



VLN<sup>®</sup> King and VLN<sup>®</sup> Menthol King  
Reduced Nicotine Cigarettes

Tobacco Products Scientific Advisory Committee Meeting

February 14, 2020

# Presentation Overview

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Modified Exposure Statutory Requirements Under §911(g)(2)

**Ed Carmines, PhD**  
Carmines Consulting, LLC

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**John D. Pritchard**

Conclusions

# Introduction

John D. Pritchard, BSc (Hons), MSc, CBiol, MRSB  
Vice President of Regulatory Science  
22nd Century Group, Inc.



# Development of Very Low Nicotine Content Cigarettes

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22nd Century Group, Inc. was founded in 1998 to develop technology to reduce the nicotine in the tobacco plant.

Since that time, 22nd Century has had numerous collaborations with many leading research institutes that have resulted in patented very low nicotine content tobacco varieties.

One of 22nd Century's discoveries became the first genetically modified (GM) tobacco variety (“Vector 21-41”).



# 22nd Century's Technology in Public Health Research

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- SPECTRUM® cigarettes were developed in collaboration with the National Institute on Drug Abuse (NIDA), a division of the National Institutes of Health (NIH), FDA, CDC and the National Cancer Institute (NCI).
- 22nd Century has provided more than 28 million proprietary SPECTRUM® research cigarettes, which have been used to research the effects of reduced nicotine content cigarettes.

# VLN<sup>®</sup> Cigarettes Are the Same As SPECTRUM<sup>®</sup> 0.5mg Nicotine Research Cigarettes

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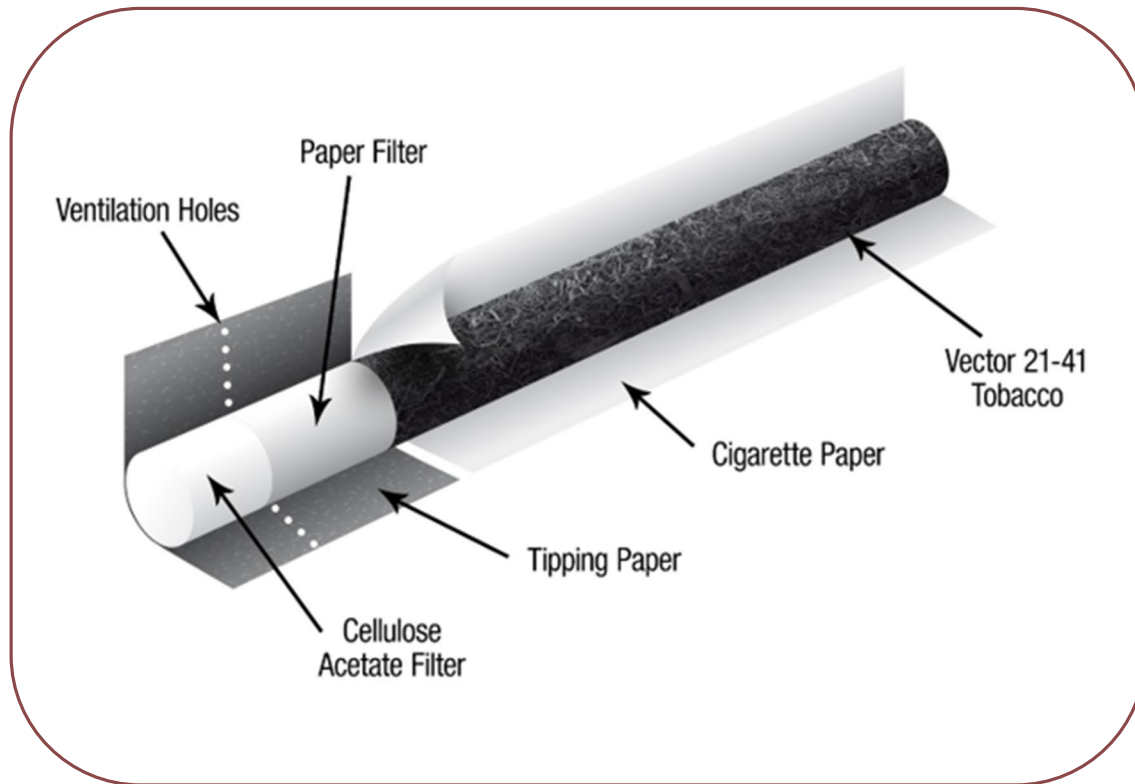


# Product & Claims Overview



# The Product

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- VLN<sup>®</sup> cigarettes are made in the same manner as conventional cigarettes, using materials, ingredients, and processes well-established in the cigarette industry.
- VLN<sup>®</sup> cigarettes are used like conventional cigarettes, there are no unique instructions for use.



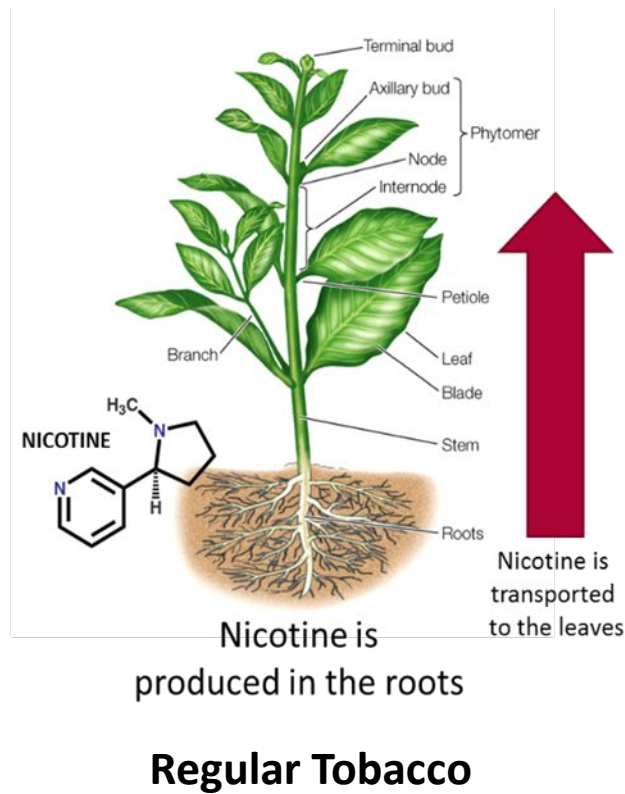
# The Tobacco

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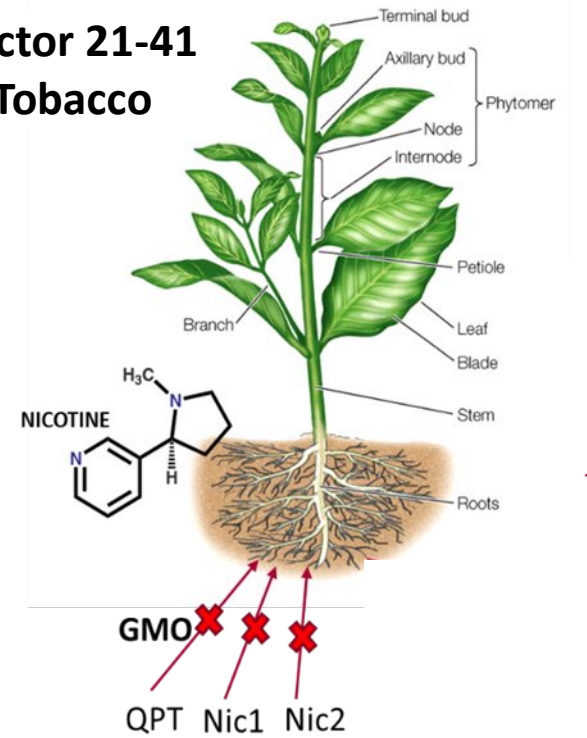
- VLN<sup>®</sup> cigarettes are made with the same proprietary tobacco as SPECTRUM<sup>®</sup> research cigarettes, with a target specification level of 0.5 mg nicotine per gram of tobacco.



# The Technology



## Vector 21-41 Tobacco



# The VLN<sup>®</sup> Claims and Voluntary Warning

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**#1**  
**“95% LESS NICOTINE”**

**#2**  
**“Helps reduce your nicotine  
consumption”**

**#3**  
**“VLN<sup>®</sup> smells, burns, and tastes like a  
conventional cigarette, but greatly  
reduces your nicotine consumption.”**

**+**

**Voluntary Warning:**  
**“Nicotine is addictive. Less  
nicotine does NOT mean safer.  
All cigarettes can cause disease  
and death.”**

# No Drug Claims

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- References to cessation, reduced dependence, and abstinence that may appear in this presentation should not be interpreted to mean that the Company intends to make any drug claims.
- The Company is requesting only Exposure Modification Orders, as set out under the statutory requirements of 911(g)(2).

# The Proposed Label



- All labeling and marketing materials will contain the reduced exposure claim “95% LESS NICOTINE.”
- The labels will comply with package marking requirements for cigarettes, including the U.S. Surgeon General’s Warnings.

# The Proposed Marketing



MAKE THE SWITCH to **95% Less Nicotine**

**REAL TOBACCO**

VLN™ smells, burns, and tastes like a conventional cigarette, but greatly reduces your nicotine consumption

For the nearest retailer, visit [vncigarettes.com/stores](http://vncigarettes.com/stores) or call: 800-225-1838 ext. 221

Nicotine is addictive. Less nicotine does NOT mean safer. All cigarettes can cause disease and death.

**SURGEON GENERAL'S WARNING: Cigarette Smoke Contains Carbon Monoxide.**

Source: Section V VLN® Marketing Outline.pdf



**95% LESS NICOTINE**

If you smoke, consider **VLN™**

VLN™ smells, burns, and tastes like a conventional cigarette, but greatly reduces your nicotine consumption

Learn more at [vncigarettes.com](http://vncigarettes.com)

**SURGEON GENERAL'S WARNING: Cigarette Smoke Contains Carbon Monoxide.**

A series of proposals to communicate product attributes to adult smokers were included in the MRTPA

# PRE-MARKET TOBACCO PRODUCT APPLICATION



# PMTA Authorized December 17, 2019

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FDA conducted a rigorous science-based review of the PMTAs and determined that these products:

- Are "**appropriate for the protection of the public health.**"
- Have "the potential to **reduce nicotine dependence** in addicted adult smokers, who may also benefit from **decreasing nicotine exposure and cigarette consumption.**"
- And "that non-smokers, including youth, are also **unlikely to start using** the products, and those who experiment are **less likely to become addicted** than people who experiment with conventional cigarettes."

<https://www.fda.gov/news-events/press-announcements/fda-permits-sale-two-new-reduced-nicotine-cigarettes-through-premarket-tobacco-product-application>



# FDA PMTA Press Announcement, December 17, 2019

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“Conventional cigarettes are designed to create and sustain addiction to nicotine. In announcing the FDA’s comprehensive plan to regulate tobacco and nicotine in July 2017, we noted our commitment to taking actions that will allow more addicted smokers to reduce their dependence and decrease the likelihood that future generations will become addicted to cigarettes.”

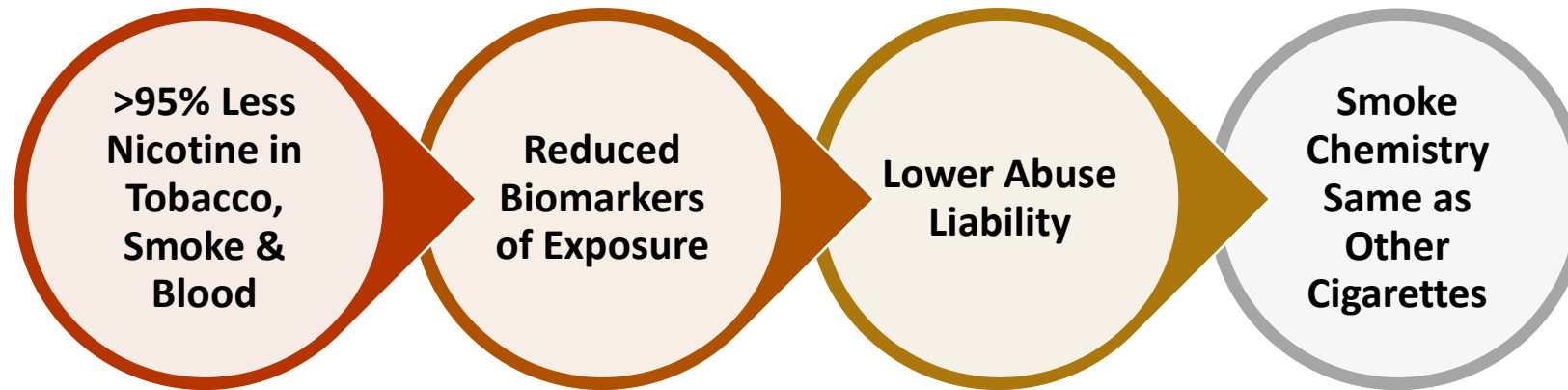
“Today’s authorization represents the first product to successfully demonstrate the potential for these types of tobacco products to help reduce nicotine dependence among addicted smokers. ”

Mitch Zeller, J.D., Director of the FDA’s Center for Tobacco Products.

<https://www.fda.gov/news-events/press-announcements/fda-permits-sale-two-new-reduced-nicotine-cigarettes-through-premarket-tobacco-product-application>

# PMTA Findings Relevant to TPSAC Review

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FDA, PMTA Scientific Review: Technical Project Lead for PM0000491 and PM000049

# Modified Exposure Statutory Requirements under §911(g)(2)



# Modified Exposure Requirements Met

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- The label, labeling, and advertising for the product is **limited to an explicit or implicit representation that the tobacco product** or its smoke does not contain or is free of a substance or contains a reduced level of a substance, or **presents a reduced exposure to a substance in tobacco smoke**;
- The **magnitude of overall reductions in exposure** to the substance or substances...**is substantial, such substance or substances are harmful**, and the product as actually used exposes consumers to the specified reduced level of the substance or substances;
- The product as actually used...**will not expose them to higher levels of other harmful substances compared to similar...tobacco products...**and the reasonably likely overall impact of product use remains a substantial and measurable reduction in overall morbidity and mortality among individual tobacco users;
- Scientific **evidence is not available...**for an application to meet the standards **for obtaining an order under Section 911(g)(1) of the FD&C Act (i.e., a risk modification order)**; and
- The exposure modification order would be **appropriate to promote the public health.**

# MRTPA Current Status: FDA Preliminary Conclusions

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- Substantiation: The three proposed claims are substantiated.
- Consumer understanding: Consumers understand the addiction risk of using the products relative to normal nicotine content cigarettes, but it is **unclear whether they understand other relative health risks of using the products; they perceive the products to be lower risk than other cigarettes.**
- Morbidity and mortality: The proposed modified risk products can reduce dependence among individual tobacco users. **The magnitude of the reduction in other morbidities and mortality from reduced dependence remains unclear.**
- Population health impact: Nonsmokers have low intentions to use the products, and current smokers have moderate intentions to use the products. All smoker groups have higher intentions to purchase VLN<sup>®</sup> cigarettes compared to Marlboro Gold cigarettes.

# FDA's Topics for Discussion

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- Discuss whether the labeling enables consumers to accurately understand the following effects of using the products:
  - a. Addiction risk
  - b. Disease risk
- Discuss the likelihood that reductions in dependence translate into substantial reductions in morbidities and mortality among individual tobacco users.
- Discuss the extent to which the following groups are likely to try and progress to regularly using the proposed modified risk tobacco products:
  - a. Never smokers
  - b. Former smokers
- Discuss the extent to which the following groups will dual use the proposed modified risk products:
  - a. Cigarette smokers who want to quit smoking
  - b. Cigarette smokers who do not want to quit smoking.

# Support for Modified Exposure Authorization

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- The scientific evidence that is available...demonstrates that a measurable and **substantial reduction in morbidity or mortality** among individual tobacco users **is reasonably likely in subsequent studies.**
- Issuance of the exposure modification order is expected to **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.**
- Testing of actual consumer perception shows that... **consumers will not be misled** into believing that the product is or has been demonstrated to be less harmful or presents or has been demonstrated to present less of a risk of disease than one or more other commercially marketed tobacco products.

# Reduction in Morbidity and Mortality

Ed Carmines, PhD  
Carmines Consulting, LLC





# Reduction in Morbidity and Mortality

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- Scientific evidence is not currently available to assess the long-term risks of the products without conducting long-term epidemiological studies, therefore 22nd Century is only making reduced exposure claims.
- However, while 22nd Century is solely seeking a modified exposure claim, the science that is available indicates a likely reduction in morbidity and mortality in smokers who switch completely.

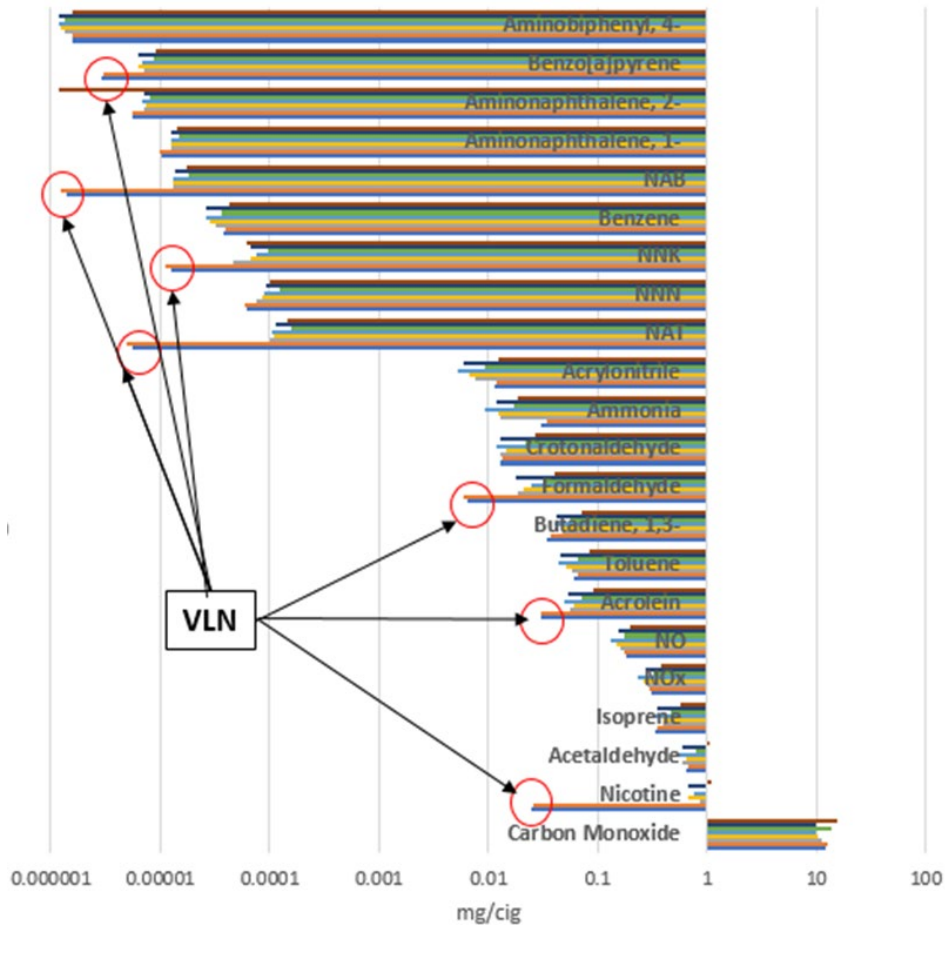
# Nicotine is a Harmful Substance

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- Nicotine causes youth, young adults, and adult users to become addicted to, and to sustain cigarette use.
- Once users become addicted to nicotine, they require nicotine to avoid withdrawal symptoms.
- Cigarette dependence caused by nicotine is a serious and life-threatening condition.
- Nicotine is classified as a Harmful and Potentially Harmful Constituent (“HPHC”) in cigarette smoke because of its addictiveness, and reproductive and developmental toxicity.

# Reduction in Nicotine and a Range of HPHCs

HPHC's Of Leading Brands and VLN

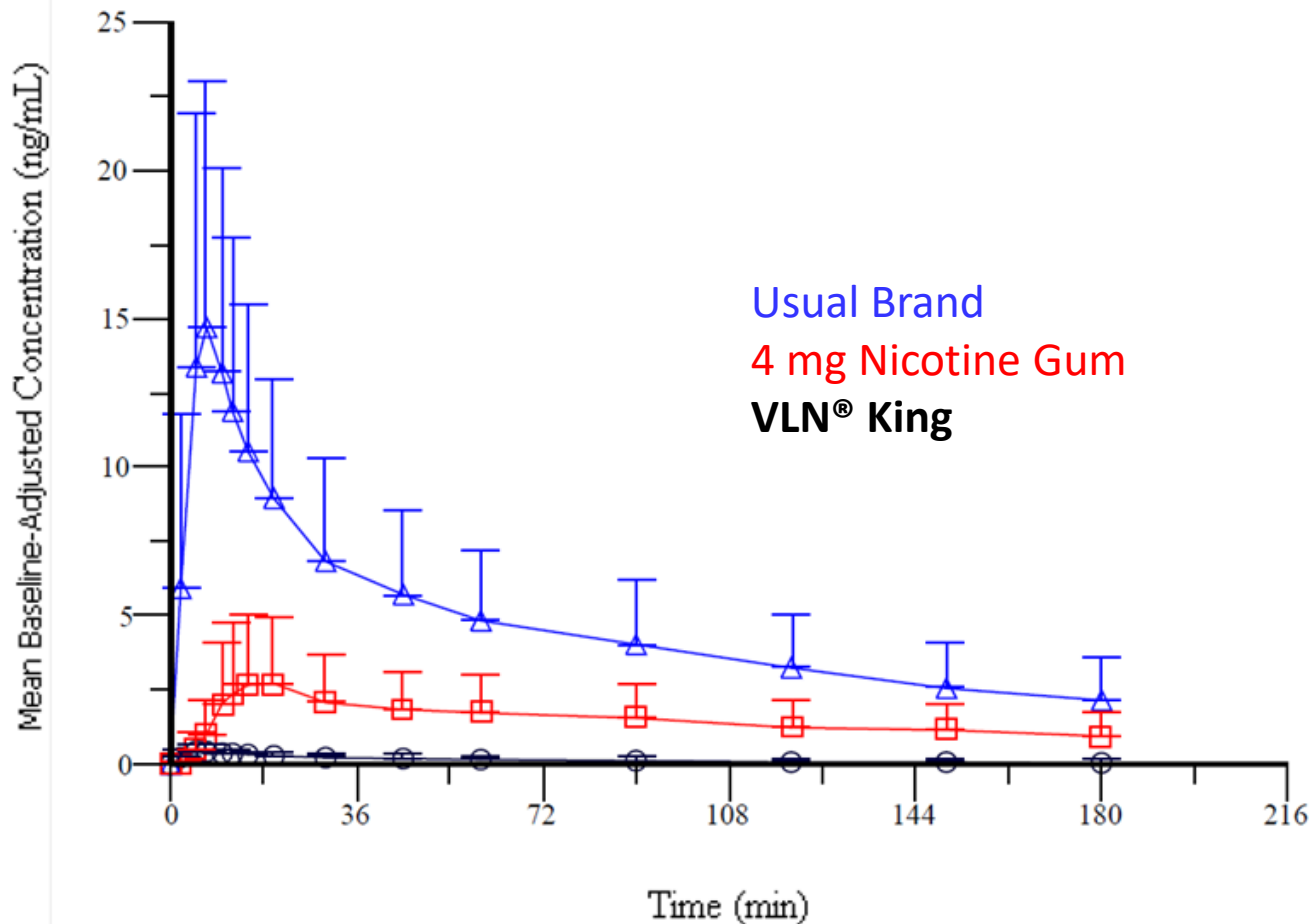


**VLN<sup>®</sup> is NOT safer:  
All cigarettes can cause  
disease and death**

- ↓ Nicotine
- ↓ Acrolein
- ↓ Formaldehyde
- ↓ NAT
- ↓ NAB
- ↓ NNK
- ↓ BaP



# VLN<sup>®</sup> Nicotine Pharmacokinetics



Mean (±SD) Baseline-Adjusted Plasma Nicotine Concentration (ng/mL) after ad libitum use

Product	AUC (ng*min/ml)
Usual Brand	879.75
Nicotine Gum	277.3
VLN <sup>®</sup>	28.3

**VLN<sup>®</sup> has Lower Abuse Liability**

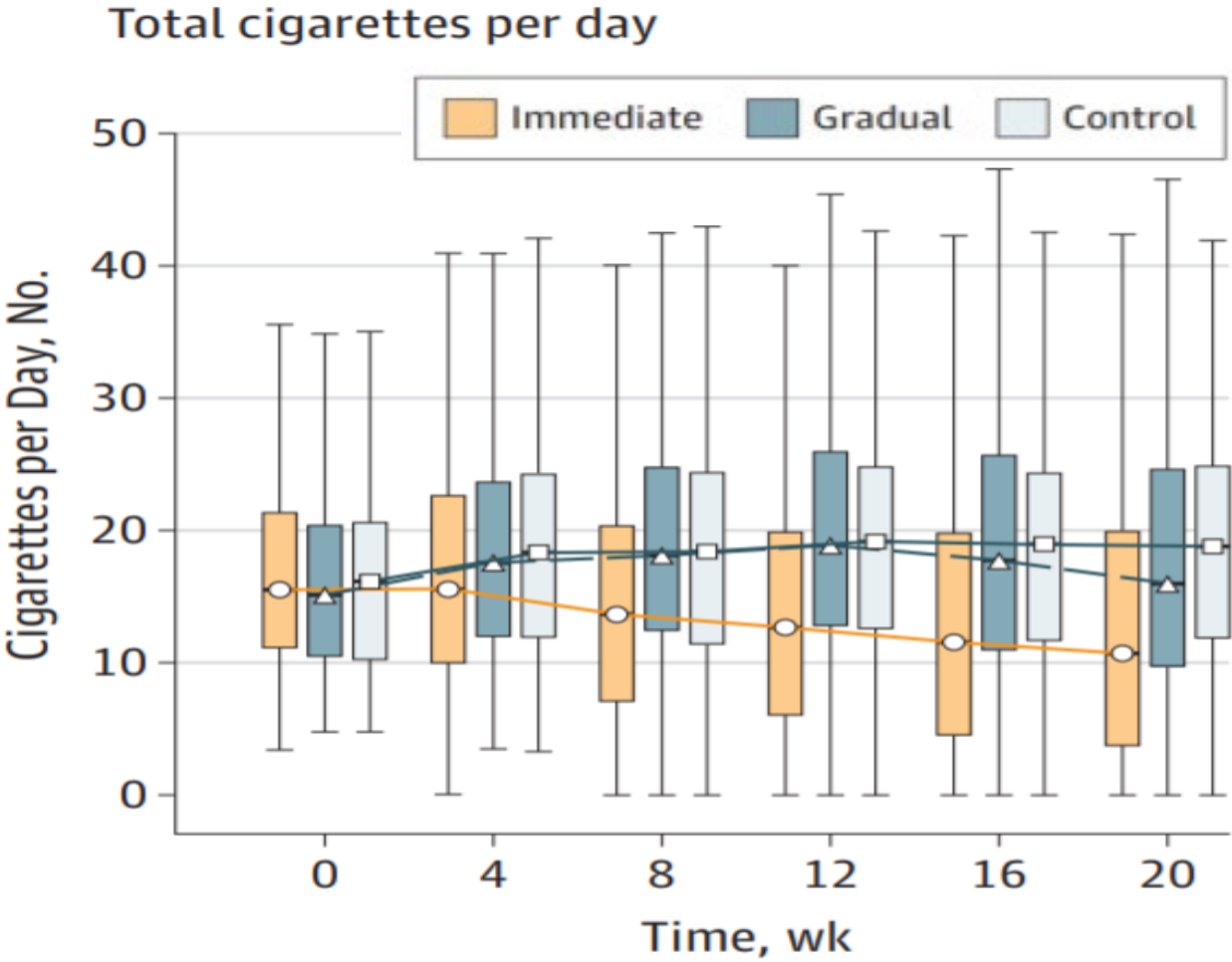
# Lower Abuse Liability

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- FDA has noted that while there is limited available evidence on very low nicotine content cigarettes, youth who experiment with such products may find them less appealing and may be less likely to develop nicotine dependence and become established cigarette smokers due to their lower abuse liability profile.
- FDA, in announcing its authorization of the PMTAs for the same product, noted:

“[t]he agency determined that non-smokers, including youth, are also unlikely to start using the products, and those who experiment are less likely to become addicted than people who experiment with conventional cigarettes.”

# Reduction in Cigarettes Per Day



50% Reduction in Cigarettes Per Day (CPD) After 20 Weeks of Use.

# Reduction in Cigarettes Per Day

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**“Lung cancer incidence in smokers is roughly proportional to dose rate (cigarettes per day) but increases much more rapidly with duration of smoking.”**

Peto, 2012

**“Reductions in CPD over the lifetime meaningfully decreased death risk; however, cessation provided a larger benefit than even large declines in CPD.”**

Inoue-Choi, 2019

“...the large American Cancer Society Prevention Study II showed **an approximately linear relation between risk of lung cancer and number of cigarettes smoked per day**, but the dose-response for cardiovascular disease is steep at low consumption and then levels off, consistent with the shape reported previously.”

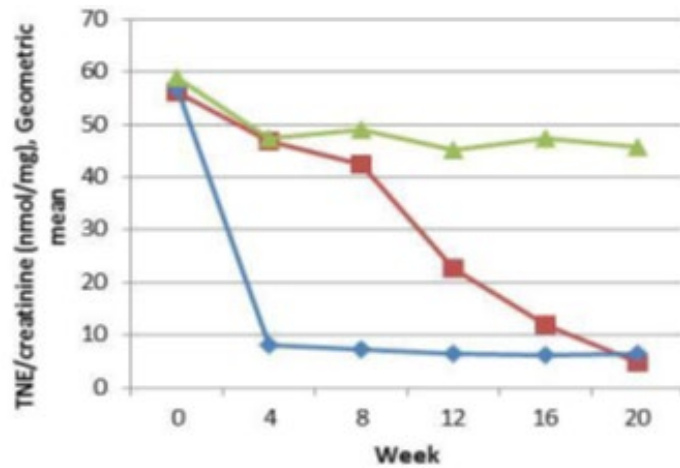
Hackshaw et al, 2018

All cigarettes can cause disease and death.

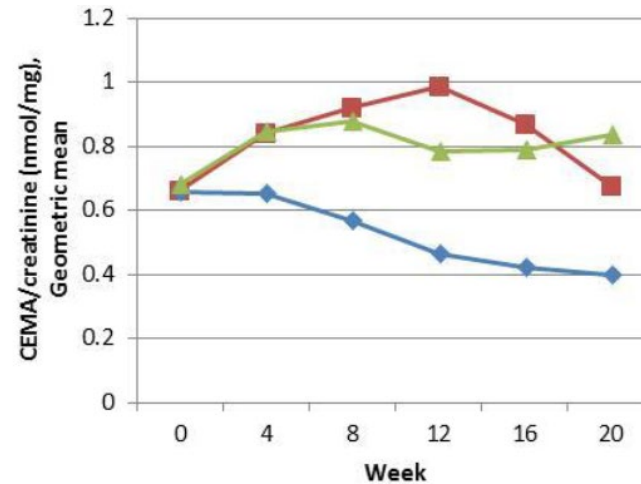
The literature reports that reducing the dose, i.e. the number of cigarettes smoked per day, has an effect on the risk of some, but **NOT** all, smoking related disease risks.

# Decreased Biomarkers of Exposure

## Reduced Nicotine Exposure

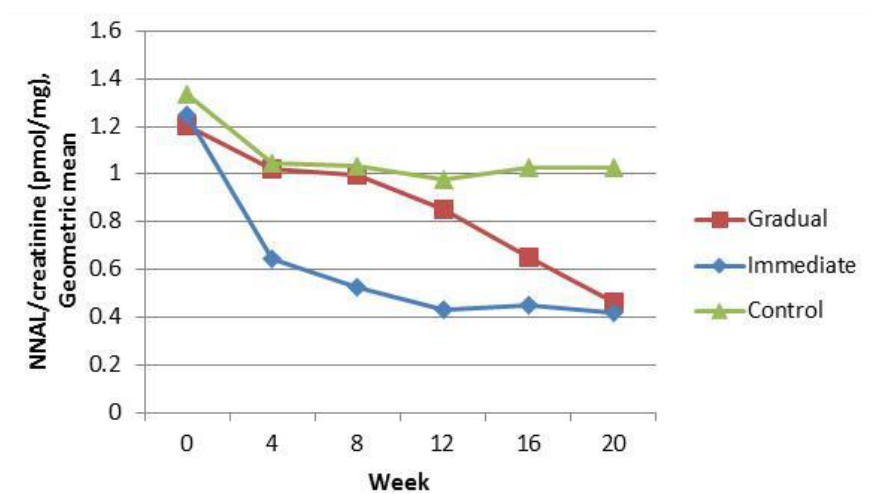


## Reduced VOC's



VOC's – Volatile Organic Compounds

## Reduced NNK





# Dual Use

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- Dual Use, i.e., “cheating” with conventional cigarettes has been widely reported in the literature.
- Hatsukami (2018) reported dual use of up to 80% by participants in the 20-week clinical study.
- The primary time for non-compliance was the first cigarette of the day. Older and more nicotine dependent smokers were more likely than younger smokers to report non-compliance (Nardone, 2019).
- Even though there was dual use, nicotine exposure, biomarkers of exposure and cigarettes per day were still reduced (Hatsukami, 2018).

# Dual Use: 6-Week VLN<sup>®</sup> Clinical Study

		Dual Use	Single Use
		ITT Population	PP Population
		LS Mean Difference (p-Value)	LS Mean Difference (p-Value)
VLN <sup>®</sup> HPHC	Biomarker	Week 6	Week 6
↓Nicotine	Urine Tneq	<b>-8.262 (&lt;.0001)</b>	<b>-14.178 (&lt;.0001)</b>
↓NNK	Urine NNAL	<b>-177.785 (&lt;.0001)</b>	<b>-271.234 (&lt;.0001)</b>
NNN	Urine NNN	-3.106 (0.1213)	-5.207 (0.0964)
↓Acrolein	Urine 3-HPMA	<b>-345.631 (0.0003)</b>	<b>-299.742 (0.0199)</b>
Benzene	Urine S-PMA	-0.312 (0.5302)	0.047 (0.9448)
↓B[a]P	Urine 1-OHP	<b>-64.058 (0.0006)</b>	<b>-92.599 (&lt;.0001)</b>
CO	Blood COHb	-0.540 (0.0457)	-0.379 (0.2247)

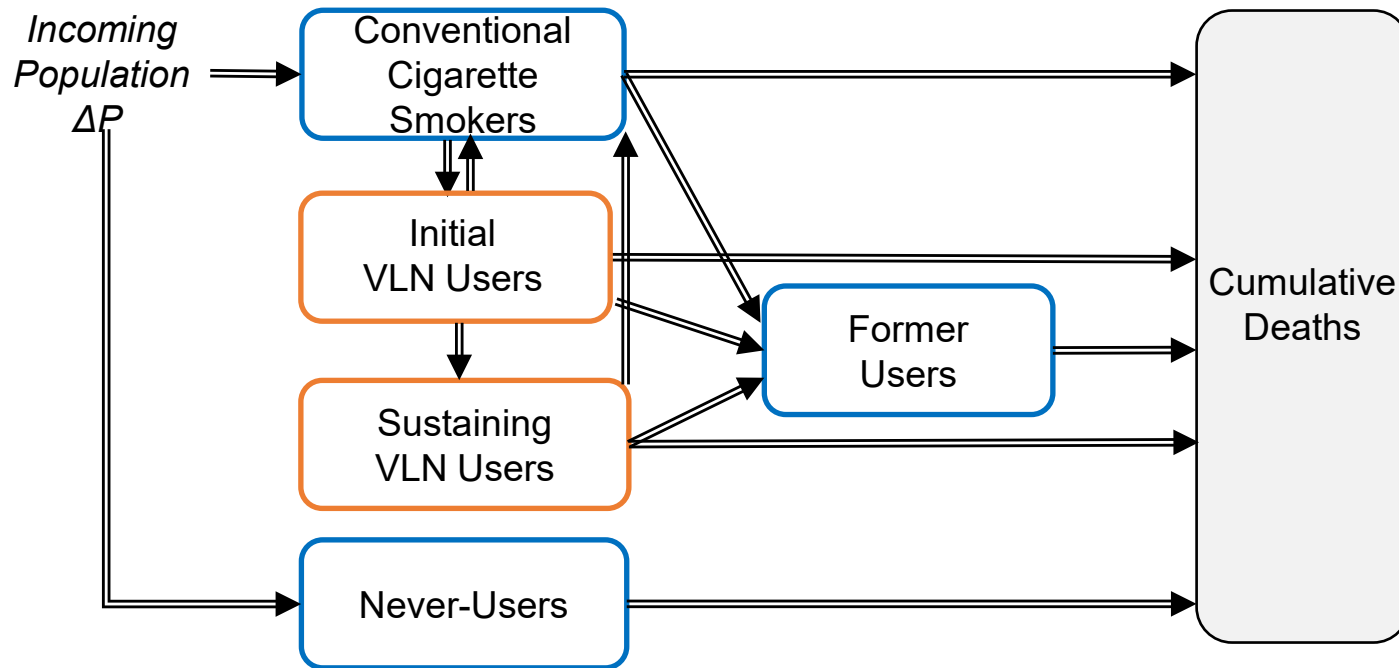
**Dual Use Still Leads to Reduced Biomarkers of Exposure**

# Summary: Individual Benefits from VLN®

	<b>Benefit to User</b>	<b>Benefit to Non-User</b>
Never Smokers	No interest to initiate	No interest to initiate, no second-hand exposure
Former Smokers	No interest to reinitiate	No interest to reinitiate, no second-hand exposure
Current Smokers	Lower abuse liability Reduced CPD	Potentially lower second-hand exposure as a result of Reduced CPD

**VLN® cigarettes yield essentially the same HPHC's as conventional cigarettes. The benefits of VLN® accrue from reduced cigarettes per day (CPD) and reduced abuse liability.**

# Simulation Model to Evaluate the Impact of VLN<sup>®</sup> Cigarettes on Population as a Whole to Year 2100



Population Flow Diagram

- Population dynamics model tracks yearly populations separated by age, sex, and tobacco use status (user type, cigarettes per day, and years since quitting for former users).
- Comparative mortality outputs (cumulative):
  - **Life-years gained**
  - **Avoided cigarette-attributable deaths**

# Simulation Model Assessments

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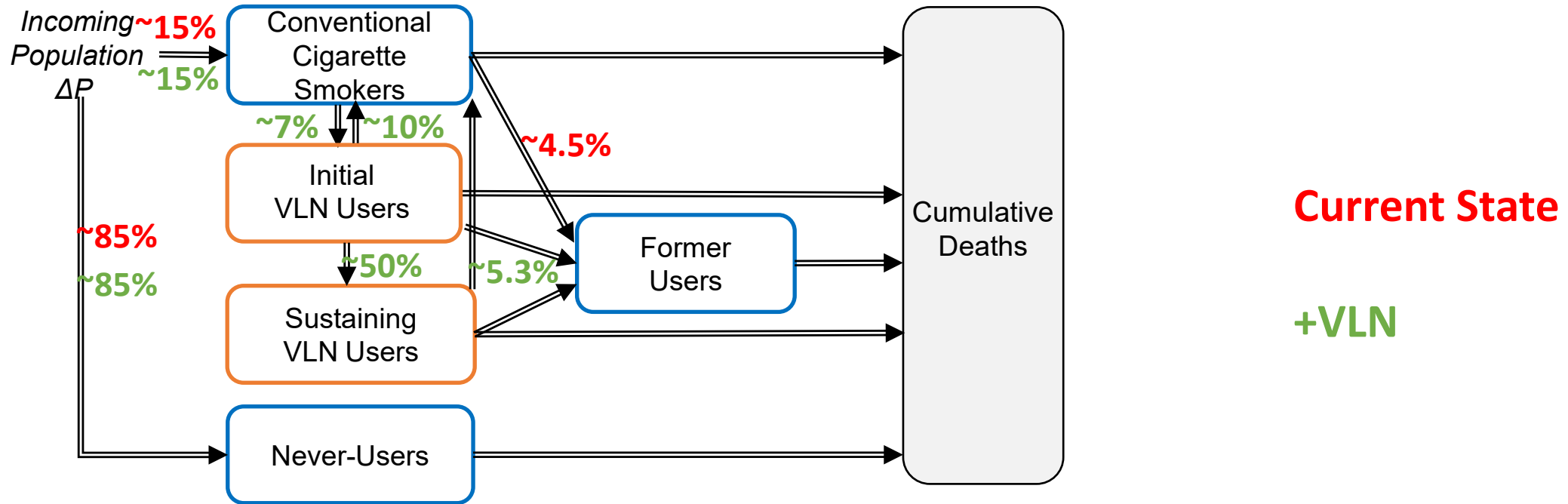
- No smoking initiation caused by VLN<sup>®</sup> and No re-initiation in former smokers caused by VLN<sup>®</sup>.
- 25% market penetration over the next 30 years.
- 50% of VLN<sup>®</sup> smokers sustain smoking VLN<sup>®</sup> after 1 year.  
10% of VLN<sup>®</sup> smokers relapse back to conventional cigarettes (Hughes, 2008).
- **50% reduction in CPD** by sustaining VLN<sup>®</sup> smokers (Hatsukami, 2018).  
Mortality risk declines with decreasing CPD (Poland, 2017).
- Mortality risk declines as a function of increased time since quitting (Poland, 2017).  
Quit rates increase from **4.5%/year to 5.3%/year** (18% increase) (Walker et al., 2012).

# VLN<sup>®</sup> Model Cases

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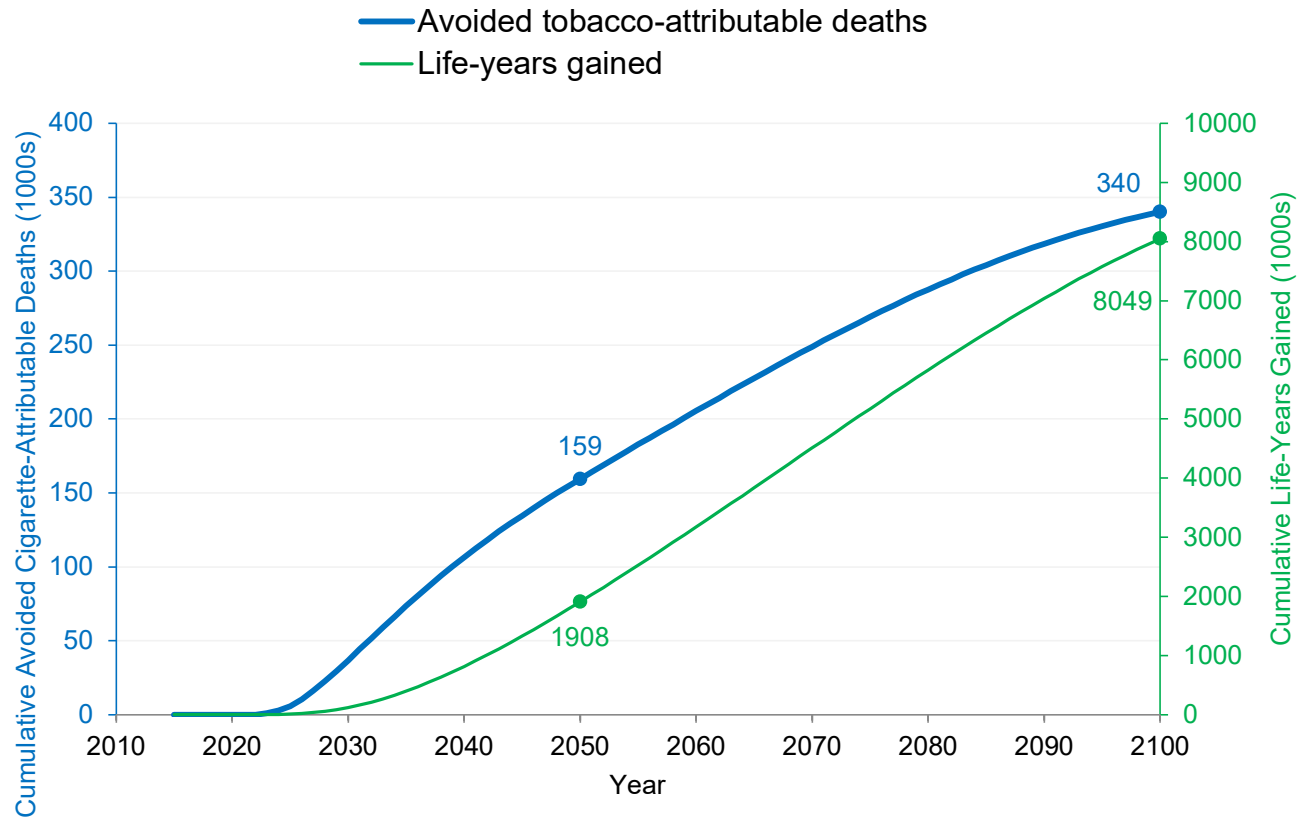
<b>Parameter</b>	<b>Base</b>	<b>Pessimistic</b>	<b>Optimistic</b>
Quit Rate	4.5% → 5.3% (Walker, 2012)	4.5% → 4.5%	4.5% → 6.75%
Relapse Rate >1 Year	10% (Hughes, 2008)	20%	0%

# Simulation Model to Evaluate the Impact of VLN<sup>®</sup> Cigarettes



Population Flow Diagram

# Model Prediction: 340,000 Avoided Cigarette-Attributable Deaths and 8.05 Million Life-years Gained (Cumulative, 2020-2100)



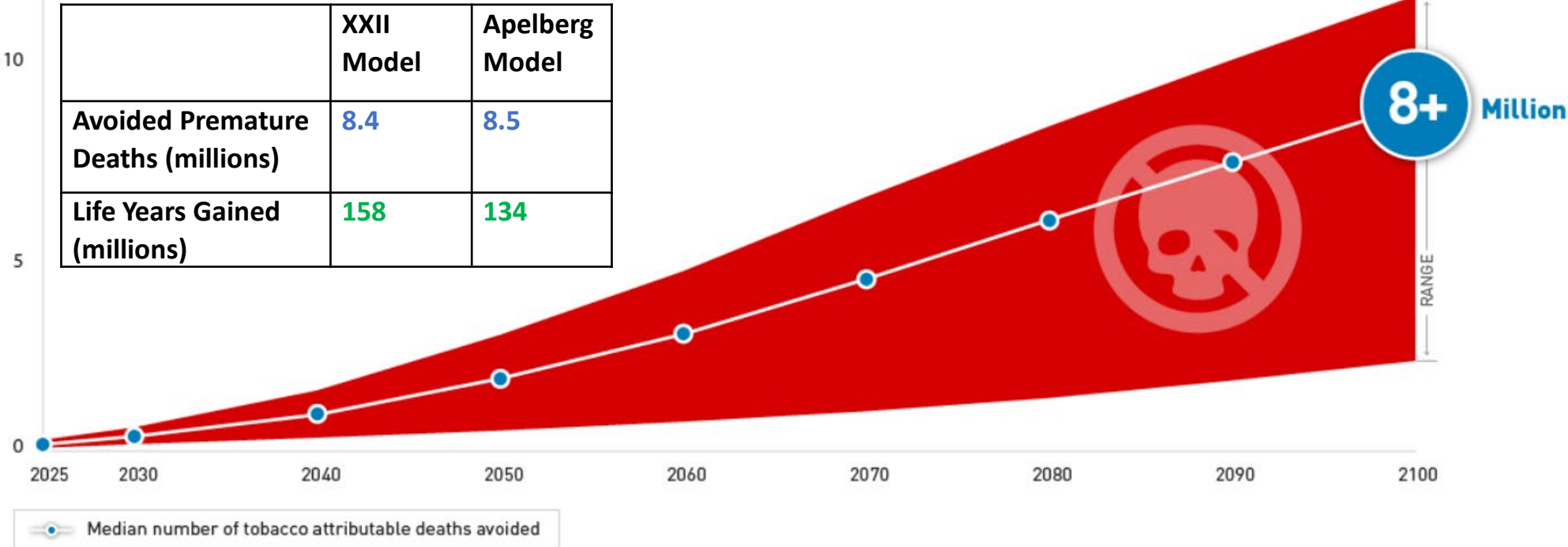
	Pessimistic	Base	Optimistic
<b>Premature Deaths Avoided</b>	<b>136K</b>	<b>340K</b>	<b>922K</b>
<b>Life Years Gained</b>	<b>4.10M</b>	<b>8.05M</b>	<b>18.7M</b>



# 22nd Century Model Mirrors FDA Model Published for Proposed Mandated Nicotine Reduction Policy

## Projected Tobacco Attributable Deaths Prevented

as a result of FDA's potential nicotine reduction policy if implemented in 2020



# Summary: Morbidity and Mortality

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- Nicotine is a harmful substance and nicotine is reduced in the smoke of VLN<sup>®</sup>.
- VLN<sup>®</sup> pharmacokinetics indicate lower abuse liability profile.
- Subjects using very low nicotine content products reduced their cigarettes per day.
- Biomarkers of exposure are reduced, even with dual use.
- Modeling shows potential benefit to the population as a whole.
- **The scientific evidence that is available demonstrates a measurable and substantial reduction in morbidity or mortality among individual tobacco users is reasonably likely in subsequent studies.**

# Consumer Perceptions



# US Adults' Pre-existing Misperceptions on Nicotine

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## **Prevalence and correlates of nicotine and nicotine product perceptions in U.S. young adults, 2016.**

Addictive Behaviors. Andrea C. Villanti, Shelly Naud, Julia C. West, Jennifer L. Pearson, Olivia A. Wackowski, Raymond S. Niaura, Elizabeth Hair, Jessica M. Rath

## **Public misperception that very low nicotine cigarettes are less carcinogenic.**

Tobacco Control. M Justin Byron, Michelle Jeong, David B. Abrams, Noel T. Brewer

## **Examining risk perceptions among daily smokers naïve to reduced nicotine content cigarettes.**

Nicotine and Tobacco Research. Melissa Mercincavage, Kirsten Lochbuehler, Andrea C. Villanti, E. Paul Wileyto, Janet Audrain-McGovern, Andrew A. Strasser

# US Adults' Pre-existing Misperceptions on Nicotine

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“Although most people (83%) believed that nicotine is the main substance in cigarettes that makes people want to smoke, about half (**49%**) incorrectly believed that nicotine is the main substance in cigarettes that **causes cancer**, and another 24% were unsure.”

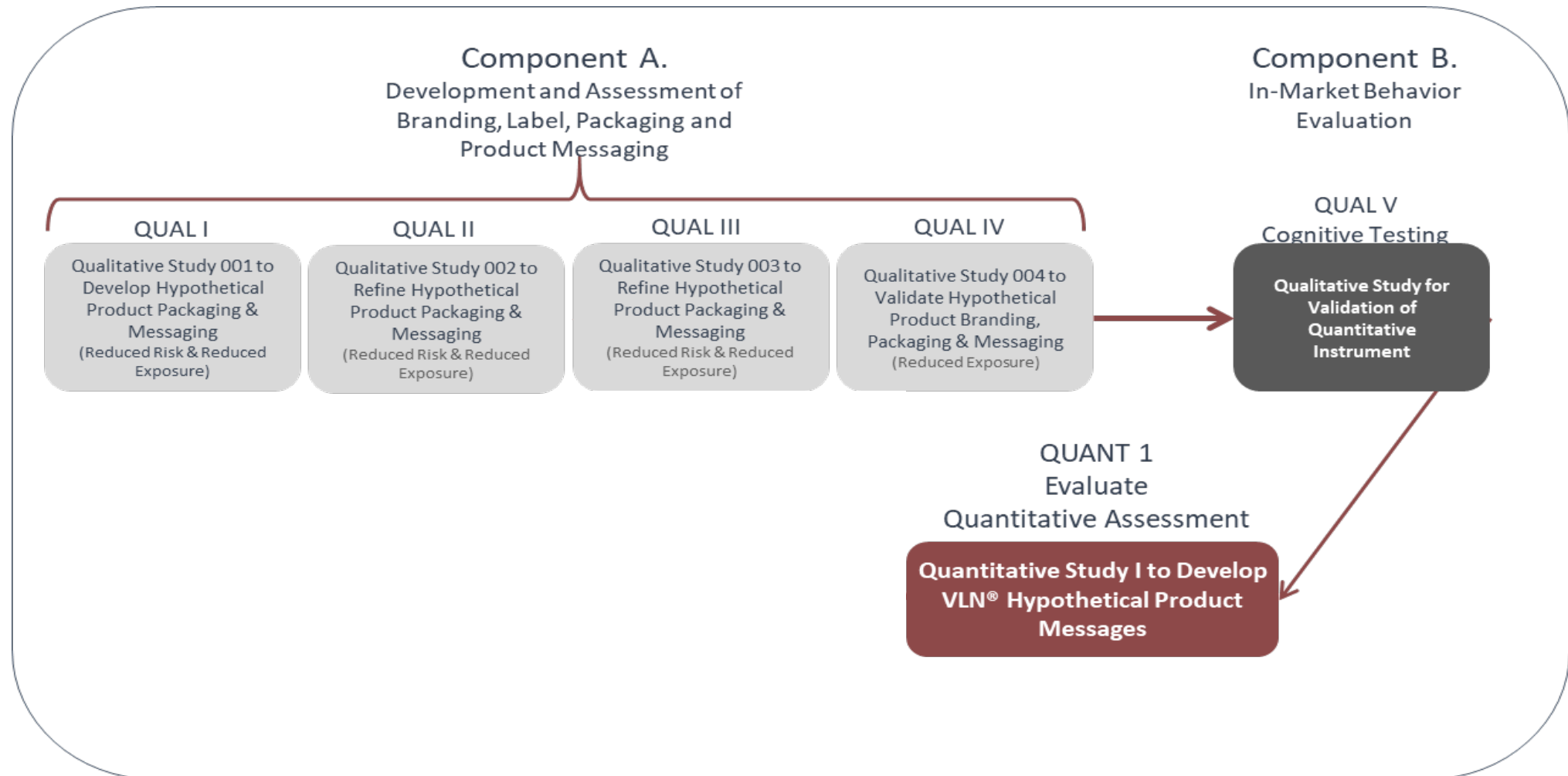
**U.S. adults' addiction and harm beliefs about nicotine and low nicotine cigarettes\***

**Erin Keely O'Brien, Anh B. Nguyen\***, Alexander Persoskie, and Allison C. Hoffman  
Center for Tobacco Products, Food and Drug Administration, United States

# Consumer Perception Studies

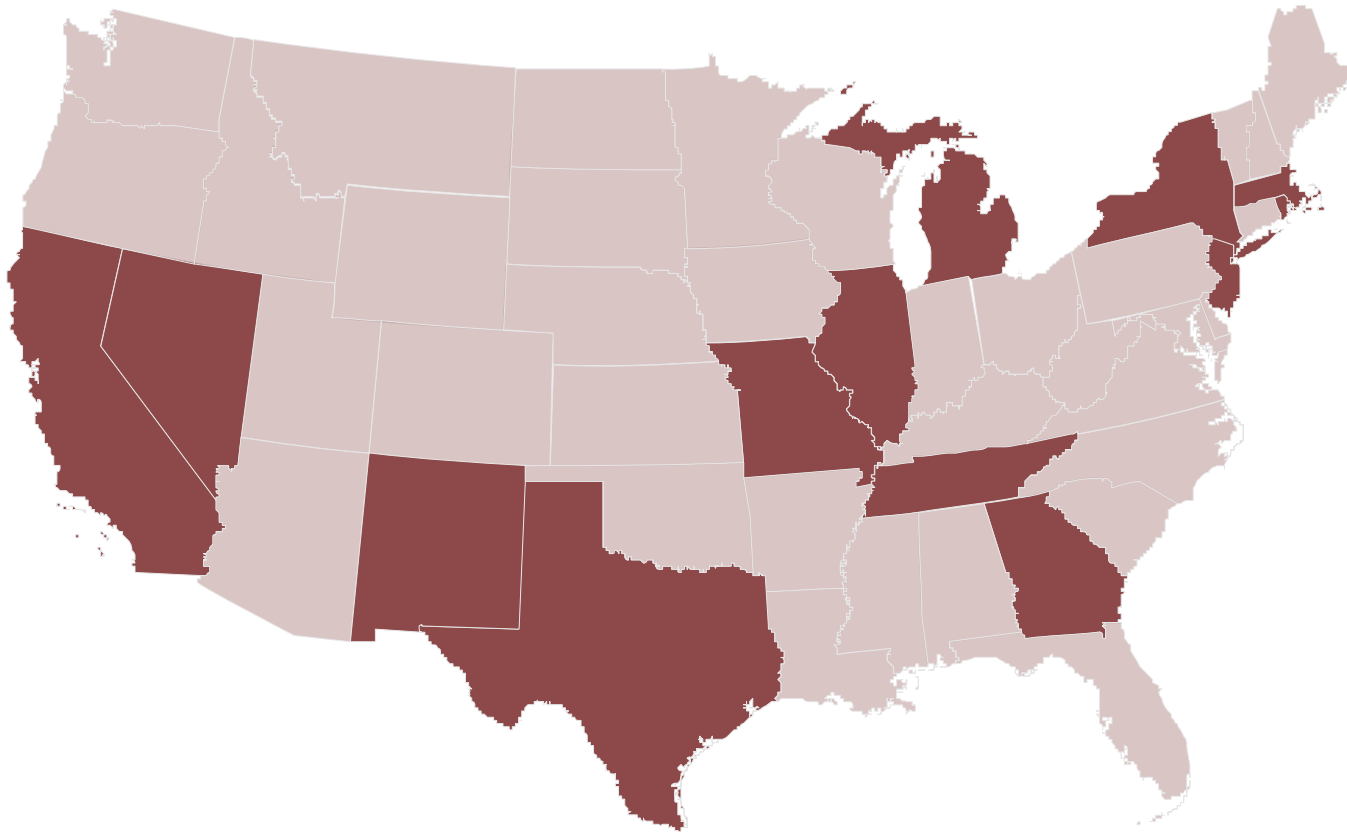


# Qualitative and Quantitative Consumer Perception Research Design



# Qualitative Studies Conducted to Develop the Claims

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- **42 focus groups and 104 in-depth one-on-one interviews across 13 states.**
- **Cities selected based on population to include a range of communities from smaller suburban to dense urban.**
- **Participant recruitment was based on age, gender, cigarette use status, ethnicity and literacy level.**



# Qualitative Findings and Labeling Evolution

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- Consumers did not interpret the VLN<sup>®</sup> labeling or the VLN<sup>®</sup> exposure modification claims to mean that the VLN<sup>®</sup> cigarettes were safer than conventional cigarettes.
- There were, however, some pre-existing misconceptions about the role of nicotine in smoking-related disease.
- 22nd Century voluntarily added a product health warning to inform people who smoke about the dangers of smoking.

# Voluntarily Warning

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Nicotine is addictive.  
Less nicotine does **NOT** mean  
safer. All cigarettes can cause  
disease and death.

# Impact of Brief Nicotine Messaging

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"Findings from the current study support the hypothesis that **a brief nicotine messaging intervention**—similar to the messages likely to be seen on warning labels or in media campaigns—**is likely to correct misperceptions of nicotine, NRT, E-cigarettes, and RNC [reduced nicotine content] cigarettes.**"

Andrea C. Villanti, PhD, MPH, Julia C. West, BA, Darren Mays, PhD, MPH, Eric C. Donny, PhD, Joseph N. Cappella, PhD, Andrew A. Strasser, PhD. "Impact of Brief Nicotine Messaging on Nicotine-Related Beliefs in a U.S. Sample." *American Journal of Preventive Medicine*, Vol. 57, Issue 4. October 1, 2019.

# A Quantitative Study to Validate the Claim Perception

- ~28,000 participants, across all 50 States, inclusive of all census subgroups including age, sex, and race (~7,000 participants per experimental condition, ~3,500 participants per control condition).
- **Measured responses to the VLN<sup>®</sup> pack label within populations of** adult smokers with an intention to quit, adult smokers with no intention to quit, adult former smokers, and adult never smokers.
- **Oversample of young adult never smokers (i.e. Legal Age to 25 years old; “LA-25”) to act as a proxy for youth.**

# Perception Study Design

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## **Comparator Categories**

Conventional Cigarettes

Moist Snuff

E-Cigarettes

NRT

## **Study Measures**

Label Comprehension

Familiarity

Intent to Use

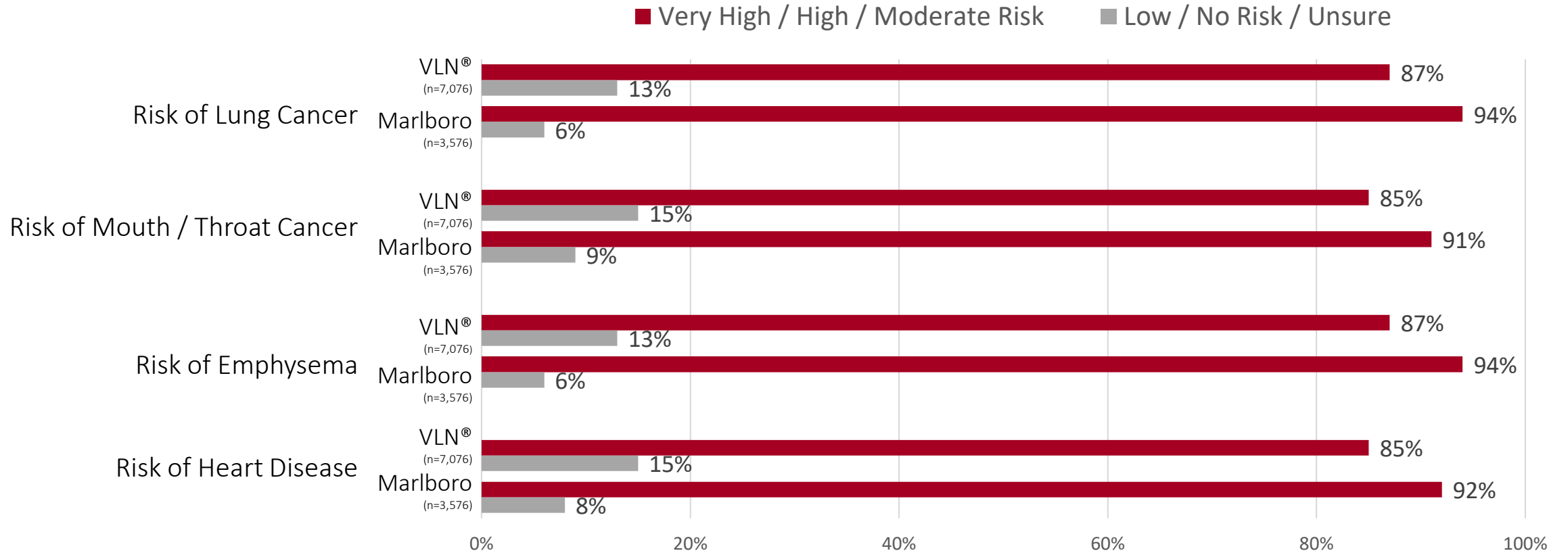
Health Risk Perception

Addiction Perception

## **Control Cell**

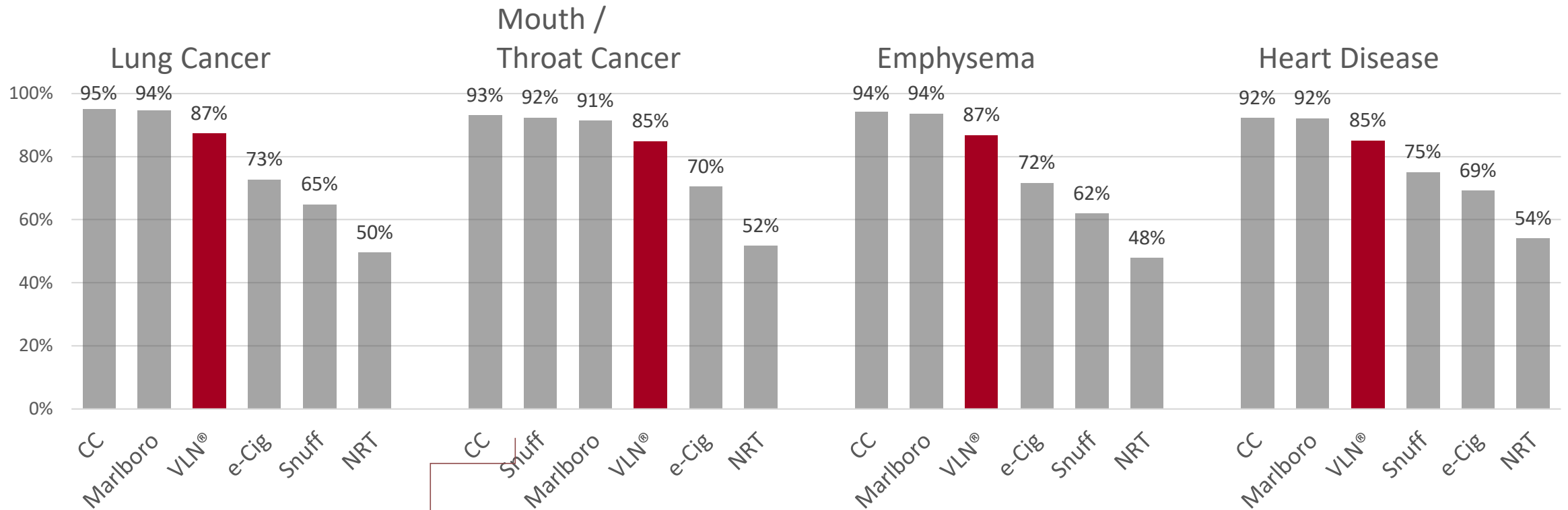
Marlboro Gold Pack

# Perceived Health Risks of VLN<sup>®</sup> Similar to Marlboro Gold



# Risk Continuum: Perception of Health Risks of VLN<sup>®</sup> Relative to Other Products Well-Understood

% of All Respondents Evaluating Comparator Category / Concept as Very High, High or Moderate Risk



*Exception: As might be expected, a higher percentage of participants perceive Moist Snuff to have risk associated with mouth or throat cancer than VLN<sup>®</sup>.*

# Label Comprehension: Less Nicotine Does Not Mean Safer

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**If I was serious about quitting smoking and was trying to get off nicotine, then I might consider it but I certainly wouldn't think it's safer in any way.**

*Dallas, Female, Age 35-49, Smoker No Intent to Quit Menthol*

**I'm going to put it up there with regular cigarettes, because it's just less nicotine. You're still getting all the smoke in your lungs. I'd say it's the same...I don't care what kind of smoke it is. It's not good for you.**

*Chattanooga, Female, Age 26-34, Recent Quitter*

**Maybe it's because people will think, "There's less nicotine. It's safer." But nicotine was never the harmful issue. So I guess it's trying to split out the addictive property versus the harmful property, and how those interact with each other.**

*Detroit, Female, Age 36-50, Current Smoker Intend to Quit*

**I would already think that it's the same as smoking. What's attractive about it is you may not smoke as much, or it'll be easier to quit after switching to this. Less cravings. But as far as cigarette for cigarette it never would have occurred to me that it's safer for somebody. You're still smoking.**

*Chicago, Male, Age 35-49, Current Smokers Intend to Quit*

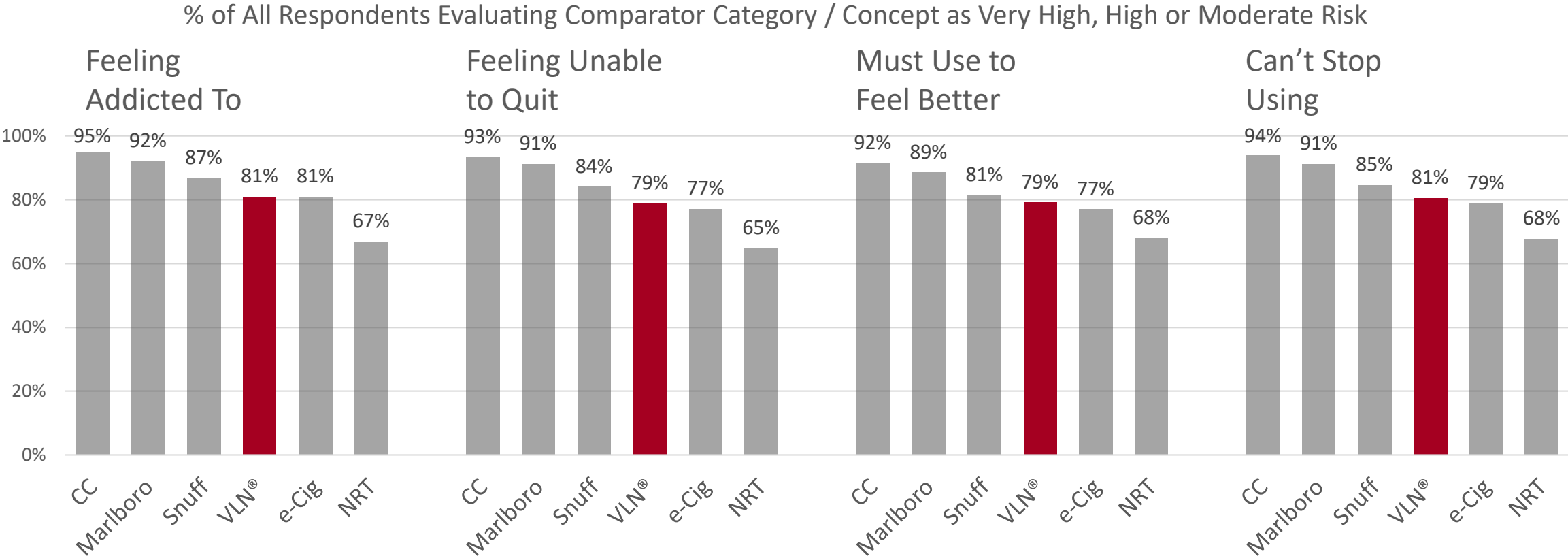


# Consumers Clearly Understood Health Risk Associated with VLN<sup>®</sup>

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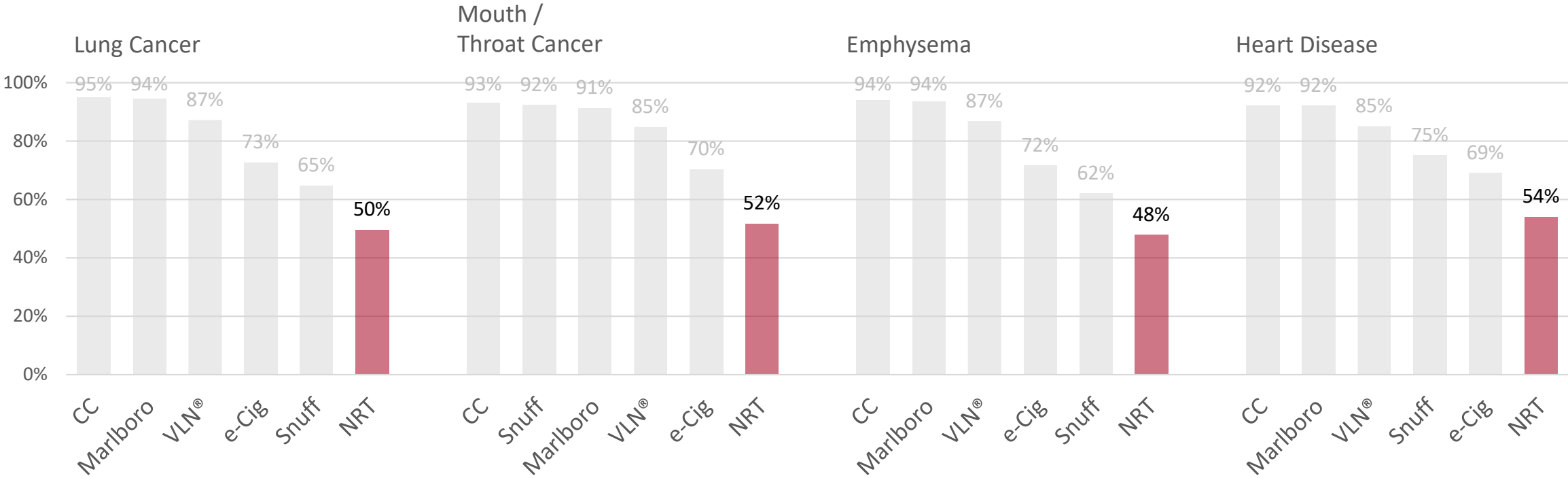
<p>When asked how to describe VLN<sup>®</sup> to a friend or family member</p>	<ul style="list-style-type: none"><li>• <b>66%</b> of participants state that the product was <b>low in nicotine</b>.</li><li>• 16% offered top-of-mind responses of health risks such as cancer or death.</li></ul>
<p>When asked about health or addiction risks</p>	<ul style="list-style-type: none"><li>• <b>31%</b> associate VLN<sup>®</sup> with the <b>same risks</b> as “regular cigarettes”</li><li>• 55% of all participants responded appropriately with diseases such as cancer, lung/respiratory disease, heart problems or general mentions of the product being “harmful.”</li></ul>
<p>When asked about health or addiction risks associated with VLN<sup>®</sup></p>	<ul style="list-style-type: none"><li>• <b>7%</b> stated that there were <b>no negative risks</b> associated with VLN<sup>®</sup>.</li></ul>

# Participants Perceived a Lower Risk of Addiction for VLN®



# Participants Perceived NRT as a Risk for Lung Cancer, Mouth/Throat Cancer, Emphysema, and Heart Disease

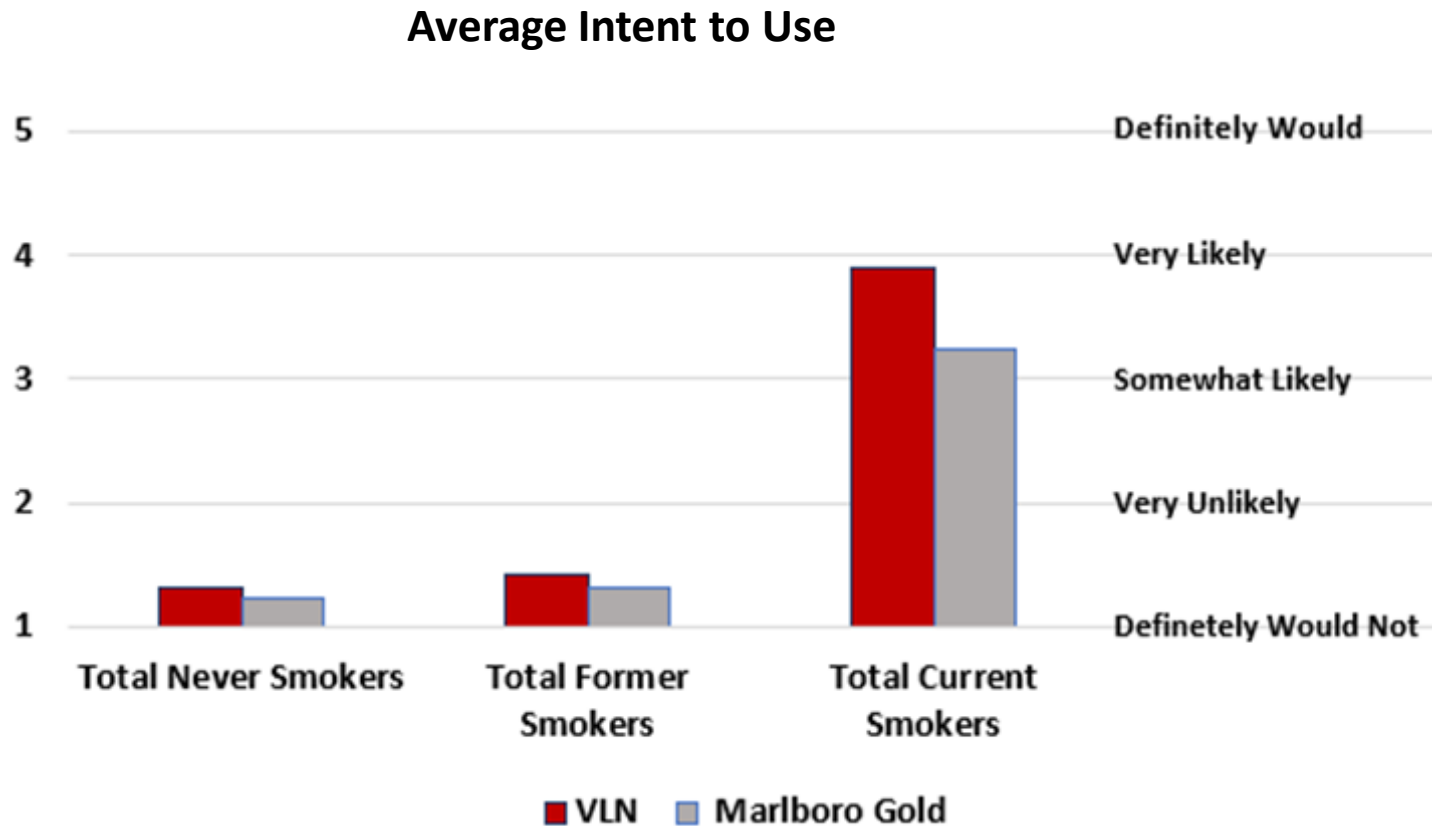
% of All Respondents Evaluating Comparator Category / Concept as Very High, High or Moderate Risk



# Consumer Interest and Intent to Use: Never Smokers and Former Smokers

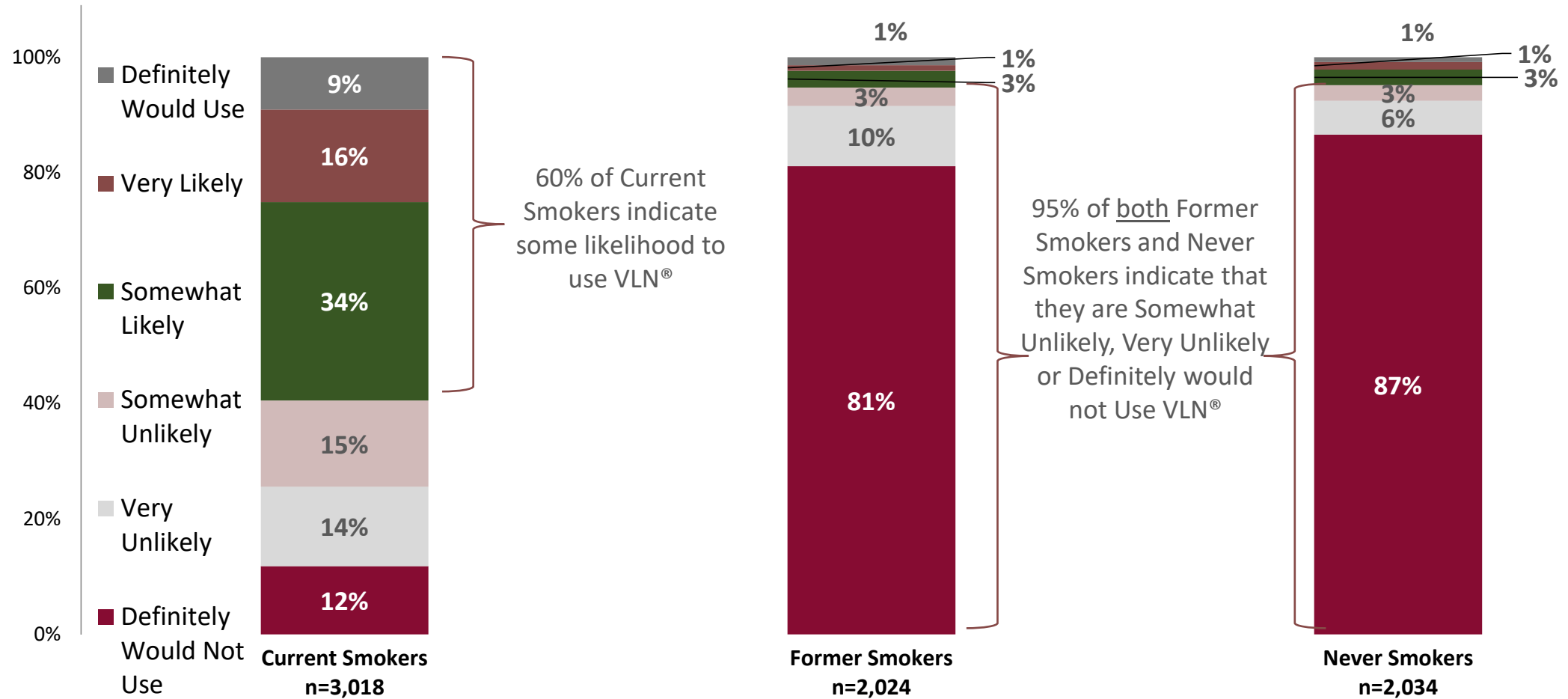


# Intent to Use VLN<sup>®</sup>

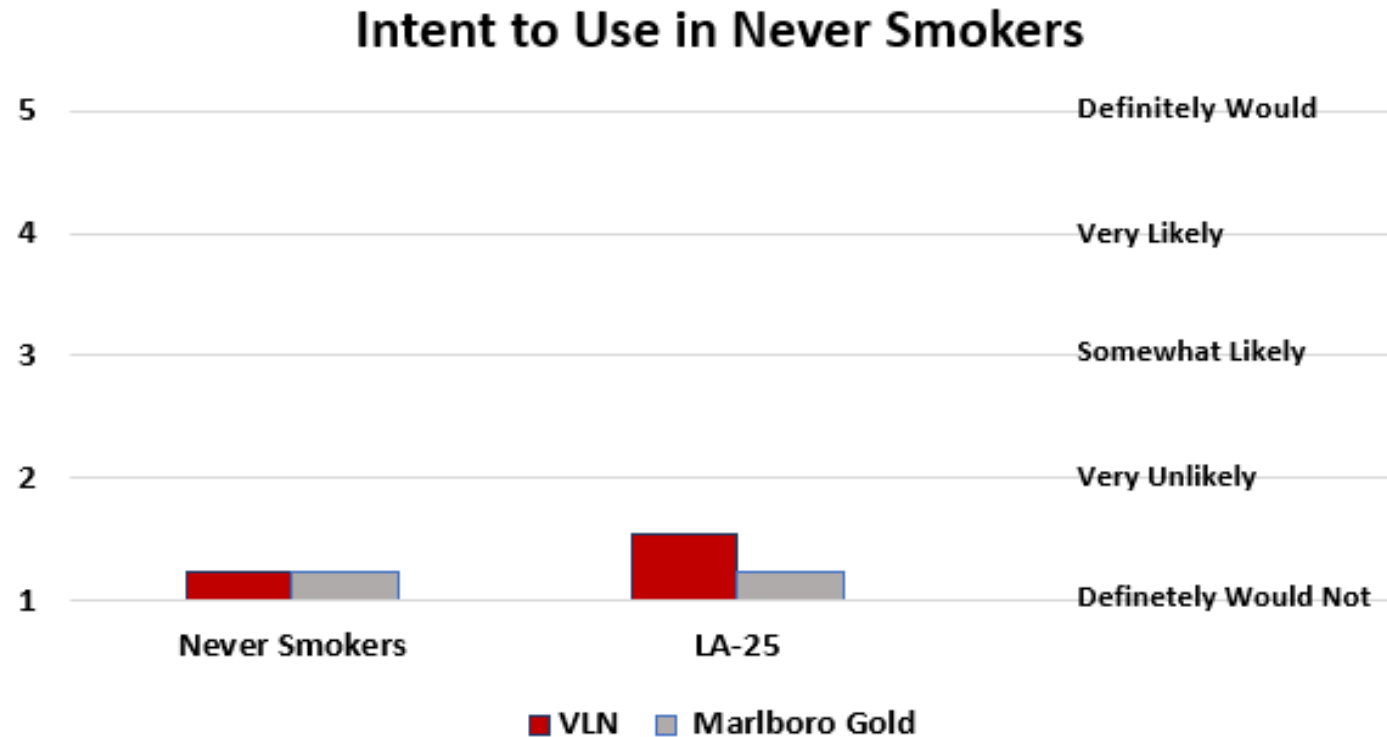


- **Never and Former Smokers Are Not Interested in VLN<sup>®</sup>.**
- **Current Smokers Are More Interested in VLN<sup>®</sup> Than Marlboro Gold.**

# Former and Never Smokers Unlikely to Use VLN®

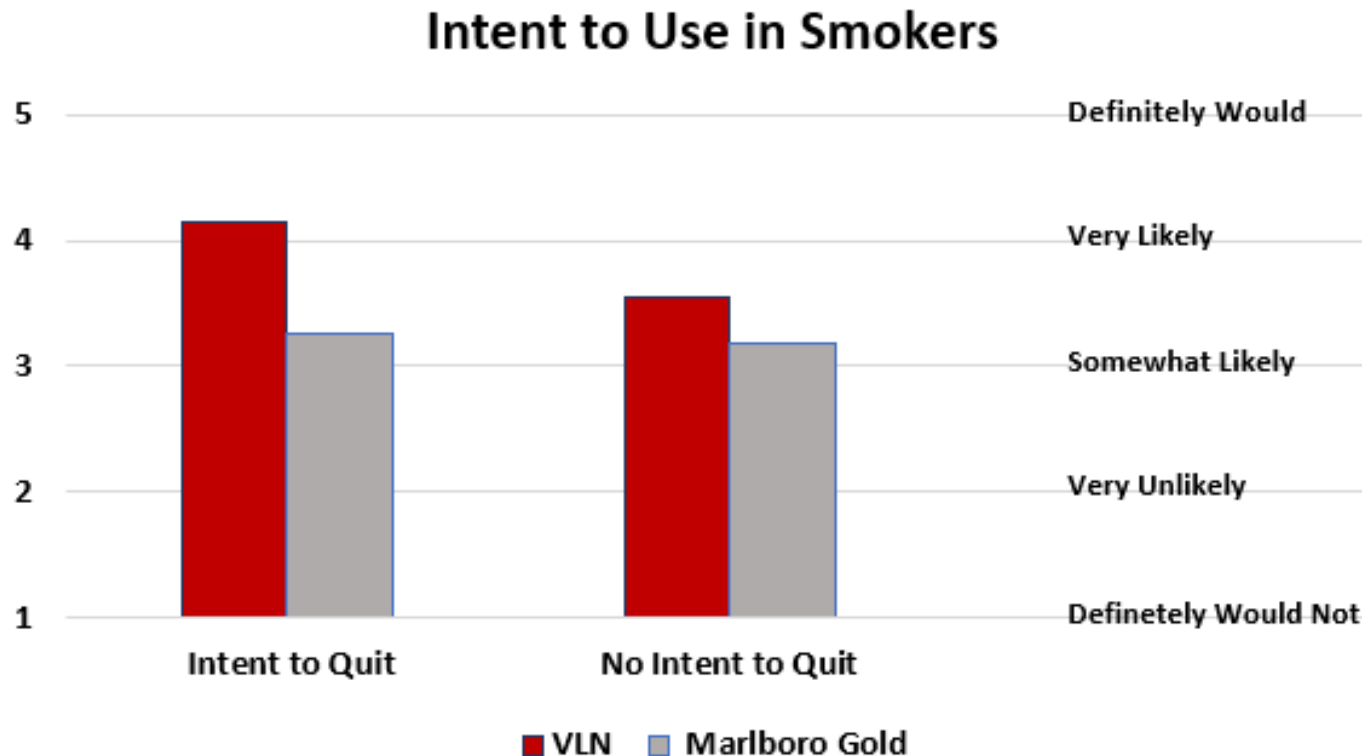


# Intent to Use VLN<sup>®</sup>: Never Smokers



- **Never Smokers Are Not Interested in VLN<sup>®</sup>.**
- **LA-25 Are Not Interested in VLN<sup>®</sup>.**
- **LA-25 Are More Interested in VLN<sup>®</sup> Than Marlboro Gold.**

# Intent to Use VLN<sup>®</sup>: Smokers



- **Smokers With Intent to Quit Are More Interested in VLN<sup>®</sup>.**
- **Smokers Are More Interested in VLN<sup>®</sup> Than Marlboro Gold.**



# Summary: Consumer Perception

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- 22nd Century made no statements on the health risk or reduced addictive nature of VLN<sup>®</sup>, we only made statements relating to 95% less nicotine.
- There are pre-existing misconceptions on the role of nicotine in disease; this is clear from the literature and from the results of our perception study.
- Perceived health risks of VLN<sup>®</sup> are similar to perceived health risks of Marlboro Gold.
- 22nd Century believes that the slight reductions seen in health risk perception are driven by pre-existing misconceptions on the role of nicotine in smoking diseases.
- Subjects understood that VLN<sup>®</sup> cigarettes had less nicotine, may be potentially less addicting, and adult never smokers, former smokers, and LA-25 are not interested in VLN<sup>®</sup>.
- **Proposed label for VLN<sup>®</sup> cigarettes did not mislead respondents into believing that the product is or has been demonstrated to be less harmful than other commercially marketed tobacco products.**

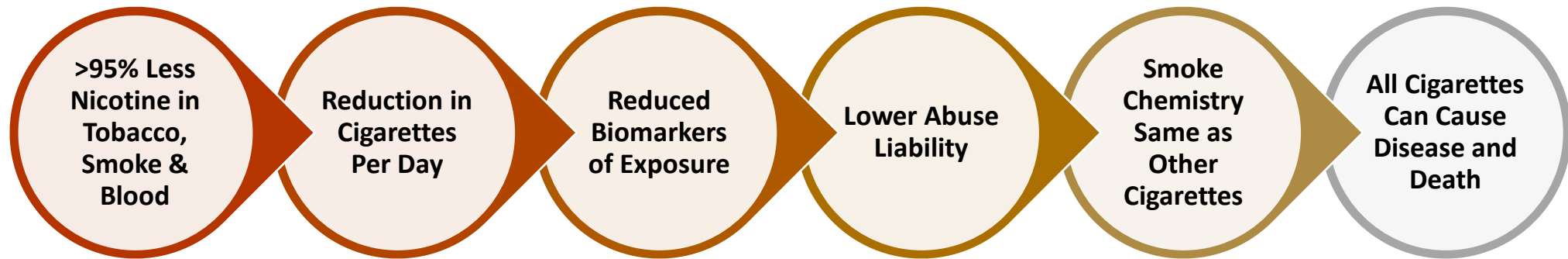
# Conclusion

John D. Pritchard, BSc (Hons), MSc, CBiol, MRSB  
Vice President of Regulatory Science  
22nd Century Group, Inc.



# VLN<sup>®</sup> Scientific Summary

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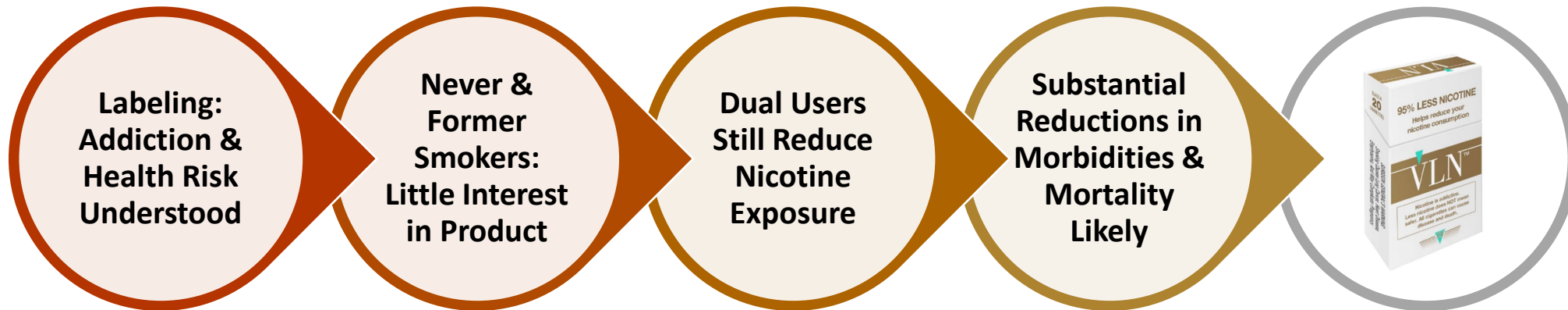
# FDA's Topics for Discussion

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- Discuss whether the labeling enables consumers to accurately understand the following effects of using the products:
  - a. Addiction risk
  - b. Disease risk
- Discuss the likelihood that reductions in dependence translate into substantial reductions in morbidities and mortality among individual tobacco users.
- Discuss the extent to which the following groups are likely to try and progress to regularly using the proposed modified risk tobacco products:
  - a. Never smokers
  - b. Former smokers
- Discuss the extent to which the following groups will dual use the proposed modified risk products:
  - a. Cigarette smokers who want to quit smoking
  - b. Cigarette smokers who do not want to quit smoking.

# VLN<sup>®</sup> MRTTP Conclusions

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**22nd Century believes it is appropriate for FDA to issue an exposure modification order for VLN<sup>®</sup>**



**22nd Century Group, Inc.**

**VLN<sup>®</sup> Reduced Nicotine Cigarettes**

**VLN<sup>®</sup> King Box and VLN<sup>®</sup> Menthol King Box**

**Tobacco Products Scientific Advisory Committee Meeting**

**February 14, 2020**