

## Quantitative Study to Develop VLN™ Hypothetical Product Messages Among U.S. Adult Cigarette Smokers, Adult Former Cigarette Smokers and Adult Never Cigarette Users

**Protocol Number:** 5180080-VLN™-B2

**Principal Investigator:** Randall Wahl  
Chief Research Officer  
M/A/R/C® Research  
7850 North Belt Line Rd  
Irving, TX 75063

**Sponsor:** 22nd Century Group, Inc.  
8560 Main Street  
Williamsville, NY 14221

**Regulatory Review:** Kinetiq  
1501 Fourth Avenue  
Suite 800  
Seattle, WA 98101

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**SIGNATURE PAGE**

**Principal Investigator:** I have read the protocol entitled “*Quantitative Study to Develop VLN™ Hypothetical Product Messages Among U.S. Adult Cigarette Smokers, Adult Former Cigarette Smokers and Adult Never Cigarette Users*” and agree to conduct the study as outlined in this document. In addition, I agree to conduct the study in compliance with all applicable regulations and guidelines as stated in the protocol and other information supplied by the Sponsor.

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Randall Wahl, Chief Research Officer  
M/A/R/C® Research

\_\_\_\_\_  
December 27, 2018

Date

(b) (6)

\_\_\_\_\_  
Brad Seipel, Vice President  
M/A/R/C® Research

\_\_\_\_\_  
December 27, 2018

Date

(b) (6)

\_\_\_\_\_  
Lynn Dagar, Vice President  
M/A/R/C® Research

\_\_\_\_\_  
December 27, 2018

Date

(b) (6)

(b) (6) \_\_\_\_\_  
Research Director  
M/A/R/C® Research

\_\_\_\_\_  
December 27, 2018

Date

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## LIST OF ABBREVIATIONS

<b>Abbreviation</b>	<b>Definition</b>
BRFSS	The Behavioral Risk Factor Surveillance System
CC	Conventional Cigarettes
CFR	Code Of Federal Regulations
CRO	Contract Research Organization
EDC	Electronic Data Capture
FDA	Food And Drug Administration
HINTS	Health Information National Trends Survey
IRB	Institutional Review Board
LA	Legal-Age
MRTTP	Modified Risk Tobacco Product
NHIS	National Health Interview Survey
NRT	Nicotine Replacement Therapy
PI	Principal Investigator
PII	Personally Identifiable Information
PATH	Population Assessment of Tobacco Use and Health
US	United States
WHO	World Health Organization

## STATEMENT OF COMPLIANCE

This study will be conducted in accordance with the specifications noted in the study protocol (Protocol Number: 5180080-VLN™-B2; "*Quantitative Study to Develop VLN™ Hypothetical Product Messages Among U.S. Adult Cigarette Smokers, Adult Former Cigarette Smokers and Adult Never Cigarette Users*") and in accordance with The Insights Association's Code of Standards and Ethics for Marketing Research and Data Analytics.

**PROTOCOL SUMMARY**

<b>Title of Study</b>	Quantitative Study to Develop VLN™ Hypothetical Product Messages Among U.S. Adult Cigarette Smokers, Adult Former Cigarette Smokers and Adult Never Cigarette Users
<b>Study Purpose</b>	<p>The purpose of this consumer perception study is to measure responses to versions of VLN™, a candidate “Modified Risk Tobacco Product” (MRTP), label and messaging within populations of (1) Adult Smokers with an intention to quit, (2) Adult Smokers without any intention to quit, (3) Adult Former Smokers and (4) Adult Never Smokers.</p> <p>This research includes two primary phases: (1) qualitative research to develop VLN™ label and messaging and (2) quantitative study to test the label and messaging. This protocol document addresses only the quantitative research.</p>
<b>Messaging To Be Tested</b>	<p>Messaging for VLN™ cigarettes, a MRTP, includes:</p> <ul style="list-style-type: none"> <li>• Primary Claim (same on all packs)             <ul style="list-style-type: none"> <li>○ 95% Less Nicotine</li> </ul> </li> <li>• Secondary (Comparative) Claim             <ul style="list-style-type: none"> <li>○ (b) (4)</li> <li>○ Helps reduce your nicotine consumption</li> <li>○ (b) (4)</li> </ul> </li> <li>• Disclaimer (same on all packs)             <ul style="list-style-type: none"> <li>○ Nicotine is addictive. Less nicotine does NOT mean safer. All cigarettes can cause disease and death.</li> </ul> </li> <li>• Back of Pack Language (same on all packs)             <ul style="list-style-type: none"> <li>○ VLN™ smells, burns, and tastes like a conventional cigarette, but greatly reduces your nicotine consumption.</li> </ul> </li> </ul>
<b>Primary Research Objectives</b>	<ul style="list-style-type: none"> <li>• Estimate impact of VLN™ using potential product messaging</li> <li>• Test hypotheses that potential product messages for VLN™:             <ul style="list-style-type: none"> <li>– Generate intent to use among those who could benefit from use (US adult smokers of cigars and cigarettes, adult smokers motivated to quit)</li> <li>– Do not generate significant intent to use among those who could be harmed by use (adult never smokers, adult former smokers)</li> <li>– Describe the product clearly and promote comprehension</li> </ul> </li> </ul>
<b>Secondary Research Objectives</b>	<ul style="list-style-type: none"> <li>• Estimate impact of VLN™ among adult never smokers, adult never smokers Legal Age to 25 years old, adult former smokers (recent &amp; long-term), adult smokers motivated to quit and adult smoker population</li> </ul>

	<ul style="list-style-type: none"> <li>• Assess risk perception for VLN™ and four alternatives (CCs, e-cigarettes, Moist Tobacco, Nicotine Replacement Therapies [NRTs])</li> <li>• Assess intent to use for VLN™ and four comparator objects (CCs, e-cigarettes, Moist Tobacco, NRTs)</li> </ul>
<b>Study Sites</b>	<p>This consumer perception research will be conducted in the United States (US) as an online study hosted by M/A/R/C® Research.</p>
<b>Design</b>	<p>Each respondent will be asked to evaluate one concept consisting of a label and messaging for VLN™. In this concept, the term label refers to the brand graphics that appear on the label on the pack, while the term messaging refers to text printed on the pack. The respondent will be asked to evaluate the messaging paired with the packaging graphics. All participants will view a 3-D image of a product package as well as flat image views of all four sides of each package.</p> <p>Assessments on product risk (exposure to harmful compounds / tobacco-related disease), addiction risk and intent to use for tobacco product categories and VLN™ will be conducted within four main subject groups, based on self-reported smoking status. Within each concept, each subject group will be composed of an approximately equal number of subjects.</p> <p>Data analysis will be descriptive and will consist of calculating measures of central tendency, dispersion and unadjusted 95% confidence intervals for each endpoint, by concept and separately for each subject group and/or for the total sample, as appropriate. Analyses to determine statistically significant variances will be performed across tobacco user types and demographic groups. Key areas of analysis will include intent to use VLN™, expected liking of using the product, differentiation from other products currently available, relative attractiveness compared to products available, perceived risk of the product, expected change in tobacco behavior/usage and preference for VLN™ concepts as well as a known cigarette brand, Marlboro Gold. These metrics will be used as a basis to understand attractiveness and likelihood of use among the populations of interest.</p> <p>The survey will be administered using a web-based self-directed platform. It will involve exposure to VLN™ packaging and messaging, control concept packaging and messaging and to direct questioning about the concept presented. Intention to Use and Risk Perception will be assessed for VLN™, CCs, e-cigarettes, Moist Snuff and NRTs. Questions about Intention to Use will be asked at multiple points throughout the survey to further mitigate against testing affects and overstatement.</p> <p>The study will be conducted solely in the US.</p>

<b>Estimated Number of Subjects</b>	<p>Subjects will be categorized into four primary subject groups, based on self-reported smoking behavior:</p> <ul style="list-style-type: none"><li>• Group 1 – Adult Smokers with no Intention to Quit CCs</li><li>• Group 2 – Adult Smokers with Intention to Quit CCs</li><li>• Group 3 – Adult Former Smokers</li><li>• Group 4 – Adult Never Smokers</li></ul> <p>These groups will be analyzed individually and they will also be analyzed together in order to estimate overall public impacts. In order to accomplish this dual purpose, (1) group samples will be stratified and over-sampled where necessary in order to carry out a meaningful analysis of each group and, then, (2) post-stratification weighting will be applied to compensate for the stratification and assure that the overall results mirror the US population as a whole.</p> <p>Each product concept (branded label and messaging) will be comprised of approximately equally-sized primary subject groups.</p> <p>Former Smokers will be further divided on the basis of how recently they quit smoking, and Current Smokers will be further subcategorized based on Intention to Quit CCs using a question from Prochaska’s and DiClemente’s Stages of Change model (Prochaska and DiClemente, 1982).</p> <p>The data will be analyzed to detect differences among Current Smokers who indicate intent to quit smoking as well as those with no intent to quit. This study will also include subjects of Legal-Age (LA) to 25 years of age who have never smoked (Never Smokers) as a proxy for youth smokers who may not be interviewed by law without parental consent. Legal-Age will be defined as the minimum age for tobacco purchase as determined by each participant’s US state of residence.</p> <p>At a broad level, the sampling frame includes adults living in the US. A main study sample size of 28,000, equivalent to 7,000 subjects per concept, is deemed to provide sufficient precision for this study and allow for reporting results by refined population segments, including special relevance populations.</p>
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**Inclusion &  
Exclusion  
Criteria**

As noted earlier, the sample will be stratified by smoking status. Goals for completed interviews within each smoking-status group using demographic variables have been established. In the event of variances from those goals, the data will be weighted so that each group reflects the overall population for that group. When analyzing the total sample, post-stratification weighting will be implemented to compensate for the effects of stratification so that overall impact on the population as a whole may be estimated accurately. Random Iterative Method (RIM) Weighting will be used for all of these procedures.

Inclusion criteria:

1. Ability to read and understand English.\*
2. Currently residing in the US.
3. Legal age of purchase (defined as the minimum age for tobacco purchase as determined by each participant's US state of residence) or older.
4. Able and willing to comply with all study requirements.
5. Provides informed consent.

Exclusion criteria:

1. Under legal age of purchase.
2. Past 3-month participation in any tobacco-related research.
3. Currently pregnant or breastfeeding or planning to become pregnant within the next 6 months.
4. Employees of tobacco or vapor companies, news or media, advertising / marketing, marketing research, healthcare, or attorney or paralegal, or having a first degree relative that is employed by these types of companies\*\*.

Sample will be further stratified into population subgroups based on a variety of characteristics including demographic criteria as well as current smoking status.

Stratification:

1. Number of cigarettes ever smoked.
2. Type of cigarette smoked (menthol/non-menthol).
3. Gender, ethnicity and annual household income to ensure representation consistent with the market.
4. Number of cigarettes smoked per day to ensure a mix of participants who are light / social smokers versus those who are heavier smokers.
5. Intent to quit smoking within the next year.
6. Cessation status - former smokers will be classified into recent versus long-term cessation defined as length of time, on the date of interview, in months / years since cessation was initiated.

*\*Only English-speaking participants will be recruited to participate as the product communication is only*

	<p><i>expected to be delivered in English at this time.</i></p> <p><i>**Employees, students and/or first-degree relatives of those who are employed by or pursuing education in sensitive industries will be excluded from the research to minimize bias and also to protect the proprietary product information that will be disclosed in the survey.</i></p>
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## 1 KEY ROLES

**Sponsor:** 22nd Century Group, Inc.  
8560 Main Street  
Williamsville, NY 14221

**Principal Investigator:** Randall Wahl  
Chief Research Officer  
M/A/R/C® Research  
7850 North Belt Line Rd  
Irving, TX 75063

**Contract Research Organization:** M/A/R/C® Research  
7850 North Beltline Road  
Irving, TX 75063

**Regulatory Review:** Kinetiq  
1501 Fourth Avenue  
Suite 800  
Seattle, WA 98101

**Protocol Author:** (b) (6)  
Research Director  
M/A/R/C® Research  
7850 North Belt Line Rd  
Irving, TX 75063

**Lead Statistician and Data Manager:** Randall Wahl  
Chief Research Officer  
M/A/R/C® Research  
7850 N. Beltline Road  
Irving, TX 75063

## 2 INTRODUCTION: BACKGROUND

### 2.1 CANDIDATE MODIFIED RISK TOBACCO PRODUCTS (MRTPs)

While cigarette smoking among US adults aged 18 and older has declined to 15.5 percent in 2016 from 20.9 percent in 2005, nearly 38 million American adults continue to smoke conventional cigarettes (CCs) most days or every day (Centers for Disease Control and Prevention, 2018). Cigarette smoking causes damage to almost every organ in the body and results in premature death (U.S. Department of Health and Human Services, 2014). 22nd Century Group, Inc. (XXII) is developing a candidate Modified Risk Tobacco Product (MRTP) designed to aid current smokers in reducing the exposure to nicotine.

The complexity in developing an MRTP is creating a product that maximizes interest in the product as a substitute for CCs among Adult Smokers (while not dissuading them from the idea that they would be better off quitting smoking entirely), yet minimizes interest among Adult Never Users and Former Smokers. Further, it is imperative that these products do not negatively impact the Intention to Quit among Adult Smokers who have the Intention to Quit CCs.

The Quantitative Study to Develop VLN™ Hypothetical Product Messages focuses on a candidate MRTP product, menthol and non-menthol cigarettes (Figures 1 and 2. Pack Example Images; images for all packs in Appendix), planned to be commercialized under the brand name of “VLN™.”

VLN™ cigarettes differ from CCs in that they are made with tobacco which has been genetically modified to contain 95% less nicotine than CCs, thereby lowering nicotine consumption. VLN™ cigarettes offer the same ritual properties of smoking and, while VLN™ may still pose the same health risks as CCs, conversion from CCs to VLN™ cigarettes significantly reduces Adult Smoker’s exposure to nicotine.

## 2.2 VLN™ CONSUMER PERCEPTION RESEARCH

Based on requirements of Section 911 of the Family Smoking Prevention and Tobacco Control Act and the FDA's recommendations as outlined in the Draft Guidance on Modified Risk Tobacco Product Applications (the "MRTP Draft Guidance"), XXII is conducting a broad program to study consumer perceptions in relation to VLN™.

The MRTP Draft Guidance states that: "FDA must ensure, for a risk or exposure modification order, that the advertising and messaging of the MRTP enable the public to comprehend the information concerning modified risk and to understand the relative significance of such information in the context of total health and in relation to all of the tobacco-related diseases and health conditions." The MRTP Draft Guidance further states that MRTP applications should address the effect of the product, label, messaging and marketing material on (1) "Tobacco use behavior among current tobacco users," (2) "Tobacco use initiation among non-users (both never users and Former users)," and (3) "Consumer understanding and perceptions."

This *Quantitative Study to Develop VLN™ Hypothetical Product Messages Among U.S. Adult Cigarette Smokers, Adult Former Cigarette Smokers and Adult Never Cigarette Users* research will include:

- Three major sample cohorts and five separate groups of US consumers based on self-stated qualification
  - Adult Current Smokers (with statistically valid representation of both menthol and non-menthol users) divided into two groups:
    - With Intention to Quit
    - Without Intention to Quit
  - Adult Former Smokers divided into two groups based on length of cessation
    - Recent Quitters (within the past year)
    - Longer-term Quitters (more than one year of cessation)
  - Adult Never Smokers

Drawing on FDA reviews of prior MRTP submissions, this study will also measure number of cigarettes smoked per day to ensure inclusion of both light smokers (less than 10 cigarettes per day) and heavy smokers (10+ cigarettes per day). This study will also include subjects of Legal-Age (LA) to 25 years of age who have never smoked (Never Smokers) as a proxy for youth smokers who are not part of the study because they may not be interviewed without parental consent by law. For the purposes of this study, Legal-Age will be defined as the minimum age for tobacco purchase as determined by each participant's US state of residence.

The study will gather quantitative data addressing each of these areas of investigation with respect to VLN™ label and messaging involving modified exposure claims.

The comprehensive research program has the following overall structure:

- Successive Four-Phase Qualitative Investigation to Develop and Refine VLN™ Label and Messaging (Completed)
  - Development of the VLN™ label and messaging.
  - Qualitative Assessment of Comprehension of the VLN™ label and messaging.
  - Qualitative Assessment of Risk Perception of VLN™ based on the VLN™ label and messaging.
  - Evaluation of Future Intention to Use VLN™ based on the VLN™ label and messaging.

- Quantitative Study to Test VLN™ Label and Messaging for Comprehension, Risk Perception and Intention to Use Among Adult Smokers, Adult Former Smokers and Adult Never Users

## 2.3 DEFINITIONS OF LABEL AND MESSAGING

XXII has defined "label" and "messaging" for the program as a whole, as:

**VLN "label"** refers to the display of brand name text or graphical material, including branding on the pack containing VLN™ cigarettes, or the packaging box of VLN™ cigarettes.

**VLN "messaging"** refers to printed statements which accompany VLN™. For example, messaging could refer to text statements printed on the front, side or back of packaging containing VLN™ cigarettes.

## 2.4 VLN™ PRODUCT DESCRIPTION

VLN™ and VLN™ menthol are 84-millimeter cigarettes (sometimes called "shorts," "regulars" or "kings") and are made with the same components found in commercial brands of cigarettes such as a filter, cigarette paper and tobacco. VLN™ and VLN™ menthol are manufactured in a manner similar to that of a typical cigarette.

The tobacco in VLN™ cigarettes is different than the tobacco used in most cigarette brands. VLN™ cigarettes are made from a tobacco plant that has been altered to contain much lower levels of nicotine than the tobacco used in traditional cigarettes.

Figure 1. VLN™ Pack Example Image – Non-Menthol.

Figure 2. VLN™ Pack Example Image – Menthol.



### 3 OBJECTIVES AND PURPOSE

#### 3.1 DESIGN OVERVIEW

In addition to requiring that a modified risk tobacco product will significantly reduce harm and the risk of tobacco-related disease to individual tobacco users, the TCA requires that a modified risk tobacco product will benefit the health of the population as a whole, taking into account both users and non-users of tobacco products (TCA Section 911(h)(1)). The *Quantitative Study to Develop VLN™ Hypothetical Product Messages Among U.S. Adult Cigarette Smokers, Adult Former Cigarette Smokers and Adult Never Cigarette Users* is planned as a randomized five-cell methodology, with each cell representing a distinct concept (label and messaging) where participants, Current Smokers as well as Former Smokers and Never Users, are assigned to each condition to evaluate a distinct and unique iteration of VLN™'s label and messaging as well as control concepts, one of which is branded as Marlboro as the brand exists in the marketplace and one that is described as the existing brand but displays the VLN™ packaging with no claim statements. This assumes three primary test concepts and one of two possible control concepts of the existing CC brand and VLN™ presented exactly the same as current marketing for the comparator CC brand.

Figure 3 gives an overview of study design and procedures, which are covered in more detail in Section 4 and Section 5.

Subjects will be categorized into four primary subject groups, based on self-reported smoking behavior:

- Group 1 – Adult Smokers with no Intention to Quit CC
- Group 2 – Adult Smokers with the Intention to Quit CC
- Group 3 – Adult Former Smokers
- Group 4 – Adult Never Smokers

Former Smokers and Current Smokers will be further divided based on cessation recency and Intention to Quit within the next six months, respectively. Among Current Smokers, light / social smokers and heavier smokers will both be profiled to ensure inclusion. In addition, an oversample of young Adult Never Smokers (from the

legal smoking age to 25 years; "LA-25 Never Smokers") will be used, to enable the collection of sufficient data to describe responses within this group. Legal-Age will be defined as the minimum age for tobacco purchase as determined by each participant's US state of residence.

Each comprehensive concept, or unique combinations of (1) Primary Claim, (2) Secondary Claim, (3) Disclaimer and (4) Back of Pack Message, will be evaluated by approximately equally-sized primary subject groups. Subjects will randomly be assigned a concept following a least-fill method (ConfirmIt, 2016) to ensure representative distribution within each concept across tobacco usage and demographic criteria.

Product stimulus including 3-D images of a product package as well as flat image views of all four sides of each package with test messaging printed on packaging as expected in final market placement will be presented to each participant. Participants will be asked to review all messaging thoroughly prior to continuing on to the next question. Checks will be employed to ensure full and complete exposure of the product packaging and messaging to each participant. For 3-D images, the software will require each participant to rotate the image prior to continuing to the next screen. For all flat packaging, a timer disallowing movement to the next screen will be placed on the page to ensure a minimum amount of time is spent reviewing packaging.

A baseline assessment of Risk Perception and future Intention to Use will be conducted on VLN™ and four comparator objects. Assessments of Intention to Use will be conducted on four comparator categories and each concept. Risk Perception will be determined using the Perceived Risk Instrument-Personal (PRI-P) developed and validated in the Phillip Morris Tobacco Heating System research (Chrea, et al, 2016.). This research will utilize the portions of this scale that address consumer perceptions of the health implications and addictiveness of using tobacco products.

In this research, one of the four comparators will be assigned randomly per subject and assessment of that comparator will occur prior to exposure to the concept (VLN™ and Control) label and messaging followed by the same assessment of VLN™ after exposure to the concept. In addition to these measurements, VLN™ will be evaluated in direct comparison to the other assigned comparator category. Additionally, the Perceived Risk Instrument-Personal (PRI-P) scale is detailed in the appendix. All comparator categories and products evaluated include:

1. CCs
2. e-cigarettes
3. Moist Tobacco
4. NRTs
5. VLN™ (three test iterations with reduced risk messaging and one control iteration with no messaging)
6. Marlboro Gold (Control Concept)

Data analyses conducted during the validation phase of the Perceived Risk Instrument-Personal (PRI-P) developed and validated in the Phillip Morris Tobacco Heating System research (Chrea, et al, 2016.) concluded that the PRI is "applicable for various types of tobacco and nicotine-containing products and provides a comparable measurement between adult smokers and adult non-smokers."

The product messages to be tested are:

#### Reduced Exposure Messaging for VLN™ cigarettes, a MRTTP

- Primary Claim (same on all packs)
  - 95% Less Nicotine
- Secondary (Comparative) Claim
  - (b) (4)
  - Helps reduce your nicotine consumption
  - (b) (4)
- Disclaimer (same on all packs)
  - Nicotine is addictive. Less nicotine does NOT mean safer. All cigarettes can cause disease and death.
- Back of Pack Language (same on all packs)
  - VLN™ smells, burns, and tastes like a conventional cigarette, but greatly reduces your nicotine consumption.

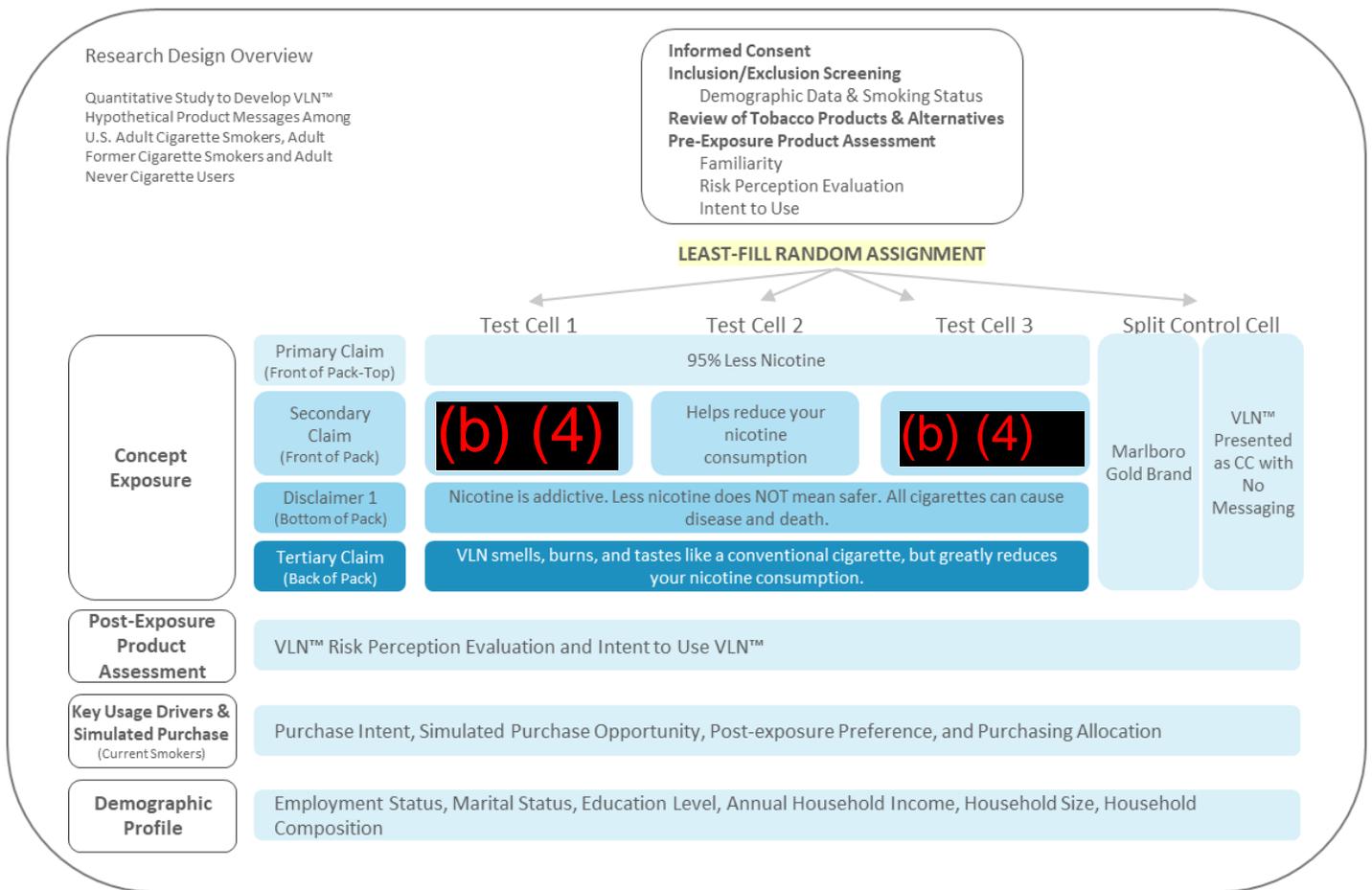
Each subject will also be presented with one of the four Surgeon General's warnings: 1) "Smoking Causes Lung Cancer, Heart Disease, Emphysema And May Complicate Pregnancy." 2) "Quitting Smoking Now Greatly Reduces Serious Risks to Your Health." 3) "Smoking By Pregnant Women May Result in Fetal Injury, Premature Birth, And Low Birth Weight." 4) "Cigarette Smoke Contains Carbon Monoxide."

This test will utilize the randomized assignment to evaluate each of the three test concepts plus a split control concept testing 1) Marlboro Gold, the leading CC brand in the US by annual sales volume, and 2) a VLN™ pack with no messaging and a description that depicts VLN™ using the same language applied for Marlboro Gold. The control cell will be divided into two groups based on stimuli with half of all subjects viewing Marlboro Gold as it exists in the marketplace at the time of interviews and the other half viewing a VLN™ pack with no claims messaging. The Marlboro Gold cell will be used to calibrate test concept responses to actual in-market behavior with a known brand while the VLN™ control cell will be used to evaluate expected change in behavior based solely on the new branding. All Current Smokers will be shown a Menthol or Non-Menthol version of the concept aligned to the type of cigarette they currently smoke.

This research will collect responses to key decision variables that drive product trial and repeat behavior, specifically, 1) Purchase Intent, 2) Expected Likeability, 3) Differentiation, 4) Need Satisfaction and 5) Simulated Purchase. Key decision criteria reflect the behavioral and psychological process consumers go through when making a selection decision. Responses across these variables will be used to create respondent-level scores that filter out the overstatement/misstatement inherent in a single measure like purchase intent. In addition, among current smokers, a simulated purchase exercise will be used to understand any expected change in product category (tobacco) use and behavior post-exposure to the concept. Additional study design details are covered in greater depth in Section 4 and Section 5.

The survey will be administered using a web-based self-directed methodology and will be conducted solely in the United States.

Figure 3. Research Design Overview.



## 3.2 PRIMARY GOALS

- Estimate population impact of VLN™ using potential product messaging
- Test hypotheses that potential product messages for VLN™:
  - Generate intent to use among those who could benefit from use (US adult smokers of cigars and cigarettes, adult smokers motivated to quit)
  - Do not generate significant intent to use among those who could be harmed by use (Adult Never Smokers, Adult Former Smokers)
  - Describe the product clearly and promote comprehension

## 3.3 SECONDARY GOALS

The secondary objectives of the study include:

- Estimated impact of VLN™ among special relevance populations (Adult Never Smokers, Adult Former Smokers, Adult Smokers Motivated To Quit)
- Assess risk perception for VLN™ and four comparator objects (CC, NRTs, e-cigarettes, and Moist Snuff)
- Assess intent to use for VLN™ and four comparator objects (CC, NRTs, e-cigarettes, and Moist Snuff)

*\* Legal-Age will be defined as the minimum age for tobacco purchase as determined by each participant's US state of residence.*

## 4 SUBJECTS

### 4.1 DEFINITIONS

- Never Users
  - Adults who have not smoked at least 100 cigarettes in their entire life and currently do not smoke at all – plus currently do not use other tobacco or nicotine products and have never done so “fairly regularly”
- Former Smokers
  - Recent Quitters: Adults who have smoked at least 100 cigarettes in their entire life and currently do not smoke at all who indicate they completely quit smoking cigarettes less than 1 year ago
  - Long-Term Quitters: Adults who have smoked at least 100 cigarettes in their entire life and currently do not smoke at all who indicate they completely quit smoking cigarettes 1 year ago or more
- Current Smokers
  - Adult Smokers will be classified by Intention to Quit CC (i.e. smokers with and without Intention to Quit CC), based on Prochaska and DiClemente's Stages of Change Model (Prochaska and DiClemente, 1982)
    - With Intention to Quit: Adults who have smoked at least 100 cigarettes in their entire life and currently smoke every day or some days – and who respond “Yes” to a question regarding whether they are seriously considering quitting smoking cigarettes in the next 6 months

- **With No Intention to Quit:** Adults who have smoked at least 100 cigarettes in their entire life and currently smoke every day or some days – and who respond “No” to a question regarding whether they are seriously considering quitting smoking cigarettes in the next 6 month
- **LA-25 (Legal-Age to 25) Never Smokers**
  - LA-25 Never Smokers are defined as Never Smokers between the legal smoking age to 25 years (inclusive).
  - This is included as an oversample of young Adult Never Smokers (from the legal smoking age to 25 years) to enable the collection of sufficient data to describe responses within this group.
  - These participants are being oversampled to ensure a proxy for participants below the regulated minimum age of purchase (under 18 years of age by federal law).
  - Legal-Age will be defined as the minimum age for tobacco purchase as determined by each participant’s US state of residence.
  - Oversampling ensures representation among a critical sample subgroup without the unnecessary burden and potential ethical conflict of sampling an audience under the legal purchase age.

## 4.2 SUBJECT GROUPS

Subjects will offer self-reported smoking status as is consistent with prior research including the World Health Organization (WHO, 1998), the The National Cancer Institute’s Health Information National Trends Survey (HINTS), and the Phillip Morris International research on “IQOS.”

The four main subject groups are defined as;

1. **Adult Smokers with no Intention to Quit CC:** Adult Smokers with no intention to Quit CC, in the pre-contemplation stage of Prochaska and DiClemente's Stages of Change model. This will include Regular Smokers.
2. **Adult Smokers with the Intention to Quit CC:** Adult Smokers in the contemplation and/or preparation stages of Prochaska and DiClemente's Stages of Change model. This will include Regular Smokers.
3. **Adult Former Smokers:** Adults who were previously regular smokers and, at the time of their participation in the study, quit CC more than 30 days ago.
4. **Adult Never Smokers:** Adults who have never smoked at all, or adults who have never been regular smokers and have smoked less than 100 cigarettes in their lives.

The National Cancer Institute’s Health Information National Trends Survey (HINTS) and the Population Assessment of Tobacco and Health (PATH) survey both use 100+ cigarettes in a lifetime plus a question about current smoking behavior to define smokers and non-smokers / never users. The threshold of 100 cigarettes was initially established in three 1954/1955 studies on Veteran’s mortality as well as a US population smoking supplement in the US Census Bureau’s Current Population Study. The 100-cigarette threshold became a staple in determining smoking status was later used in the 1964 Adult Use of Tobacco Survey and the first US National Health Interview Survey (NHIS, 1965) where it became the key criterion for smoking status definitions.

## 4.3 SAMPLING

At a broad level, the sampling frame is adults living in the US. A main study sample size of 28,000, equivalent to 7,000 subjects per concept, is deemed to provide sufficient precision for this study and allow for reporting results by defined population segments, including special relevance populations.

## 4.4 MAIN STUDY SAMPLING

The main samples will be stratified with the following variables:

### 1. Smoking status

For each unique concept there will be approximately the same number of subjects from each of the main subject groups:

1. Adult Smokers with No Intention to Quit CC
2. Adult Smokers with Intention to Quit CC
3. Adult Former Smokers
4. Adult Never Smokers

### 2. Gender

There will be a representative number of male and female subjects.

### 3. Age

For each study cell there will be approximately the same number of subjects from each of the following age categories:

- o Legal Age to 25 years (oversample)
- o Legal Age to 24 years
- o 25 to 44 years
- o 45 to 64 years
- o 65+ years

This will enable separate analysis of each age group. Post-stratification weighting will be used to correct for the effects of stratification by age so that the total sample will reflect the age distribution of the population as a whole.

The main sample for this study will be recruited into the study from an online non-probability based opt-in panel. Potential subjects will receive an invitation to participate in a research study or will self-select a new survey opportunity from the panel website or an external referring partner via a panel-specific app to access the study's online consent, which describes the study and requested participation. Respondents will provide consent prior to being asked any questions. After screening for eligibility, subjects will be assigned to a concept following a randomized least-fill method to ensure representative distribution of the full n=7000 interviews within each concept across tobacco usage and demographic criteria (ConfirmIt, 2016).

Table 1 shows the estimated representation **per concept across all relevant groups**. The sample design will be focused on these key mutually exclusive analytical groups.

Table 2 details the distribution of completes **per concept and per analytic group** for all **Test Concept Cells** to be assessed on a total base of n=7,000 and the expected distribution percentages across demographic subgroups.

Table 3 details the distribution of completes **per concept and per analytic group** for both **Split Control Concept Cells** to be assessed on a total base of n=3,500 per cell and the distribution percentages across demographic subgroups.

Table 1. Sampling Plan by Tobacco Usage (per concept).

	Sample Size	Margin of Error (at 95% Confidence Intervall)
<b>Never Users</b>	<b>2000</b>	<b>2.2%</b>
Adult Consumers	1000	3.1%
Oversample of Legal Age to 25	1000	3.1%
<b>Former Smokers</b>	<b>2000</b>	<b>2.2%</b>
Recent Quitters	1000	3.1%
Long-Term Quitters	1000	3.1%
<b>Current Smokers</b>	<b>3000</b>	<b>1.8%</b>
With Intention to Quit	1500	2.5%
With No Intention to Quit	1500	2.5%

Table 2. Planned Demographic Representation by Tobacco Usage (per concept) for VLN™ Concepts with Messaging.

		Never Users	Never Users Oversample - LA to 25	Long-Term Quitter	Recent Quitters	Current Smokers With Intention to Quit	Current Smokers With No Intention to Quit
Quotas		1000	1000	1000	1000	1500	1500
Gender	Male	41%	41%	52%	51%	49%	51%
	Female	59%	59%	48%	49%	51%	49%
Age (Oversample)	LA-25***		100%				
Age	21-24	13%		1%	11%	10%	8%
	25-44	32%		27%	42%	43%	37%
	45-64	31%		5%	31%	45%	40%
	65+	24%		67%	15%	2%	16%
Race/ Ethnicity	White, Non-Hispanic	66%	66%	82%	71%	71%	76%
	Black, Non-Hispanic	12%	12%	7%	11%	15%	12%
	Asian, Non-Hispanic	6%	6%	3%	4%	3%	2%
	American Indian/ Alaska Native, Non-Hispanic	1%	1%	1%	**%	2%	1%
	Hispanic	14%	14%	7%	13%	8%	8%
	Non-Hispanic Multi-race	1%	1%	1%	**%	1%	1%
US Census Regions	Northeast	17%	16%	20%	13%	16%	15%
	Midwest	21%	21%	23%	28%	26%	28%
	South	36%	35%	31%	36%	37%	35%
	West	27%	27%	26%	24%	21%	22%

\*Data for illustrative purposes: Proportions estimated based on referencing NHIS 2015, NHIS 2016, BRFSS, and HINTS

\*\*Less than one-half of one percent. \*\*\*For the purposes of this study, Legal-Age will be defined as the minimum age for tobacco purchase as determined by each participant's US state of residence.

Table 3. Planned Demographic Representation by Tobacco Usage for Split Control Concept Cells (per concept).

		Never Users	Never Users Oversample - LA to 25	Long-Term Quitter	Recent Quitters	Current Smokers With Intention to Quit	Current Smokers With No Intention to Quit
Quotas		500	500	500	500	750	750
Gender	Male	41%	41%	52%	51%	49%	51%
	Female	59%	59%	48%	49%	51%	49%
Age (Oversample)	LA-25***		100%				
Age	21-24	13%		1%	11%	10%	8%
	25-44	32%		27%	42%	43%	37%
	45-64	31%		5%	31%	45%	40%
	65+	24%		67%	15%	2%	16%
Race/Ethnicity	White, Non-Hispanic	66%	66%	82%	71%	71%	76%
	Black, Non-Hispanic	12%	12%	7%	11%	15%	12%
	Asian, Non-Hispanic	6%	6%	3%	4%	3%	2%
	American Indian/Alaska Native, Non-Hispanic	1%	1%	1%	**%	2%	1%
	Hispanic	14%	14%	7%	13%	8%	8%
	Non-Hispanic Multi-race	1%	1%	1%	**%	1%	1%
US Census Regions	Northeast	17%	16%	20%	13%	16%	15%
	Midwest	21%	21%	23%	28%	26%	28%
	South	36%	35%	31%	36%	37%	35%
	West	27%	27%	26%	24%	21%	22%

\*Data for illustrative purposes: Proportions estimated based on referencing NHIS 2015, NHIS 2016, BRFSS, and HINTS

\*\*Less than one-half of one percent. \*\*\*For the purposes of this study, Legal-Age will be defined as the minimum age for tobacco purchase as determined by each participant's US state of residence.

#### 4.5 INCLUSION CRITERIA & STRATIFICATION

The study will be based on a sample that will be as representative of the US population as possible. However, certain groups, such as those who do not speak English with some level of proficiency or those under the age of 18, will be excluded. The sample will be stratified by smoking status and demographic criteria.

Quota sampling for completed interviews within each smoking-status group using demographic variables will be utilized. In the event of variances from those goals, the data will be weighted so that each group reflects the overall population for that group and the sample for each smoking-status group is likewise representative of the population as a whole. When analyzing the total sample, post-stratification weighting will be implemented to compensate for the effects of stratification so that overall impact on the population as a whole may be estimated accurately. In addition to quota sampling, Random Iterative Method (RIM) Weighting will be used to ensure a final distribution of completed interviews that is representative of the population.

For example, participants will be screened for:

1. Ability to read and understand English\*.
2. Currently residing in the US.
3. Legal age of purchase (defined as the minimum age for tobacco purchase as determined by each participant's US state of residence) or older.
4. Able and willing to comply with all study requirements.
5. Provides informed consent.

Sample will be further stratified into population subgroups based on a variety of characteristics including demographic criteria as well as current smoking status:

1. Number of cigarettes ever smoked.
2. Type of cigarette smoked (menthol/non-menthol)
3. Gender, ethnicity and annual household income to ensure representation consistent with the market.
4. Number of cigarettes smoked per day to ensure a mix of participants who are light / social smokers versus those who are heavier smokers.
5. Intent to quit smoking within the next year.
6. Cessation status - former smokers will be classified into recent versus long-term cessation.

#### 4.6 EXCLUSION CRITERIA

1. Past 3-month participation in any tobacco-related research.
2. Currently pregnant or breastfeeding or planning to become pregnant within the next 6 months.
3. Employees of tobacco or vapor companies, news or media, advertising / marketing, marketing research, healthcare, or attorney or paralegal, or having a first degree relative that is employed by these types of companies\*\*.

*\*Only English-speaking participants will be recruited to participate as the product communication is only expected to be delivered in English at this time.*

*\*\*Employees, students and/or first-degree relatives of those who are employed by or pursuing education in sensitive industries will be excluded from the research to minimize bias and also to protect the proprietary product information that will be disclosed in the survey.*

## 5 PROCEDURES AND ASSESSMENTS

### 5.1 RECRUITMENT

Subjects will be recruited through (b) (4), an opt-in online panel company to which subjects have granted permission to be contacted to participate in market research studies. Panel companies house proprietary databases and dynamically recruit participants who are profiled on basic demographic information which may be used in targeting potential subjects for inclusion into the study. Each participant will be provided a unique, anonymous link to use for participation in the study and no personally identifiable information (PII) about any participant will be provided by the participants or panel company. All participants will be screened for demographic and smoking status as noted below.

### 5.2 SCREENING

Potential subjects will receive an invitation to participate in a "Study About Products" or will self-select a new survey opportunity from the panel website or an external referring partner. Those who click on the survey link will be redirected to the web-based survey and, after reviewing two general introduction screens, will be presented with an Informed Consent screen.

Participants will then be screened on the basis of the inclusion and exclusion criteria. The screening process will assess smoking status, age, gender, ethnicity and US Census Region. The survey will programmatically determine which concepts each participant is eligible for based on smoking status, age, gender, ethnicity and Census Region quota availability within each concept and will then randomly select from all possible concepts with open quotas for that given participant based on a combination of tobacco use and demographic characteristics.

Eligible participant who fit the requirements of the sampling plan will pass the screener and proceed to the full survey. Non-eligible participant's interviews will be immediately terminated and they will see a "Thank you" page with a redirect designated by the panel company. Potential subjects will be compensated a nominal amount in line with US market research industry and each independent panel's standards.

### 5.3 INFORMED CONSENT

Participants will see a screen with the informed consent form (ICF). Participants will be asked to review the informed consent information carefully and, at the conclusion of the form, will be asked if they agree to participate in the survey with an option to select "Yes – I agree to participate in this research" or "No – I do not agree to participate in this research." Selecting "Yes" will move to the next screen with the first survey question. A selection of "No" will immediately terminate the participant and they will see a "Thank you" page with a redirect designated by the individual panel company.

Regardless of smoking status, all participants will view exactly the same ICF verbiage. This will prevent any bias or variance in responses based on the possibility that different messages were viewed upon survey entry. Subjects will be informed that their participation is completely voluntary. Subjects will also be informed that they may voluntarily suspend or withdraw from the survey at any time during the interview by closing the browser or app.

## 5.4 SURVEY FLOW AND MEASUREMENTS

After passing all screening requirements and freely consenting to participation in the research, subjects will begin the survey. The survey instrument follows this general outline:

- Introduction to Detailed Subject Matter
- Detailed Review of Tobacco Products and Alternatives
  - CCs
  - e-cigarettes
  - Moist Snuff
  - NRTs
- Initial Evaluation of Tobacco Products and Alternatives
  - All four comparator categories will be evaluated on:
    - Familiarity
    - Intention to Use
  - Risk Perception
    - Percieved Risk Instrument – Personal (PRI-P) used for measurement
    - One product comparator category will be assessed by each participant (CC, e-cigarettes, Moist Snuff, and Nicotine Replacement Therapies [NRTs])
    - Subjects will be assigned to a product comparator category following a randomized least-fill method to ensure representation across tobacco usage and demographic criteria
- Presentation of Product Package with Messaging
  - 3-D and flat packaging is presented
    - Participants will see instructions to read all text on the packaging in its entirety
    - Programmatic checks will be implemented to ensure respondent does not proceed until a sufficient amount of time to review has elapsed
  - Open-ended Questions to Measure Recall and Comprehension
    - Describe the concept to a friend or family member
    - Describe the benefits of the concept
    - Describe the health or addiction risks of the concept
  - Evaluation of VLN™/Control Conept on:
    - Risk Perception
      - Percieved Risk Instrument – Personal (PRI-P) used for measurement
      - Direct (head-to-head) comparison of one comparator category and VLN™/Control Conept
    - Intention to Use
      - VLN™/Control Conept
- Concept Screen (where appropriate – for example, non-users will not have an evoked set of brands and will, therefore, skip related questions)
  - Product Package with Messaging will be available for additional review throughout the survey (via link – “Click here to see the concept”)
  - Simulated repurchase opportunity (Current Smokers only)

- Measurement of preference for test concept versus evoked product alternatives\* (evoked products are those selected by participants as product category (tobacco) items purchased / used in the past)
- Expected purchase behavior for evoked products vs. test product\*
- Anticipated test concept purchasing
- Performance versus expectations

*\*Post-exposure preference and purchasing allocation questions would be asked after the simulated purchase question in the concept interview only for Current Smokers*

- Second Evaluation of VLN™/Control Conept on:
  - Risk Perception
    - Direct (head-to-head) comparison of one comparator category and VLN™/Control Conept
  - Intention to Use
    - CCs
    - e-cigarettes
    - Moist Snuff
    - NRTs
    - VLN™/Control Conept
- Demographic Profile

## 5.5 INTERVIEW LENGTH

The study duration is expected to be approximately 15-20 minutes for each subject and this will be specified in the ICF.

## 5.6 WITHDRAWAL FROM RESEARCH

As will be noted in the ICF, subjects may cease and withdraw from the research at any time of their choosing without penalty or loss of benefits. Subjects may do so by closing their web browser or app.

# 6 STATISTICAL CONSIDERATIONS

## 6.1 STATISTICAL HYPOTHESES

The purpose of this study is to measure responses to versions of VLN™, a “Modified Risk Tobacco Product” (MRTP), and Control Products on label and messaging within populations of (1) Adult Smokers with an intention to quit, (2) Adult Smokers without any intention to quit, (3) Adult Former Smokers and (4) Adult Never Smokers.

### Primary Objectives:

- Estimate impact of VLN™ using potential product messaging
- Test hypotheses that potential product messages for VLN™:
  - Generate intent to use among those who could benefit from use (Adult Current Smokers, Adult Current Smokers motivated to quit)

- Do not generate significant intent to use among those who could be harmed by use (adult never smokers, adult former smokers)
- Describe the product clearly and promote comprehension

#### Secondary Objectives:

- Estimate population impact of VLN™ among Adult Never Smokers, Adult Former Smokers, Adult Current Smokers motivated to quit CCs and Adult Current Smokers with no Intent to Quit CCs population subsets
- Assess risk perception for VLN™ and four alternatives (CC, Nicotine Replacement Therapies [NRTs], e-cigarettes, Moist Snuff)
- Assess intent to use for VLN™ and four comparator objects (CC, Nicotine Replacement Therapies [NRTs], e-cigarettes, Moist Snuff)

## 6.2 ANALYSIS SAMPLES

### **Full Sample**

All subjects invited to participate in the study who satisfy the inclusion and exclusion criteria, fully complete the survey and meet all data quality requirements will be included in the full final sample.

### **Main Study Sample**

The main study sample will include the four primary subject groups (Adult Never Smokers, Adult Former Smokers, Adult Current Smokers With Intent to Quit CCs, Adult Current Smokers With No Intent to Quit CCs) and a representative percentage of LA-25 Never Smokers. These participants must satisfy all inclusion and exclusion criteria to fully complete the survey and meet all data quality requirements.

### **LA-25 Never Smokers Oversample**

The LA-25 Never Smokers sample will include those subjects in the main sample who are LA-25 Never Smokers as well as those who fulfill in the LA-25 "oversample." This group may be considered a fifth subject group.

## 6.3 METHOD

### **General Principles**

The number of subjects in each subject group (Total Base) as well as the count and proportion of subjects selecting each response option in each question will be presented in all categorical outcome measures. Proportions will be calculated on the total base for each subject group or subset of interest who have non-missing data. Effective base will be used for statistical testing on all data weighted to the population.

The number of subjects in each subject group with non-missing score values will serve as the total base for each subject group or subset of interest. These measures will also be represented with the mean, standard deviation, median, minimum and maximum. Unadjusted 95% confidence intervals will be calculated for the point estimates of the outcome variables.

Analyses will be performed with SPSS® software (Statistical Package for the Social Sciences, Version 16.0 or higher) and/or Quantum tabulation software.

## **Demographics and Subject Characteristics**

Descriptive statistics for all demographics and subject characteristics (such as smoking status, age, sex, race/ethnicity, education level, employment details, marital status, and household income) will be presented overall and by subject group within each concept separately.

### **Subject Disposition**

Descriptive statistics will be presented as the proportion of subjects who screened, agreed, and completed the study within each concept separately.

## **6.4 ANALYSIS OF OBJECTIVES**

### **Intent to Use VLN™ / Control Concepts, CC, e-cigarettes and Moist Snuff**

Descriptive statistics and 95% confidence intervals of the proportion of responses for each comparator category will be presented by subject group within each concept separately for the items related to Intention to Use. Intention to Use each concept and comparator categories will be assessed both pre- and post-exposure to the concepts to understand any change in intention for future product usage as would be influenced by exposure to product concept.

### **Risk Perception**

The Perceived Risk Scale-Personal (PRI-P) scale was validated in the prior PMI IQOS research (Chrea, et al, 2016.). The Perceived Risk Scale-Personal (PRI-P) will be presented to participants in two groups of attributes including (1) Risk of Exposure / Tobacco-Related Diseases and (2) Risk of Addiction. Response data will be presented in descriptive statistics and 95% confidence intervals of the proportion of responses. Risk Perception scores will be offered by subject group and VLN™ / Control concepts will be compared to the four comparator categories directly.

### **Comprehension**

Because VLN™ messaging was tested extensively in the qualitative phases of this research and no clear measurement precedent has been established for testing comprehension to market a tobacco product, the need to validate comprehension will be assessed simply using three open-ended responses to ensure recall and basic comprehension. Open-ended responses will be coded for each post-exposure question so that responses may be evaluated in tabulated data.

Descriptive statistics and 95% confidence intervals will be presented on the proportion of participants indicating responses in the coded, tabulated data who provide clear, logical and relevant responses to each question as well as the proportion offering unclear, irrelevant or “Unsure / Don’t Know” responses.

## **6.5 MISSING DATA**

No imputation of missing data will be undertaken. All reported percentages will be based on non-missing data.

## 6.8 SAMPLE SIZE

To establish sufficient measurement precision across all objectives on both an unweighted and weighted basis, a sample size within each subgroup including smoker status, age, gender, ethnicity and concept cell was calculated to result in n=7,000 completed interviews per concept cell. The sample sizes within each concept will be equal. As outlined in Table 4, these sample sizes are deemed sufficient to present comparative analyses across the various populations at a 95% confidence interval. Quota sampling for demographic distribution by gender, age, ethnicity and Census Region will be used to ensure completed interviews across subgroups within each concept cell and smoking-status group is sufficient for statistical testing.

The exceptions to this are three ethnicity groups including Asian Non-Hispanic, American Indian / Alaska Native Non-Hispanic, Non-Hispanic Multi-race. These three groups will be treated as a single entity in any analysis that may be conducted by ethnicity. Subsequent research would be required to focus analyses on these difficult-to-reach population groups.

Table 4 details the sample quotas **per concept and per analytic group** for all **Test Concept Cells** to be assessed on a total base of n=7,000 and the expected distribution across demographic subgroups.

Table 5 details the distribution of completes **per concept and per analytic group** for both **Split Control Concept Cells** to be assessed on a total base of n=3,500 per cell and the distribution percentages across demographic subgroups.

Table 4. Quota Sampling Plan by Tobacco Usage (per concept) for VLN™ Concepts with Messaging.

		Never Users	Never Users Oversample - LA to 25	Long-Term Quitter	Recent Quitters	Current Smokers With Intention to Quit	Current Smokers With No Intention to Quit
Quotas		1000	1000	1000	1000	1500	1500
Gender	Male	410	410	520	510	735	765
	Female	590	590	480	490	765	735
Age (Oversample)	LA-25***		1000				
Age	21-24	130		10	115	150	120
	25-44	320		270	425	645	550
	45-64	310		50	310	675	595
	65+	240		670	150	30	235
Race/Ethnicity	White, Non-Hispanic	660	660	820	710	1065	1140
	Black, Non-Hispanic	120	120	70	110	225	180
	Asian, Non-Hispanic	60	60	30	40	45	30
	American Indian/Alaska Native, Non-Hispanic	10	10	5	5	30	15
	Hispanic	140	140	70	130	120	120
	Non-Hispanic Multi-race	10	10	5	5	15	15
US Census Regions	Northeast	165	165	200	125	240	225
	Midwest	210	210	230	280	390	420
	South	355	355	310	360	555	525
	West	270	270	260	235	315	330

\*Data for illustrative purposes: Proportions estimated based on referencing NHIS 2015, NHIS 2016, BRFSS, and HINTS

\*\*\*For the purposes of this study, Legal-Age will be defined as the minimum age for tobacco purchase as determined by each participant's US state of residence.

Table 5. Quota Sampling Plan by Tobacco Usage for Split Control Concept Cells (per concept).

		Never Users	Never Users Oversample - LA to 25	Long-Term Quitter	Recent Quitters	Current Smokers With Intention to Quit	Current Smokers With No Intention to Quit
Quotas		500	500	500	500	750	750
Gender	Male	205	205	260	255	368	383
	Female	295	295	240	245	383	368
Age (Oversample)	LA-25***		500				
Age	21-24	65		5	57	75	60
	25-44	160		135	213	322	275
	45-64	155		25	155	338	298
	65+	120		335	75	15	117
Race/ Ethnicity	White, Non-Hispanic	330	330	410	355	533	570
	Black, Non-Hispanic	60	60	35	55	112	90
	Asian, Non-Hispanic	30	30	15	20	23	15
	American Indian/ Alaska Native, Non-Hispanic	5	5	3	3	15	8
	Hispanic	70	70	35	65	60	60
	Non-Hispanic Multi-race	5	5	2	2	7	7
US Census Regions	Northeast	83	82	100	62	120	112
	Midwest	105	105	115	140	195	210
	South	178	178	155	180	278	263
	West	135	135	130	118	157	165

\*Data for illustrative purposes: Proportions estimated based on referencing NHIS 2015, NHIS 2016, BRFSS, and HINTS

\*\*\*For the purposes of this study, Legal-Age will be defined as the minimum age for tobacco purchase as determined by each participant's US state of residence.

## 7 SOURCE DOCUMENTS AND ACCESS TO SOURCE DATA / DOCUMENTS

The contract research organization (CRO) and PI will maintain documentation to permit evaluation of the conduct of the study, including assessing the quality and integrity of the study data and protection of human subjects. The PI will have access to all data from participants and will make these data available for inspection at the request of the Sponsor or regulatory agencies.

## 8 ETHICS / PROTECTION OF HUMAN SUBJECTS

### 8.1 ETHICAL STANDARD

The PI has worked to ensure that this study is conducted in full conformity with Regulations for the Protection of Human Subjects of Research codified in 45 CFR Part 46 and any additional human subjects protections as determined necessary.

### 8.2 INSTITUTIONAL REVIEW BOARD

Given the nature of this online perception study and the limited opportunity for subject exposure to harm or risk, XXII Century, Inc. has declined IRB review and approval.

### 8.3 INFORMED CONSENT PROCESS

#### 8.3.1 CONSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Consent language describing in detail the study product(s), study procedures, and risks are given to the participant and documentation of informed consent is required prior to participant entry into the online survey. The following consent materials are submitted with this protocol:

- Overview of the study and its purpose
- Informed consent language (Appendix 3)

#### 8.3.2 CONSENT PROCEDURES AND DOCUMENTATION

Description of risks and possible benefits of participation will be provided to the participants in the informed consent. Participants will be asked to review the informed consent information carefully and, at the conclusion of the form, will be asked if they agree to participate in the survey. The participant will electronically indicate their consent. A selection of “No” will immediately terminate the participant and they will see a “Thank you” page with a redirect designated by the individual panel company. The participants may withdraw consent at any time throughout the course of the study.

Subjects will also be informed that they may voluntarily suspend or withdraw from the survey at any time during the interview by closing their browser button or app.

## 8.4 PARTICIPANT AND DATA CONFIDENTIALITY

Participant confidentiality is strictly held in trust by the participating investigators, their staff, the Sponsor and its agents. Therefore, the data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the Sponsor.

Authorized representatives of the Sponsor may inspect all documents and records required to be maintained by the PI, including the online data from participants in this study. The Contract Research Organization (CRO) will permit access to such records. At the end of the study, source documents/ primary data will be securely maintained by the CRO for a minimum of five years after market authorization of a MRTP (or two years after formal discontinuation of development of the MRTP). Study participant data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at 22nd Century Group, Inc. This will not include the participant's contact or other PII. Rather, individual participants and their research data will be identified by a unique study identification number. The study management systems used will be secured and password protected. At the end of the study, all study databases will be archived at 22nd Century Group, Inc.

## 9 DATA HANDLING AND RECORD KEEPING

### 9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

All data captured from participants using the online assessment system will be stored in an electronic data capture (EDC) system. Edit checks will be built into the system to minimize data entry errors. Data management will be responsible for reviewing these data as defined in the study protocol. The contract research organization is HIPAA compliant.

Participants enter the EDC system with masked (not tied to PII) unique identifiers, and system access privileges will be strictly controlled and documented. Whenever data are modified after the initial data entry process, a computer-generated audit trail will be generated.

### 9.2 STUDY RECORDS RETENTION

Study documents should be retained for a minimum of 5 years after the authorization of a MRTP application or until at least 2 years have elapsed since the formal discontinuation of development of the MRTP. These documents should be retained for a longer period, however, if required by regulations. No records will be destroyed without the written consent of the Sponsor, if applicable.

### 9.3 PROTOCOL DEVIATIONS

A protocol deviation is any nonadherence with the study protocol. The nonadherence may be either on the part of the participant, the PI, or the other study staff. As a result of deviations, corrective actions are to be developed by the PI in consultation with the Sponsor and implemented promptly.

### 9.4 PUBLICATION AND DATA SHARING POLICY

Participant responses will be kept confidential. Data could be shared with other entities only when: 1) the participant gives explicit permission to release this data, or 2) data are shared with an entity who agrees in writing that the data will be held strictly confidential and that the data will be used for research purposes only, or 3) the release of this data is required by a regulatory agency.

These data are being collected to support an MRTP application for VLN™. Any publications arising from this work will report data in aggregate form and will not include any personally identifying information.

## 10 CONFLICT OF INTEREST POLICY

None.

## APPENDIX 1 – QUANTITATIVE SURVEY INSTRUMENT

**Study Name:** Quantitative Study to Develop VLN™ Hypothetical Product Messages Among U.S. Adult Cigarette Smokers, Adult Former Cigarette Smokers and Adult Never Cigarette Users

**Protocol Number:** 5180080-VLN™-B2

**Sponsor:** 22nd Century Group, Inc.  
8560 Main Street  
Williamsville, NY 14221

**Version Number:** 1.2

**Author:** (b) (6)



**22nd Century Group, Inc.**  
**VLN™ QUANTITATIVE FINAL EVALUATE PHASE ASSESSOR® RESEARCH**  
 Matter #: 5180080 10-30-v0

<b>QUOTAS</b>	
TOTAL COMPS .....	28,000
<b>QUOTA PER CONCEPT.....7000</b>	
<b>CONCEPTS</b>	
1. URGE.....	7000
2. CONSUMPTION .....	7000
3. LESS.....	7000
4. CONTROL CELL A.....	3500
5. CONTROL CELL B.....	3500
<b>TOBACCO USE (PER CONCEPT)</b>	
NEVER USERS (Q16/17).....	1000
NEVER USERS OVERSAMPLE (Q16/17)	1000
FORMER SMOKER – LONG-TERM (Q16/17)	1000
FORMER SMOKER – RECENT (Q16/17)	1000
CURRENT SMOKER – INTEND TO QUIT (Q16/17)	1500
CURRENT SMOKER – NO INTENT (Q16/17)	1500
<b><u>SEE CUSTOM QUOTA GRID FOR FULL BREAKOUT</u></b>	

<b>ALL QUOTAS PER CONCEPT CELLS 1, 2, 3</b>		<b>Never Users</b>	<b>Never Users Oversample Age 21 to 25</b>	<b>Long-Term Quitter</b>	<b>Recent Quitters</b>	<b>Current Smokers With Intent to Quit</b>	<b>Current Smokers With No Intent to Quit</b>
<b>Total Quotas</b>		<b>1000</b>	<b>1000</b>	<b>1000</b>	<b>1000</b>	<b>1500</b>	<b>1500</b>
<b>Gender</b>	Male	410	410	520	510	735	765
	Female	590	590	480	490	765	735
<b>Oversample Age</b>	<b>21 to 25</b>		<b>1000</b>				
<b>Age</b>	21-24	130		10	115	150	120
	25-44	320		270	425	645	550
	45-64	310		50	310	675	595
	65+	240		670	150	30	235
<b>Race/ Ethnicity</b>	White, Non-Hispanic	660	660	820	710	1065	1140
	Black, Non-Hispanic	120	120	70	110	225	180
	Asian, Non-Hispanic	60	60	30	40	45	30
	American Indian/ Alaska Native, Non- Hispanic	10	10	5	5	30	15
	Hispanic	140	140	70	130	120	120
	Non-Hispanic Multi-race	10	10	5	5	15	15
<b>US Census Regions</b>	Northeast	165	165	200	125	240	225
	Midwest	210	210	230	280	390	420
	South	355	355	310	360	555	525
	West	270	270	260	235	315	330

ALL QUOTAS PER CONCEPT CELLS 4 & 5		Never Users	Never Users Oversample Age 21 to 25	Long-Term Quitter	Recent Quitters	Current Smokers With Intent to Quit	Current Smokers With No Intent to Quit
Total Quotas		500	500	500	500	750	750
Gender	Male	205	205	260	255	368	383
	Female	295	295	240	245	383	368
Oversample Age	21 to 25		500				
Age	21-24	65		5	57	75	60
	25-44	160		135	213	322	275
	45-64	155		25	155	338	298
	65+	120		335	75	15	117
Race/ Ethnicity	White, Non-Hispanic	330	330	410	355	533	570
	Black, Non-Hispanic	60	60	35	55	112	90
	Asian, Non-Hispanic	30	30	15	20	23	15
	American Indian/ Alaska Native, Non- Hispanic	5	5	3	3	15	8
	Hispanic	70	70	35	65	60	60
	Non-Hispanic Multi-race	5	5	2	2	7	7
US Census Regions	Northeast	83	82	100	62	120	112
	Midwest	105	105	115	140	195	210
	South	178	178	155	180	278	263
	West	135	135	130	118	157	165

**[WELCOME SCREEN]**

- # INT) Welcome. You're invited to participate in this research survey about consumer products. This survey will take approximately 15-17 minutes to complete.
- Individual answers will be kept strictly confidential and used for marketing research purposes only.
  - Use the "forward arrow" button on the bottom of each page to move within the survey.
  - Answer every question to the best of your ability. There are no right or wrong answers; we are only interested in your opinions.
- To start your survey, click on the "forward arrow" button below.**
- # QS1) Thanks for taking the time to participate in our survey. Your responses provided in this survey will only be used in connection with this research project and will not be shared with any third parties. Thank you in advance for your thoughtful input.
- # QICF) **[INSERT INFORMED CONSENT SCREEN – TERMINATE IF RESPONDENT SELECTS 2 “No – do not voluntarily participate”]**
- # QS2) What is your 5-digit zip code?
- # CENSUSSTATE) State **[SET FROM ZIP CODE DB LOOKUP]**
- # CENSUSREG) Region **[SET FROM ZIP CODE DB LOOKUP]**
- Northeast..... 1
  - Midwest ..... 2
  - South ..... 3
  - West ..... 4
- [CHECK QUOTAS; IF FULL, TERM AND SKIP TO END; OTHERWISE CONTINUE]**
- # CENSUSDIV) Division **[SET FROM ZIP CODE DB LOOKUP]**
- New England ..... 1
  - Middle Atlantic ..... 2
  - East North Central ..... 3
  - West North Central ..... 4
  - South Atlantic ..... 5
  - East South Central ..... 6
  - West South Central ..... 7
  - Mountain ..... 8
  - Pacific ..... 9

# QS6) Are you...?  
Male.....1  
Female .....2  
**[CHECK QUOTAS; IF FULL, TERM AND SKIP TO END; OTHERWISE CONTINUE]**

# QS7) What is your age?  
[ \_\_\_\_\_ ]  
**[EDIT: 10 – 99]**  
**[IF AGE 21+ CONTINUE; OTHERWISE TERMINATE AND SKIP TO END]**

# QS8) To confirm, what is your date of birth?  
**[MONTH] [DAY] [YEAR]**  
MIN/MAX CHARS: [2] [2] [4]  
**[CALCULATE AGE AND VALIDATE BACK TO ENTRY AT QS7. IF AGE IS NOT EQUAL, ASK:  
“You mentioned that you were [INSERT AGE FROM QS7] but your date of birth indicates that you are  
[INSERT CALCULATED AGE IN YEARS FROM QS8]. Is the birthdate that you entered correct? Yes/No.  
IF YES, DATAWRITE QS7 WITH CORRECT AGE AND CONTINUE TO QS9. IF NO, TRIGGER ERROR  
MESSAGE TO RE-ENTER DOB. IF VALIDATION FAILS TWICE, TERMINATE.]**

# AGEGRP) **[PUNCH AGEGRP BASED ON EXACTAGE]**  
**[HIDDEN QUESTION. PUNCH BASED ON EXACT AGE CALCULATION FROM QS8]**  
[21-24 years.....1  
25-44 years .....2  
45-64 years .....3  
65+ years .....4  
**[CHECK QUOTAS; IF FULL, TERM AND SKIP TO END; OTHERWISE, CONTINUE]**

# QS9) Are you of Hispanic or Latino origin?  
Yes .....1  
No.....2

# QS10) With which of the following do you most closely identify?  
Caucasian/White .....1  
Black/African American .....2  
Hispanic (e.g., Latin American, Mexican, Puerto Rican, Cuban) .....3  
Asian or Pacific Islander .....4  
Native American or Alaskan Native .....5  
Multi-racial background .....6  
Another ethnic background.....7

# S10a) **[PUNCH ETHNICITY FROM QS9 AND QS10]**  
**IF QS9 = 1 OR IF QS10 = 3, PUNCH 5**  
**IF QS9 = 2 AND QS10 = 1, PUNCH 1**  
**IF QS9 = 2 AND QS10 = 2, PUNCH 2**  
**IF QS9 = 2 AND QS10 = 4, PUNCH 3**  
**IF QS9 = 2 AND QS10 = 5, PUNCH 4**  
**IF QS9 = 2 AND QS10 = 6, PUNCH 6**  
**IF QS9 = 2 AND QS10 = 7, PUNCH 6**  
**White, Non-Hispanic.....1**  
**Black, Non-Hispanic.....2**  
**Asian, Non-Hispanic.....3**  
**American Indian or Alaskan Native, Non-Hispanic.....4**  
**Hispanic .....5**  
**Non-Hispanic, Multi-race, Other ..... 6]**  
**[CHECK ETHNICITY QUOTAS, IF FILLED, TERMINATE AND SKIP TO END; OTHERWISE, CONTINUE]**

- # QS11) Do you, or does anyone in your household, work in or go to school for any of the following? Please select all that apply.
- [RANDOMIZE LIST]..... [M]
  - Advertising.....1
  - Market Research.....2
  - Health / Medical Industry.....3
  - Journalism.....4
  - Public Relations.....5
  - Manufacture, sale or distribution of tobacco products.....6
  - Marketing.....7
  - Political Lobbying / Legal Field.....8
  - Newsagent / Supermarket / Cash & Carry retailing.....9
  - None of these [ANCHOR] [EXCLUSIVE].....10
- [IF QS11 = 1-8, TERMINATE AND SKIP TO END, OTHERWISE CONTINUE]
- # QS12) Have you ever participated in a market research survey?
- Yes.....1
  - No.....2
- [ASK QS13 IF QS12= 1 (YES); OTHERWISE SKIP TO QS14]
- # QS13) Approximately how long ago did you take a survey on each of these?
- [RANDOMIZE LIST]
  - Laundry Detergent.....1
  - Fast Food Restaurants.....2
  - Tobacco Products.....3
  - Bottled Water.....4
- [SCALE:]
- Within the last 3 months.....1
  - 3 to 6 months ago.....2
  - 6 to 12 months ago.....3
  - Over 12 months ago.....4
  - Never.....6
  - Don't know / Not sure.....5
- [IF QS13 = 1 (P3MO FOR TOBACCO), TERMINATE AND SKIP TO END, OTHERWISE CONTINUE]
- [ASK QS14 & QS15 IF QS6 = 2 (FEMALE); OTHERWISE, SKIP TO QS16]
- # QS14) Are you currently pregnant?
- Yes.....1
  - No.....2
- [IF QS14 = 1 (YES), TERMINATE AND SKIP TO END, OTHERWISE CONTINUE]
- # QS15) Are you currently breastfeeding?
- Yes.....1
  - No.....2
- [IF QS15 = 1 (YES), TERMINATE AND SKIP TO END, OTHERWISE CONTINUE]
- # QS16) Do you currently smoke cigarettes...?
- Every day.....1
  - Some days.....2
  - Not at all.....3
- # QS17) Have you ever smoked 100 cigarettes or more in your life?
- Yes.....1
  - No.....2
- [TOBACCO USAGE QUOTA GROUP CLASSIFICATION:  
 IF QS16=1 OR 2 (EVERY DAY OR SOME DAYS) AND QS17=1 (YES), CLASSIFY AS "CURRENT SMOKERS."  
 IF QS16=3 (NOT AT ALL) AND QS17=1 (YES), CLASSIFY AS "FORMER SMOKERS"  
 IF QS16=1 OR 2 (EVERY/SOME DAYS) AND QS17=2 (NO), CLASSIFY AS "EXPERIMENTAL CURRENT SMOKERS"  
 IF QS16=3 (NOT AT ALL) AND QS17=2 (NO), CLASSIFY AS "NEVER SMOKERS."  
 IF "EXPERIMENTAL CURRENT SMOKERS," TERMINATE; OTHERWISE, CONTINUE.]

# QS18) To confirm, please indicate which of these you have **used in the past 30 days**. Select **all** that apply.  
**[RANDOMIZE LIST]**

	Used in the past 30 days
Cigarettes (Marlboro, Camel, Newport, etc.)	1
Electronic cigarettes/E-cigarettes/Vapor products	2
Loose tobacco to roll your own cigarettes	3
Loose leaf chewing tobacco (Red Man, Levi Garrett, etc.)	4
Moist snuff or dip in a can (Skoal, Copenhagen, etc.)	5
Large cigars, little cigars or cigarillos	6
Nicotine replacement therapies such as patches, gum, lozenges, or inhalers	7
Other tobacco or nicotine-based product(s)	98
None of these <b>[ANCHOR] [EXCLUSIVE]</b>	99

**[IF QG=NEVER USERS, SKIP TO QINT]**

**[IF QG=FORMER SMOKERS, ASK QS19; OTHERWISE, SKIP TO QS20.]**

**[IF QG= CURRENT SMOKERS AND QS18 DOES NOT EQUAL CODE 1 (CIGARETTES), ASK QS18a; OTHERWISE, SKIP TO QS20.]**

# QS18a) Just to confirm, have you smoked cigarettes in the past 30 days?

Yes ..... 1  
 No ..... 2

**[IF QS18a=2 (NO) TERMINATE; OTHERWISE AUTOCODE QS18 = CODE 1 (CIGARETTES) AND CONTINUE.]**

# QS19) For how long have you quit smoking cigarettes now?

Less than 2 weeks ..... 1  
 2 weeks to less than 1 month ago ..... 2  
 1 month to less than 3 months ago ..... 3  
 3 months to less than 6 months ago ..... 4  
 6 months to less than 1 year ago ..... 5  
 1 year ago to less than 5 years ago ..... 6  
 5 years to less than 15 years ago ..... 7  
 15 or more years ago ..... 8

**[FORMER SMOKER SUBQUOTA CLASSIFICATION:**

**IF QS19=1 – 5 (WITHIN PAST YEAR), CLASSIFY AS “RECENT QUITTERS.”**

**IF QS19=6 – 8 (1+ YEAR AGO), CLASSIFY AS “LONG-TERM QUITTERS.”]**

**[IF QG=CURRENT SMOKERS, ASK QS20-QS29; OTHERWISE, SKIP TO QINT]**

**[DISPLAY QS20 AND QS22 ON ONE SCREEN]**

# QS20) Which brand of cigarettes do you, yourself, buy and smoke most often?

**[INSERT CIGARETTE BRAND LIST]**

[OMIT QS21] [CHECK VALID FLAVOR BACK TO BRAND FAMILY LIST]

# QS22) And is this usual brand...?

Menthol ..... 1  
 Non-menthol ..... 2

# QS23) Approximately, how many cigarettes do you smoke each day? Please enter the **total** number of cigarettes you smoke **each day** on average. Your closest estimate is fine. One pack equals 20 cigarettes.

**[EDIT: 1 – 99]**

# QS24) In the last year, how many times have you quit smoking cigarettes for at least 24 hours?

Zero ..... 1  
 One to two times ..... 2  
 Three to four times ..... 3  
 Five times or more ..... 4

- # QS25) Are you seriously considering quitting smoking within the next **6 months**?
- Yes .....1  
 No .....2

**[CURRENT SMOKER SUBQUOTA CLASSIFICATION:  
 IF QS25=1 (YES), CLASSIFY AS “CURRENT SMOKER – INTEND TO QUIT”  
 IF QS25=2 (NO), CLASSIFY AS “CURRENT SMOKER – NO INTENT TO QUIT”]**

[OMIT QS25b]

- # QS26) **[ASK QS26 IF QS25 = YES; OTHERWISE, SKIP TO QS27.]**  
 Are you planning to quit smoking in the next **30 days**?
- Yes .....1  
 No .....2

- # QS27) When was the last time you seriously tried to quit smoking?
- Less than 6 months ago .....1  
 More than 6 months ago .....2  
 Never .....3

- # QS28) How concerned are you, if at all, about the effects of smoking on **your health**?

Not Concerned At All										Very Concerned
1	2	3	4	5	6	7	8	9	10	

- # QS29) How concerned are you, if at all, about the effects of smoking on the **health of others**?

Not Concerned At All										Very Concerned
1	2	3	4	5	6	7	8	9	10	

**[CHECK ALL QUOTAS. IF QUOTA FULL, TERMINATE & SKIP TO END. OTHERWISE, CONTINUE.]  
 [RANDOMLY ASSIGN RESPONDENT TO ONE CONCEPT QUOTA CELLS BASED ON GREATEST TOBACCO USAGE / DEMOGRAPHIC NEED ACROSS ALL CONCEPT/DEMO QUOTA GROUPS.]  
 [EXCEPTION: IF QG=CURRENT SMOKER & QS20 = MARLBORO, DO NOT ASSIGN TO CELL 5 – CONTROL CELL B.]**

1. URGE
2. CONSUMPTION
3. LESS
4. CONTROL CELL A
5. CONTROL CELL B

**EACH RESPONDENT WILL SEE ONLY ONE CONCEPT.]**

**[END OF SCREENER]**

- # QINT) Thank you for agreeing to participate in this important public health study. This study is about tobacco products, both those currently on the market as well as potential new products in development.

**[IF QG=FORMER SMOKER / NEVER USER:** We understand that you do not currently use tobacco products. This research is not being conducted to help a manufacturer market or promote a new product. Rather, this research is to help understand how the release of a new product might affect health risk and harm reduction. Gathering perceptions of non-users of tobacco products is extremely important for this research and we appreciate the time that you are taking to participate.]

- # Q1c) **[ASK Q1c-Q1g IF QG = CURRENT SMOKER; OTHERWISE, SKIP TO Q1.]** These first few questions ask about the cigarette brand(s) you typically purchase. First, if the brand you buy most often, **[INSERT BRAND FROM QS20]** was not available, what **one other** cigarette brand would you buy?  
**[DISPLAY BRAND FAMILY AND FLAVOR QUESTIONS]**

\_\_\_\_\_ ]  
**[2<sup>nd</sup> CHOICE BRAND CODE]**

# Q1d) What other tobacco cigarette brands have you bought **for yourself** in the **last 30 days**? Please select **up to 3** brands or select "None" in the first row.

**[DISPLAY BRAND FAMILY AND FLAVOR QUESTIONS.]**

[ \_\_\_\_\_ ]  
 [3<sup>rd</sup> CHOICE BRAND CODE]  
 [ \_\_\_\_\_ ]  
 [4<sup>th</sup> CHOICE BRAND CODE]  
 [ \_\_\_\_\_ ]  
 [5<sup>th</sup> CHOICE BRAND CODE]

**[CREATE EVOKED SET USING BRAND AND FLAVOR FROM QS20, Q1c, Q1d\_1, Q1d\_2, Q1d\_3; SET WILL INCLUDE UP TO 5 OPTIONS (A-E); WRITE NUMBER OF BRANDS IN THE EVOKED SET TO DATA.]**  
**[IF MORE THAN ONE BRAND IN EVOKED SET, CONTINUE; OTHERWISE, SKIP TO Q.1]**

# Q1e) Now, you will see some brands of cigarettes, two at a time. Please divide **11** points between each pair of brands, considering everything you know about each brand. You can divide the points any way you like; just keep in mind that the two numbers you assign to the brands in each pair must add to **11**. Always give the brand you prefer, for whatever reason, the larger of the two numbers.

**[ON EACH SCREEN ASK: Please allocate 11 points to the following two brands.]**

The **[FIRST/NEXT]** pair of brands is [ \_\_\_\_\_ ] and [ \_\_\_\_\_ ].

How many points would you give [ \_\_\_\_\_ ]? How many points would you give [ \_\_\_\_\_ ]?

**[REPEAT FOR ALL COMPARISONS]**

	# OF POINTS		# OF POINTS	TOTAL POINTS PER PAIR
A. _____	<input type="checkbox"/>	B. _____	<input type="checkbox"/>	=11
B. _____	<input type="checkbox"/>	C. _____	<input type="checkbox"/>	=11
C. _____	<input type="checkbox"/>	A. _____	<input type="checkbox"/>	=11
D. _____	<input type="checkbox"/>	B. _____	<input type="checkbox"/>	=11
A. _____	<input type="checkbox"/>	D. _____	<input type="checkbox"/>	=11
D. _____	<input type="checkbox"/>	C. _____	<input type="checkbox"/>	=11
E. _____	<input type="checkbox"/>	A. _____	<input type="checkbox"/>	=11
B. _____	<input type="checkbox"/>	E. _____	<input type="checkbox"/>	=11
E. _____	<input type="checkbox"/>	D. _____	<input type="checkbox"/>	=11
C. _____	<input type="checkbox"/>	E. _____	<input type="checkbox"/>	=11

**[Q1f-Q1g ARE IN A GRID FORMAT.]**

# Q1f-g) These next two questions will sound very similar. However, the first question is asking **how many times** you purchase each brand of cigarettes in an average 30-day period. And, the second question is asking **how many packs** you purchase in an average 30-day period.

For each brand listed below, please indicate the **number of times** you buy this brand for yourself in an average 30-day period. **If none, please enter "0"**.

Then, for each brand you buy, please indicate the **number of packs** you buy for yourself in an average 30-day period.

Remember, if you buy by the carton, please enter number of packs at this question - there are 10 packs in a carton.

**[INSERT EACH BRAND IN EVOKED SET INTO THE GRID; IF 0 AT Q1f\_XX, DO NOT ACCEPT AN ANSWER ON Q1g\_XX FOR THAT BRAND; THE ANSWER AT Q1g\_XX MUST BE GREATER THAN OR EQUAL TO THE ANSWER AT Q1f\_XX; MIN = 0; MAX = 99]**

[

	# Q1f Number of times bought	# Q1g Number of packs purchased
A. _____	_____	_____
B. _____	_____	_____
C. _____	_____	_____
D. _____	_____	_____
E. _____	_____	_____]

**[PRODUCT CATEGORY REVIEW]**

# Q1) Please carefully read each of the following product descriptions.

**[DISPLAY ONE PRODUCT PER SCREEN WITH PRODUCT NAME AND DESCRIPTION. PLACE A MINIMUM 5-SECOND TIMER ON EACH PAGE. DISALLOW SELECTION OF THE 'NEXT' BUTTON FOR 5 SECONDS TO ALLOW PARTICIPANT TO THOROUGHLY REVIEW.] [DO NOT RANDOMIZE PRODUCT ORDER]**

Cigarettes	A cigarette is a narrow cylinder of finely cut tobacco leaves that are rolled into thin paper for smoking. The cigarette is ignited at one end, causing the cigarette to smolder and allowing smoke to be inhaled from the other end. Most modern manufactured cigarettes are filtered. Here are some examples of traditional cigarettes: <b>[DISPLAY PRODUCT IMAGE]</b>
E-Cigarettes	Electronic cigarettes, also known as e-cigarettes, e-vaporizers, or electronic nicotine delivery systems, are battery-operated devices that people use to inhale an aerosol, which typically contains nicotine (though not always), flavorings, and other chemicals. Here are some examples of e-cigarettes: <b>[DISPLAY PRODUCT IMAGE]</b>
Moist Snuff	Moist snuff is a smokeless tobacco product that is consumed by placing it into your mouth between the lip and the gum. You don't burn it, and users often spit when they use it. Here are some examples of moist snuff: <b>[DISPLAY PRODUCT IMAGE]</b>
Nicotine Replacement Therapy (NRT)	Nicotine Replacement Therapy are products that contain nicotine but no tobacco and are used to help people quit cigarettes or other tobacco products. Nicotine Replacement Therapy products usually come in the form of gum, patches, inhalers, lozenges or tablets. Here are some examples of NRTs: <b>[DISPLAY PRODUCT IMAGE]</b>

# Q2) Considering everything you know or may have seen or heard, even if you have never used the product, please indicate how familiar you believe you are with each of these.

<b>[DO NOT RANDOMIZE LIST]</b>	Not At All Familiar	Not Very Familiar	Somewhat Familiar	Very Familiar	Extremely Familiar
Cigarettes (Marlboro, Camel, Newport, etc.)	1	2	3	4	5
Electronic cigarettes/E-cigarettes/Vapor products	1	2	3	4	5
Moist snuff or dip in a can (Skoal, Copenhagen, etc.)	1	2	3	4	5
Nicotine replacement therapies such as patches, gum, lozenges, or inhalers	1	2	3	4	5

**[PRE-EXPOSURE HEALTH RISK PERCEPTION MEASUREMENT]**  
**[ASK Q3a & Q3b FOR THESE FOUR PRODUCT CATEGORIES PER RESPONDENT. ENSURE REPRESENTATIVE DISTRIBUTION (ACROSS SMOKING STATUS) OF EACH PRODUCT CATEGORY USING LEAST FILL METHOD FOR A TOTAL OF 7000 EVALUATIONS PER PRODUCT CATEGORY.] [INSERT BRACKETED TEXT AS APPROPRIATE FOR EACH CATEGORY.]**

CATEGORY #	CATEGORY	TOTAL EVALUATIONS	EVALUATIONS PER CONCEPT CELL
1	Cigarettes (Marlboro, Camel, Newport, etc.)	7000	1400
2	Electronic cigarettes/E-cigarettes/Vapor products	7000	1400
3	Moist snuff or dip in a can (Skoal, Copenhagen, etc.)	7000	1400
4	Nicotine Replacement Therapies	7000	1400

# Q3a) The next questions ask for your views about the **health and addiction risks** of **[INSERT CATEGORY]**.

After reading each question, select the answer that best reflects how you feel, keeping in mind that there are no right or wrong answers. Please answer all questions. If you are unsure about how to answer a question, give the best answer that you can.

Taking into consideration everything you know about **[INSERT CATEGORY]**, indicate what you believe is the **risk** of each of the following long-term or lifetime **health-related** issues because of **[INSERT CATEGORY]** **[IF CATEGORY = 1-4: use]**.  
**[RANDOMIZE LIST]**

<b>Measurement:</b>					
1	2	3	4	5	99
No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Unsure
<b>Scale:</b>					
1. Having a bad cough that lasts for days					
2. Having poor gum health					
3. Having lung cancer					
4. Occasional wheezing (i.e., difficult breathing that produces a sound)					
5. Having mouth or throat cancer					
6. Aging faster (e.g., wrinkles on the face)					
7. Being sick with frequent minor illnesses (e.g., coughs and colds)					
8. Having regular respiratory infections (e.g., bronchitis, pneumonia)					
9. Having a serious illness (e.g., chest pain, vascular disorder, diabetes)					
10. Having reduced stamina					
11. Having emphysema (i.e., serious lung disease)					

12. Having a cough early in the morning
13. Losing some sense of taste
14. Having heart disease
15. An earlier death
16. Having sores of the mouth or throat
17. Being physically unfit
18. Having other types of cancer (besides mouth, throat, or lung)

# Q3b) Now think about the **addiction risks** associated with [INSERT CATEGORY] [IF CATEGORY = 1-4: use].

Taking into consideration everything you know about [INSERT CATEGORY], indicate what you believe is the **risk** of each of the following long-term or lifetime **addiction-related** issues because of [INSERT CATEGORY] [IF CATEGORY = 1-4: use].  
 [RANDOMIZE LIST]

Measurement:					
1	2	3	4	5	99
No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Unsure
1. Being unable to quit [INSERT CATEGORY]					
2. Being addicted to [INSERT CATEGORY]					
3. Having to use [INSERT CATEGORY] to feel better					
4. Feeling like you <b>have</b> to use [INSERT CATEGORY]					
5. Feeling like you can't stop using [INSERT CATEGORY] even though you know it is not good for you					
6. Feeling unable to quit [INSERT CATEGORY]					

# Q7) Now think about **your personal intent to use** each of the following. By intent to use, we mean that you personally [IF NEVER / FORMER SMOKER: “, as a non-smoker,”] **now intend to use the product on a regular, ongoing basis**.

Overall, what is your current intent to use each of the following products **on a regular, ongoing basis**?

[DO NOT RANDOMIZE]	Definitely Would Not Use	Very Unlikely	Somewhat Unlikely	Somewhat Likely	Very Likely	Definitely Would Use
1. Cigarettes (Marlboro, Camel, Newport, etc.)	1	2	3	4	5	6
2. Electronic cigarettes/E-cigarettes/Vapor products	1	2	3	4	5	6
3. Moist snuff or dip in a can (Skoal, Copenhagen, etc.)	1	2	3	4	5	6
4. Nicotine replacement therapies such as patches, gum, lozenges, or inhalers	1	2	3	4	5	6

[CONCEPT EXPOSURE]

[SHOW Q8a IF CELL = 1, 2, OR 3]

[IF QG=CURRENT SMOKER AND S22=1 (MENTHOL) = SHOW MENTHOL IMAGES]

[IF QG=CURRENT SMOKER AND S22=2 (NON-MENTHOL) = SHOW NON-MENTHOL IMAGES]

[IF QG=FORMER SMOKER OR QG=NEVER USERS, SHOW HALF OF RESPONDENTS MENTHOL AND HALF OF RESPONDENTS NON-MENTHOL IMAGES AND SET QUOTAS BY FORMER SMOKERS OR NEVER SMOKERS (CONCEPT/CELL)]

# Q8a) A new tobacco product called VLN™ (Very Low Nicotine) is currently in development. Please read the entire description of VLN™ thoroughly, as the questions that follow will be related to this product concept.

**VLN™ and VLN™ menthol are 84-millimeter cigarettes (sometimes called “shorts,” “regulars” or “kings”) and are made with the same components found in commercial brands of cigarettes such as a filter, cigarette paper and tobacco. VLN™ and VLN™ menthol are manufactured in a manner similar to that of a typical cigarette.**

**The tobacco in VLN™ cigarettes is different than the tobacco used in most cigarette brands. VLN™ cigarettes are made from a tobacco plant that has been altered to contain much lower levels of nicotine than the tobacco used in traditional cigarettes.**

Click the “forward arrow” button [to continue](#).

# 8a1) Next you will see a 3D image of the product package. Once it loads, (please allow up to 1 minute) and don't close your browser), place your mouse pointer on the image and click and move it around to turn the package 360 degrees so you can view all sides. Once you have fully viewed the product press the “NEXT” button to continue back to the survey.

To proceed to the 3D image, press the “forward arrow” button.

# 8a2) [SEND RESPONDENT TO 3<sup>RD</sup> PARTY WEBSITE FOR VIEWING 3D AND RETURN BACK]

[SHOW Q8b IF CELL = CONTROL CELL A]

[IF QG=CURRENT SMOKER AND S22=1 (MENTHOL) = SHOW MENTHOL IMAGES]

[IF QG=CURRENT SMOKER AND S22=2 (NON-MENTHOL) = SHOW NON-MENTHOL IMAGES]

[IF QG=FORMER SMOKER OR QG=NEVER USERS, SHOW HALF OF RESPONDENTS MENTHOL AND HALF OF RESPONDENTS NON-MENTHOL IMAGES]

# Q8b) A new tobacco product called VLN™ is currently in development. Please read the entire description of VLN™ thoroughly, as the questions that follow will be related to this product concept.

**VLN™ and VLN™ menthol cigarettes are timeless originals. VLN™ combines Bright, Burley and Oriental tobaccos to create a rich, flavored blend legendary for its smoothness.**

Click the “forward arrow” button to continue.

# 8b1) Next you will see a 3D image of the product package. Once it loads, (please allow up to 1 minute) and don't close your browser), place your mouse pointer on the image and click and move it around to turn the package 360 degrees so you can view all sides. Once you have fully viewed the product press the “NEXT” button to continue back to the survey.

To proceed to the 3D image, press the “forward arrow” button.

# 8b2) [SEND RESPONDENT TO 3<sup>RD</sup> PARTY WEBSITE FOR VIEWING 3D AND RETURN BACK]

[SHOW Q8c IF CELL = CONTROL CELL B UNLESS QG=CURRENT SMOKER AND QS20=MARLBORO. DO NOT ASSIGN THESE RESPONDENTS TO CONTROL CELL B.]

[IF QG=CURRENT SMOKER AND Q20 ≠ MARLBORO OR QGFORMER SMOKER OR QG=NEVER USERS, SHOW HALF OF RESPONDENTS MENTHOL AND HALF OF RESPONDENTS NON-MENTHOL IMAGES]

# Q8c) Marlboro Gold is a conventional cigarette that is currently available to consumers. Please read the entire description of Marlboro Gold thoroughly, as the questions that follow will be related to this product concept.

**Marlboro Gold™ and Marlboro Gold™ menthol cigarettes are timeless originals. Marlboro Gold combines Bright, Burley and Oriental tobaccos to create a rich, flavored blend legendary for its smoothness.**

Click the “forward arrow” button to continue.

# Q9) On the next few screens you will see several additional images of the product package. Please review each image and click the “forward arrow” button to proceed to the next screen.

**[INSERT CONCEPT ASSIGNED TO RESPONDENT HERE: TEXT FOR REST OF THE SURVEY SHOULD BE THE SAME AS THE CONCEPT VIEWED PER CELL ASSIGNMENT AND MENTHOL/NON-MENTHOL SELECTION.] [KEEP FRONT & BACK IMAGE OPEN FOR MINIMUM OF 3 SECONDS BEFORE ALLOWING RESPONDENT TO CLOSE – DO NOT FORCE TIMER ON SIDE IMAGES.]**

**[SHOW QCMP1 AND QCMP2 IF CELL = 1, 2, 3, or 4]**

# QCMP1) If you were asked to describe **[INSERT CONCEPT]** to a friend or family member, what would you say? Please be specific.  
**[OPEN TEXT. MAX CHARS=250.]**

# QCMP2) What do you think are the **benefits** of **[INSERT CONCEPT]**? Please be specific.  
**[OPEN TEXT. MAX CHARS=250.]**

# QCMP3) What do you think are the **health or addiction risks** associated with **[INSERT CONCEPT]**? Please be specific.  
**[OPEN TEXT. MAX CHARS=250.]**

# QRE1\_1) Now that you have seen this product, the next section asks for your views about the long-term or lifetime **health or addiction risks** of smoking **[INSERT CONCEPT]**. These questions are the same as those you saw previously, but now we are asking about the **product you just reviewed**.

**[INSERT REVIEW BUTTON]** “Click here to review the product”

Taking into consideration everything you know about **[INSERT CONCEPT]**, indicate what you believe is the **risk** of each of the following long-term or lifetime **health-related** issues because of smoking **[INSERT CONCEPT]**.  
**[RANDOMIZE LIST SAME ORDER AS Q3A]**

Measurement:					
1	2	3	4	5	99
No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Unsure
<b>Scale:</b>					
1. Having a bad cough that lasts for days					
2. Having poor gum health					
3. Having lung cancer					
4. Occasional wheezing (i.e., difficult breathing that produces a sound)					
5. Having mouth or throat cancer					
6. Aging faster (e.g., wrinkles on the face)					
7. Being sick with frequent minor illnesses (e.g., coughs and colds)					
8. Having regular respiratory infections (e.g., bronchitis, pneumonia)					
9. Having a serious illness (e.g., chest pain, vascular disorder, diabetes)					
10. Having reduced stamina					
11. Having emphysema (i.e., serious lung disease)					
12. Having a cough early in the morning					
13. Losing some sense of taste					
14. Having heart disease					
15. An earlier death					
16. Having sores of the mouth or throat					
17. Being physically unfit					
18. Having other types of cancer (besides mouth, throat, or lung)					

# QRE1\_2) Now think about the **addiction risks** associated with smoking **[INSERT CONCEPT]**.

Taking into consideration everything you know about **[INSERT CONCEPT]**, indicate what you believe is the **risk** of each of the following long-term or lifetime **addiction-related** issues because of smoking **[INSERT CONCEPT]**.  
**[RANDOMIZE LIST SAME ORDER AS Q3B]**

Measurement:					
1	2	3	4	5	99
No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Unsure
Scale:					
1. Being unable to quit smoking <b>[INSERT CONCEPT]</b>					
2. Being addicted to <b>[INSERT CONCEPT]</b>					
3. Having to smoke <b>[INSERT CONCEPT]</b> to feel better					
4. Feeling like you <b>have</b> to smoke <b>[INSERT CONCEPT]</b>					
5. Feeling like you can't stop smoking <b>[INSERT CONCEPT]</b> even though you know it is not good for you					
6. Feeling unable to quit smoking <b>[INSERT CONCEPT]</b>					

# QRE1a) After reviewing this product and the possible **health or addiction risks** to you, personally, of using this product, how do you think **[INSERT CONCEPT]** compares to **[INSERT OTHER PRODUCT CATEGORY SELECTED FOR Q3]**?

	No Risk Compared to <b>[INSERT CATEGORY FROM Q3]</b>	Low Risk Compared to <b>[INSERT CATEGORY FROM Q3]</b>	Moderate Risk Compared to <b>[INSERT CATEGORY FROM Q3]</b>	High Risk Compared to <b>[INSERT CATEGORY FROM Q3]</b>	Very High Risk Compared to <b>[INSERT CATEGORY FROM Q3]</b>	Don't Know
<b>[INSERT CONCEPT]</b>	1	2	3	4	5	99

# QIU1) Now think about your personal intent to use **[INSERT CONCEPT]**. By intent to use, we mean that you personally **[IF NEVER / FORMER SMOKER: “, as a non-smoker,”]** **now intend to smoke [INSERT CONCEPT] on a regular, ongoing basis.**

Overall, what is your intent to smoke **[INSERT CONCEPT] on a regular, ongoing basis?**

	Definitely Would Not Use	Very Unlikely	Somewhat Unlikely	Somewhat Likely	Very Likely	Definitely Would Use
<b>[INSERT CONCEPT]</b>	1	2	3	4	5	6

**[KEY PURCHASE DRIVERS]**

**[FORMAT Q11-Q14 WITH ANSWER BUTTONS HORIZONTALLY WITH NEGATIVE OPTIONS TO THE LEFT]  
 [IF RESPONDENT SAW MENTHOL IMAGE IN Q8A, B, OR C, SHOW MENTHOL IMAGE IN Q10/Q11/Q12/Q13/Q14] [IF RESPONDENT SAW NON-MENTHOL IMAGE IN Q8A, B, OR C, SHOW NON-MENTHOL IMAGE IN Q10/Q11/Q12/Q13/Q14]**

# Q10) For the remainder of the survey please assume that **[INSERT CONCEPT]** is available where you shop.

**[INSERT REVIEW BUTTON “Click here to review the product package.”]**

**[PREPI]**

# Q11) How likely would you be to buy **[INSERT CONCEPT]**? Assume it's priced equivalently to a pack of cigarettes.

- Definitely Would.....5
- Probably Would .....4
- Might or Might Not .....3
- Probably Would Not.....2
- Definitely Would Not .....1



**[PRELIKE]**

# Q12) How well do you think you might like **[INSERT CONCEPT]**?

[INSERT REVIEW BUTTON “Click here to review the product package.”]

Extremely Well.....6  
 Very Much .....5  
 Quite Well .....4  
 Somewhat.....3  
 Slightly .....2  
 Not At All .....1

**[PREDIFF]**

# Q13) How different is **[INSERT CONCEPT]** from other tobacco products you have seen?

[INSERT REVIEW BUTTON “Click here to review the product package.”]

Extremely Different .....5  
 Very Different.....4  
 Somewhat Different .....3  
 Not Very Different.....2  
 Not Different At All .....1

**[PREIMP]**

# Q14) How important are the benefits of **[INSERT CONCEPT]** to you?

[INSERT REVIEW BUTTON “Click here to review the product package.”]

Extremely Important .....6  
 Very Important.....5  
 Quite Important.....4  
 Somewhat Important .....3  
 Slightly Important .....2  
 Not At All Important .....1

**[PURCHASE DYNAMICS]**

**[IF QG=FORMER OR NEVER SMOKER, SKIP TO RE2a.]**  
**[IF QG=CURRENT SMOKERS AND Q11 = 5, 4 OR 3 (POSITIVE OR NEUTRAL PI), CONTINUE; OTHERWISE, SKIP TO Q30]**  
**[INSERT VLN MENTHOL FOR TEST BRAND IF QS22=1 (MENTHOL); INSERT VLN NON-MENTHOL IF QS22=2 (NON-MENTHOL)]**

# Q16a) Again, you will see some brands of cigarettes two at a time. Please divide 11 points between each pair of brands, considering everything you know about each brand. You can divide the points any way you like, just keep in mind that the two numbers you assign to the brands in each pair must add to 11. Always give the brand you prefer most, for whatever reason, the larger of the two numbers.  
**[ON EACH SCREEN ASK: Please allocate 11 points to the following two brands.]**

The **[FIRST/NEXT]** pair of brands is **[\_\_\_\_\_]** and **[\_\_\_\_\_]**.  
 How many points would you give **[\_\_\_\_\_]**? How many points would you give **[\_\_\_\_\_]**?

**[DISPLAY BRANDS IN EVOKED SET PLUS CONCEPT] [REPEAT FOR ALL COMPARISONS]**

		# OF POINTS		# OF POINTS	TOTAL POINTS PER PAIR
H.	<b>[TEST BRAND]</b> _____	<input type="checkbox"/>	B.	_____	=11
C.	_____	<input type="checkbox"/>	H.	<b>[TEST BRAND]</b> _____	=11
H.	<b>[TEST BRAND]</b> _____	<input type="checkbox"/>	E.	_____	=11
H.	<b>[TEST BRAND]</b> _____	<input type="checkbox"/>	D.	_____	=11
H.	<b>[TEST BRAND]</b> _____	<input type="checkbox"/>	A.	_____	=11 ]

**[NEXT 4 WEEK PURCHASES]**

# Q19) Please assume that **[INSERT CONCEPT]** is available where you normally purchase your tobacco and/or nicotine-replacement products.

Now, thinking about tobacco and nicotine-replacement products, over the **next 4 weeks** of purchases you make, how many would be for the following? If you're not sure, enter your best estimate.

**[INCLUDE PRODUCTS MENTIONED AT QS18; EDIT EACH 0-99; ALLOW BLANKS]  
 [SHOW RUNNING TOTAL]**

<b>[DO NOT RANDOMIZE LIST]</b>	<b># Purchase in Next 4 Weeks</b>
Cigarettes (Marlboro, Camel, Newport, etc.)	[ ]
Electronic cigarettes/E-cigarettes/Vapor products	[ ]
Loose tobacco to roll your own cigarettes	[ ]
Loose leaf chewing tobacco (Red Man, Levi Garrett, etc.)	[ ]
Moist snuff or dip in a can (Skoal, Copenhagen, etc.)	[ ]
Large cigars, little cigars or cigarillos	[ ]
Nicotine replacement therapies such as patches, gum, lozenges, or inhalers	[ ]
Other tobacco or nicotine-based product(s)	[ ]
<b>[INSERT CONCEPT]</b>	[ ]
None of these <b>[ANCHOR] [EXCLUSIVE]</b>	99

**[SUBSTITUTABILITY]  
 [POSUB1-POSUBn]**

# Q20) Would your purchase(s) of **[INSERT CONCEPT]** replace any tobacco or nicotine-replacement products that you currently use?

**[RANDOMIZE]**

- No, I would just buy **[INSERT CONCEPT]** in addition to my current products..... 1
- Yes, buying **[INSERT CONCEPT]** would result in fewer purchases of other tobacco or nicotine-replacement products..... 2

**[IF Q20=2 (YES, BUYING WOULD REDUCE TOBACCO PURCHASES), ASK Q21; OTHERWISE SKIP TO Q30]**

# Q21) Which tobacco or nicotine-replacement products would you cut back on, as a result of buying **[INSERT CONCEPT]**? Select **all** that apply.

<b>[INCLUDE ANSWERS FROM QS18]</b>	<b>[M]</b>
Cigarettes (Marlboro, Camel, Newport, etc.) .....	1
Electronic cigarettes/E-cigarettes/Vapor products .....	2
Loose tobacco to roll your own cigarettes.....	3
Loose leaf chewing tobacco (Red Man, Levi Garrett, etc.) .....	4
Moist snuff or dip in a can (Skoal, Copenhagen, etc.) .....	5
Large cigars, little cigars or cigarillos .....	7
Nicotine replacement therapies such as patches, gum, lozenges, or inhalers.....	8
Other tobacco or nicotine-based product(s).....	98

**[ASK Q30 IF QG=CURRENT SMOKERS; OTHERWISE SKIP TO QRE2a.]  
 [FEELINGS ABOUT TOBACCO USE]**

# Q30) How much do you **agree or disagree** with each of the following statements?

**[RANDOMIZE LIST]**

	Disagree Strongly	Disagree Somewhat	Neither Agree Nor Disagree	Agree Somewhat	Agree Strongly
1. Sometimes I worry if my tobacco / nicotine product use could hinder my professional success	1	2	3	4	5
2. I enjoy using tobacco / nicotine products with my friends	1	2	3	4	5

3. I hide my tobacco / nicotine use from non-users	1	2	3	4	5
4. My tobacco / nicotine use causes tension in my family life	1	2	3	4	5
5. I do not feel ashamed about my tobacco / nicotine product use	1	2	3	4	5
6. My tobacco / nicotine product use is no one's business but my own	1	2	3	4	5
7. Nicotine without tobacco has no appeal to me	1	2	3	4	5

**[ASK ALL QRE2a AND QIU2]**

# QRE2a) After reviewing this potential new product and the related risks of use, how do you think **[INSERT CONCEPT]** compares to **[INSERT OTHER PRODUCT CATEGORY SELECTED FOR Q3]**?

	No Risk Compared to <b>[INSERT Q3]</b>	Low Risk Compared to <b>[INSERT Q3]</b>	Moderate Risk Compared to <b>[INSERT Q3]</b>	High Risk Compared to <b>[INSERT Q3]</b>	Very High Risk Compared to <b>[INSERT Q3]</b>	Don't Know
<b>[INSERT CONCEPT]</b>	1	2	3	4	5	99

# QIU2) By intent to use, we mean that you personally **[IF NEVER / FORMER SMOKER: “, as a non-smoker,”]** ***now intend to use the product on a regular, ongoing basis.***

Overall, what is your current intent to use each of the following ***on a regular, ongoing basis?***

	Definitely Would Not Use	Very Unlikely	Somewhat Unlikely	Somewhat Likely	Very Likely	Definitely Would Use
<b>[DO NOT RANDOMIZE LIST]</b>						
Cigarettes (Marlboro, Camel, Newport, etc.)	1	2	3	4	5	6
Electronic cigarettes/E-cigarettes/Vapor products	1	2	3	4	5	6
Moist snuff or dip in a can (Skoal, Copenhagen, etc.)	1	2	3	4	5	6
Nicotine replacement therapies such as patches, gum, lozenges, or inhalers	1	2	3	4	5	6
<b>[INSERT CONCEPT]</b>	1	2	3	4	5	6

**[DEMOGRAPHICS]**

**[MARITAL]**

# QD1) Which of the following best describes your marital status?

- Married or living with partner ..... 1
- Single, never married ..... 2
- Separated or divorced ..... 3
- Widowed..... 4
- Prefer not to answer ..... 5

**[HHSIZE]**

# QD2) Including yourself and any children of all ages, how many people currently live in your household?

- One..... 1
- Two..... 2
- Three ..... 3
- Four ..... 4
- Five or more ..... 5
- Prefer not to answer ..... 6

**[IF QD2=2-5 ASK QD3; OTHERWISE SKIP TO QD4]**

**[CHILD1-N] [ALLOW BLANK ANSWERS; IF ANY BLANKS THEN 0 FILL]**

# QD3) How many children younger than 18, if any, are there in your household? Please enter a number in each box. If none, enter 0.

Younger than 6 years old .....	[ ]
Between 6 and 12 years old .....	[ ]
Between 13 and 17 years old .....	[ ]

**[SCHOOL]**

# QD4) Which best represents the highest level of education that you completed?

Some high school or less .....	1
High school graduate.....	2
Some college/Technical trade school.....	3
College graduate .....	4
Post-graduate school.....	5
Prefer not to answer .....	6

**[EMPLOY]**

# QD5) Which of the following best describes your employment status?

Employed full-time .....	1
Employed part-time .....	2
Homemaker .....	3
Student .....	4
Retired .....	5
Unemployed .....	6
Prefer not to answer .....	7

**[INCOME]**

# QD6) Which of the following groups represents your total annual household income before taxes?

Less than \$25,000 .....	1
\$25,000 but less than \$35,000 .....	2
\$35,000 but less than \$50,000 .....	3
\$50,000 but less than \$75,000 .....	4
\$75,000 but less than \$100,000 .....	5
\$100,000 but less than \$150,000 .....	6
\$150,000 or more .....	7
Prefer not to answer .....	8

# QDB) Thank you again for your time and participation. Before you close your browser or app, please review these reminders regarding the dangers of tobacco use.

- Smoking causes serious and fatal diseases such as lung cancer, heart disease and emphysema in smokers. Smokers are far more likely to develop serious diseases like lung cancer than non-smokers.
- Cigarette smoking during pregnancy is associated with increased risk of pregnancy complications, spontaneous abortion, low birth weight infants, and stillbirth.
- Cigarette smoking is addictive. It can be very difficult to quit smoking, but this should not deter adult smokers who want to quit from trying to do so.
- There is no such thing as a safe cigarette.
- **[IF VIEWING MRTP (CELLS 1, 2, 3):** Modified Risk Tobacco Products or MRTPs like what you have reviewed today have not been shown to be safer than smoking conventional cigarettes and MRTPs should not be viewed as an alternative to quitting smoking.
- Anything communicated during this research is not in any way intended to promote smoking, to promote a particular MRTP or to promote MRTPs in general.]

**INFORMED CONSENT TO TAKE PART IN A QUANTITATIVE STUDY**  
to Develop VLN Cigarettes Consumer Messaging

Please review this screen carefully before continuing. When you believe you understand the purpose of this study and you agree to take part, select “Yes – I agree to participate in this research” and click the “forward arrow” button to continue.

**M/A/R/C® Research** is conducting a public health research study with current smokers, former smokers and people who have never smoked cigarettes to help understand how the release of a new product might affect the *greater public health*. Also, to develop product messages for modified risk tobacco products (MRTPs). MRTPs are new tobacco products for existing smokers. This research is about various tobacco products including a new MRTP product.

If you participate in this survey, you will read and respond to questions about various tobacco products. You will not be asked to smoke or otherwise try any tobacco products, the new MRTP product, and no promotion of any tobacco brand or product will occur. You will be compensated **the amount you were offered prior to entering the survey** for participating in this survey.

Some sensitive information (Confidential Information) about the product may be shared. Any confidential information **may not be disclosed** to anyone outside of this research. Your input will be analyzed as part of a broader study where your specific opinions will be anonymous relative to thousands of other participants.

Using tobacco products is known to cause disease and early death. Talking about tobacco products could cause you to crave tobacco. There is no direct benefit to you for taking part in this study, outside of the incentive paid for your time. It is your decision to take part in this research study. Participation is voluntary and you may change your mind and stop at any time.

By signing selecting “Yes – I agree to participate in this research” you:

- Are providing electronic confirmation that you have read and understand this Informed Consent Form & Confidentiality Declaration
- Have read and understand the purposes of this research
- Understand what will happen in this survey
- Understand the risks associated with the research
- Will be compensated for your participation

You should contact (b) (6) at **1-800-884-6272 (1425 Greenway Drive, Suite 300, Irving, TX 75038)** if you have questions or concerns after taking this survey.

Do you agree to participate in this study?

1. Yes – I voluntarily agree to participate in this study
2. No – I do not agree to participate in this study

## APPENDIX 2 – TOBACCO PRODUCT COMPARATORS DESCRIPTIONS

**Study Name:** Quantitative Study to Develop VLN™ Hypothetical Product Messages Among U.S. Adult Cigarette Smokers, Adult Former Cigarette Smokers and Adult Never Cigarette Users

**Protocol Number:** 5180080-VLN™-B2

**Sponsor:** 22nd Century Group, Inc.  
8560 Main Street  
Williamsville, NY 14221

**Version Number:** 1.2

**Author:** (b) (6)

## Traditional Cigarettes

A cigarette is a narrow cylinder of finely cut tobacco leaves that are rolled into thin paper for smoking. The cigarette is ignited at one end, causing the cigarette to smolder and allowing smoke to be inhaled from the other end. Most modern manufactured cigarettes are filtered. Here are some examples of traditional cigarettes:

Figure A2.1 Example Image – Traditional Cigarettes



## e-cigarettes

Electronic cigarettes, also known as e-cigarettes, e-vaporizers, or electronic nicotine delivery systems, are battery-operated devices that people use to inhale an aerosol, which typically contains nicotine (though not always), flavorings, and other chemicals. Here are some examples of e-cigarettes:

Figure A2.2 Example Image – e-cigarettes



## Moist Snuff

Moist snuff is a smokeless tobacco product that is consumed by placing it into your mouth between the lip and the gum. You don't burn it, and users often spit when they use it. Here are some examples of moist snuff:

Figure A2.3 Example Image – Moist Snuff



## Nicotine Replacement Therapy (NRT)

Nicotine Replacement Therapy are products that contain nicotine but no tobacco and are used to help people quit cigarettes or other tobacco products. Nicotine Replacement Therapy products usually come in the form of gum, patches, inhalers, lozenges or tablets. Here are some examples of NRTs:

Figure A2.4 Example Image – Nicotine Replacement Therapy Products



## APPENDIX 3 – INFORMED CONSENT

**Study Name:** Quantitative Study to Develop VLN™ Hypothetical Product Messages Among U.S. Adult Cigarette Smokers, Adult Former Cigarette Smokers and Adult Never Cigarette Users

**Protocol Number:** 5180080-VLN™-B2

**Sponsor:** 22nd Century Group, Inc.  
8560 Main Street  
Williamsville, NY 14221

**Version Number:** 1.2

**Author:** (b) (6)

**INFORMED CONSENT TO TAKE PART IN A QUANTITATIVE STUDY**  
to Develop VLN Cigarettes Consumer Messaging

Please review this screen carefully before continuing. When you believe you understand the purpose of this study and you agree to take part, select “Yes – I agree to participate in this research” and click the “forward arrow” button to continue.

**M/A/R/C® Research** is conducting a public health research study with current smokers, former smokers and people who have never smoked cigarettes to help understand how the release of a new product might affect the *greater public health*. Also, to develop product messages for modified risk tobacco products (MRTPs). MRTPs are new tobacco products for existing smokers. This research is about various tobacco products including a new MRTP product.

If you participate in this survey, you will read and respond to questions about various tobacco products. You will not be asked to smoke or otherwise try any tobacco products, the new MRTP product, and no promotion of any tobacco brand or product will occur. You will be compensated **the amount you were offered prior to entering the survey** for participating in this survey.

Some sensitive information (Confidential Information) about the product may be shared. Any confidential information ***may not be disclosed*** to anyone outside of this research. Your input will be analyzed as part of a broader study where your specific opinions will be anonymous relative to thousands of other participants.

Using tobacco products is known to cause disease and early death. Talking about tobacco products could cause you to crave tobacco. There is no direct benefit to you for taking part in this study, outside of the incentive paid for your time. It is your decision to take part in this research study. Participation is voluntary and you may change your mind and stop at any time.

By signing selecting “Yes – I agree to participate in this research” you:

- Are providing electronic confirmation that you have read and understand this Informed Consent Form & Confidentiality Declaration
- Have read and understand the purposes of this research
- Understand what will happen in this survey
- Understand the risks associated with the research
- Will be compensated for your participation

You should contact (b) (6) at **1-800-884-6272 (1425 Greenway Drive, Suite 300, Irving, TX 75038)** if you have questions or concerns after taking this survey.

Do you agree to participate in this study?

3. Yes – I voluntarily agree to participate in this study
4. No – I do not agree to participate in this study

## APPENDIX 4 – VLN™ AND CONTROL CELL PACK IMAGES

**Study Name:** Quantitative Study to Develop VLN™ Hypothetical Product Messages Among U.S. Adult Cigarette Smokers, Adult Former Cigarette Smokers and Adult Never Cigarette Users

**Protocol Number:** 5180080-VLN™-B2

**Sponsor:** 22nd Century Group, Inc.  
8560 Main Street  
Williamsville, NY 14221

**Version Number:** 1.2

**Author:** (b) (6)

Figure A4.1 Example VLN™ Non-Menthol Image – “Helps”  
Figure A4.2 Example VLN™ Menthol Image – “Helps”

Statement to be tested: (b) (4)



Figure A4.3 Example VLN™ Non-Menthol Image – “Nicotine”  
Figure A4.4 Example VLN™ Menthol Image – “Nicotine”

Statement to be tested:       Helps reduce your nicotine consumption



Figure A4.5 Example VLN™ Non-Menthol Image – “Urge”

Figure A4.6 Example VLN™ Menthol Image – “Urge”

Statement to be tested:

(b) (4)



Figure A4.7 Example VLN™ Non-Menthol Image – No Claims Messaging  
Figure A4.8 Example VLN™ Menthol Image – No Claims Messaging

Statement to be tested: None



Figure A4.9 Example Marlboro Gold™ Non-Menthol Image – No Claims Messaging

Figure A4.10 Example Marlboro Gold™ Menthol Image – No Claims Messaging

Figure A4.11a Example Marlboro Gold™ Non-Menthol & Menthol Images – Marketing Images from Brand Website

Figure A4.11b Example Marlboro Gold™ Non-Menthol & Menthol Images – Marketing Images from Brand Website

Statement to be tested:      None



## APPENDIX 5 – PARTICIPANT DEBRIEFING SCRIPT

**Study Name:** Quantitative Study to Develop VLN™ Hypothetical Product Messages Among U.S. Adult Cigarette Smokers, Adult Former Cigarette Smokers and Adult Never Cigarette Users

**Protocol Number:** 5180080-VLN™-B2

**Sponsor:** 22nd Century Group, Inc.  
8560 Main Street  
Williamsville, NY 14221

**Version Number:** 1.2

**Author:** (b) (6)

## Participant Debriefing Script

Thank you again for your time and participation. Before you close your browser or app, please review these reminders regarding the dangers of tobacco use.

- Smoking causes serious and fatal diseases such as lung cancer, heart disease and emphysema in smokers. Smokers are far more likely to develop serious diseases like lung cancer than non-smokers.
- Cigarette smoking during pregnancy is associated with increased risk of pregnancy complications, spontaneous abortion, low birth weight infants, and stillbirth.
- Cigarette smoking is addictive. It can be very difficult to quit smoking, but this should not deter adult smokers who want to quit from trying to do so.
- There is no such thing as a safe cigarette.
- [IF VIEWING MRTP (CELLS 1, 2, 3): Modified Risk Tobacco Products or MRTPs like what you have reviewed today have not been shown to be safer than smoking conventional cigarettes and MRTPs should not be viewed as an alternative to quitting smoking.
- Anything communicated during this research is not in any way intended to promote smoking, to promote a particular MRTP or to promote MRTPs in general.]

## APPENDIX 6 – PERCEIVED RISK INSTRUMENT

**Study Name:** Quantitative Study to Develop VLN™ Hypothetical Product Messages Among U.S. Adult Cigarette Smokers, Adult Former Cigarette Smokers and Adult Never Cigarette Users

**Protocol Number:** 5180080-VLN™-B2

**Sponsor:** 22nd Century Group, Inc.  
8560 Main Street  
Williamsville, NY 14221

**Version Number:** 1.2

**Author:** (b) (6)

**PRI-P CC**

*This survey asks for your views about the **risks of smoking cigarettes**. After reading each question, select the answer that best reflects how you feel, keeping in mind that there are no right or wrong answers. Please answer all questions. If you are unsure about how to answer a question, give the best answer that you can.*

**[PRI-P- Perceived Health Risk scale SCREEN 1/3]**

**[CC smokers] What do you think is the risk, if any, to you personally of getting the following (sometime during your lifetime) because you smoke cigarettes...**

**[never CC smokers] If you were to start smoking, what do you think would be the risk, if any, to you personally of getting the following (sometime during your lifetime) because you smoke cigarettes...**

**[former CC smokers] If you were to resume smoking, what do you think would be the risk, if any, to you personally of getting the following (sometime during your lifetime) because you smoke cigarettes...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Having a bad cough that lasts for days	<input type="checkbox"/>					
Having poor gum health	<input type="checkbox"/>					
Having lung cancer	<input type="checkbox"/>					
Occasional wheezing (difficult breathing that produces a sound)	<input type="checkbox"/>					
Having mouth or throat cancer	<input type="checkbox"/>					
Aging faster (for example, wrinkles on the face)	<input type="checkbox"/>					

**[PRI-P- Perceived Health Risk scale SCREEN 2/3]**

[CC smokers] **What do you think is the risk, if any, to you personally of getting the following (sometime during your lifetime) because you smoke cigarettes...**

[never CC smokers] **If you were to start smoking, what do you think would be the risk, if any, to you personally of getting the following (sometime during your lifetime) because you smoke cigarettes...**

[former CC smokers] **If you were to resume smoking, what do you think would be the risk, if any, to you personally of getting the following (sometime during your lifetime) because you smoke cigarettes...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Being sick with frequent minor illnesses (for example, coughs and colds)	<input type="checkbox"/>					
Having regular respiratory infections (for example, bronchitis, pneumonia)	<input type="checkbox"/>					
Having a serious illness (for example, chest pain, vascular disorder, diabetes)	<input type="checkbox"/>					
Having reduced stamina	<input type="checkbox"/>					
Having emphysema (serious lung disease)	<input type="checkbox"/>					
Having a cough early in the morning	<input type="checkbox"/>					

**[PRI-P- Perceived Health Risk scale SCREEN 3/3]**

[CC smokers] **What do you think is the risk, if any, to you personally of getting the following (sometime during your lifetime) because you smoke cigarettes...**

[never CC smokers] **If you were to start smoking, what do you think would be the risk, if any, to you personally of getting the following (sometime during your lifetime) because you smoke cigarettes...**

[former CC smokers] **If you were to resume smoking, what do you think would be the risk, if any, to you personally of getting the following (sometime during your lifetime) because you smoke cigarettes...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Losing some sense of taste	<input type="checkbox"/>					
Having heart disease	<input type="checkbox"/>					
An earlier death	<input type="checkbox"/>					
Having sores of the mouth or throat	<input type="checkbox"/>					
Being physically unfit	<input type="checkbox"/>					
Having other types of cancer (besides mouth, throat, or lung)	<input type="checkbox"/>					

**[PRI-P- Perceived Harm to Others items]**

[CC smokers] **What do you think is the risk, if any, to others because you smoke cigarettes...**

[never CC smokers] **If you were to start smoking, what do you think would be the risk, if any, to others because you smoke cigarettes...**

[former CC smokers] **If you were to resume smoking, what do you think would be the risk, if any, to others because you smoke cigarettes...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Harming others through your second hand smoke	<input type="checkbox"/>					
Harming the unborn baby because you (the mother or the father) smoke cigarettes during pregnancy	<input type="checkbox"/>					

**[PRI-P- Perceived Addiction Risk scale]**

[CC smokers] **What do you think is the risk, if any, to you personally of experiencing the following because you smoke cigarettes...**

[never CC smokers] **If you were to start smoking, what do you think would be the risk, if any, to you personally of experiencing the following because you smoke cigarettes...**

[former CC smokers] **If you were to resume smoking, what do you think would be the risk, if any, to you personally of experiencing the following because you smoke cigarettes...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Being unable to quit cigarettes	<input type="checkbox"/>					
Feeling addicted to cigarettes	<input type="checkbox"/>					
Having to smoke cigarettes to feel better	<input type="checkbox"/>					
Feeling like you have to smoke cigarettes	<input type="checkbox"/>					
Feeling like you can't stop smoking cigarettes even through you know it is not good for you	<input type="checkbox"/>					
Feeling unable to quit cigarettes	<input type="checkbox"/>					

**PRI-P NRT**

*This survey asks for your views about the risks of using nicotine replacement therapy products (NRTs). After reading each question, select the answer that best reflects how you feel, keeping in mind that there are no right or wrong answers. Based on the information you have about NRTs, please answer all questions. If you are unsure about how to answer a question, give the best answer that you can.*

**[PRI-P- Perceived Health Risk scale SCREEN 1/3]**

**[CC smokers] If you were to stop smoking cigarettes and start using NRTs instead, what do you think is the risk, if any, to you personally of getting the following (sometime during your lifetime) because you use NRTs...**

**[former CC smokers] If you were to start using NRTs, what do you think would be the risk, if any, to you personally of getting the following (sometime during your lifetime) because you use NRTs...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Having a bad cough that lasts for days	<input type="checkbox"/>					
Having poor gum health	<input type="checkbox"/>					
Having lung cancer	<input type="checkbox"/>					
Occasional wheezing (difficult breathing that produces a sound)	<input type="checkbox"/>					
Having mouth or throat cancer	<input type="checkbox"/>					
Aging faster (for example, wrinkles on the face)	<input type="checkbox"/>					

**[PRI-P- Perceived Health Risk scale SCREEN 2/3]**

[CC smokers] **If you were to stop smoking cigarettes and start using NRTs instead, what do you think is the risk, if any, to you personally of getting the following (sometime during your lifetime) because you use NRTs...**

[former CC smokers] **If you were to start using NRTs, what do you think would be the risk, if any, to you personally of getting the following (sometime during your lifetime) because you use NRTs...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Being sick with frequent minor illnesses (for example, coughs and colds)	<input type="checkbox"/>					
Having regular respiratory infections (for example, bronchitis, pneumonia)	<input type="checkbox"/>					
Having a serious illness (for example, chest pain, vascular disorder, diabetes)	<input type="checkbox"/>					
Having reduced stamina	<input type="checkbox"/>					
Having emphysema (serious lung disease)	<input type="checkbox"/>					
Having a cough early in the morning	<input type="checkbox"/>					

**[PRI-P- Perceived Health Risk scale SCREEN 3/3]**

[CC smokers] **If you were to stop smoking cigarettes and start using NRTs instead, what do you think is the risk, if any, to you personally of getting the following (sometime during your lifetime) because you use NRTs...**

[former CC smokers] **If you were to start using NRTs, what do you think would be the risk, if any, to you personally of getting the following (sometime during your lifetime) because you use NRTs...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Losing some sense of taste	<input type="checkbox"/>					
Having heart disease	<input type="checkbox"/>					
An earlier death	<input type="checkbox"/>					
Having sores of the mouth or throat	<input type="checkbox"/>					
Being physically unfit	<input type="checkbox"/>					
Having other types of cancer (besides mouth, throat, or lung)	<input type="checkbox"/>					

**[PRI-P- Perceived Harm to Others items]**

[CC smokers] **If you were to stop smoking cigarettes and start using NRTs instead, what do you think is the risk, if any, to others because you use NRTs...**

[former CC smokers] **If you were to start using NRTs, what do you think would be the risk, if any, to others because you use NRTs...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Harming the unborn baby because you (the mother or the father) use NRTs during pregnancy	<input type="checkbox"/>					

**[PRI-P- Perceived Addiction Risk scale]**

[CC smokers] **If you were to stop smoking cigarettes and start using NRTs instead, what do you think is the risk, if any, to you personally of experiencing the following because you use NRTs...**

[former CC smokers] **If you were to start using NRTs, what do you think would be the risk, if any, to you personally of experiencing the following because you use NRTs...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Being unable to quit NRTs	<input type="checkbox"/>					
Feeling addicted to NRTs	<input type="checkbox"/>					
Having to use NRTs to feel better	<input type="checkbox"/>					
Feeling like you have to use NRTs	<input type="checkbox"/>					
Feeling like you can't stop using NRTs even through you know it is not good for you	<input type="checkbox"/>					
Feeling unable to quit NRTs	<input type="checkbox"/>					

**PRI-P RRP**

*This section asks for your views about **the risks of using <RRP>**. After reading each question, select the answer that best reflects how you feel, keeping in mind that there are no right or wrong answers. Based on the information you have read about <RRP> please answer all questions. If you are unsure about how to answer a question, give the best answer that you can.*

**[PRI-P- Perceived Health Risk scale SCREEN 1/3]**

[current RRP user] **What do you think is the risk, if any, to you personally of getting the following (sometime during your lifetime) because you use <RRP>...**

[non RRP user] **If you were to start using <RRP>, what do you think would be the risk, if any, to you personally of getting the following (sometime during your lifetime) because you use <RRP> ...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Having a bad cough that lasts for days	<input type="checkbox"/>					
Having poor gum health	<input type="checkbox"/>					
Having lung cancer	<input type="checkbox"/>					
Occasional wheezing (difficult breathing that produces a sound)	<input type="checkbox"/>					
Having mouth or throat cancer	<input type="checkbox"/>					
Aging faster (for example, wrinkles on the face)	<input type="checkbox"/>					

**[PRI-P- Perceived Health Risk scale SCREEN 2/3]**

[current RRP user] **What do you think is the risk, if any, to you personally of getting the following (sometime during your lifetime) because you use <RRP>...**

[non RRP user] **If you were to start using <RRP>, what do you think would be the risk, if any, to you personally of getting the following (sometime during your lifetime) because you use <RRP> ...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Being sick with frequent minor illnesses (for example, coughs and colds)	<input type="checkbox"/>					
Having regular respiratory infections (for example, bronchitis, pneumonia)	<input type="checkbox"/>					
Having a serious illness (for example, chest pain, vascular disorder, diabetes)	<input type="checkbox"/>					
Having reduced stamina	<input type="checkbox"/>					
Having emphysema (serious lung disease)	<input type="checkbox"/>					
Having a cough early in the morning	<input type="checkbox"/>					

**[PRI-P- Perceived Health Risk scale SCREEN 3/3]**

[current RRP user] **What do you think is the risk, if any, to you personally of getting the following (sometime during your lifetime) because you use <RRP>...**

[non RRP user] **If you were to start using <RRP>, what do you think would be the risk, if any, to you personally of getting the following (sometime during your lifetime) because you use <RRP> ...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Losing some sense of taste	<input type="checkbox"/>					
Having heart disease	<input type="checkbox"/>					
An earlier death	<input type="checkbox"/>					
Having sores of the mouth or throat	<input type="checkbox"/>					
Being physically unfit	<input type="checkbox"/>					
Having other types of cancer (besides mouth, throat, or lung)	<input type="checkbox"/>					

**[PRI-P- Perceived Harm to Others items]**

[current RRP user] **What do you think is the risk, if any, to others because you use <RRP>...**

[non RRP user] **If you were to start using <RRP>, what do you think would be the risk, if any, to others because you use <RRP> ...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Harming others through your second hand smoke	<input type="checkbox"/>					
Harming the unborn baby because you (the mother or the father) use <RRP> during pregnancy	<input type="checkbox"/>					

**[PRI-P- Perceived Addiction Risk scale]**

[current RRP user] **What do you think is the risk, if any, to you personally of experiencing the following because you use <RRP>...**

[non RRP user] **If you were to start using <RRP>, what do you think would be the risk, if any, to you personally of experiencing the following because you use <RRP> ...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Being unable to quit <RRP>	<input type="checkbox"/>					
Feeling addicted to <RRP>	<input type="checkbox"/>					
Having to use <RRP> to feel better	<input type="checkbox"/>					
Feeling like you have to use <RRP>	<input type="checkbox"/>					
Feeling like you can't stop using <RRP> even through you know it is not good for you	<input type="checkbox"/>					
Feeling unable to quit <RRP>	<input type="checkbox"/>					

**PRI-P CESSATION**

*This section asks for your views about the **risks that remain after having stopped smoking cigarettes**. After reading each question, select the answer that best reflects how you feel, keeping in mind that there are no right or wrong answers. Please answer all questions. If you are unsure about how to answer a question, give the best answer that you can.*

**[PRI-P- Perceived Health Risk scale SCREEN 1/3]**

[CC smokers] **If you were to successfully quit smoking, what do you think would be the risk, if any, to you personally of getting the following (sometime during your lifetime) because you smoked cigarettes in the past...**

[former CC smokers] **If you remain a former smoker, what do you think is the risk, if any, to you personally of getting the following (sometime during your lifetime) because you smoked cigarettes in the past...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Having a bad cough that lasts for days	<input type="checkbox"/>					
Having poor gum health	<input type="checkbox"/>					
Having lung cancer	<input type="checkbox"/>					
Occasional wheezing (difficult breathing that produces a sound)	<input type="checkbox"/>					
Having mouth or throat cancer	<input type="checkbox"/>					
Aging faster (for example, wrinkles on the face)	<input type="checkbox"/>					

**[PRI-P- Perceived Health Risk scale SCREEN 2/3]**

[CC smokers] **If you were to successfully quit smoking, what do you think would be the risk, if any, to you personally of getting the following (sometime during your lifetime) because you smoked cigarettes in the past...**

[former CC smokers] **If you remain a former smoker, what do you think is the risk, if any, to you personally of getting the following (sometime during your lifetime) because you smoked cigarettes in the past...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Being sick with frequent minor illnesses (for example, coughs and colds)	<input type="checkbox"/>					
Having regular respiratory infections (for example, bronchitis, pneumonia)	<input type="checkbox"/>					
Having a serious illness (for example, chest pain, vascular disorder, diabetes)	<input type="checkbox"/>					
Having reduced stamina	<input type="checkbox"/>					
Having emphysema (serious lung disease)	<input type="checkbox"/>					
Having a cough early in the morning	<input type="checkbox"/>					

**[PRI-P- Perceived Health Risk scale SCREEN 3/3]**

[CC smokers] **If you were to successfully quit smoking, what do you think would be the risk, if any, to you personally of getting the following (sometime during your lifetime) because you smoked cigarettes in the past...**

[former CC smokers] **If you remain a former smoker, what do you think is the risk, if any, to you personally of getting the following (sometime during your lifetime) because you smoked cigarettes in the past...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Losing some sense of taste	<input type="checkbox"/>					
Having heart disease	<input type="checkbox"/>					
An earlier death	<input type="checkbox"/>					
Having sores of the mouth or throat	<input type="checkbox"/>					
Being physically unfit	<input type="checkbox"/>					
Having other types of cancer (besides mouth, throat, or lung)	<input type="checkbox"/>					

**[PRI-P- Perceived Addiction Risk scale]**

[CC smokers] **If you were to successfully quit smoking, what do you think would be the risk, if any, to you personally of experiencing the following because you smoked cigarettes in the past...**

[former CC smokers] **If you remain a former smoker, what do you think is the risk, if any, to you personally of experiencing the following because you smoked cigarettes in the past...**

	No Risk	Low Risk	Moderate Risk	High Risk	Very High Risk	Don't Know
Still feeling addicted to cigarettes	<input type="checkbox"/>					
Having to smoke cigarettes to feel better	<input type="checkbox"/>					
Feeling like you have to smoke cigarettes	<input type="checkbox"/>					
Feeling anxiety when in a situation where people smoke	<input type="checkbox"/>					

## APPENDIX 7 – 3D IMAGES

**Study Name:** Quantitative Study to Develop VLN™ Hypothetical Product Messages Among U.S. Adult Cigarette Smokers, Adult Former Cigarette Smokers and Adult Never Cigarette Users

**Protocol Number:** 5180080-VLN™-B2

**Sponsor:** 22nd Century Group, Inc.  
8560 Main Street  
Williamsville, NY 14221

**Version Number:** 1.2

**Author:** (b) (6)

## APPENDIX 8 – REFERENCES

**Study Name:** Quantitative Study to Develop VLN™ Hypothetical Product Messages Among U.S. Adult Cigarette Smokers, Adult Former Cigarette Smokers and Adult Never Cigarette Users

**Protocol Number:** 5180080-VLN™-B2

**Sponsor:** 22nd Century Group, Inc.  
8560 Main Street  
Williamsville, NY 14221

**Version Number:** 1.2

**Author:** (b) (6)

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**APPENDIX 10 – PROTOCOL REVISIONS**

<b>Version</b>	<b>Date</b>	<b>Significant Revisions</b>