

Swedish Match North America

Protocol for Observational Study

ZYN® Likelihood of Use Study

(b) (4)

Status: Approved

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Prepared by: (b) (4)

Confidentiality Statement

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2. LIST OF ABBREVIATIONS

| | |
|--------------------|--|
| CAPTCHA | Completely Automated Public Turing Test To Tell Computers and Humans Apart |
| CASRO | Council of American Survey Research Organizations |
| CTP | Center for Tobacco Products |
| FDA | Food and Drug Administration |
| FTP | File Transfer Protocol |
| IP | Internet Protocol |
| IRB | Institutional Review Board |
| MRTP | Modified Risk Tobacco Product |
| MTSS | Motivation to Stop Scale |
| NCHS | National Center for Health Statistics |
| NON-USERS | Never and Former users of tobacco/nicotine products |
| OMB | Office of Management and Budget |
| PATH | Population Assessment of Tobacco and Health |
| PII | Personally Identifiable Information |
| PMTA | Premarket Tobacco Product Application |
| RESPONDENTS | Total sample which includes current, never, and former users of tobacco/nicotine products |
| SAP | Statistical Analysis Plan |
| SMNA | Swedish Match North America |
| TNP | Tobacco/Nicotine Products, including cigarettes, e-cigarettes, moist snuff, chewing tobacco, snus, nicotine pouches, cigars, cigarillos, and filtered cigars filled with tobacco, pipe tobacco, hookah and water pipe tobacco, and aids to help stop smoking |
| U.S. | United States |

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3. RESPONSIBLE PARTIES

3.1. Investigator(s) and Contributors

Investigator:

(b) (4), (b) (6)

(b) (4)

Project Team:

(b) (4), (b) (6)

3.2. Sponsor

Swedish Match North America

(b) (4), (b) (6)

4. SYNOPSIS

| | |
|---|------------------------------|
| Title | ZYN® Likelihood Of Use Study |
| Protocol version identifier | Version 1.0, Amendment 2 |
| Date of last version of protocol | November 16, 2017 |
| Protocol number | (b) (4) |
| Author | (b) (4), (b) (6) |

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| Rationale and background | <p>Swedish Match North America (SMNA) began selling ZYN[®] in 2014. ZYN[®] delivers nicotine derived from tobacco, but the ZYN[®] product itself does not contain tobacco leaves. It comes in a small pouch that contains nicotine flavoring elements and other ingredients required to ensure shelf stability. SMNA has no current intention of marketing ZYN[®] as a smoking cessation product, but rather as a nicotine-delivery product that requires no spitting, produces no off-putting odors, is smoke-free, and comes in a variety of flavors and nicotine strengths. The output of this research will be submitted to the FDA as part of the ZYN[®] PMTA.</p> |
| Research question and objective | <p>The overarching research questions within the ZYN[®] Likelihood of Use Study can be stated as follows: <i>(i) How does the exposure to a ZYN[®] description and package label affect intentions, behaviors, and perceptions of TNP users and TNP non-users, when compared pre- to post-exposure, and (ii) how does exposure to a ZYN[®] description and packaging label have a different impact on intentions, behaviors, and perceptions across TNP user and TNP non-user groups?</i> These questions will be evaluated by way of an observational study with a pre-/post-exposure design. No formal hypotheses are specified for the ZYN[®] Likelihood of Use Study.</p> <p>These questions will be studied among both TNP users and non-users (all of whom are of legal age to use TNP in their residential geography). The primary intent of the survey will be to have respondents evaluate a single description and packaging label for ZYN[®] to elicit intention to change TNP behavior, perceptions of health risk associated with TNP, and the appeal of the product. Respondents will be shown the description and packaging label.</p> <p>The description will provide a picture of the canister, details about the product, such as smoke-free, spit-free, tobacco leaf-free, and a general description of the contents of each pouch. Additionally, the description provides instructions on use, strengths and flavors available, as well as the required warning that nicotine is addictive chemical (see Attachment 1).</p> <p>Respondents will also be exposed to a schematic of the label for the top, bottom, and side of the canister for ZYN[®]. The packaging label will provide the flavor, strength, number of pouches in the canister, and the nicotine warning statement on the top; description of contents, strength, flavor, best-before date, bar code, and customer call number/company identifier on the bottom; and the nicotine warning statement, flavor, strength, and number of pouches in canister along the side (see Attachment 2).</p> <p>The primary objectives of this study are:</p> |

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| | <ol style="list-style-type: none"> 1. Among all respondents, assess whether being exposed to a ZYN[®] description and packaging label impacts perceptions and intentions related to the use of TNP. <ol style="list-style-type: none"> i. Among TNP never-users legal age to 24, TNP never-users older than 24, and former TNP users evaluate: <ul style="list-style-type: none"> - Current likelihood to initiate or reinstate TNP based on intention to buy TNP - Future likelihood to initiate or reinstate TNP based on intention to buy ZYN[®] after being exposed to a ZYN[®] description and packaging label ii. Among cigarette smokers with intent to quit, cigarette smokers without intent to quit, and current tobacco users (excluding cigarettes) evaluate: <ul style="list-style-type: none"> - Current use of TNP - Future intention to buy ZYN[®] after being exposed to a ZYN[®] description and packaging label - Future intention to use current TNP after being exposed to a ZYN[®] description and packaging label iii. Among cigarette smokers with intent to quit, cigarette smokers without intent to quit, and current tobacco users (excluding cigarettes) evaluate: <ul style="list-style-type: none"> - Current intention to quit use of TNP - Future intention to quit use of TNP after being exposed to a ZYN[®] description and packaging label 2. Among all respondents, measure the appeal of various ZYN[®] brand and product attributes after being exposed to a ZYN[®] description and packaging label. Attributes include: <ol style="list-style-type: none"> i. Overall look and feel; ii. Variety of flavors; iii. Product design; iv. Physical product; v. Child-safety lid. <p>The secondary objectives of this study are:</p> <ol style="list-style-type: none"> 1. Among all respondent cohorts, explore variation in perceptions of absolute risk associated with never having used any TNP, smoking cigarettes, and using ZYN[®]. |
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| | <p>i. Measurement of absolute risk of non-usage and smoking to occur prior to showing respondents the ZYN[®] description and packaging label.</p> <p>ii. Measurement of absolute risk of ZYN[®] to occur after showing respondents the ZYN[®] description and packaging label.</p> <p>The health conditions under consideration when considering absolute risk are:</p> <ul style="list-style-type: none"> - Adult tooth loss - Gum disease - Mouth cancer - Serious health problems <p>2. Among all respondent cohorts, explore variation in perceptions of <u>relative</u> risk of using ZYN[®] as opposed to:</p> <ul style="list-style-type: none"> i. Using other tobacco products; ii. Using aids to help stop smoking; iii. Quitting all TNP; and iv. Never using any TNP. <p>All measurements of relative risk will be collected after respondents are exposed to the ZYN[®] description and packaging label.</p> <p>The health conditions under consideration when considering relative risk are:</p> <ul style="list-style-type: none"> - Adult tooth loss - Gum disease - Mouth cancer - Serious health problems |
| Study design | <p>The ZYN[®] Likelihood of Use Study consists of a pre-/post-exposure, repeated measures study design. Study participants will be exposed to the ZYN[®] description and packaging label, which will provide a picture of the canister and a schematic of the label for the top, bottom, and side of the canister. The ZYN[®] description and packaging label will indicate product information, including instructions on use, strengths, number of pouches in canister, and flavors, as well as the required warning that nicotine is an addictive chemical.</p> <p>Cognitive interviews will be conducted prior to launching the web-based survey to determine any potential problems with how consumers</p> |

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| | understand, interpret, and answer each survey question, including questions or response options which may be confusing or misinterpreted. |
| Population | <p>The survey will be administered to (b) (4) U.S. consumers who meet all of the following criteria:</p> <ul style="list-style-type: none"> • Minimum legal age for TNP use per local state requirements • Able to read and speak English • Currently a resident of the United States • Provide electronic informed consent <p>Individuals who meet any of the following criteria will be excluded:</p> <ul style="list-style-type: none"> • Respond as “don’t know” or “decline to answer” to specific demographics (gender, geographical region, ethnicity, or education), used for balancing cohorts. • Unwilling or unable to provide electronic informed consent • Employed in any of the following fields or professions: market research, marketing, advertising, manufacturers of TNP, or physicians • Taken part in a consumer research study on tobacco in the past 2 weeks <p>Please see Data Sources below for more detail about where the sample is sourced.</p> |
| Variables | The primary intent of the survey will be to have respondents evaluate a single description and packaging label for ZYN® to elicit intention to change TNP behavior, perceptions of health risk associated with TNP, and the appeal of the product. Respondents will be shown the description and packaging label. |
| Data sources | <p>Consumers will initially be recruited from verified online consumer panels, including Lightspeed Research Panel, Survey Sampling International, and Research Now. As verified panels, these are large commercial consumer panels that profile panelists on self-reported characteristics such as age, gender, location, income, ethnicity, household size, marital status, presence of young children, and education.</p> <p>Based on panelist self-reported background information, a representative sample reflecting socio-demographic characteristics of the adult population based on U.S. Census data will be selected from these panels reflecting the marginal distribution of age, gender, geographical region, ethnicity, race, and education. Next, a sampling frame consisting of all legal age panelists from each state will be created. The invited sample will</p> |

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| | <p>then be derived from a stratified sampling framework based on socio-demographic characteristics of the adult population from the Population Assessment of Tobacco and Health (PATH) study data².</p> <p>Like the socio-demographic variables, panel source will also be balanced across cohorts through sample assignments, daily monitoring, and sample management, as well as extended duration of fielding. Although perfect balance is the goal with panel source, as with the socio-demographic variables, perfect balance is unlikely achievable in the recruitment for this study and will be discussed in the Limitations (Section 8.9).</p> <p>To ensure successful oversampling of key segments, an organization named (b) (4) will work with additional partners. Specifically, (b) (4) will be utilized for the current cigarette smokers with intention to quit from legal age to 24 years of age cohort. (b) (4) is an aggregator resource, with the ability to leverage sample from different sources, such as Branded Research Inc., for Good, P2, and Prodege. These sources recruit from social networks, targeted environments and websites, advertisement campaigns, reward companies, such as Swagbucks.com, to recruit hard-to-reach quota groups, especially younger age groups.</p> |
| Study size | <p>(b) (4) consumers will be recruited, (b) (4) from each of the following seven cohorts:</p> <ul style="list-style-type: none"> • Never tobacco users from legal age to 24 years of age • Never tobacco users older than 24 years of age • Former tobacco users from legal age and older • Current cigarette smokers <u>with</u> intent to quit from legal age to 24 years of age • Current cigarette smokers <u>with</u> intent to quit older than 24 years of age • Current cigarette smokers <u>without</u> intent to quit, legal age and older • Current tobacco users (excluding cigarettes) from legal age and older |

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| Data analysis | <p>Cognitive interviews will be conducted prior to launching the web-based surveys. The series of individual comments obtained in the cognitive interviews, pertaining to separate questions across multiple interviews, will be compiled into a coherent set of summary findings that transcend the individual interview level. In-depth analysis will include looking for themes that indicate that respondents have issues with comprehension, retrieval, decision-judgment, and response for questions in the survey.¹³ The results will then be compiled to determine which changes to the survey instrument are necessary for greater content validity.</p> <p>Descriptive statistics for accomplishing primary objectives will be reported for current intention to buy TNP, future intention to buy ZYN®, current use of TNP, future intention to use TNP, current and future intention to quit TNP, and appeal of ZYN® brand and product attributes. Descriptive statistics will include the number of non-missing observations, frequencies, percentages, and 95% CIs for the percentage of respondents endorsing each category for categorical variables.</p> <p>Descriptive statistics for accomplishing secondary objectives will be reported for absolute risk outcomes, and relative risk outcomes. Descriptive statistics will include the number of non-missing observations, frequencies, percentages, and 95% CIs for the percentage of respondents endorsing each category for categorical variables.</p> | | | | |
| Milestones | <table> <tr> <td>Start of data collection</td><td>December 2017</td></tr> <tr> <td>End of data collection</td><td>February 2018</td></tr> </table> | Start of data collection | December 2017 | End of data collection | February 2018 |
| Start of data collection | December 2017 | | | | |
| End of data collection | February 2018 | | | | |

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5. AMENDMENTS AND UPDATES

| Number | Date | Section of study protocol | Amendment or update | Reason |
|--------|------------|---------------------------|---------------------|--|
| 1 | 11/16/2017 | Throughout | Amendment | Changes based on initial Center of Tobacco Products (CTP) feedback on different MRTP protocol |
| 2 | 5/28/18 | Throughout | Amendment | Changes based on new information and additional background obtained from: <ul style="list-style-type: none"> • January 24-25, 2018 Tobacco Products Scientific Advisory Committee Meeting • Public availability of Camel Snus/RJ Reynolds Tobacco Company MRTP application |
| ... | | | | |

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6. BACKGROUND AND RATIONALE

In 2009, the Family Smoking Prevention and Tobacco Control Act was signed into law, giving the FDA the power to regulate the tobacco industry and establishing the Center for Tobacco Products (CTP) within the FDA. This law gives the CTP authority to regulate the marketing/advertising content and sale of tobacco/nicotine products (TNP). The FDA requires that the marketing of a new tobacco product be appropriate for the protection of the public health as determined “on the basis of well-controlled investigations” (Section 910).¹

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 the tobacco product.¹ In making this evaluation the FDA will assess the product under review and take into account (1) the increased or decreased likelihood that existing users of tobacco products will stop using such products; and (2) the increased or decreased likelihood that those who do not use tobacco products will start using such products.¹ This evidence must be submitted for all currently marketed products as part of a premarket tobacco product application (PMTA). Products marketed in the U.S. after February 15, 2007 must obtain a marketing authorization from the FDA (i.e., through a premarket tobacco product application [PMTA] application or a Substantial Equivalence [SE] report) or they can no longer be sold in the U.S.¹

Swedish Match North America (SMNA) began selling ZYN[®] in 2014. ZYN[®] delivers nicotine derived from tobacco, but the ZYN[®] product itself does not contain tobacco leaves. It comes in a small pouch that contains nicotine flavoring elements and other ingredients required to ensure shelf stability. SMNA has no current intention of marketing ZYN[®] as a smoking cessation product, but rather as a nicotine-delivery product that requires no spitting, produces no off-putting odors, is smoke-free, and comes in a variety of flavors and nicotine strengths. As a result of the Tobacco Control Act requirements, SMNA must submit a PMTA to continue marketing the ZYN[®] product. The output of this research will be submitted to the FDA as part of the ZYN[®] PMTA.

7. OBJECTIVES AND HYPOTHESES

The overarching research questions within the ZYN[®] Likelihood of Use Study can be stated as follows: *(i) How does the exposure to a ZYN[®] description and package label affect intentions, behaviors, and perceptions of TNP users and TNP non-users, when compared pre- to post-exposure, and (ii) how does exposure to a ZYN[®] description and packaging label have a different impact on intentions, behaviors, and perceptions across TNP user and TNP non-user groups?* These questions will be evaluated by way of an observational study with a pre-/post-exposure design. No formal hypotheses are specified for the ZYN[®] Likelihood of Use Study.

7.1. Primary Objectives:

1. Among all respondents, assess whether being exposed to a ZYN[®] description and packaging label impacts perceptions and intentions related to the use of TNP.

- i. Among TNP never-users legal age to 24, TNP never-users older than 24, and former TNP users evaluate:
 - Current likelihood to initiate or reinitiate^a TNP based on intention to buy TNP.
 - Future likelihood to initiate or reinitiate TNP based on intention to buy ZYN® after being exposed to a ZYN® description and packaging label.
 - ii. Among cigarette smokers with intent to quit, cigarette smokers without intent to quit, and current tobacco users (excluding cigarettes) evaluate:
 - Current use of TNP.
 - Future intention to buy ZYN® after being exposed to a ZYN® description and packaging label.
 - Future intention to use current TNP after being exposed to a ZYN® description and packaging label.
 - iii. Among cigarette smokers with intent to quit, cigarette smokers without intent to quit, and current tobacco users (excluding cigarettes) evaluate:
 - Current intention to quit use of TNP.
 - Future intention to quit use of TNP after being exposed to a ZYN® description and packaging label.
2. Among all respondents, measure the appeal of various ZYN® brand and product attributes after being exposed to a ZYN® description and packaging label. Attributes include:
- i. Overall look and feel;
 - ii. Variety of flavors;
 - iii. Product design;
 - iv. Physical product;
 - v. Child-safety lid.

^a The term “initiate” refers to entering the category of TNP user and is only pertinent to TNP never, i.e., those not currently using TNP. Similarly, the term “re-initiate” is only pertinent to TNP former users.

7.2. Secondary Objectives:

1. Among all respondent cohorts, explore variation in perceptions of absolute risk associated with never having used any TNP, smoking cigarettes, and using ZYN®.
 - i. Measurement of absolute risk of non-usage and smoking to occur prior to showing respondents the ZYN® description and packaging label.
 - ii. Measurement of absolute risk of ZYN® to occur after showing respondents the ZYN® description and packaging label.

The health conditions under consideration when considering absolute risk are:

- Adult tooth loss
 - Gum disease
 - Mouth cancer
 - Serious health problems
2. Among all respondent cohorts, explore variation in perceptions of relative risk of using ZYN® as opposed to:
 - iii. Using other tobacco products;
 - iv. Using aids to help stop smoking;
 - v. Quitting all TNP; and
 - vi. Never using any TNP.

All measurements of relative risk will be collected after respondents are exposed to the ZYN® description and packaging label.

The health conditions under consideration when considering relative risk are:

- Adult tooth loss
- Gum disease
- Mouth cancer
- Serious health problems

8. RESEARCH METHODS

8.1. Data Source

Data for the ZYN® Likelihood of Use Study will be obtained using responses from a customized web-based survey of invited consumers who meet inclusion and exclusion criteria (explained in [Section 8.5.1](#) and [Section 8.5.2](#)) and who agree to participate. Consumers will initially be recruited from verified online consumer panels Lightspeed Research Panel, Survey Sampling International, and Research Now. These are large commercial consumer panels profile their panelists on self-reported characteristics such as age, gender, location, income, ethnicity, household size, marital status, presence of young children, and education. The panels are reflective of the U.S. population; however, they are not balanced to the U.S. census. They are sizeable enough to generate ending samples that are representative of the U.S. population. This ensures that our sample source is a reliable representation of the U.S. online population.

The online panels are opt-in panels where consumers who join make a conscious decision to participate regularly in surveys. Several methodologies, such as email, e-newsletter campaigns, banner placement, partnerships, direct mail, etc. are used by the panel companies to recruit panelists. Potential panelists are asked to complete an in-depth registration profile which includes numerous logic checks to ensure quality. Steps taken to ensure quality include, but are not limited to:

- Use of proxy detection which detects a proxy server used to mask the registrant's true IP address and past fraudulent activity;
- IP GeoFencing which detects the registrant's location via his/her IP address and determines his/ her eligibility for registration based on location-specific rules;
- CAPTCHA technology which prevents automated programs from joining our site through challenge-response tests; and
- Email address verification which queries our database to ensure the email address is unique (all registrants must verify their email addresses through a double opt-in registration process).

In addition, registrants' postal address and zip/postal code are verified against a current local address directory. Each computer is also tagged with a unique ID to ensure only one respondent per computer can participate in a survey. This 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. Extensive analysis is conducted to understand and measure panelist activity. These analyses include the following: recruitment source, panel composition, longevity on panel, response, participation and dropout rate, and response quality.

The panel member details are maintained in confidence and are used purely for research purposes only. No information that could personally identify the respondent can be released, nor can personal information be sought from the panelists or about the panelists without their prior knowledge and consent.

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Based on panelist self-reported background information, a representative sample reflecting socio-demographic characteristics of the adult population based on U.S. Census data will be selected from these panels reflecting the marginal distribution of age, gender, geographical region, ethnicity, race, and education. Next, a sampling frame consisting of all legal age panelists from each state will be created. The invited sample will then be derived from a stratified sampling framework based on socio-demographic characteristics of the adult population from the Population Assessment of Tobacco and Health (PATH) study data². Panelists with required demographic profiles will be randomly selected for inclusion in the invited sample until demographic profile quotas are met in each study cohort. This recruitment methodology is expected to provide socio-demographic profiles consistent with the adult population based on PATH study data for each of the study cohorts.

Online panel sampling tools will be used to generate traffic to the survey, based on the targeted demographics and considering expected response rates for the different demographic strata. During the fieldwork, sample performance will be monitored daily; analysis of response rates and qualifying rates will be done for each demographic quota within cohorts. The panels will utilize manual monitoring and dynamic automated tools to ensure that the sampling process results in the desired demographic quotas. As quota targets are achieved, the random sample selection process will be refined to target only panelists matching those demographic characteristics whose quotas have not yet been reached.

Like the socio-demographic variables, panel source will also be balanced across cohorts through sample assignments, daily monitoring, and sample management, as well as extended duration of fielding. Although perfect balance is the goal with panel source, as with the socio-demographic variables, perfect balance is unlikely achievable in the recruitment for this study and will be discussed in the Limitations (Section 8.9).

To ensure successful oversampling of key segments, an organization named (b) (4) will work with additional partners. Specifically, (b) (4) will be utilized for the current cigarette smokers with intention to quit from legal age to 24 years of age cohort. (b) (4) is an aggregator resource, with the ability to leverage sample from different sources, such as Branded Research Inc., for Good, P2, and Prodege. These sources recruit from social networks, targeted environments and websites, advertisement campaigns, reward companies, such as Swagbucks.com, to recruit hard-to-reach quota groups, especially younger age groups. All partners, like the online panels, have automated and manual sample quality assurance measures. The Limitations section (Section 8.9) will provide some further detail on the challenges associated with acquiring sample for this difficult cohort.

Prior to launching the study in full, (b) (4) will execute a soft launch. The primary objective of the soft launch process is to confirm that all facets of the data collection process function according to protocol; items of specific interest include the initial incidence rate, the length of interview, and the accuracy of the web-based instrument (i.e., survey), all of which work to ensure the primary objectives of the research are met. Soft launch data will be used as part of the final data set, unless quality control checks suggest an error or unintended issue that may have

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compromised the data. In that event, the data will be saved but not included in the final data set. The soft launch will account for no greater than 10% of the total sample.

Once the accuracy of the web-based instrument is verified through soft launch, the study will be fully launched with invitations being sent to a broader number of potential respondents. Potential respondents will receive their invitations from their respective panels to participate in the survey. To be clear that the study is relevant for all consumers, the invitation will specify that the opinions of both users and non-users of TNP will be important. The email will include the following: (1) general invitation; and (2) a link to the panelist welcome page. Approximately 2 to 4 days after the initial invitation, non-responders will be sent an e-mail reminder regarding the availability of the survey. New invitations will be sent until the target sample size is reached. Panelists previously invited will still be able to participate if their desired quota is not reached.

If invited panelists are interested in participation, they click on the link at the bottom of the invitation or copy and paste the link into their browser. The link takes respondents to the panelist welcome page where they are presented with another link to the screener followed by the statement of informed consent for this study. The informed consent advises potential respondents that participation is voluntary and that responses will remain confidential. It also includes information about the goals of the study, the approximate length of the survey, and compensation for participation. Lastly, the statement of informed consent provides potential respondents with the contact information for panel managers to address any concerns they may have.

If potential respondents agree to participate in the study after reading the statement of informed consent, they will select “I agree to participate” and will then be taken to the survey instrument. Those who select “I do not agree to participate” will be thanked before exiting.

Respondents will be able to complete the online survey via computer, tablet, or smartphone. Following the completion of the survey by each of the respondents, a debriefing statement will be shown to clarify that the intent of the survey was not to market, sell or promote any tobacco or nicotine product, and that no products will be offered in exchange for survey completion. Respondents who complete the survey will receive compensation, typically reward points or currency offered by the panel of which they are a member, which are of fair market value for their time.

8.2. Study Design

Qualitative cognitive interviews will precede quantitative data collection. These cognitive interviews will walk through key components of the survey instrument to assess interpretation of each question by respondents. See [Section 8.3](#) for more details about cognitive interviews.

The ZYN® Likelihood of Use Study consists of a pre-/post-exposure, repeated measures study design. Study participants will be exposed to the ZYN® description and packaging label, which will provide a picture of the canister and a schematic of the label for the top, bottom, and side of the canister. The ZYN® description and packaging label will indicate product information, including instructions on use, strengths, number of pouches in canister, and flavors, as well as the required warning that nicotine is an addictive chemical.

8.3. Cognitive Interviews

Cognitive interviews will be conducted prior to executing the quantitative phase of the Likelihood of Use Study. The cognitive interviews will be conducted in accordance with the Office of Management and Budget (OMB) Statistical Policy Directive No. 2 Addendum: Standards and Guidelines for Cognitive Interviews.³ Cognitive interviewing is used as a means for applying qualitative research methods to the understanding of the functioning of survey questions.⁴ The premise of this approach is that intensive interviewing of a single individual provides rich information that is useful for providing the questionnaire designer with information concerning how questionnaires and individual survey questions, provide (or fail to provide) desired information.

The cognitive interviewing approach, used to evaluate sources of response error in survey questionnaires, has been tested and is used by the National Center for Health Statistics (NCHS) Centers for Disease Control and Prevention.⁵ The cognitive assessments will determine any potential problems with how consumers understand, interpret, and answer each survey question, including questions or response options which may be confusing or misinterpreted. It will also provide input into the clarity, understandability, and interpretation of the patterns of TNP use.

To ensure that the materials are appropriate and sufficiently clear to consumers, the Likelihood of Use online survey will be piloted among 24 respondents defined by the cohorts established for this study, across two rounds of qualitative in-depth, in-person, interviews. The second round of cognitive interviews will take place a week after the initial round of interviews to allow for revisions between rounds. We anticipate reaching saturation and not requiring additional rounds of cognitive testing; however, if saturation is not met, additional rounds of testing may be required.

The study team will collaboratively develop an interview guide around the survey instrument to standardize each interview with the purpose of collecting information with respect to the content validity of the instrument. As outlined by the guideline, the interview guide will “contain the questions to be evaluated along with interviewer instructions, such as follow-up probe questions.” The purpose of the questions are to “to measure the processes by which a respondent interprets and responds to a question.”

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Recruitment of respondents will be a convenience sample. However, the cognitive testing sample will be recruited to best represent the population of interest including age, gender, race/ethnicity, education, and tobacco/nicotine use behavior. Recruitment will be done by (b) (4) at a local level, utilizing their databases of consumers. Panel members will be contacted via email with a link to the screener. The email would include a general introduction to the availability of a new study, those interested would complete an online screener for qualification based on cohorts as well as all the inclusion and exclusion criteria (see [Section 8.5.1](#) and [Section 8.5.2](#)). The screener will also include an introduction explaining the purpose and scope of the study. Once qualified, consumers will indicate interest and the field agency will schedule the in-person interview.

Table 1: Cognitive Interview Sample Plan by Cohort

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8.4. Study Population

The study population consists of U.S. population of legal age for TNP use. To meet the objectives of the Likelihood of Use Study, the research will include respondents from the following cohorts:

| | |
|------------------------------------|---|
| <p>Never tobacco users</p> | <ul style="list-style-type: none"> • Have NEVER used the following products: <ul style="list-style-type: none"> ▪ Cigarettes ▪ E-cigarettes ▪ Cigars, cigarillos, filtered cigars ▪ Pipe filled with tobacco ▪ Nicotine pouches ▪ Hookah or water pipe filled with tobacco ▪ Smokeless tobacco (snus pouches, moist snuff, dip, or chewing tobacco) • OR ALL of the following: <ul style="list-style-type: none"> ▪ Smoked fewer than 100 cigarettes during their lifetime AND now do not smoke every day or some days AND ▪ For each of the following products, have never been a regular user AND now do not use the product every day or some days: <ul style="list-style-type: none"> - E-cigarettes - Cigars, cigarillos, filtered cigars - Pipe filled with tobacco - Nicotine pouches - Hookah or water pipe filled with tobacco - Smokeless tobacco (snus pouches, moist snuff, dip, or chewing tobacco) |
| <p>Former tobacco users</p> | <ul style="list-style-type: none"> • Have smoked 100 or more cigarettes during lifetime AND currently do not smoke cigarettes every day or some days <p>AND/OR</p> <ul style="list-style-type: none"> • For any of the following products, have been a regular user BUT now do not use every day or some days: <ul style="list-style-type: none"> ▪ E-cigarettes ▪ Cigars, cigarillos, filtered cigars ▪ Pipe filled with tobacco ▪ Nicotine pouches ▪ Hookah or water pipe filled with tobacco ▪ Smokeless tobacco (snus pouches, moist snuff, dip, or chewing tobacco) |

(b) (4)

| | |
|---|---|
| Current cigarette smokers <u>with</u> intention to quit | <ul style="list-style-type: none"> • Have smoked 100 or more cigarettes during lifetime AND • Currently smoke cigarettes every day or some days AND • Have intention to quit (score 5-7 on the Motivation to Stop Scale [MTSS]⁶) |
| Current cigarette smokers <u>without</u> intention to quit | <ul style="list-style-type: none"> • Have smoked 100 or more cigarettes during lifetime AND • Currently smoke cigarettes every day or some days AND • Have no intention to quit (score of 1-4 on MTSS⁶) |
| Current tobacco users (excluding cigarettes) | <ul style="list-style-type: none"> • For any of the following products, have been a regular user AND now uses the product every day or some days: <ul style="list-style-type: none"> ▪ E-cigarettes ▪ Cigars, cigarillos, filtered cigars ▪ Pipe filled with tobacco ▪ Nicotine pouches ▪ Hookah or water pipe filled with tobacco ▪ Smokeless tobacco (snus pouches, moist snuff, dip, or chewing tobacco) <p>AND</p> <ul style="list-style-type: none"> • Have smoked cigarettes during lifetime (fewer than 100 <u>or</u> 100 or more in lifetime) AND currently do not smoke cigarettes every day or some days <p>OR have never smoked</p> |

(b) (4)

8.5. Sample Size

A precision analysis was used to inform the sample sizes for all cohorts of interest, with the purpose of ensuring that study samples allow for robust evaluation of the objectives. The precision analysis was performed under the following assumptions: a confidence interval of 95% ($\alpha=.05$), a standard deviation of 3.74,^b a small interval half-width, and a probability of achieving the desired precision of .99.

The precision analysis suggested a sample size of (b) (4) per cohort would be appropriate. In total, the planned study sample is (b) (4), with (b) (4) respondents in each cohort. Table 2 presents the sample size for each cohort, along with the percent of sample per cohort, and the estimated percent of the adult population that each cohort represents based on PATH estimates.² In compliance with the CTP's guidance regarding intended use and risk assessment in vulnerable populations, this study will oversample the young adult population among never users and current cigarette smokers, specifically people who fall between the legal age for tobacco use in their states, to age 24.⁷ The age breaks are based on those used in PATH.²

Table 2: Proposed Sample Size

(b) (4)

^b The standard deviation used in these power calculations are taken from data provided by Swedish Match, "A market research report (January 2017)" which uses the Juster Scale to measure purchase intentions for moist snuff. The standard deviation is an average of the 3 standard deviations taken from Question #9, 13, and 17.

Figure 1: Respondent Identification Flowchart



8.5.1. Subject Selection: Inclusion Criteria

In addition to the cohorts to be included in this study, respondents must meet the following criteria to be included:

- Minimum legal age per local requirements
- Able to read and speak English
- Currently a resident of the United States
- Individuals who provide electronic informed consent

8.5.2. Subject Selection: Exclusion Criteria

Respondents who meet any of the following criteria will be excluded:

- Respond as “don’t know” or “decline to answer” to specific demographics (gender, geographical region, ethnicity, or education), used for balancing cohorts
- Unwilling or unable to provide electronic informed consent
- Employed in any of the following fields or professions: market research, marketing, advertising, manufacturers of TNP, or physicians
- Have taken part in a consumer research study on tobacco in the past 2 weeks

8.6. Variables

8.6.1. Exposure

The length of interview for this survey instrument is estimated to be 15-20 minutes. Respondents will be able to complete the online survey via computer, tablet, or smartphone.

The primary intent of the survey will be to have respondents evaluate a single description and packaging label for ZYN® to elicit intention to change TNP behavior, perceptions of health risk

(b) (4)

associated with TNP, and the appeal of the product. Respondents will be shown the description and packaging label.

The description will provide a picture of the canister, details about the product, such as smoke-free, spit-free, tobacco leaf-free, and a general description of the contents of each pouch. Additionally, the description provides instructions on use, strengths and flavors available, as well as the required warning that nicotine is addictive chemical (see [Attachment 1](#)).

Respondents will also be exposed to a schematic of the label for the top, bottom, and side of the canister for ZYN®. The packaging label will provide the flavor, strength, number of pouches in the canister, and the nicotine warning statement on the top; description of contents, strength, flavor, best-before date, bar code, and customer call number/company identifier on the bottom; and the nicotine warning statement, flavor, strength, and number of pouches in canister along the side (see [Attachment 2](#)).

8.6.2. Outcomes

Pre-exposure outcomes that will be used to evaluate the primary objectives are as follows:

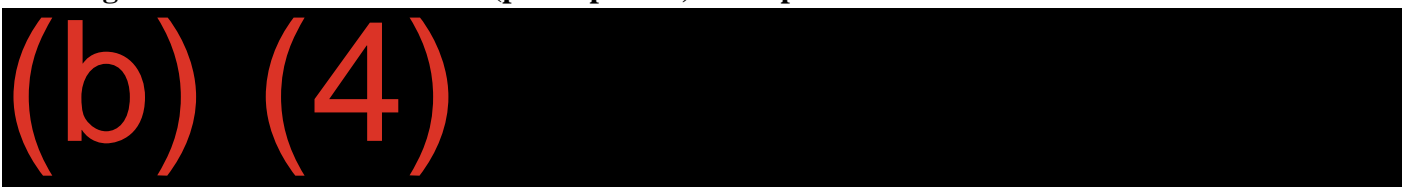
Current intention to buy TNP will be assessed with the 11-point Juster Scale, one survey item per TNP type. The Juster Scale is a probability scale that can be used to produce estimates of the average probability that a population will perform a certain behavior by a future time.⁸ As the Juster Scale measures probability, the mean response predicts the proportion of the population that will perform the behavior.⁹ Research has shown that the Juster Scale is effective in predicting consumers' future purchasing behaviors.¹⁰ See Figure 2 for an example.

Figure 2: Current Intention to Buy TNP (pre-exposure) Example

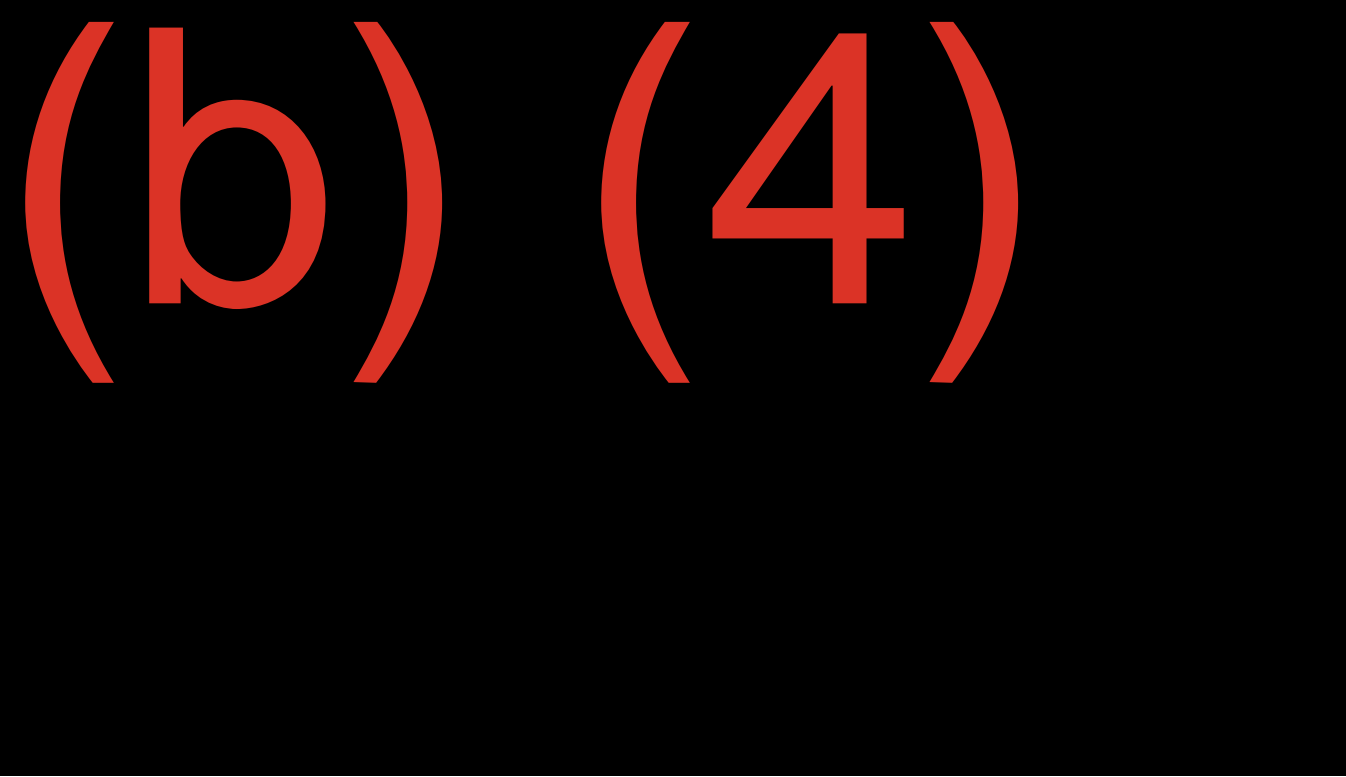


Current use of TNP will be assessed by measuring present frequency of use for each TNP, utilizing one survey item per TNP type. This approach mimics methodology measuring current TNP use employed in PATH.² Response options for frequency of use include “Every day,” “Some days,” “Not at all,” “Don’t know” and “Decline to answer.” See Figure 3 for an example.

Figure 3: Current Use of TNP (pre-exposure) Example



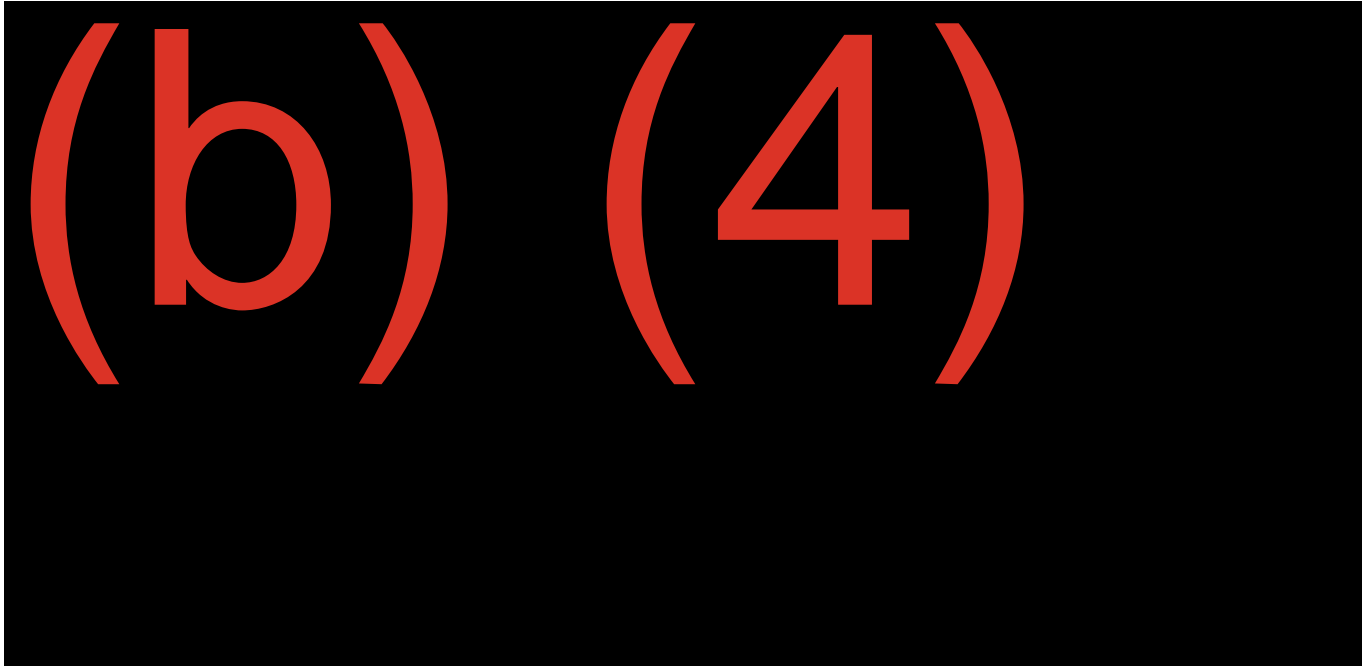
(b) (4)



Current intention to quit TNP will be measured by the one-item validated instrument, MTSS.⁶ The MTSS consists of one item with seven response options ranging from 1 (lowest level of motivation to stop smoking), also including “Don’t know.” Scale developers found that odds of quit attempts increased linearly with increasing levels of motivation. In the current study, we use the MTSS both for assessing intention to quit cigarettes and for other TNPs. Consistent with published research using the MTSS, we will report the mean MTSS score.¹¹ See [Figure 4](#) for an example.

(b) (4)

Figure 4: Current Intention to Quit TNP (MTSS; pre-exposure)



Pre-exposure outcomes that will be used to evaluate the secondary objectives are as follows:

Pre-exposure perceptions of absolute health risk of non-usage and smoking will be assessed using one item (5-point Likert scale; from 1= Very low chance to 5= Very high chance, also including “Don’t know” and “Decline to answer”) for each of four health conditions (adult tooth loss, gum disease, mouth cancer, and serious health problems). This scale was modified from the risk perception scale in HINTS.¹² The 5-point Likert scale used in HINTS had response options where 1= Much less harmful to 5= Much more harmful; we changed the response options to fit with the structure of the question in the survey. See Figure 5 for an example.

Figure 5: Perceptions of Absolute Health Risk (pre-exposure) Example



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8.6.2.1 Post-exposure to ZYN®

Note that for all questions following the review of the ZYN® description and packaging label, respondents will be able to click a link to review the description and label again, if needed.

Outcomes captured post-exposure to ZYN® that will be used to evaluate the primary objectives are as follows:

Future intention to buy ZYN® will be assessed post-exposure to the ZYN® description and packaging label via the 11-point Juster Scale. The Juster Scale is explained in more detail under “Current intention to buy TNP” above. See Figure 6 for an example.

Figure 6: Future Intention to Buy ZYN® (post-exposure) Example

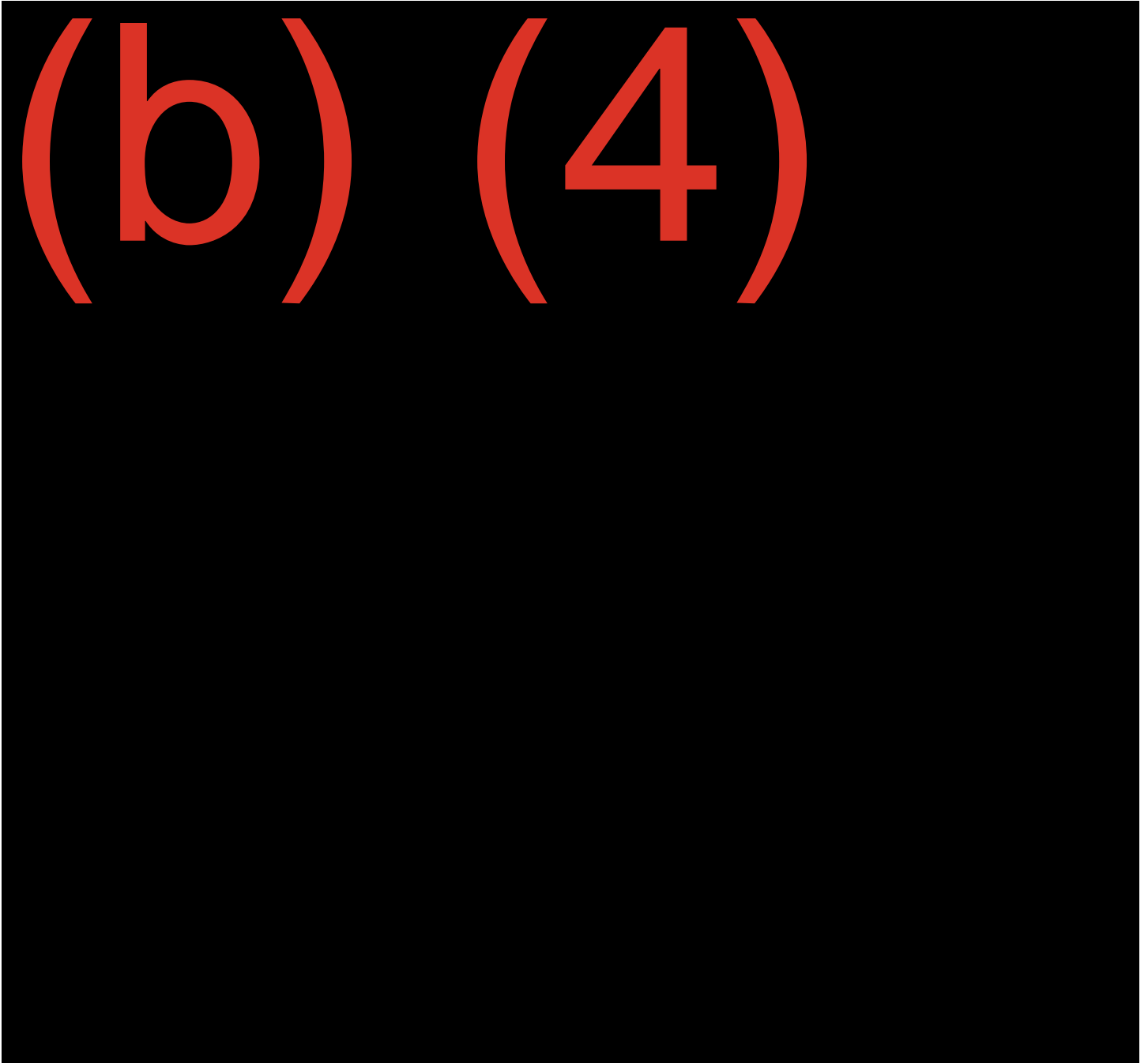
For all questions following the review of the ZYN® description and packaging label, respondents will be able to click a link to be able to review the description and label again, if needed.

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Future intention to use TNP will be assessed post-exposure to the ZYN® description and packaging label using a custom, single-item 4-point ordinal scale for each TNP currently used. Response options for the item will include “Quit completely,” “Cut back use,” “Use the same amount” and “Use more”; “Don’t know” and “Decline to answer” will be available as answer options outside of the scale. See [Figure 7](#) for an example.

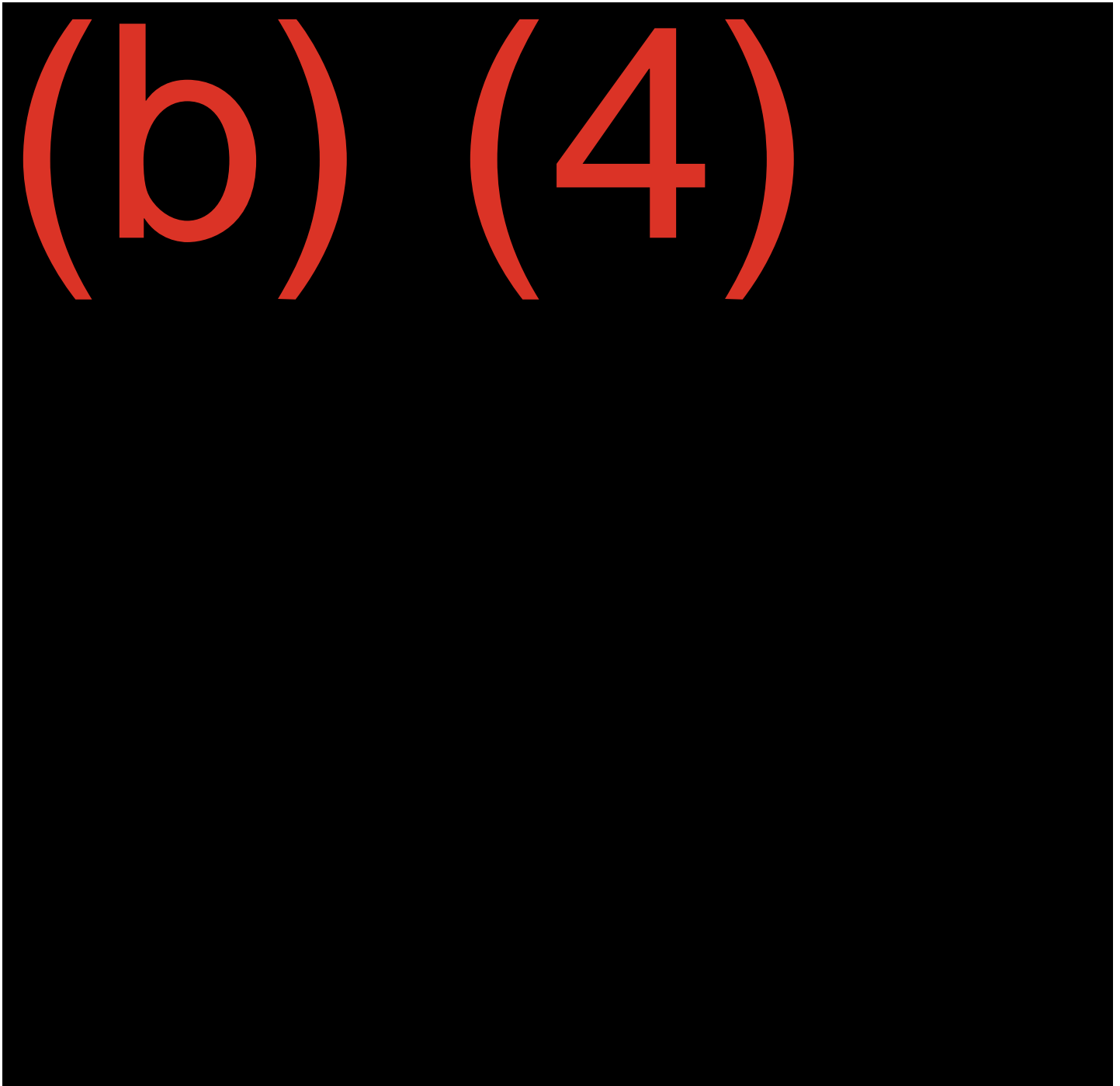
(b) (4)

Figure 7: Future Intention to Use TNP (post-exposure) Example



(b) (4)

Figure 8: Future Intention to Quit TNP (MTSS; post-exposure)



Post-exposure outcomes that will be used to evaluate the secondary objectives are as follows:

Perceptions of absolute health risk of the daily use of only ZYN® and no other TNP will be assessed using one item (5-point Likert scale; from 1= Very low chance to 5= Very high chance, also including “Don’t know” and “Decline to answer”) for each of four health conditions (adult

(b) (4)

tooth loss, gum disease, mouth cancer, and serious health problems). This scale was modified from the risk perception scale in HINTS.¹² The 5-point Likert scale used in HINTS had response options where 1= much less harmful to 5= much more harmful; we changed the response options to fit with the structure of the question in the survey. See Figure 10 for an example.

Figure 10: Perceptions of Absolute Health Risk of Daily Use of Only ZYN® (post-exposure) Example



Perceptions of relative health risk will be assessed using one item (5-point Likert scale; from 1= A much lower chance to 5= A much higher chance, also including “Don’t know” and “Decline to answer”) for each of the four health conditions (adult tooth loss, gum disease, mouth cancer, and serious health problems). In this battery, respondents will evaluate ZYN® use against several other risk exposures. The risk exposures to be assessed for each health condition include use of ZYN® versus: the daily use of other TNP, aids to help stop smoking, never having used any TNPs, and quitting all TNP relative to quitting all TNP except for ZYN®. This scale was modified from the risk perception scale used in HINTS.¹² The 5-point Likert scale used in HINTS had response options where 1= Much less harmful to 5= Much more harmful; we changed the response options to fit with the structure of the question in the survey. See Figure 11 for an example.

Figure 11: Perceptions of Relative Health Risk (post-exposure) Example



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(b) (4)



8.6.3. Potential Confounders

As discussed in Data Sources, [Section 8.1](#), the sampling approach will ideally mitigate potential confounding factors. Nevertheless, confounding variables may include respondent demographics (age, gender, ethnicity, education, and geographic region), frequency of tobacco use, current tobacco products used, intentions to quit, and method of recruitment. Although efforts will be made to ensure a representative sample using stratified sampling, the precise ratio of subgroups which may appear in the population cannot be fully controlled. If deemed appropriate, weighting socio-demographic variables will be employed to bring the sample more in line with the distribution of the underlying population and mitigate the effects of over- and under-representation.

Further, as compared to the other six study cohorts an additional data source (b) (4) will be used to obtain the required sample in the current cigarette smokers with intent to quit from legal age to 24 years of age cohort. While the utilization of an additional data source for this cohort may also introduce potential confounding factors when comparing outcomes across cohorts, confounding factors should be limited for test versus control comparisons within cohort.

A description of potential impact and subsequent handling of confounding variables will be described in the Statistical Analysis Plan (SAP) which will be submitted as a follow-up to the study protocol.

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8.6.4. Other Variables

Baseline characteristics of age, gender, ethnicity, education, and geographical region will be collected to help achieve a representative sample.

8.7. Data Management

(b) (4) will be responsible for all study data management. The protocol specifies data sources, data collection modes, software products and servers used for data collection, data management and data transfer procedures, as well as the measures that will be taken to protect the security and integrity of the data as they are collected and stored during the study.

(b) (4) subscribes to Safe Harbor and pledges to follow the Council of American Survey Research Organizations (CASRO) Code of Conduct, both providing principles and guidelines to ensure respondent confidentiality and privacy.

Examples of best practices include but are not limited to:

- The implementation of controls and procedures to maintain the confidentiality, integrity, and availability of personal information in accordance to company policy and applicable local legislation;
- Data handling procedures ensuring secure transfer and storage of personal identifiable information;
- Restricting access to personal information to only those that require access to perform their job;
- Properly informing respondents about the survey's aim and how their personal information will be used and protected.

8.7.1. Data Quality Control

The data collected for this study will be monitored for adherence with the study protocol. All data will be collected using a programmed web survey. Prior to initiating the study, appropriate edit programming will be conducted to ensure the final dataset requires minimal cleaning of invalid responses. The questionnaire will be designed so that instructions are as easy to understand and clear as possible to help avoid missing data. These programming procedures for the web-based survey data entry tool will include response ranges, consistency checks, skip patterns, and other special edit procedures where applicable. At every step of data processing, results or data manipulations will be cross-checked by (b) (4) team members who independently replicate the results and/or verify that the data have been handled appropriately and accurately. Any inconsistencies identified during this process are corrected before any further analysis is completed.

Other quality control procedures include the identification of respondents with little variability in their responses, for example due to disinterest in the project (“straight liners”), respondents that complete the survey much faster than expected (“speeders”), and/or that provide disproportionate

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or nonsensical numeric responses compared to the average (outliers). Removed respondents will be held in a separate data file with that will be utilized for the analysis.

In addition, respondents with clearly inconsistent responses will be removed and replaced from the main study. Problematic cases will be monitored during field and considered for deletion. Deleted cases will be replaced during field to ensure the completion of the sample. A separate file with the removed cases will be stored for future reference. Further explanation of the handling of suspect respondents will be provided in the study SAP.

8.7.2. Data Base Lock

After data collection is complete, data quality and completeness will be evaluated. Once the data quality check is complete, the database will be locked, and the data will no longer be subject to change.

8.7.3. Data Transfer

Until the approval and signing of the SAP by SMNA, the data will remain blinded and locked to the analytical team.

Once data are transferred, the analytical team will perform further checks prior to conducting data analyses specified in the SAP.

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will transfer final data files to SMNA in a zipped file via a secure FTP site after the study. SMNA will confirm receipt of these files. File name will include the study name and date of transfer.

8.7.4. Data Storage and Archiving

All electronic data files will be kept on secure servers, with backup processes in place. Paper data files will be scanned and filed accordingly.

Only de-identified data will be transferred for analysis purposes.

Personally Identifiable Information (PII) will be stored separately from the study data. Electronic records of data files and study documents will be transferred in a secure manner to SMNA and retained and stored on a secured server maintained by SMNA as required by law.

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8.8. Data Analysis

A formal and more detailed SAP will be prepared by (b) (4) This SAP will be submitted after finalization of the study protocol and survey.

8.8.1. Cognitive interview data analysis

The cognitive interviews will be conducted in accordance with the Office of Management and Budget (OMB) Statistical Policy Directive No.2 Addendum: Standards and Guidelines for Cognitive Interviews.³ Systematic content analysis will provide the data to be analyzed thus assuring we are hearing the participants own words as they “think aloud” while completing the survey. The series of individual comments obtained in the cognitive interviews, pertaining to separate questions and the product information sheet, across multiple interviews will be compiled into a coherent set of summary findings that transcend the individual interview level. In-depth analysis will include looking for themes that indicate whether questions have issues with comprehension, retrieval, decision-judgment, and response across all subjects.¹³ If a question or element in the survey is misunderstood from what was intended, the moderator will identify the statements/descriptions/terms that caused the misunderstanding. These will then be reworked or adjusted and reassessed, so that the terms achieve universal understanding of the intent of the question. The results will then be compiled to determine which changes are necessary for greater content validity. From this analysis, recommendations will be made to revise the language and content of study materials.

8.8.2. Quantitative data analysis

All analyses performed for the ZYN[®] Likelihood of Use Study will be descriptive in nature.

Descriptive statistics for accomplishing primary objectives will be reported for current intention to buy TNP, future intention to buy ZYN[®], current use of TNP, future intention to use TNP, current and future intention to quit TNP, and appeal of ZYN[®] brand and product attributes.

Descriptive statistics will include the number of non-missing observations, frequencies, percentages, and 95% CIs for the percentage of respondents endorsing each category for categorical variables.

Descriptive statistics for accomplishing secondary objectives will be reported for absolute risk outcomes, and relative risk outcomes. Descriptive statistics will include the number of non-missing observations, frequencies, percentages, and 95% CIs for the percentage of respondents endorsing each category for categorical variables.

The study team will format and properly label the data sets (including all responses from respondents and the date that the survey was completed) using SAS[®] software (Statistical Analysis System, version 9.3)¹⁴ so they are suitable for analysis. The data sets will contain a subject ID number and will not contain any information that could be used to identify individual respondents.

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8.8.3. Quality control

There are several aspects to quality control as described below:

Survey Instrument Programming

- The web-based survey will be created by the (b) (4) programming team using the (b) (4) software for web-based survey programming ((b) (4)).
- Then, the survey will be checked by another programmer independent of the day-to-day project to ensure all programming is correct.
- After the survey has been programmed and tested, the survey link and content will be reviewed by a separate team within (b) (4) fielding operations group from the perspective of the respondent (i.e. the link is reviewed online and not within the (b) (4) software).
- Prior to initiating the study, appropriate edit programming will be conducted to assure the final dataset requires minimal cleaning of invalid responses. These programming procedures for the web-based survey data entry tool will include response ranges, consistency checks, skip patterns, and other special edit procedures where applicable. At every step of data processing, results or creation of grouping variables will be cross-checked by (b) (4) operations team members who independently replicate the results and/or verify that the data have been handled appropriately and accurately. Any inconsistencies identified during this process are corrected before data are provided to (b) (4) analytical team to begin study analysis.

Qualitative Study

- As mentioned in [Section 8.3](#) “Cognitive Interviews,” a qualitative study will be conducted to assess the online survey instrument in a live setting with 24 total respondents matching the inclusion and exclusion criteria. During this time, any areas in the survey instrument that require clarification or improvements will be updated.

Data Management and Analyses

- When conducting online research, invariably some respondents will find a way to complete the survey without attempting to provide accurate, relevant responses. To ensure that those respondents do not compromise the integrity of the data, measures are taken to identify them in a systematic and objective way prior to actual analyses. No respondent will be removed from the full study analyses. However, should the process below identify outliers, sensitivity analyses will be conducted without these respondents to determine whether results differ from the full sample analyses. The process will seek to identify the following respondent types:
 - Respondents who lack variability in their responses to a battery of questions (“straight liners”) will be identified using standard deviations customized for each outcome found in the survey. Respondents whose responses have a standard

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deviation of zero or greater than four times the overall standard deviation will be flagged and examined individually.

- Similarly, respondents who demonstrate a discernable pattern in their answers inconsistent with any coherent understanding of the question (e.g., selecting 1, 2, 3, 4, 5, 1, 2, 3, 4, 5, 1... etc.) will also be flagged and examined individually.
- Respondents who are straight lining or giving patterned responses consistently throughout the survey (i.e., across multiple sections of the survey) will be individually scrutinized.
- Respondents found to lack credibility will be identified, handled consistently and transparently, and documented in the final report. This said, the a priori assumption is that all data reported is true and accurate, and preliminary outliers will be identified based on the underlying distribution of the data and through descriptive analysis.
- Data from non-credible respondents will be flagged in the data file. Additionally, the number of respondents flagged and the rationale for their identification as outliers will be reported in the final report.

8.9. Limitations of the Research Methods

The data collected will be based on responses post-exposure to a description and package label for a TNP. The perceived health risk assessments are intended to simulate real world perceptions after exposure to real world information on ZYN® but obviously do not have the same contextual, social, and emotional consequences of actual decisions. Similarly, one can only expect so much accuracy and extrapolation while capturing behavioral intentions, as unforeseen market factors can impact actual behaviors. Thus, differences can arise between stated and actual choices, and stated and actual behaviors. Potential hypothetical bias can be limited by constructing questions that mimic realistic perceptions and behaviors as closely as possible.

In addition, since data from this study will depend on respondent self-reporting, subsequently reported variables may also be subjected to recall bias. Self-reported data collection is a standard approach and any potential problems with recall bias are anticipated to be constant across time points.

Respondents will be recruited based on their membership with an online market research panel. As a result, recruitment could be considered a convenience sample. While multiple panels will be used, similar to any other data source used (e.g. random dialing), consumers who are not part of these data sources will not have the opportunity to participate. Further, due to sample selection during recruitment, respondents who are more interested in research or, perhaps healthy enough to participate, may be over-represented, hence the possibility of selection bias. Although these issues raise concerns about the external validity of the findings (e.g., our sample may not be fully generalizable to all consumers), the recruitment plan is designed to mirror the underlying populations (see [Section 8.4](#) “Study Population” for more detail). Even with efforts to ensure a representative sample using stratification, the precise proportion of subgroups which will appear

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in the study sample cannot be completely controlled. In fact, regardless of how respondents are recruited, there will always exist the possibility that the people who decline the opportunity to participate in the research differ in a systematic way from the people who accept the opportunity. Weighting may be used to bring the study sample more in line with the distribution of the population, and mitigate the effects of over-representation.

9. PROTECTION OF HUMAN SUBJECTS

This study is an observational study; there is no assignment of a respondent to any TNP, or vice versa. No additional diagnostic or monitoring process is required for participation or during the study. This study will test the effect that exposure to product information sheet and labels with warning indications has on health risk perceptions and behavior intentions. All stimuli will be presented in such a way that all information is visible and legible to respondents and ensures the respondent views the nicotine warning as it would appear on the product package in the real world. Additionally, the study will end with a debriefing statement to inform all respondents that all information within stimuli is for market research purposes only and not approved or endorsed by the FDA.

9.1. Regulatory authority approvals/authorizations

The study will be carried out in accordance with CTP guidance on data for human studies designed to evaluate the risks and benefits to the population as a whole¹. Additionally, (b) (4) conducts all our research in accordance with the requirements of our Quality System, which confirms to ISO 20252:2012 the International Standard for Market Research, Certification Number: 1019.

9.1.1. Institutional review board (IRB)

Documented approval from an appropriate IRB in the U.S. will be obtained prior to study start. When necessary, an extension, amendment or renewal of the IRB approval will be obtained and forwarded to SMNA. The IRB will supply to SMNA, upon request, a list of the IRB members involved in the vote and a statement to confirm that the IRB is organized and operates according to applicable laws and regulations.

9.1.2. Respondent information and consent

Prior to beginning the survey, potential respondents will be provided with an electronic statement of informed consent. The consent informs potential respondents that participation in the study is voluntary and that responses will remain confidential. It also includes information about the goals of the study, the approximate length of the survey, incentives for participation. Lastly, the statement of informed consent provides potential respondents with the resource references to address any concerns they may have. A link to each panel is given if the respondent has any specific questions about the survey instrument or incentives for participation. Contact information for the IRB is also provided if the respondent has any questions or concerns about their rights as a research participant

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(b) (4)

After potential respondents read the statement of informed consent, they will be asked, “Do you voluntarily agree to participate in this study?” Respondents who select “I agree to participate” will be able to complete the survey. At any time during survey completion, the respondent may choose to exit the survey should they decide not to participate any further. Data provided by a respondent who exits the survey prematurely will not be utilized in any analyses. Respondents who select “I do not agree to participate” will be thanked for their time before exiting. IRB written approval/ favorable opinion of the electronic informed consent form and any other written information provided to respondents will be obtained prior to the initiation of the study.

9.1.3. Confidentiality

Swedish Match North America as well as all investigators ensure adherence to applicable data privacy protection regulation. Data are transferred in encoded form only. The entire documentation made available to Swedish Match North America does not contain any data which, on its own account or in conjunction with other freely available data, can be used to re-identify natural persons. The investigators are obligated to ensure that no documents contain such data.

All records identifying the subject will be kept confidential and will not be made publicly available. Respondent names will not be supplied to SMNA. If the respondent name appears on any document, it must be obliterated before a copy of the document is supplied to SMNA. Study findings stored on a computer will be stored in accordance with local data protection laws.

The investigator will maintain a list to enable respondents’ records to be identified in case of queries.

10. REFERENCES

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(b) (4)

ATTACHMENTS

ATTACHMENT 1: ZYN® DESCRIPTION

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

ZYN NICOTINE POUCHES



SMOKE-FREE
SPIT-FREE
TOBACCO LEAF-FREE
15 NICOTINE POUCHES

What's in the pouch?
ZYN combines nicotine extracted from tobacco leaves, food-grade flavorings, and natural additives and sweeteners in a pouch that is completely tobacco leaf-free.

How to use ZYN

1. Align arrows on either side of the child safety lid. Squeeze and lift.
2. Place a pouch under your upper lip.
3. Use for up to 60 minutes.
4. Discard the pouch when finished.

ZYN nicotine pouches come in six flavors, each offered at 3 mg or 6 mg of nicotine.

| | | |
|---|--|---|
|  Cool Mint |  Spearmint |  Cinnamon |
|  Peppermint |  Wintergreen |  Coffee |

(b) (4)

ATTACHMENT 2: ZYN® LABEL

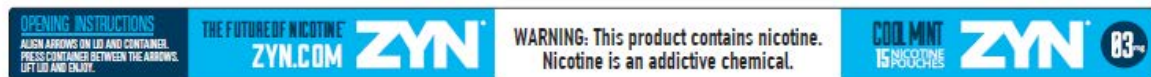
Below is an example of the package label on one ZYN® package. For purposes of illustration, this package label is for Cool Mint flavor and 3mg nicotine content. Aside from the flavor and strength, the information shown here would be shown on all packages.



Top Label



Bottom Label



Side Label

(b) (4)

INVESTIGATOR SIGNATURE

I have read this protocol and agree that it contains all necessary details for carrying out this study. I will conduct the study as outlined herein and will complete the study within the time designated.

I will provide copies of the protocol and all pertinent information to all individuals responsible to me who assist in the conduct of this study. I will discuss this material with them to ensure that they are fully informed regarding the conduct of the study and the obligations of confidentiality.

Investigator (Main Author):

Name (typed or printed):

(b) (4), (b) (6)

Company:

(b) (4)

Signature:

(b) (6)

Date: 1 June 2018

(Day Month Year)

Note: If the address or telephone number of the investigator changes during the course of the study, written notification will be provided by the investigator to SMNA; a protocol amendment will not be required.

SPONSOR SIGNATURE

Sponsor:

Name (typed or printed):

(b) (4), (b) (6)

Company:

Swedish Match North America

Signature:

(b) (6)

Date: 31 May 2018

(Day Month Year)