Report Every Day MarkTen[®] Use¹

Perception
and Behavior
Assessment



¹ Data shared at Society for Research on Nicotine and Tobacco 2018 Annual Meeting. Largo et al., USE PATTERNS ASSOCIATED WITH SWITCHING AND DUAL USE AMONG CURRENT CONSUMERS OF MARKTEN[®]XL E-VAPOR PRODUCTS

Beyond “satisfying nicotine cravings” Reasons for MarkTen® Use Vary by Users¹

Perception
and Behavior
Assessment

Reasons	Switchers (n=349)	Dual Users (n=1,465)
To satisfy my nicotine cravings	81%	71%
To help prevent relapse	63%	15%
To not smell like smoke/not bother other people with smoke	60%	43%
It might be less harmful than cigarettes/other tobacco products	58%	29%
Enjoy the taste	53%	45%
Has a flavor I like	46%	39%
To help cut back or quit smoking/using other tobacco products	41%	65%
It might be less harmful for other people around me	40%	30%
More affordable than cigarettes/other tobacco products	37%	25%
To use in places where I cannot/shouldn't smoke	30%	61%
So I would not have to quit using tobacco products altogether	26%	16%
Advertising or promotion (e.g., magazine ad, sign in store, coupon)	23%	34%
Interested in using this type/brand of e-cigarette	20%	24%
Curiosity	9%	16%
All other reasons	3%	2%
Don't know	1%	1%



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Source: ALCS In-Market Adult Consumer Study – e-Cigarettes Currently Marketed as MarkTen®XL e-Vapor:
A Cross-Sectional Survey of Adult MarkTen®XL e-Vapor Ever Triers (ALCS-CMI-16-16-EV)

Consumer Perception and Behavioral Assessment

Perception
and Behavior
Assessment

Key Takeaways:

1 Perception and behavioral intentions

Sizable portion of AS perceive MarkTen® as equally or more harmful than cigarettes

MarkTen® flavor portfolio appeals primarily to current tobacco users

2 Actual use studies

Flavor varieties are necessary to maximize switching

3 In market study

In-market data indicate every day use is associated with exclusive use of e-vapor

4 Product instruction comprehension

Product instructions are easily understood

ALCS Framework for Reduced Harm Tobacco Products



Population Assessment¹

Risks and
Benefits to the
Population

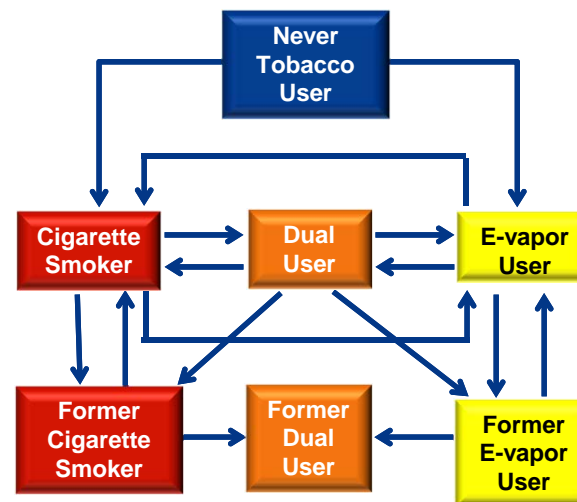
1 Population Modeling

Projection of likely impact on the population

Base Case



Modified Case



Modified Case – Base Case = Estimated change as a result of Introduction of E-vapor Product

Population Assessment

Risks and
Benefits to the
Population

2 Post-Market Surveillance

Passive and active monitoring the impact of the introduction of the new product into the market

	Active Surveillance				Passive Surveillance		
Consumer Health		■	■	■	■		
Consumer Behavior	■	■	■	■	■		
Consumer Perception	■	■	■	■	■		
Adverse Events			■		■	■	■
	In-market cross-sectional surveys	Prospective observational studies	Literature reviews	National surveys and studies (e.g. PATH)	Internet forum monitoring (pending validation)	Call center AEs monitoring	Poison center registration



Overall Conclusions

- E-vapor products present an opportunity to reduce the harm from cigarette smoking
- Need for collaboration to advance harm reduction
 - Generate and share sound science
 - Reframe debate about nicotine
 - Truthful and accurate communications about relative risk



For additional
information visit our
science website at
[Altria.com/ALCS-
Science](http://Altria.com/ALCS-Science).



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