

# **Quantitative Study to Assess Perceptions of and Likelihood to Use ZYN® with Modified Risk Claims Among US Adults**

PROTOCOL SMNA 5240072

**Principal Investigator:**

(b) (4)

**Sponsor:**

**Swedish Match North America, LLC**

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## INVESTIGATOR SIGNATURE

**Principal Investigator:** I have read the protocol entitled “*Quantitative Study to Assess Perceptions of and Likelihood of Use ZYN® with Modified Risk Claims Among US Adults*” 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.

\_\_\_\_\_  
Name

\_\_\_\_\_  
(b) (4)

\_\_\_\_\_  
Date

## SPONSOR SIGNATURE

**Sponsor:** I have read the protocol entitled “*Quantitative Study to Assess Perceptions of and Likelihood of Use ZYN® with Modified Risk Claims Among US Adults*” 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.

\_\_\_\_\_  
Name

\_\_\_\_\_  
Swedish Match North America, LLC

\_\_\_\_\_  
Date

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## LIST OF ABBREVIATIONS

| Abbreviation | Definition   |
|--------------|--|
| AIAN         | American Indian/Alaska Native  |
| APPH         | Appropriate for the Protection of Public Health                            |
| CAPTCHA      | Completely Automated Public Turing Test to Tell Computers and Humans Apart |
| CC           | Conventional Cigarettes  |
| CFR          | Code of Federal Regulations  |
| CRO          | Contract Research Organization   |
| CTP          | Center for Tobacco Products  |
| EDC          | Electronic Data Capture  |
| ENDS         | Electronic Nicotine Delivery System  |
| FDA          | Food and Drug Administration   |
| HIPAA        | Health Insurance Portability and Accountability Act                        |
| ICF          | Informed Consent Form  |
| ID           | Identification   |
| IP           | Internet Protocol  |
| IPF          | Iterative Proportional Fitting   |
| IRB          | Institutional Review Board   |
| mg           | Milligrams   |
| ml           | Milliliters  |
| M RTP        | Modified Risk Tobacco Product  |
| MTSS         | Motivation to Stop Scale   |
| NHIS         | National Health Interview Survey   |
| NP           | Nicotine Pouch   |
| NRT          | Nicotine Replacement Therapy   |
| PATH         | Population Assessment of Tobacco and Health                                |
| PMTA         | Premarket Tobacco Product Application                                      |
| PI           | Principal Investigator   |
| PII          | Personally Identifiable Information  |

|      |                                  |
|------|----------------------------------|
| SMNA | Swedish Match North America, LLC |
| STP  | Smokeless Tobacco Products       |
| TNP  | Tobacco/Nicotine Product         |
| US   | United States                    |

## STATEMENT OF COMPLIANCE

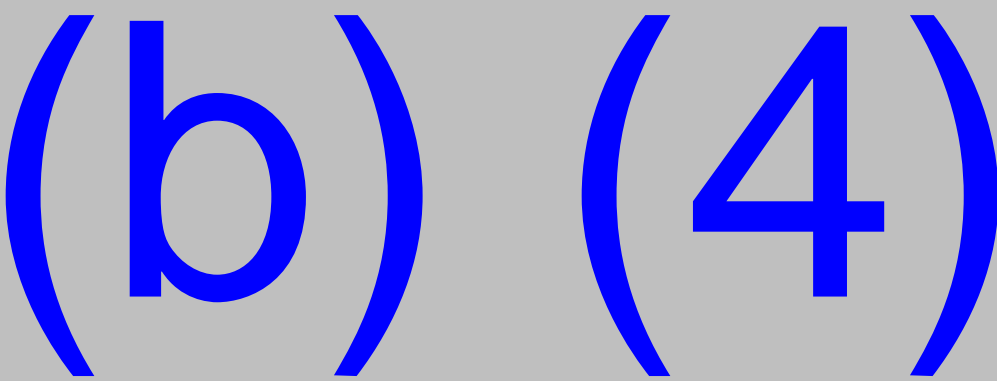
This study will be conducted in accordance with the specifications noted in the study protocol (PROTOCOL-ZYN® *Quantitative Study to Assess Perceptions of and Likelihood of Use ZYN(R) with Modified Risk Claims Among US Adults* Version 2.0, January 17, 2024); “*Quantitative Study to Assess Perceptions of and Likelihood of Use ZYN(R) with Modified Risk Claims Among US Adults*” and in accordance with The Insights Association’s Code of Standards and Ethics for Marketing Research and Data Analytics.

## STUDY SUMMARY

|                              |   |
|------------------------------|---|
| <b>Title of Study</b>        | Quantitative Study to Assess Perceptions of and Likelihood of Use ZYN® with Modified Risk Claims Among US Adults  |
| <b>Methodology</b>           | An internet-based cross-sectional study with stratified sampling of five (5) sub-populations defined according to self-reported tobacco / nicotine use at the time of data collection.  |
| <b>Study Purpose</b>         | The overall purpose of the Quantitative Study to Assess Perceptions of and Likelihood of Use ZYN® with Modified Risk Claims Among US Adults is to assess consumer reaction to the ZYN® product if marketed with the modified risk claims and how it compares to other in market TNP categories.   |
| <b>Study Site</b>            | This research will be conducted in the United States (US) as an online self-administered survey. It will be hosted by (b) (4) and fielded in English language only.   |
| <b>Products to be Tested</b> | <p>This <i>Quantitative Study to Assess Perceptions of and Likelihood of Use ZYN® with Modified Risk Claims Among US Adults</i> focuses on currently marketed candidate PMTA product, ZYN® (nicotine pouches), as available in market across the 10 varieties and 2 strengths plus the inclusion of modified risk claims.</p> <ol style="list-style-type: none"> <li>1. Chill</li> <li>2. Cinnamon</li> <li>3. Citrus</li> <li>4. Coffee</li> <li>5. Cool Mint</li> <li>6. Menthol</li> <li>7. Peppermint</li> <li>8. Smooth</li> <li>9. Spearmint</li> <li>10. Wintergreen</li> </ol>  |
| <b>Study Population</b>      | <p>The sampling frame includes adults (age 21+) living in the US. A total sample of 3,400 US adults (age 21+) will be interviewed, split equally ((b) (4)) between a Test (ZYN® specific to current varieties inclusive of modified risk claims) and Control (ZYN® specific to current varieties exclusive of modified risk claims)) cell. Respondents will be categorized into five primary respondent groups based on self-reported tobacco/nicotine product use:</p> <ul style="list-style-type: none"> <li>• Group 1 –Current Smokers <ul style="list-style-type: none"> <li>○ Intention to Quit in Next 12 Months</li> <li>○ No Intention to Quit in Next 12 Months</li> </ul> </li> </ul> |



|                       |  |
|-----------------------|--|
|                       | <ul style="list-style-type: none"> <li>Group 2 –Former Users/Other TNP Users (not CC or smokeless)</li> <li>Group 3 –Non-Established Users (b) (4)</li> <li>Group 4 – Non-Established Users (b) (4)</li> <li>Group 5 – Current Smokeless Users</li> </ul> <p>These groups will be analyzed individually and as part of the overall respondent pool to assess study outcomes.</p> <p>The sampling approach will involve, (1) group sample stratification and over-sampling where necessary and (2) post-stratification weighting will be applied to compensate for the stratification and ensure that the overall results mirror the populations specific to each group.</p>  |
| Objectives            | <p><b><u>Primary Objectives:</u></b></p> <ul style="list-style-type: none"> <li>Assess whether being exposed to the ZYN® product with modified risk claims impacts perceptions and likelihood to use ZYN® (overall in general and inclusive of varieties/ strengths), among all respondent groups.</li> <li>Assess how marketing of ZYN® Nicotine Pouches with modified risk claims would be appropriate for the protection of the public health (APPH) in terms of: <ul style="list-style-type: none"> <li>Generation of Intent to Use among Current Smokers and Current Smokeless Users</li> <li>No generation of significant Intent to Use among Never Users and Former Users/Other TNP Users</li> </ul> </li> <li>Assess current use of TNPs across all respondents, categorizing use status specific to never use, former use, and current use.</li> <li>Measure the understanding of ZYN® as presented during concept exposure.</li> </ul> <p><b><u>Secondary Objectives:</u></b></p> <ul style="list-style-type: none"> <li>Explore variation in perceptions of absolute risk associated with ZYN® and other types of TNPs (including categories of CCs, Vapor, Smokeless, Nicotine Pouches), across the specific health conditions (including 5 primary conditions of lung cancer, mouth cancer, throat cancer, emphysema, and heart disease).</li> <li>Explore variation in perceptions of relative risk of using ZYN® as opposed to: <ul style="list-style-type: none"> <li>Smoking cigarettes;</li> <li>Using other smokeless/ nicotine products;</li> <li>Using Electronic Nicotine Delivery Systems (ENDS);</li> <li>Using Nicotine Replacement Therapies (NRTs);</li> <li>Cessation of CC use;</li> <li>Cessation of all TNP use and using nothing.</li> </ul> </li> </ul> |
| Inclusion / Exclusion | <p><b><u>Inclusion criteria:</u></b></p> <ol style="list-style-type: none"> <li>Currently residing in the US</li> </ol>  |

|                        |  |
|------------------------|--|
| <p><b>Criteria</b></p> | <ol style="list-style-type: none"> <li>2. Legal-Age (21 years of age and above)</li> <li>3. Able and willing to comply with all study requirements</li> <li>4. Provided informed consent</li> </ol> <p><b><u>Exclusion criteria:</u></b></p> <ol style="list-style-type: none"> <li>1. Under legal age of purchase (21 years of age)</li> <li>2. Participated in a market research survey about tobacco products in the past 3 months</li> <li>3. Employees of or household member employed in manufacturing, sales or distribution TNPs, advertising / marketing, market research, healthcare, legal field, or news and media, to minimize bias and to protect any proprietary product information that will be disclosed in the survey</li> <li>4. Have started smoking within the last 30 days or started using a smokeless tobacco/nicotine product within the last 30 days</li> <li>5. Employed in any of the following fields or professions: market research, marketing, advertising, media or journalism, law, or manufacturers or distributors of TNPs</li> </ol> |
| <p><b>Design</b></p>   | <p>The impact of the ZYN<sup>®</sup> product profile will be assessed via repeated measures analysis and independent measures across defined TNP user groups.</p> <p>This study is planned to include randomized assignment to one of two product exposure cells. In the study, each cell represents a distinct product concept where participants are assigned to evaluate the ZYN<sup>®</sup> test (ZYN<sup>®</sup> specific to current varieties inclusive of modified risk claims) or control (ZYN<sup>®</sup> specific to current varieties exclusive of modified risk claims).</p> <p>The hypotheses of this study, which correspond with the research objectives are:</p> <div style="text-align: center; background-color: #cccccc; padding: 20px;">  </div>   |

AMENDMENTS AND UPDATES

| Version | Date | Section | Description | Rationale |
|---------|------|---------|-------------|-----------|
|         |      |         |             |           |
|         |      |         |             |           |

## 1 RESPONSIBLE PARTIES

**Sponsor:**

**Swedish Match North America, LLC**

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Richmond, VA 23219

**Contract Research Organization:**

(b) (4)

**Principal Investigator:**

(b) (4)

## 2 BACKGROUND AND RATIONALE

The Family Smoking Prevention and Tobacco Control Act, signed into law in 2009, gave the FDA the power to regulate the tobacco industry and established the Center for Tobacco Products (CTP) within the FDA. The law gives the CTP authority to regulate marketing/ advertising content and sale of TNPs. The FDA requires that the marketing of a new tobacco product is appropriate for the protection of the public health as determined “on the basis of well-controlled investigations” (section 910)<sup>1</sup>.

The CTP has provided draft guidance on data for human studies designed to evaluate the risks and benefits to the population as a whole, including users and non-users of TNPs. Essentially, CTP requires research-based evidenced that: (1) Existing TNP users do not increase consumption; (2) Non-TNP users do not start using; (3) Former TNP users do not re-start using. Products marketed in the US after February 15, 2007 must obtain a marketing authorization through a Premarket Tobacco Product Application (PMTA) or a Modified Risk Tobacco Product Application (MRPTA) inclusive of modified risk claims. A product cannot be sold in the US without a marketing authorization.

Swedish Match North America, LLC (SMNA) officially began selling ZYN® in 2014. ZYN® delivers tobacco-derived nicotine (does not contain tobacco leaves) via a small pouch, containing flavoring elements and food-grade ingredients for shelf-stability. SMNA markets ZYN® as a nicotine delivery product which is smoke-free, is spitless, tobacco-leaf free, and comes in multiple varieties and nicotine strengths. SMNA filed a PMTA for ZYN® on March 4, 2020 and is awaiting approval.

Additionally Swedish Match is exploring including modified risk claims for ZYN®, specific to the product as currently in-market.

This *Quantitative Study to Assess Perceptions of and Likelihood of Use ZYN® with Modified Risk Claims Among US Adults* focuses on currently marketed candidate PMTA product, ZYN® (nicotine pouches), as available in market across the 10 varieties and 2 strengths.

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<sup>1</sup> US Department of Health and Human Services, Food and Drug Administration, Center for Tobacco Products. Applications for Premarket Review of New Tobacco Products: Draft Guidance Sept-2011.

### 3 OVERVIEW AND OBJECTIVES

#### 3.1 DESIGN OVERVIEW AND HYPOTHESES

The overall purpose of the *Quantitative Study to Assess Perceptions of and Likelihood of Use ZYN® with Modified Risk Claims Among US Adults* is to evaluate how exposure to the ZYN® product description (including description/ varieties/ strengths) inclusive of modified risk claims compares to other in market TNP categories.

The impact of the ZYN® product profile will be assessed via repeated measures analysis and independent measures across defined TNP user groups.

This study is planned to include randomized assignment to one of two product exposure cells. In the study, each cell represents a distinct product concept where participants are assigned to evaluate the ZYN® test (specific to current varieties inclusive of modified risk claims) or control (specific to current varieties inclusive of modified risk claims). The details of the concepts for each cell are described in Appendix 2 (Test Cell) and Appendix 3 (Control Cell).

The hypotheses of this study, which correspond with the research objectives (described in Section 3.2), are:

(b) (4)

Figure 1 gives an overview of study design and procedures, which are covered in more detail in Section 3 and Section 4.

Figure 1. Research Design Overview.

(b) (4)

### 3.2 OBJECTIVE(S)

The primary objectives of this study are:

1. Assess whether being exposed to the ZYN® product description with modified risk claims impacts perceptions and likelihood to use ZYN® (overall in general and inclusive of varieties/ strengths), among all respondents:
  - a. Current likelihood to initiate on in-market TNPs including the branded ZYN® product.
  - b. Future likelihood to initiate based on exposure to the ZYN® product generally (brand name plus general shelf set) versus detailed ZYN® product/ varieties/ strengths description (product description, varieties/ strengths labeling, and shelf set) inclusive of modified risk claims.
  - c. Comparison by age, (b) (4) in self-reported likelihood to start using tobacco/ nicotine products.
2. Assess current use of TNPs across all respondents, categorizing use status specific to never use, former use, and current use.
  - a. Establish current use status in the context of CCs, Smokeless, and other types of products.
  - b. Current intention to quit current TNPs used
    - i. Impact of exposure to ZYN® self-reported intention to quit current TNP used (quit intention before/ after exposure to ZYN®).
3. Measure the understanding that ZYN® as presented during concept exposure, specific to:
  - a. Containing nicotine
  - b. Is not risk free
  - c. Available in both 3mg and 6mg nicotine strengths
  - d. For adult use only

The secondary objectives of this study are:

1. Explore variation in perceptions of absolute risk associated with ZYN® and other types of TNPs (including categories of CCs, ENDS, Smokeless, Nicotine Pouches), across the specific health conditions of (including 5 primary conditions of lung cancer, mouth cancer, throat cancer, emphysema, and heart disease):

(b) (4)



2. Explore variation in perceptions of relative risk of using ZYN® as opposed to:
- a. Smoking cigarettes;

b. Using other smokeless/ nicotine products;

c. Never using any TNP;

d. Quitting all TNPs and using nothing.

3.3 STUDY SAMPLING

Within each of the five (5) respondent groups, and for each cell, there will be a representative number of respondents for gender/age, race/ethnicity and geography based on the National Health Interview Survey (NHIS) 2022 survey:

1. Gender / Age

For each cell there will be a representative number of respondents from each of the following age categories, within gender, based on the NHIS 2022 survey:

(b) (4)

2. Ethnicity/ Race

There will be a representative distribution by Ethnicity and Race based on the NHIS 2022 survey.

3. Geography

There will be a representative distribution by Census Region based on the NHIS 2022 survey.

Potential respondents for this study will be recruited into the study from an online non-probability-based opt-in panel aggregator. Each contact 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 application. After screening for eligibility and establishment of TNP use status, respondents will provide consent prior to moving on to the remainder of the survey. Respondents will then be assigned to one of the two cells following a least-filled method to ensure representative distribution of the full (b) (4) respondents per cell across TNP usage and demographic criteria.

Table 1 shows the estimated representation per cell across relevant analytic groups (b) (4)

The sample design will be focused on the primary analytic groups. These primary analytic groups are defined in mutually exclusive

terms, so any single respondent will only be referenced as associated with a single primary group.

Table 1. Sampling Plan by TNP Usage (per cell).

(b) (4)

There are no specific targets among sub-designations (For example, AIAN current smokeless users) of interest, the demographic representation is expected to fall naturally across primary groups and sub-designations.

### 3.4 INCLUSION CRITERIA & STRATIFICATION

The study will be based on a sample that will be as representative of the Adult US population, 21 years of age or older, as possible. The sample will be stratified by TNP use status and demographic criteria.

(b) (4)

For example, participants will be screened for:

5. Currently residing in the US
6. Legal-Age (21 years of age and above)
7. Able and willing to comply with all study requirements
8. Provided informed consent

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

1. Number of cigarettes ever smoked (>100 Cigarettes)
2. Prior usage of any other type of TNPs
3. Gender, race / ethnicity, and US Census Region to ensure representation consistent with the market
4. Intention to Quit smoking within the next 12 months
5. Use of Smokeless

### 3.5 EXCLUSION CRITERIA

1. Under legal age of purchase (21 years of age)
2. Participated in a market research survey about tobacco products in the past 3 months
3. Employees of or household member employed in manufacturing, sales or distribution of TNPs, advertising / marketing, market research, healthcare, legal field, or news and media, to minimize bias and to protect any proprietary product information that will be disclosed in the survey
4. Have started smoking within the last 30 days or started using a smokeless tobacco/nicotine product within the last 30 days
5. Employed in any of the following fields or professions: market research, marketing, advertising, media or journalism, law, or manufacturers or distributors of TNPs

## 4 PROCEDURES AND ASSESSMENTS

### 4.1 RECRUITMENT

Respondents will be recruited through (b) (4)

Each participant will be provided a unique, anonymous link for participation in the study and no personally identifiable information (PII) about any respondent will be provided by the respondents or panel company. All respondents will be screened for demographic and tobacco/ nicotine product use status.

It is anticipated that fielding will occur in 2024 from late January through February .

### 4.2 SCREENING

Potential respondents 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 questions around inclusion / exclusion criteria and smoking status, potential respondents will be presented via an online ICF for review/ agreement.

Respondents will then be screened based on the inclusion and exclusion criteria. The screening process will assess TNP use status, gender/ age, ethnicity/ race, and US Census Region. The survey will programmatically determine which cell each respondent is eligible for based on TNP use status, gender/age, ethnicity/ race, and US Census Region quota availability within each cell. Respondents will be assigned to one of the two cells depending on which cell is least-filled.

Eligible respondents who fit the requirements of the sampling plan, pass the screening, and agree to informed consent will proceed to the full survey. Non-eligible participant's interviews will be immediately terminated. They will see a "Thank You" note with a redirect designated by the panel company. Potential respondents who do not qualify to participate due to non-qualification or closed quotas may be compensated a nominal amount that is in line with US market research industry and each independent panel's standards.

### 4.3 INFORMED CONSENT

The informed consent process in this survey will be documented using an ICF presented online for review and agreement to participate.

The ICF will explain the nature of the survey and all procedures and risks will be explained in a form understandable to respondents. Prospective respondents will be given the option to participate or not, and is free to terminate participation in the survey at any time without reason.

### 4.4 SURVEY FLOW AND MEASUREMENTS

(b) (4)

(b) (4)

Cognitive testing of the survey instrument will occur prior to fielding. This will consist of (b) (4) one-on-one interviews (conducted using a web conference interface), (b) (4)

(b) (4)

to assess understanding and answerability of each question, as well as ensure the respondent accurately comprehends what is being asked.

#### 4.5 Survey Length

The survey length is expected to be approximately 20 minutes for each respondent; this will be specified in the ICF.

#### 4.6 WITHDRAWAL FROM RESEARCH

As noted in the ICF, respondents may cease and withdraw from the research at any time of the individual's choosing without penalty or loss of benefits. Respondents may do so by closing their web browser or application.

### 5 STATISTICAL CONSIDERATIONS

#### 5.1 HYPOTHESES AND DATA ANALYSIS

The purpose of this study is to measure responses to the ZYN® (test) and ZYN® (control) within populations of (1) Current Smokers, (2) Former Users/ Other TNP Users (not CC or Smokeless), (3) Never Users, and (4) Current Smokeless Users. (b) (4)

#### Primary Objectives:

- Assess perceptions of ZYN® (overall)
- Assess Intent to Buy ZYN®
- Assess Intent to Use each of ZYN® varieties and nicotine strengths among Current Smokers, Former Users/Other TNP Users (Not CC or Smokeless), Never Users, and Current Smokeless Users
- Assess how marketing of ZYN® would be appropriate for the protection of the public health (APPH):
  - Generation of Intent to Use among Current Smokers and Current STP/ NP Users
  - No generation of significant Intent to Use among Never Users and Former Smokers

## **Secondary Objectives:**

- Comprehension check of the product label and labeling among primary respondent groups and any sub-designations
- Assess perceptions of the health and addiction risks associated with use of ZYN® among the primary respondent groups and sub-designations
- Evaluate Intention to Quit pre- and post-exposure among current TNP users
- Assess perceptions of the health and addiction risks associated with the use of each of the six (6) comparator categories of product use and cessation in each of the primary respondent groups and any sub-designations:
  - CCs
  - ENDS
  - STPs or NPs
  - NRTs
  - Cessation of CC use
  - Cessation of any TNP use
- Assess Intent to Use ZYN® and four (4) comparator categories of product use (descriptions shown in the appendix) among each of the primary respondent groups and any sub-designations:
  - CCs
  - ENDS
  - STPs/ NPs
  - NRTs

## **5.2 REPORTING AND ANALYSIS GROUPS**

All participants must satisfy all inclusion and exclusion criteria to fully complete the survey.

The groups for reporting will include the primary respondent groups and any sub-designations:

- Current Smokers
  - Current Smokers with Intention to Quit in Next 12 Months
  - Current Smokers with No Intention to Quit in Next 12 Months
  - Exclusive CC Users
- Former Users/Other TNP Users (Not CC or Smokeless)
- Never Users (b) (4)
- Current STP/ NP Users

(b) (4)



### 5.3 METHOD

#### **General Principles**

The number of respondents in each respondent group as well as the count and proportion of respondents 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 respondent 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 respondents in each respondent group with non-missing score values will serve as the total base for each respondent 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), SAS® statistical software (Version 9.4) and / or Quantum tabulation software.

#### **Demographics and Respondent Characteristics**

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

#### **Respondent Disposition**

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

### 5.4 ANALYSIS OF OBJECTIVES

#### **Intent to Use ZYN® and Comparator Categories**

Descriptive statistics and 95% confidence intervals of the proportion of responses for each comparator category will be presented by respondent group within each cell separately for the items related to Intention to Use. Intention to Use for each cell and comparator categories will be assessed both pre- and post-exposure to the ZYN® (test) / ZYN® (control) to understand any change in intention for future product usage would be influenced by exposure to these products.

#### **Risk Perception**

Risk perceptions will be presented to participants in three groups of attributes including: (1) Risk of Exposure / Tobacco-Related Diseases, (2) Risk of Addiction, and (3) Risk of Harm to Others. Response data will be presented in descriptive statistics and 95% confidence intervals of the proportion of responses. Risk perceptions will be offered by respondent group; ZYN® (test) / ZYN® (control) will be compared to the six (6) comparator categories directly.

## Comprehension Check

(b) (4)

### 5.5 MISSING DATA

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

### 5.6 SAMPLE SIZE

To ensure measurement precision across all objectives on both an unweighted and weighted basis, a sample size, within each of the primary respondent groups, including TNP use status, age, gender, race / ethnicity, and US Census Region was calculated to result in (b) (4) completed interviews per cell. As outlined in Table 1, 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, race / ethnicity, and US Census Region will be used to ensure completed interviews across subgroups within each cell and smoking-status group is sufficient for statistical testing.

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

There are no specific targets among sub-designations of interest and the demographic representation is expected fall naturally within sub-designations. These estimates are based on patterns of tobacco/nicotine use found in previous tobacco/nicotine product perceptions research, among US adults, conducted by (b) (4) (b) (4)

## 6 SUPPORTING DOCUMENTATION

The contract research organization (CRO) and Principal Investigator (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.

## 7 ETHICS / PROTECTION OF HUMAN SUBJECTS

### 7.1 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 21 CFR Part 50 and any additional human subject protections as determined necessary.

### 7.2 INSTITUTIONAL REVIEW BOARD

In accordance with applicable human subjects research regulations, the protocol, ICF, respondent recruitment materials, and any other written information provided to respondents will be reviewed and approved by Advarra Review IRB. The Investigator is responsible for submitting all such documents to the IRB for review and approval. The Investigator must also submit any other information that the IRB may request for review and approval. Verification of the IRB unconditional approval of the protocol and the written ICF statement will be transmitted to the Investigator. Approval of both the protocol and ICF must be obtained before the study commences and any participant is enrolled. The Investigator will maintain all IRB-approved documents in the study file. Copies of the IRB response/approval and all other IRB-approved documents will be provided to the Sponsor.

The IRB will be informed of any subsequent protocol amendments and of events that meet reportable event criteria. Approval for protocol amendments will be transmitted in writing to the Investigator.

The IRB to which study materials will be submitted is:

(b) (4)

The IRB will be provided with progress reports at appropriate intervals (not to exceed 1 year) and a Study Progress Report following the completion, termination, or discontinuation of the Investigator's participation in the study.

### 7.3 CONSENT PROCEDURES AND DOCUMENTATION

Description of risks and possible benefits of participation will be provided to the respondents in the informed consent. Respondents will be asked to review the informed consent information carefully and, at the end of the form, will be asked if they agree to participate in the survey. The respondent will electronically indicate their consent. A selection of "No" will immediately terminate the respondent 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.

Respondents 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.

#### 7.4 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 PMTA (or two years after formal discontinuation of development of the PMTA). Study participant data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at ZYN®. 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 ZYN®.

## 8 DATA HANDLING AND RECORD KEEPING

### 8.1 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 CRO 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.

The panels are reflective of the US population and are sizeable enough to ensure it is a reliable representation of the US Online population.

Steps taken to ensure quality include, but are not limited to:

- Use of proxy detection with detects registrant's true IP address and past fraudulent activity;
- IP geofencing which detects the registrant's location via her/ his IP address and determines her/ his eligibility for registration bases on location-specific rules;
- CAPTCHA technology which prevents automated programs from joining our site through challenge-response tests.

In addition, registrants; zip/ postal code are verified against relevant geography of data collection. Each computer is also tagged with a unique ID to ensure only one respondent per computer can participate in the survey. The ID would block survey respondents who attempt to complete the same survey from multiple panels and those who attempt to take a survey multiple times using different identities.

## 8.2 STUDY RECORDS RETENTION

Study documents should be retained for a minimum of 5 years after the authorization of a PMTA or until at least 2 years have elapsed since the formal discontinuation of development of the PMTA. 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.

## 8.3 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.

## 8.4 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 a PMTA for ZYN®. Any publications arising from this work will report data in aggregate form and will not include any personally identifying information.

# 9 CONFLICT OF INTEREST POLICY

(b) (4) is consulting firm focused on consumer research providing qualitative and quantitative research services to clients including design, fielding, analysis, and reporting. This work was funded by ZYN®, a company that is dedicated to the marketing and distribution of ZYN® products.

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## APPENDIX 1 – SURVEY INSTRUMENT

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INFORMED CONSENT STATEMENT

INVESTIGATOR:

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You are being invited to take part in a research survey which will take approximately 20 minutes. Taking part in this research is voluntary. Whether you take part is up to you. You can choose not to take part or agree to take part and later change your mind. There will be no penalty or loss of benefits to which you are otherwise entitled.

The purpose of this research is to gather perceptions about tobacco products. You will be asked to complete a survey now.

If you take part in this research, you will be responsible to answer questions as honestly as you can. There are no known risks to completing this research survey. Participation will not cost you anything.

There are no benefits to you if you take part in this research. We cannot promise any benefits to others if you take part in this research. However, possible benefits to others include an improved understanding of tobacco products. Your alternative is to not take part in the research.

Your private information and your medical history will not be collected. The answers to this survey may be shared with individuals and organizations that conduct or watch over this research, including:

- The research sponsor
- People who work with the research sponsor
- Government agencies, such as the Food and Drug Administration

We may publish the results of this research. However, we will not collect your name or other identifying information. We protect your information from disclosure to others to the extent required by law. We cannot promise complete secrecy.

If you have questions, concerns, or complaints, contact the research team at (b) (4) (b) (4) ). Ask to speak to (b) (6) 1.

By proceeding to the next screen, you confirm that you have read, understand, and accept the points above and are consenting to participate in this study.

Yes, I agree [CONTINUE]

No, I do not agree [TERMINATE]

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2

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S32)

[END OF SCREENER]

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## APPENDIX 2 – ZYN® SHELF SET AND MODIFIED RISK CONCEPT IMAGES – TEST CELL



**WARNING: This product contains nicotine.**  
Nicotine is an addictive chemical.

**ZYN**  
NICOTINE POUCHES

AVAILABLE IN  
10 VARIETIES &  
2 STRENGTHS

**3mg** | **6mg**

**SMOKE-FREE**

**SPIT-FREE**

**HANDS-FREE**

**ZYN** (Tobacco) | **ZYN** (Menthol) | **ZYN** (Tobacco) | **ZYN** (Tobacco) | **ZYN** (Tobacco)  
**ZYN** (Tobacco) | **ZYN** (Tobacco) | **ZYN** (Tobacco) | **ZYN** (Tobacco) | **ZYN** (Tobacco)

**FIND YOUR ZYN at [ZYN.com](https://www.zyn.com)**

**USING ZYN INSTEAD OF CIGARETTES PUTS YOU AT A LOWER RISK OF MOUTH CANCER, HEART DISEASE, LUNG CANCER, STROKE, EMPHYSEMA, AND CHRONIC BRONCHITIS.**

### APPENDIX 3 - ZYN® SHELF SET AND CONCEPT (CONTROL CELL)



**WARNING: This product contains nicotine.  
Nicotine is an addictive chemical.**

# ZYN

NICOTINE POUCHES

AVAILABLE IN  
10 VARIETIES &  
2 STRENGTHS

**3mg** | **6mg**

**SMOKE-FREE**

**SPIT-FREE**

**HANDS-FREE**

**FIND YOUR ZYN at [ZYN.com](http://ZYN.com)**

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