



Observational Study

ZYN[®] Likelihood of Use Study

Study Report

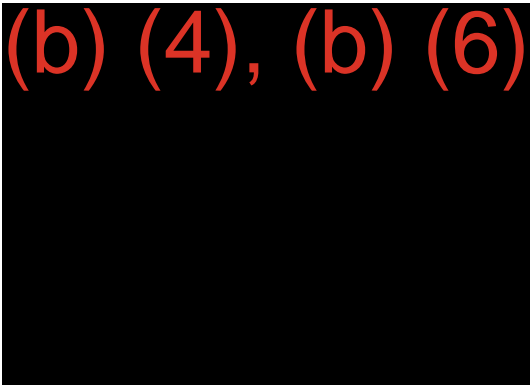
(b) (4)

Product Name:	ZYN [®]
First Respondent Enrolled:	05 December 2017
Last Respondent Completed:	16 February 2018
Principal Investigators:	(b) (4), (b) (6)
Sponsor:	Swedish Match North America (b) (4), (b) (6)
Sponsor Signatory:	(b) (6)
Version:	3.0
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Confidentiality Statement

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2. SYNOPSIS

Sponsor: Swedish Match North America (SMNA) Two James Center 1021 East Cary Street, Suite 1600 Richmond, VA 23219
Name of Finished Product: ZYN®
Name of Active Ingredient: Not applicable
Study Title: ZYN® Likelihood of Use Study
Investigators: (b) (4), (b) (6) 
Publication (reference): Not applicable
Studied Period: First respondent participation: 05 December 2017 Last respondent completed: 16 February 2018
Objectives: The overarching research questions within this project were: <ul style="list-style-type: none">• “How does exposure to the ZYN description and packaging label (referred to as

‘stimuli’ going forward) affect intentions, behaviors, and perceptions of Tobacco/Nicotine Product (TNP) users and TNP non-users, when compared pre- to post-exposure?”, and

- “Does exposure to the ZYN stimuli have a different impact on intentions, behaviors, and perceptions across TNP user and TNP non-user groups?”

TNP was defined as cigarettes, e-cigarettes, moist snuff, chewing tobacco, snus, nicotine pouches, cigars/cigarillos/filtered cigars filled with tobacco, pipe tobacco, or hookah/water pipe tobacco.

These questions were evaluated by way of an observational study with a pre-/post-exposure design. No formal hypotheses were specified for the ZYN Likelihood of Use Study.

Primary Objectives:

1. Among all respondents, assess whether being exposed to ZYN stimuli has an impact on perceptions and intentions related to the use of TNP.
 - 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 TNP based on intention to buy TNP; the term “initiate” is only pertinent to TNP never-users, i.e., those not currently using TNP. Similarly, the term “reinitiate” is only pertinent to TNP former users.
 - Future likelihood to initiate or reinitiate TNP based on intention to buy ZYN after being exposed to ZYN stimuli.
 - Among cigarette smokers with intention to quit, cigarette smokers without intention to quit, and current tobacco users (excluding cigarettes), evaluate:
 - Current use of TNP.
 - Future intention to buy ZYN after being exposed to ZYN stimuli.
 - Future intention to use current TNP after being exposed to ZYN stimuli.
 - Among cigarette smokers with intention to quit, cigarette smokers without intention 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 ZYN stimuli.

2. Among all respondents, measure the appeal of various ZYN brand and product attributes after being exposed to ZYN stimuli. Attributes include:

- Overall look and feel.
- Variety of flavors.
- Product design.
- Physical product.
- Child-safety lid.

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.

- Measurement of absolute risk of non-usage and smoking to occur prior to showing respondents the ZYN stimuli.
- Measurement of absolute risk of ZYN to occur after showing respondents the ZYN stimuli.

The health conditions under consideration when assessing absolute risk were:

- 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:

- Using other tobacco products.
- Using aids to help stop smoking.

- Quitting all TNP.
- Never using any TNP.

All measurements of relative risk were collected after respondents were exposed to the ZYN stimuli.

The health conditions under consideration when assessing relative risk were:

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

Methodology: The Likelihood of Use study followed a pre- and post-exposure design assessing intended behavior regarding TNP use and perceptions of health risk before and after exposure to ZYN stimuli. The ZYN stimuli provided a picture of the canister and a schematic of the label for the top, bottom, and side of the canister. Further, the ZYN stimuli indicated product information, including instruction on use, strengths, number of pouches in canister, and flavors, as well as the required warning that nicotine is an addictive chemical.

Data were obtained using responses from a customized web-based survey of invited consumers who met inclusion and exclusion criteria and agreed to participate in the study. Consumers were initially recruited from verified online consumer survey panels, including (b) (4), (b) (4), and (b) (4). The study population was derived from the invited sample using a stratified sampling framework, based on socio-demographic characteristics of the adult population from the Population Assessment of Tobacco and Health (PATH) study. The overall recruitment methodology was expected to provide socio-demographic profiles consistent with the adult population based on PATH study data for each of the study cohorts.

After recruitment, participants accessed a 15-20 minute survey where they were asked to self-report current TNP use. Cognitive interviews preceded survey finalization to ensure that the survey materials were appropriate and sufficiently clear to respondents.

Number of Respondents (Planned and Analyzed)

Planned: The study sample consisted of a U.S. adult population of legal age for TNP use. The study was planned to have a total sample of (b) (4) respondents for seven cohorts, with (b) (4) respondents in each cohort. Sample size was determined by an a priori precision analysis

considering a confidence interval of 95% ($\alpha=0.05$), a standard deviation of 3.74, a small interval half-width, and a probability of achieving the desired precision of 0.99.

Analyzed: There were (b) (4) respondents who met the study eligibility criteria, completed the survey, and were retained for study analysis. Of these respondents, (b) (4) were of legal age to 24 years of age and never used tobacco, (b) (4) were >24 years of age and never used tobacco, (b) (4) were former tobacco users from legal age and older, (b) (4) of respondents (b) (4) were of legal age to 24 years of age and current cigarette smokers with intention to quit, (b) (4) of respondents (b) (4) were >24 years of age and current cigarette smokers with intention to quit, (b) (4) of respondents (b) (4) were of legal age and older without intention to quit, and (b) (4) of respondents (b) (4) were current tobacco users (excluding cigarettes) from legal age and older.

Inclusion Criteria:

- 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.

Exclusion Criteria:

- Respond as “Don’t know” or “Decline to answer” to specific demographics (U.S. residency, state of residence, age, gender, racial or ethnic background, or education), since used for balancing cohorts.
- Unwilling or unable to provide electronic informed consent.
- Individual employed in any of the following fields or professions: market research, marketing, advertising, employee of a TNP manufacturer, or physician.
- Individuals who have taken part in a consumer research study on tobacco in the past 2 weeks, or respond as “Don’t know” or “Decline to answer” when asked.

Statistical Methods: All analyses performed for the ZYN Likelihood of Use Study were descriptive in nature. Descriptive statistics were used to understand the distribution of outcomes and socio-demographic variables were calculated prior to any recoding or aggregation that might be utilized for the presentation of results. Respondents with values for variables that were illogical or deemed unreliable, as determined by the underlying distribution and individual examination, were considered for removal prior to performing the main analyses. Numeric

variables were described using total sample size, number of missing observations (if applicable), means, standard deviations, medians, minimums, and maximums. Categorical variables were described using frequencies, percentages, and the number of missing observations (if applicable).

Descriptive statistics that were reported for the main analyses included the number of non-missing observations, means, standard deviations, and 95% confidence intervals (CIs) for numeric variables. For categorical variables, these included the number of non-missing observations, frequencies, percentages, and 95% CIs for the percentage of respondents relevant for each outcome.

The study team formatted and properly labelled the data sets (including all responses from respondents and the date that the survey was completed) using Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows [Version 23, Armonk, NY: IBM Corp 2015]) and SAS[®] software (Statistical Analysis System [SAS] [Version 9.4, Cary, NC]) so that they were suitable for analyses. The data sets contained a subject ID number and did not contain any information that could be used to identify individual respondents.

Results and Discussion:

The demographic data were comparable between the seven cohorts in this study. The outcomes associated with each objective revealed how exposure to the ZYN stimuli affected the intentions, behaviors, and perceptions of TNP users and non-users. Respondents demonstrated comprehension of ZYN stimuli.

Primary Objective 1

Among all respondents, assess whether being exposed to ZYN stimuli had an impact on perceptions and intentions related to the use of TNP.

Likelihood to initiate or reinstate TNP: All TNP non-users and former users were unlikely to buy any kind of TNP in the future, including ZYN. Exposure to ZYN stimuli did not create any interest in the product.

Future intention to buy ZYN among TNP users: After exposure to the ZYN stimuli, the likelihood that cigarette smokers would buy ZYN in the future ranged between 2.26 - 2.97 points on an 11-point Juster scale (from 0 = no chance, almost none – 10 = certain, practically certain). The mean likelihood that current tobacco users, excluding cigarettes, would purchase ZYN in the future was 1.83. Notably, cigarette smokers with intention to quit showed higher likelihood to buy ZYN than cigarette smokers without intention to quit.

Current use of TNP and future intention to use current TNP after exposure to ZYN: The majority of TNP users reported smoking cigarettes every day, with the highest frequency among those without intention to quit (b) (4). After exposure to ZYN stimuli, nearly (b) (4) of cigarette

smokers with intention to quit and (b) (4) of cigarette smokers without intention to quit reported intending to cut back or quit completely future cigarette smoking.

Current and future intention to quit TNP: The future intention of TNP users to quit TNPs did not change after exposure to the ZYN stimuli. Prior to exposure to the ZYN stimuli, cigarette smokers with intention to quit already had high levels of desire to quit TNP use (mean Motivation to Stop Scale [MTSS] scores ranging from 3.69 – 5.89), whereas most cigarette smokers without intention to quit (mean MTSS scores ranging from 2.47 – 3.35) and tobacco users (mean MTSS scores ranging from 2.40 – 3.59) had less desire to quit their TNP use. Scores on MTSS range from 1=“I don’t want to stop smoking”; 2=“I think I should stop smoking but don’t really want to”; 3=“I want to quit smoking but haven’t thought about when”; 4=“I really want to stop smoking but I don’t know when I will”, 5=“I really want to stop smoking and hope to soon”; 6=“I really want to stop smoking and intend to in the next 3 months”; 7=“I really want to stop smoking and intend to next month.”

Primary Objective 2

Among all respondents, measure the appeal of various ZYN brand and product attributes after being exposed to ZYN stimuli.

TNP users considered the ZYN brand and its various product attributes (flavor variety, product design, physical product) to be more appealing compared with TNP non-users. In particular, the child-safety lid was the most appealing attribute among both TNP and non-TNP users.

Secondary Objective 1

Among all respondent cohorts, explore variation in perceptions of absolute risk associated with never having used any TNP, smoking cigarettes, and using ZYN.

Across all health conditions (adult tooth loss, mouth cancer, gum disease, and serious health problems), most respondents perceived low absolute risks for never having used any TNPs, moderate absolute risks for using only ZYN daily, and high absolute risks for smoking cigarettes daily.

Secondary Objective 2

Among all respondent cohorts, explore variation in perceptions of relative risk of using ZYN as opposed to using other tobacco products, aids to help stop smoking, quitting all TNP, and never using any TNP.

Respondents consistently attributed high risk to the presence of cigarette usage, whether in the presence of ZYN or otherwise. However, the majority of respondents across all cohorts perceived the daily use of only ZYN to carry the same or lower risk of each health condition as cigarettes, both cigarettes/ZYN, moist snuff, chewing tobacco, and snus. Additionally, ZYN

was perceived to carry higher risk relative to quitting all TNP and never using TNP.

Strengths and Limitations of the Study: This study was conducted following the guidance of the Center for Tobacco Products ([FDA Guidance for Industry, 2011](#)) within the FDA on data for human studies designed to evaluate the risks and benefits to the population, including users and non-users of tobacco products. The Likelihood of Use study relied on relevant statutes, and information obtained from the Tobacco Products Scientific Advisory Committee Meeting to frame the research questions addressed in the General Snus MRTP study ([FDA CTP Response Letter, 2017](#)). The study also benefited from guidance for best practices in consumer research for Tobacco Product Perception and Intention Studies (TPPIS), based on a March 2017 meeting between the FDA and SMNA ([CTP Addendum, 2017](#)).

The study featured many strengths, the first being the extensive number of individuals included in the survey panels, which ensured robustness of findings. The study also benefitted from the use of qualitative cognitive interviews prior to the execution of the quantitative survey, which informed and strengthened the design of the web-based survey. Cognitive interviews ensured that the materials were appropriate and sufficiently clear to respondents. As a result, the questionnaire offered both completeness and simplicity. Additionally, the administration of the web-based survey allowed for improved survey designs and accurate data capture. Importantly, the study results were robust enough to withstand the inclusion of outliers. As the pattern of results were similar in both the full sample analysis and the sensitivity analysis, it appeared that the inclusion of outliers did not have a substantive impact on the findings.

Finally, in virtually all cases survey questions utilized validated scales, or scales directly comparable to studies in literature. In particular, usage of the Juster Scale and Motivation to Stop Scale allowed for simple, justifiable interpretation. Scales used in risk perception questions line up with other tobacco-related research, such as HINTS.

There were limitations to the current study, arguably none of which should draw concern regarding data integrity. The data collected were based on post-exposure responses to stimuli for ZYN. The perceived health risk assessments were intended to simulate real-world perceptions after exposure to real-world information on ZYN, but obviously they did not have the same contextual, social, and emotional consequences of actual decisions. Similarly, one could only expect a limited degree of accuracy and extrapolation while capturing behavioral intentions, as unforeseen factors can impact actual behaviors. Thus, differences may arise between stated and actual choices, and stated and actual behaviors. Potential hypothetical bias may be limited by constructing questions that mimic realistic perceptions and behaviors as closely as possible. In addition, since data from this study were dependent on respondent self-reporting, subsequently reported variables may also be subjected to recall bias and the inability to confirm actual tobacco use behavior. Self-reported data collection is a standard approach and any potential problems with recall bias were anticipated to be constant across time points.

Every effort was made to approximate the socio-demographic profiles of the adult population enrolled in the PATH study, though it was difficult to recruit the full cohort for current cigarette

smokers with intention to quit from legal age to 24 years (cohort 4; (b) (4)), which was under-sampled by over (b) (4) respondents. Although we intended to follow CTP guidance which requires oversampling in vulnerable populations, specifically the young adult population (legal age for tobacco use in their states, to age 24) among current cigarette smokers, due to insufficient numbers of active panel members in the desired age range who also met the precise requirements of being smokers and intending to quit, we were not able to recruit a full cohort as planned. It may be that younger smokers were more likely to have started smoking recently and thus would be less likely to already have intentions to quit smoking. Thus, the population base for sampling this cohort is small relative to older smokers. In the end, the achieved socio-demographic proportions in the current study were within $\pm 20\%$ of the corresponding PATH demographics.

Respondents were recruited based on their membership with an online market research panel. As a result, recruitment could be considered a convenience sample. While multiple panels were used, similar to any other data source used (e.g. random dialing), consumers who were not part of these data sources did not have the opportunity to participate. Further, due to sample selection during recruitment, respondents who were more interested in research, or perhaps healthy enough to participate, may be over-represented, hence the possibility of selection bias. Although these issues raised concerns about the external validity of the findings (e.g., our sample may not be fully generalizable to all consumers), the recruitment plan was designed to mirror the underlying populations. Even with efforts to ensure a representative sample using stratification, the precise proportion of subgroups in the study sample could not be completely controlled.

Conclusion: Study findings support the conclusion that overall, the introduction of ZYN does not appear to compromise public health in any way, based on likelihood of use and perceptions of risk as assessed in the current study. Specifically, results demonstrated that:

- Respondents who did not use TNPs were not likely to initiate or reinstate TNPs after viewing the ZYN description and packaging label ('stimuli').
- Current tobacco users and current cigarette smokers demonstrated some interest in purchasing ZYN in the future. Additionally, cigarette smokers with intention to quit showed greater interest in purchasing ZYN than cigarette smokers without intention to quit.
- Among TNP users, exposure to the ZYN stimuli did not affect their intention to quit TNP, as reflected in MTSS scores. However, according to future intention to use TNP, the majority of smokers with intention to quit did report that they would cut back or completely quit the use of cigarettes, moist snuff, cigars/cigarillos/filtered cigars filled with tobacco, and/or pipe tobacco after exposure to the ZYN stimuli.

- Respondents perceived that there are risks of certain health conditions associated with using ZYN, but those risks are 1) the same or lower for cigarettes, both cigarettes/ZYN, moist snuff, chewing tobacco, and snus; and 2) higher than using no TNP.

Final Date: 3 August 2018

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4. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation or Specialist Term	Explanation
CI	Confidence Interval
CTP	Center for Tobacco Products
FDA	Food and Drug Administration
GED	General Educational Development
IRB	Institutional Review Board
MRTTP	Modified Risk Tobacco Product
MTSS	Motivation to Stop Scale
NA	Not applicable
NCHS	National Center for Health Statistics
PATH	Population Assessment of Tobacco and Health
PMTA	Premarket Tobacco Product Application
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SE	Substantial Equivalence
SMNA	Swedish Match North America

Abbreviation or Specialist Term	Explanation
SPSS	Statistical Package for the Social Sciences
TNP	Tobacco/nicotine products
TPPIS	Tobacco Product Perception and Intention Studies
U.S.	United States

5. RESPONSIBLE PARTIES

5.1 Investigator and Contributors

Principal Investigator:	(b) (4), (b) (6)
(b) (4) Project Team:	(b) (4), (b) (6)

5.2 Sponsor

Sponsor:	Swedish Match North America (b) (4), (b) (6)
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6. ETHICS

6.1 Institutional Review Board (IRB)

Documented approval from a central IRB in the U.S. was obtained prior to to the initiation of the study. Sterling, IRB (Atlanta, Georgia) approved this study. When necessary, an extension, amendment or renewal of the IRB approval was obtained from Sterling, IRB and forwarded to Swedish Match North America (SMNA).

6.2 Ethical Conduct of the Study

The study was carried out within an approved indication and in accordance with Center for Tobacco Products (CTP) guidance on data for human studies designed to evaluate the risks and benefits to the population as a whole. Additionally, (b) (4) conducted all research in accordance with the requirements of a Quality System, which conforms to ISO 20252:2012 the International Standard for Market Research, Certification Number: 1019.

6.3 Respondent Information and Consent

Prior to beginning the survey, potential respondents were provided with an electronic statement of informed consent. The consent informed potential respondents that participation in the study was voluntary and that responses remained confidential. It also included information about the goals of the study, the approximate length of the survey, incentives for participation, and the resource references to address any concerns they could have. A link to each panel was given if the respondent had any specific questions about the survey instrument or incentives for participation.

After potential respondents read the statement of informed consent, they were asked, “Do you voluntarily agree to participate in this study?”. Respondents who selected “I agree to participate” were able to complete the survey. At any time during survey completion, the respondent could choose to exit the survey should they decide not to participate any further. Data provided by a respondent who exited the survey prematurely was not utilized in any analyses. Respondents who selected “I do not agree to participate” were 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 was obtained prior to the initiation of the study.

7. INTRODUCTION

7.1 Background

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 is appropriate for the protection of the public health as determined “on the basis of well-controlled investigations” ([FDA Guidance for Industry, 2011](#)).

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 ([FDA Guidance for Industry, 2011](#); [FDA Guidance for Industry, 2016](#)). 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 ([FDA Guidance for Industry, 2011](#)). 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 PMTA or a Substantial Equivalence [SE] report) or they can no longer be sold in the U.S ([FDA Guidance for Industry, 2011](#); [FDA Guidance for Industry, 2016](#)).

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.

7.2 Rationale

As a result of the Tobacco Control Act requirements, SMNA must submit a PMTA to continue marketing the ZYN product. The output of the Likelihood of Use study will be submitted to the FDA as part of the ZYN PMTA. For this purpose, the objective of this study was to determine consumer perceptions of health risks of TNP and how the likelihood to use TNP changes after becoming aware of ZYN among cohorts of adults, separated by age, usage history of TNP, and intention to quit TNP.

8. STUDY OBJECTIVES

The overarching research questions within this study can be stated as follows: “How does exposure to the ZYN description and packaging label (referred to as ‘stimuli’ going forward) affect intentions, behaviors, and perceptions of TNP users and TNP non-users, when compared pre- to post-exposure?”, and “Does exposure to the ZYN stimuli have a different impact on intentions, behaviors, and perceptions across TNP user and TNP non-user groups?”

TNP was defined as cigarettes, e-cigarettes, moist snuff, chewing tobacco, snus, nicotine pouches, cigars/cigarillos/filtered cigars filled with tobacco, pipe tobacco, or hookah/water pipe tobacco.

These questions were evaluated by way of an observational study with a pre- and post-exposure design. No formal hypotheses were specified for the ZYN Likelihood of Use study.

8.1 Primary Objectives

The two primary objectives were:

8.1.1 Primary Objective 1

Among all respondents, assess whether being exposed to ZYN stimuli had an impact on perceptions and intentions related to the use of TNP.

- Among TNP never-users legal age to 24, TNP never-users older than 24, and former TNP users evaluate:
 - Current likelihood to initiate or reinstate TNP based on intention to buy TNP; the term “initiate” is only pertinent to TNP never-users, i.e., those not currently using TNP. Similarly, the term “reinstate” is only pertinent to TNP former users.
 - Future likelihood to initiate or reinstate TNP based on intention to buy ZYN after being exposed to ZYN stimuli.
- Among cigarette smokers with intention to quit, cigarette smokers without intention to quit, and current tobacco users (excluding cigarettes) evaluate:
 - Current use of TNP.
 - Future intention to buy ZYN after being exposed to ZYN stimuli.
 - Future intention to use current TNP after being exposed to ZYN stimuli.
- Among cigarette smokers with intention to quit, cigarette smokers without intention 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 ZYN stimuli.

8.1.2 Primary Objective 2

Among all respondents, measure the appeal of various ZYN brand and product attributes after being exposed to ZYN stimuli. Attributes included:

- Overall look and feel;
- Variety of flavors;
- Product design;
- Physical product;
- Child-safety lid.

8.2 Secondary Objectives

The two secondary objectives were:

8.2.1 Secondary Objective 1

Among all respondent cohorts, explore the variation in perceptions of absolute risk associated with never having used any TNP, smoking cigarettes, and using ZYN.

- Measurement of absolute risk of non-usage and smoking prior to showing respondents the ZYN stimuli.
- Measurement of absolute risk of ZYN to occur after showing respondents the ZYN stimuli.

The health conditions under consideration when assessing absolute risk were:

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

8.2.2 Secondary Objective 2

Among all respondent cohorts, explore variation in perceptions of relative risk of using ZYN as opposed to:

- Using other tobacco products;
- Using aids to help stop smoking;
- Quitting all TNP; and
- Never using any TNP.

All measurements of relative risk were collected after respondents were exposed to the ZYN stimuli.

The health conditions under consideration when assessing relative risk were:

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

9. INVESTIGATIONAL PLAN

9.1 Quantitative Study Design

The ZYN Likelihood of Use Study consisted of a pre-/post-exposure, repeated measures study design. Study stimuli consisted of a one-page ZYN description (Figure 1) and packaging label (Figure 2) that indicated product information, including instruction on use, strengths, number of pouches in canister, and flavors, as well as the required warning that nicotine is an addictive chemical. Note that while stimuli focused on the cool mint flavor 3 mg strength, respondents were informed that all other packaging was identical except for flavor and strength (3 mg versus 6 mg).

Figure 1: ZYN Description



Figure 2: ZYN Packaging Label



Data for the ZYN Likelihood of Use Study were obtained using responses from a customized web-based survey of invited consumers who met inclusion ([Section 9.2.1](#)) and exclusion criteria ([Section 9.2.2](#)) and who agreed to participate in the study. Consumers were initially recruited from verified online consumer survey panels, including Lightspeed Research Panel, Survey Sampling International, and Research Now. If these panels did not satisfy sampling needs, additional panels were included such as Lucid. Study recruitment resulted in a representative sample (based on U.S. Census data and including age, gender, geographic region, racial or ethnic background, and education) that was utilized in the study. The study sample was then recruited from the invited sample using a sampling framework based on socio-demographic characteristics of the adult population from the Population Assessment of Tobacco and Health (PATH) study ([U.S. Department of Health and Human Services, PATH, 2017](#)). The overall recruitment methodology was expected to provide socio-demographic profiles consistent with the adult population based on PATH ([U.S. Department of Health and Human Services, PATH, 2017](#)) study data for each of the study cohorts. In compliance with CTP's guidance ([FDA CTP Response Letter, 2017](#)), regarding intended use and risk assessment in vulnerable populations, the study intended to oversample the young adult population, specifically people who fall between legal age for tobacco use (by state) and 24 years of age. Additionally, the study intended to oversample cigarette smokers with intention to quit as assessed by the Motivation to Stop Scale (MTSS) ([Kotz et al., 2013](#)). More information on recruitment of study cohorts is available in the ZYN Likelihood of Use Study protocol ([Attachment 17.4](#)).

After recruitment, participants in the ZYN Likelihood of Use Study accessed a 15-20 minute survey where they were asked to self-report current TNP use. Cognitive interviews informed the survey design to ensure that the survey materials were appropriate and sufficiently clear to respondents. More information about cognitive interviews can be found in Protocol Section 8.3 ([Attachment 17.4](#)) and in the cognitive interview report ([Attachment 17.6](#)), while more information on the study survey is available in the ZYN Likelihood of Use Study survey ([Attachment 17.3](#)).

9.2 Study Cohorts

The study population consisted of the U.S. population of legal age for TNP use. To meet the objectives of the ZYN Likelihood of Use Study, the study included respondents from the following cohorts described in Table 1. Cohorts of interest were defined based on self-reported TNP use. The definition of TNP use, and the product types constituting TNP for this study, were adapted from the PATH study ([U.S. Department of Health and Human Services, PATH, 2017](#)). The PATH study suggests a definition for lifetime cigarette use, which is having smoked 100+ cigarettes in a lifetime. For all other TNP, usage was based on recollection of ever using any particular TNP fairly regularly ([U.S. Department of Health and Human Services, PATH, 2017](#)). Current use was based on now using the product every day or some days ([U.S. Department of Health and Human Services, PATH, 2017](#)). Cohorts with and without intention to quit cigarettes were defined using the MTSS ([Kotz et al., 2013](#)) which is described in more detail in [Section 9.4.1](#).

Table 1: Study Cohorts

Never tobacco users	<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
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	<p>smoke every day or some days AND</p> <ul style="list-style-type: none"> ▪ 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)
Former tobacco users	<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)
Current cigarette smokers with 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]) (Kotz et al., 2013)
Current cigarette smokers	<ul style="list-style-type: none"> • Have smoked 100 or more cigarettes during lifetime AND

<u>without</u> intention to quit	<ul style="list-style-type: none">• Currently smoke cigarettes every day or some days AND• Have no intention to quit (score of 1-4 on MTSS) (Kotz et al., 2013)
Current tobacco users (excluding cigarettes)	<ul style="list-style-type: none">• For any of the following products, have been a regular user AND now 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>AND</p> <ul style="list-style-type: none">• Have smoked cigarettes during lifetime (fewer than 100 or 100 or more in lifetime) AND currently do not smoke cigarettes every day or some days <p>OR have never smoked</p>

9.2.1 Inclusion Criteria

In addition to the cohorts included in this study, respondents had to meet all of 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.

9.2.2 Exclusion Criteria

Respondents were excluded if any of the following criteria were met:

- Respond as “Don’t know” or “Decline to answer” to specific demographics (U.S. residency, state of residence, age, gender, racial or ethnic background, or education), since used for balancing cohorts.
- Unwilling or unable to provide electronic informed consent.
- Individual employed in any of the following fields or professions: market research, marketing, advertising, employee of a TNP manufacturer, or physician.
- Individuals who have taken part in a consumer research study on tobacco in the past 2 weeks, or respond as “Don’t know” or “Decline to answer” when asked.

9.3 Determination of 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 allowed for robust evaluation of the objectives. The precision analysis was performed under the following assumptions: a confidence interval of 95% ($\alpha=0.05$), a standard deviation of 3.74 (derived from the average of 3 standard deviations taken from Questions 9, 13, and 17 of a [2017 SMNA market research report](#)), a small interval half-width, and a probability of achieving the desired precision of 0.99.

The precision analysis suggested a sample size of 814 respondents per cohort would be appropriate. In total, the planned study sample was $N=5,698$ with $n=814$ respondents in each cohort. Table 2 presents the sample size for each cohort, the percent of sample per cohort, and the estimated percent of the adult population that each cohort represents based on PATH estimates ([U.S. Department of Health and Human Services, PATH, 2017](#)). In compliance with the CTP’s guidance regarding intended use and risk assessment in vulnerable populations, this study intended to oversample the young adult population among never users and current cigarette smokers, specifically subjects who fall between the legal age for tobacco use in their states, to age 24 ([FDA CTP Response Letter, 2017](#)).

Table 2: Definition and Target Sample Size of Each Cohort



(b) (4)

9.4 Variables of Relevance to the Study

This was an observational study; there was no assignment of a respondent to any TNP, or vice versa. No additional diagnostic or monitoring processes were required for participation during the study. This study tested the effect of exposure to product information sheet and labels with warning indications on health risk perceptions and behavior intentions.

9.4.1 Outcomes

9.4.1.1 Pre-Exposure

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

- **Current intention to buy TNP** was 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 (Juster, 1966). As the Juster Scale measures probability, the mean response predicts the proportion of the population that will perform the behavior (Juster, 1966). Research has shown that the Juster Scale is effective in predicting consumer future purchasing behaviors (McDonald & Albert, 2001).
- **Current use of TNP** was 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 (U.S. Department of Health and Human Services, PATH, 2017). Response options for frequency of use included “Every day,” “Some days,” “Not at all,” “Don’t know” and “Decline to answer.”

- **Current intention to quit TNP** was measured by the one-item validated instrument, the MTSS (Kotz et al., 2013). The MTSS consisted of one item with seven response options ranging from 1 (lowest) to 7 (highest 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, the MTSS was used both for assessing intention to quit cigarettes and for other TNPs. Consistent with published research using the MTSS, we reported the mean MTSS score (Hummel et al., 2017).

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

- **Pre-exposure perceptions of absolute health risk of non-usage and smoking** was 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”; Likert, 1932) 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 (National Cancer Institute, HINTS, 2005). 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. Additionally, this measure achieved saturation during cognitive interviewing. Saturation was defined at 80% or more of the respondents being able to verbalize a logical thought process when answering the question that fit with the intent of the question.

9.4.1.2 Post-Exposure to ZYN

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

- **Future intention to buy ZYN** was assessed post-exposure to the ZYN stimuli via the 11-point Juster Scale. The Juster Scale is explained in more detail under “Current intention to buy TNP” above.
- **Future intention to use TNP** was assessed post-exposure to the ZYN stimuli using a custom, single-item 4-point ordinal scale for each TNP currently used. Response options for the item included “Quit completely,” “Cut back use,” “Use the same amount” and “Use more”; “Don’t know” and “Decline to answer” were available as answer options outside of the scale. Cognitive interviewing demonstrated that saturation was achieved for this measure.
- **Future intention to quit TNP** was measured by the one-item validated instrument, the MTSS (Kotz et al., 2013). The MTSS is explained in more detail under “Current intention to quit TNP” above.

- **Appeal of various ZYN brand and product attributes** were assessed using one item for each brand and product attribute. Specific attributes investigated included the overall ZYN product, ZYN packaging, ZYN pouches (i.e., the product itself), ZYN child-safety lid, and ZYN variety of flavors. Response options included “Not at all appealing,” “Slightly appealing,” “Moderately appealing,” “Very appealing” and “Extremely appealing”; “Don’t know” and “Decline to answer” were available as answer options outside of the scale.

Post-exposure outcomes that were 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** were 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 ([National Cancer Institute, HINTS, 2005](#)). 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. Additionally, this measure achieved saturation during cognitive interviewing.
- **Perceptions of relative health risk** were 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 evaluated ZYN use against several other risk exposures. The risk exposures assessed for each health condition included 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 ([National Cancer Institute, HINTS, 2005](#)). The 5-point Likert scale used in HINTS had response options where 1= Much less harmful to 5= Much more harmful; the response options were changed to fit with the structure of the question in the survey. Additionally, this measure achieved saturation during cognitive interviewing.

Summaries of the outcomes for primary and secondary objectives, including measurement domain, subcategories, measurement details, and metrics are presented in [Table 3](#) to [Table 4](#) and [Table 5](#) to [Table 6](#), respectively.

Table 3: Outcomes Table for Primary Objective 1 - Impacts of ZYN on Perceptions and Intentions Related to the use of TNP

(b) (4)

(b) (4)

(b) (4)

(b) (4)

Table 4: Outcomes Table for Primary Objective 2 – Appeal of Various ZYN Brand and Product Attributes

(b) (4)

Table 5: Outcomes Table for Secondary Objective 1 – Perceptions of Absolute Risk

(b) (4)



Table 6: Outcomes Table for Secondary Objective 2 – Perceptions of Relative Risk

(b) (4)

(b) (4)

(b) (4)

9.4.2 Respondent Characteristics

9.4.2.1 Sociodemographic Variables

- **State of residence**, used to derive U.S. census region, was assessed using a single item asking the respondent what state they spend most days of the year in. State of residence was categorized into the four U.S. census geographic regions to summarize data collection results: Northeast, South, Midwest, and West.
- **Age** of the respondent was assessed using a single item asking the respondent how many years old they are. Age of respondents was categorized for reporting using the following age groups: 18-20, 21-24, 25-34, 35-44, 45-54, and 55+ years old.
- **Gender** was assessed using a single item asking the respondent if they are male or female.
- **Racial or ethnic background** was assessed using a single item asking the respondent which best describes their racial/ethnic background. Response options included: Caucasian/White, Black/African American, Hispanic (e.g., Latin American, Mexican, Puerto Rican, Cuban), Asian or Pacific Islander, Native American or Alaskan native, mixed racial background, or other.
- **Highest grade or level of school completed** was assessed using a single item asking the respondent which response corresponds to the highest level of education they have attained. Response options included: Less than high school, some high school – no diploma, General Educational Development (GED), high school graduate – diploma, some college but no degree, Associate degree, Bachelor’s degree (e.g., BA, AB, BS), or a post-graduate degree (e.g., MBA, PhD, JD, etc.).
- **Marital status** was assessed using a single item asking the respondent their marital status. Response options included: Now married, widowed, divorced, separated, never married, and decline to answer.
- **Pregnancy status** was assessed using a single item asking female respondents their pregnancy status. Response options included: I am currently pregnant, I am intending on getting pregnant in the next 6 months, none of the above, don’t know, and decline to answer.
- **Number of adults who live in the household** was assessed using a single item asking the respondent for the number of individuals living in the household who are over 18 years old. Decline to answer was also available as a response option. The number of adults in the household was categorized for reporting as 1, 2, 3, 4, or 5+.

- **Number of children who live in the household** was assessed using a single item asking the respondent for the number of individuals living in the household who are under 18 years old. Decline to answer was also available as a response option. The number of children in the household was categorized for reporting as 1, 2, 3, 4, or 5+.
- **Household income** in the last 12 months was assessed using a single item asking respondents which category best describes their total household income in the last 12 months. Response options included: Less than \$10,000, \$10,000 to \$14,999, \$15,000 to \$24,999, \$25,000 to \$34,999, \$35,000 to \$49,999, \$50,000 to \$74,999, \$75,000 to \$99,999, \$100,000 to \$199,999, \$200,000 or more, don't know, or decline to answer. Household income was categorized for reporting as less than \$25,000, \$25,000-49,999, \$50,000-74,999, \$75,000-99,999, \$100,000 or more.

9.4.2.2 Comprehension Check

Comprehension of the ZYN stimuli was assessed by using one item measuring comprehension of the various pieces of information presented in the ZYN stimuli. The multiple-choice response options included: ZYN contains nicotine, the packaging label includes a warning that nicotine is an addictive chemical, ZYN comes in the form of chewing gum, ZYN comes in a total of three flavors, ZYN comes in both 3 mg of nicotine and 6 mg of nicotine varieties, don't know, and decline to answer.

10. STATISTICAL ANALYSIS

10.1 Study Analysis

All analyses performed were descriptive in nature. Descriptive statistics were used to understand the distribution of outcomes and socio-demographic variables were calculated prior to any recoding or aggregation that might be utilized for the presentation of results. Respondents with values for variables that were illogical or deemed unreliable, as determined by the underlying distribution and individual examination, were considered for removal prior to performing the main analyses (See [Section 11.2](#) and [Section 11.3](#) for details regarding this process). Numeric variables were described using total sample size, number of missing observations (if applicable), means, standard deviations, medians, minimums, and maximums. Categorical variables were described using frequencies, percentages, and the number of missing observations (if applicable). Unless otherwise specified in the table shells ([Section 10 of SAP, Attachment 17.5](#)), descriptive statistics that were reported for the main analyses included the number of non-missing observations, means, standard deviations, and 95% confidence intervals (CIs) for numeric variables. For categorical variables, these included the number of non-missing observations, frequencies, percentages, and 95% CIs for the percentage of respondents relevant for each outcome.

The study team formatted and properly labelled the data sets (including all responses from respondents and the date that the survey was completed) using Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows [Version 23, Armonk, NY: IBM Corp 2015]) and SAS[®] software (Statistical Analysis System [SAS] [Version 9.4, Cary, NC]) so that they were suitable for analysis. The data sets contained a subject ID number and did not contain any information that could be used to identify individual respondents.

10.2 Socio-demographics and Comprehension Check

Descriptive statistics were reported for all socio-demographic variables, as well as the comprehension check outlined in [Section 9.4.2](#). Specifically, U.S. census region, age of respondent, gender, racial or ethnic background, highest grade or level of school completed, marital status, pregnancy status, number of adults who live in the household, number of children who live in the household, household income in the last 12 months, and comprehension of the ZYN stimuli were reported for all cohorts.

10.3 Statistical Analysis by Study Objective

10.3.1 Primary Objective

Descriptive statistics for accomplishing primary objectives were reported for current intention to buy TNP ([Table 7](#)), future intention to buy ZYN ([Table 7](#)), current use of TNP ([Table 7](#)), future intention to use TNP ([Table 7](#)), current and future intention to quit TNP ([Table 7](#)), and appeal of ZYN brand and product attributes ([Table 8](#)). Descriptive statistics included the number of non-

missing observations, frequencies, percentages, and 95% CIs for the percentage of respondents endorsing each category for categorical variables.

Table 7: Analysis Table for Primary Objective 1 – Impacts of ZYN on Perceptions and Intentions Related to the use of TNP

(b) (4)

Table 8: Analysis Table for Primary Objective 2 – Appeal of Various ZYN Brand and Product Attributes

(b) (4)

10.3.2 Secondary Objective

Descriptive statistics for accomplishing secondary objectives were reported for absolute ([Table 9](#)) and relative ([Table 10](#)) risk outcomes. Descriptive statistics included the number of non-missing observations, frequencies, percentages, and 95% CIs for the percentage of respondents endorsing each category for categorical variables.

The health conditions under consideration when assessing absolute risk were:

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

Table 9: Analysis Table for Secondary Objective 1 – Perception of Absolute Risk

(b) (4)

Table 10: Analysis Table for Secondary Objective 2 – Perceptions of Relative Risk

(b) (4)

10.4 Changes in the Conduct of the Study or Planned Analyses

There were two amendments to the protocol. The summary of changes in the conduct of the study from the procedures outlined in the original protocol are briefly listed below:

- Amendment 1 (issued on November 16, 2017): The changes were based on initial feedback from the Center of Tobacco Products (CTP) on a different Modified Risk Tobacco Product (MRTP) protocol.
- Amendment 2 (issued on May 28, 2018): The changes were based on new information and additional background obtained from January 24-25, 2018 Tobacco Products Scientific Advisory Committee Meeting and public availability of the Camel Snus/RJ Reynolds Tobacco Company MRTP application.

In addition to the amendments to the protocol listed above, there were necessary changes during the fielding of the study. First, qualifying incidences for some of the sub-quotas were too low to reach the targets, within a sample frame that is reflective of marginal distribution of age, gender, geographical region, ethnicity, race, and education. Second, to achieve the overall cohort sample sizes, demographic quotas based on PATH were relaxed. However, the achieved demographic quotas were within $\pm 20\%$ of the PATH demographics.

There was one amendment made to the SAP issued on June 6, 2018. These changes did not pertain to the planned analyses in the SAP. A summary of the changes to the original SAP are briefly listed below:

- Format edits to the table shells and accompanying footnotes were made for better representation and accuracy.

11. STATISTICAL AND ANALYTICAL ISSUES

11.1 Data Capture and Management

11.1.1 Data Capture

The web-based survey was created by the (b) (4) programming team using (b) (4) software for web-based survey programming ((b) (4)). After the survey was programmed and tested, the survey link and content were reviewed by a separate team within (b) (4) fielding operations group from the perspective of the respondent (i.e. the link was reviewed online and not within the (b) (4) software).

The data collected for this study was monitored for adherence with the study protocol ([Attachment 17.4](#)). All data were collected using a programmed web survey ([Attachment 17.3](#)). Prior to initiating the study, appropriate edit programming was conducted to assure the final dataset required minimal cleaning of invalid responses. The questionnaire was designed so that instructions were as easy to understand and clear as possible to help avoid missing data. These programming procedures for the web-based survey data entry tool included response ranges, consistency checks, skip patterns, and other special edit procedures where applicable. At every step of data processing, results or data manipulations were cross checked by (b) (4) team members who independently replicated the results and/or verified that the data was handled appropriately and accurately. Any inconsistencies identified during this process were corrected before data were provided to (b) (4) analytical team to begin study analysis.

11.1.2 Data Management and Analysis QC Process

- Until the approval of the SAP by SMNA, the data remained blinded and locked to the analytical team.
- Once data were unlocked, the analytical team performed the following checks prior to conducting data analyses specified in the SAP:
 - The classification of participants into the study cohorts based on self-reported use or non-use of TNP were checked.
 - Completion of the survey was verified and any respondent who did not complete the full survey was removed from analysis.
 - It was verified that respondents fulfilled the inclusion and exclusion criteria.
 - The actual quota frequencies for each study cohort in the data set were compared against the quota frequencies specified in the study protocol. All discrepancies were documented in the final report.

- All variable coding followed as specified in the SAP (e.g., grouping age by age brackets, grouping the number of adults/children in the household, and total household income in the last 12 months).
- All statistical analyses and results output were checked by another researcher on the analytical team for quality control. These checks included:
 - Correct coding of variables.
 - Correct use of statistical tests as specified in the analysis section.
 - Correct export of results from SAS[®] output to Excel tables.

11.2 Missing Data

The structure of the questionnaire did not have “true” missing data. The online survey did not allow respondents to proceed without receiving an answer to the present question. No partially completed surveys were included in the final data set or analyses. Data points were either missing because the respondent selected “Don’t know” or “Decline to answer,” or they did not qualify to answer the question due to survey skip logic. Thus, these types of missing data were kept as is and were reported descriptively (percentages and counts). The questionnaire was designed (and tested through cognitive interviewing) so that instructions were as easy to understand and as clear as possible, to help avoid missing data.

The rationale and utilization of “Don’t know” and “Decline to answer” response options were as follows:

- In this study, a “Decline to answer” response option without a “Don’t know” option was provided for any question where there was personally sensitive information, but the answer would be known to the respondent (e.g., age, gender, etc.).
- “Don’t know” and “Decline to answer” options were provided for all other questions.

11.3 Identification of Outliers

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 did not compromise the integrity of the data, measures were taken to identify them in a systematic and objective way prior to actual analyses. No respondent was removed from the full study analyses. However, (b) (4) outliers were identified per SAP guidelines ([Section 8.3 of SAP, Attachment 17.5](#)) and sensitivity analyses ([Attachment 17.2](#)) were conducted without these respondents to determine whether results differed from the full sample analyses. Specifically, these respondents met the outlier criteria as follows:

- Lacked variability in their responses across batteries of questions or provided a discernable pattern in their answers (e.g., 1, 2, 3, 4, 5, 1, 2, 3, 4, 5... etc.) inconsistent with any coherent understanding of questions A2, A3, B3, B4, B5, and B6 (perceptions of absolute risk for TNP use, perceptions for relative risk of TNP use, and appeal of ZYN).

Sensitivity analyses ([Attachment 17.2](#)) were conducted for every outcome with the (b) (4) outliers removed. The results of the sensitivity analyses were reported ([Section 13.5](#)) as to whether the exclusion of the outliers changed or did not change the descriptive results from the full sample analyses in a substantive way.

12. STUDY RESPONDENTS

12.1 Study Fielding Summary

The fielding summary for number of respondents who entered the survey, those who did not complete the survey, and those who were terminated (and the reasons for termination) are summarized below.



During the cohort data management check, it was discovered that (b) (4) of the (b) (4) retained respondents, all initially classified as never tobacco users, legal age to 24 years and older than 24 years cohorts, could not be verified as never users. These respondents had responded with “don’t know” or “decline to answer” to some of the TNP products asked in Question S8 in the survey (“have you ever used any...”). Thus, these (b) (4) respondents were removed from study analysis.

12.2 Final Sample

In total, there were (b) (4) respondents who met the study eligibility criteria and were included in the study analysis after data management.

Of the respondents, (b) (4) (b) (4) were of legal age to 24 years of age and never used tobacco, (b) (4) (b) (4) were older than 24 years of age and never used tobacco, (b) (4) (b) (4) were former tobacco users from legal age and older, (b) (4) of respondents (b) (4) were of legal age to 24 years of age and current cigarette smokers with intention to quit, (b) (4) of respondents (b) (4) were older than 24 years of age and current cigarette smokers with intention to quit, (b) (4) of respondents (b) (4) were of legal age and older without intention to quit, and (b) (4) of respondents (b) (4) were current tobacco users (excluding cigarettes) from legal age and older. Legal age was per local state law; all the respondents were of legal age to use TNP in their residential geography.

The number of respondents in each of the seven cohorts met the planned sample size except for cohort 4 (current cigarette smokers with intention to quit from legal age to 24 years of age) which was under-sampled (b) (4) by over (b) (4) respondents. Although we intended to follow CTP guidance which requires oversampling in vulnerable populations, specifically the young adult population (legal age for tobacco use in their states, to age 24) among current cigarette

smokers, due to insufficient numbers of active panel members in the desired age range who also met the precise requirements of being smokers and intending to quit, we were not able to recruit a full cohort as planned.

Respondents were recruited from all 50 U.S. states and Washington D.C. Enrollment ranged from (b) (4) of respondents from the states of Alaska (b) (4), North Dakota (b) (4), Rhode Island (b) (4), Vermont (b) (4), Washington D.C. (b) (4), and Wyoming (b) (4) to (b) (4) of respondents from California (b) (4) (Descriptive Table 1a, Attachment 17.1). The greatest proportion of respondents were enrolled from the Southern region (b) (4), (b) (4), followed by the Midwestern (b) (4), (b) (4), Western (b) (4), (b) (4), and Northeastern (b) (4), (b) (4) regions (Descriptive Table 1a, Attachment 17.1).

Respondents self-reported on their TNP use, both in the TNP type and frequency of use (Descriptive Table 2, Attachment 17.1). The majority of respondents used cigarettes (b) (4), (b) (4) and e-cigarettes (b) (4), (b) (4) fairly regularly, with (b) (4), (b) (4) reported having smoked 100 or more cigarettes in their entire life and (b) (4), (b) (4) of respondents currently smoked cigarettes daily (Descriptive Table 2, Attachment 17.1).

13. STUDY RESULTS

13.1 Descriptive Results

All respondents were included in the descriptive analyses (Statistical Tables 11–24, Appendix 16.1).

13.2 Demographics and Respondent Characteristics

13.2.1 Demographics

The overall demographic results (not by cohort) are summarized in Descriptive Tables 1a – 14, Attachment 17.1. Demographics are summarized by cohort in Statistical Table 11, Appendix 16.1.

Respondent mean age was 41.94 years (range: 18-92 years) (Descriptive Table 1b, Attachment 17.1). Overall, (b) (4) ((b) (4)) and (b) (4) ((b) (4)) of respondents were 18-24 years and ≥55 years of age, respectively (Descriptive Table 1a, Attachment 17.1). Respondent gender was similar in 4 of the 7 cohorts, except for the never tobacco users, which had a majority of females, and current tobacco users from legal age and older, which had a majority of males (Statistical Table 11, Appendix 16.1). The majority of respondents were Caucasian ((b) (4), (b) (4)), followed by Black/African American ((b) (4), (b) (4)) (Descriptive Table 1a, Attachment 17.1).

Approximately half of all respondents had at least a high school degree ((b) (4), (b) (4)) or some college experience with no degree ((b) (4), (b) (4)) (Descriptive Table 1a, Attachment 17.1). A higher proportion of never tobacco users >24 years of age ((b) (4), (b) (4)) had post-graduate degrees compared with former ((b) (4), (b) (4)) and current ((b) (4), (b) (4)) tobacco users (Statistical Table 11, Appendix 16.1).

A nearly equivalent percentage of respondents were reported to be currently ((b) (4), (b) (4)) or never married ((b) (4), (b) (4)) (Descriptive Table 1a, Attachment 17.1). Approximately (b) (4) of younger respondents (legal age to 24 years; cohorts 1 ((b) (4)) and 4 ((b) (4))) were never married (Statistical Table 11, Appendix 16.1). Overall, pregnancy status showed < (b) (4) ((b) (4)) of the female respondents were pregnant and (b) (4) ((b) (4)) of the female respondents intended on getting pregnant within the next 6 months (Descriptive Table 1a, Attachment 17.1).

On average, half of the respondents from each cohort reported having 2-3 adults (≥18 years) living in the household (Descriptive Table 1b, Attachment 17.1). The majority of respondents (>(b) (4)) had no children in the household (Descriptive Table 1b, Attachment 17.1). Approximately half of the total respondents reported a household income of <\$49,999 in the last 12 months (Statistical Table 11, Appendix 16.1).

13.2.2 Comprehension Check

About (b) (4) of all respondents (range: (b) (4) - (b) (4)) understood that the ZYN product contains nicotine and (b) (4) (range: (b) (4) - (b) (4)) understood the packaging label's warning that nicotine is an addictive chemical ([Descriptive Table 9, Attachment 17.1; Table 11](#)). Less than (b) (4) (range: (b) (4) - (b) (4)) of respondents answered that ZYN comes in the form of chewing gum and (b) (4) (range: (b) (4) - (b) (4)) thought it came in a total of three flavors. Approximately half of all respondents answered that ZYN comes in both 3 mg and 6 mg nicotine varieties. However, more current TNP users ((b) (4) - (b) (4)) answered that ZYN came in both 3 and 6 mg nicotine varieties.

Overall, these measures demonstrated that the majority of respondents comprehended the ZYN stimuli.

Table 11: ZYN Stimuli Comprehension



(b) (4)

13.3 Results for Primary Objectives

Descriptive statistical analyses by cohort are presented in [Statistical Tables 12–17](#), [Appendix 16.1](#). Sensitivity analyses were conducted for every outcome with the outliers removed to determine whether results differed from the full sample analyses. Identification of outliers can be found in [Section 11.3](#).

13.3.1 Primary Objective 1 – Impacts of ZYN on Perceptions and Intentions Related to the use of TNP

13.3.1.1 Likelihood to Initiate or Reinitiate TNP

The current likelihood to buy a TNP among TNP non-users (cohorts 1 – 3) was measured pre-exposure to the ZYN stimuli and was assessed using an 11-point Juster scale where 0 = no chance, almost none to 10 = certain, practically certain ([Table 12](#)).

Overall, TNP non-users and former users were unlikely to initiate or reinitiate TNPs prior to being exposed to the ZYN stimuli. After exposure to the ZYN stimuli, the likelihood to buy ZYN among TNP never-users was low for both those legal age to age 24 ((b) (4)) and those older than 24 ((b) (4)). The likelihood to buy ZYN among former tobacco users from legal age and older was even lower ((b) (4)).

Across cohorts, the mean Juster scores were higher for the future likelihood to buy ZYN compared with the current likelihood to buy other TNPs, however this increase (0.2 or lower) was negligible on the 11-point Juster scale.

Table 12: Mean Juster Scores - Likelihood to buy TNP

(b) (4)

13.3.1.2 Future Intention to Buy ZYN among TNP Users

Among TNP user groups, the likelihood to buy ZYN after exposure to the ZYN stimuli ranged from a mean Juster score of 1.83 to 2.97 ([Table 13](#)). After exposure to the ZYN stimuli, cigarette smokers intending to quit were more likely to buy ZYN than cigarette smokers not intending to quit.

Table 13: Mean Juster Scores - Future Intention to Buy ZYN among TNP Users

(b) (4)

13.3.1.3 Current Use of TNP among TNP Users

The current use of TNPs (both TNP type and frequency [every day, some days, not at all, don't know, decline to answer]) among TNP users were evaluated (Table 14). The majority of cigarette smokers reported smoking cigarettes daily (range: (b) (4) - (b) (4)); those without intention to quit showing the highest frequency of use ((b) (4)). A larger proportion ((b) (4)) of cigarette smokers older than 24 with intention to quit smoke daily compared with half the population ((b) (4)) of the smokers legal age to 24 with intention to quit. Among current tobacco users (excluding cigarettes), (b) (4) used moist snuff and (b) (4) used snus daily.

Table 14: Type and Frequency of Current TNP Use among TNP Users

(b) (4)

(b) (4)

(b) (4)

13.3.1.4 Future Intention to Use Current TNP after Exposure to ZYN

The future intention to use TNP among TNP users was assessed post-exposure to the ZYN stimuli (Table 15). The majority of cigarette smokers reported that they would cut back or completely quit TNPs, specifically cigarettes (except for those with no intention to quit), moist snuff, snus, cigars/cigarillos/filtered cigars with tobacco, and pipe tobacco after being exposed to the ZYN stimuli. Notably, (b) (4) of cigarette smokers with intention to quit reported that they would cut back or completely quit their cigarette use after exposure to ZYN stimuli.

In general, the majority of TNP users reported intentions to quit completely, cut back use or use the same amount of the TNPs after exposure to the ZYN stimuli (Table 15).

Table 15: Future Intention to Use TNP after Exposure to ZYN

(b) (4)

(b) (4)

(b) (4)

13.3.1.5 Intention to Quit TNP

Respondents' intention to quit TNPs pre- and post- exposure to the ZYN stimuli was assessed using the MTSS. The MTSS consisted of one item with seven response options ranging from 1 ("I don't want to stop smoking") to 7 ("I really want to stop smoking and intend to in the next month") ([Table 16](#)).

As expected, prior to exposure to the ZYN stimuli, current smokers with intention to quit had high levels of desire to quit TNP use (range: (b) (4)), whereas current smokers without intention to quit ((b) (4)) and tobacco users ((b) (4)) had less desire to quit their TNP use. After exposure to the ZYN stimuli, the intention to quit moist snuff and snus increased slightly (by (b) (4) points or less on the MTSS) across cohorts, except for cigarette smokers legal age to 24 with intention to quit. The range of MTSS scores for tobacco users still signified less desire to quit. Overall, among TNP users, the intention to quit TNP after exposure to the ZYN stimuli was similar to the intention to quit TNP before exposure to the ZYN stimuli.

Table 16: Pre-Exposure Intention to Quit and Post-Exposure Intention to Quit TNP (MTSS)

(b) (4)

13.3.2 Primary Objective 2 – Appeal of Various ZYN Brand and Product Attributes

The appeal of several ZYN product attributes including the overall brand, packaging, the physical product itself (pouches), the child-safety lid, and flavor variety was investigated ([Table 17](#)).

In general, TNP users considered the ZYN brand to be more appealing compared with TNP non-users. About one-third to one-half of TNP users considered the ZYN brand, overall packaging, flavor variety, and pouches to be moderately to very appealing.

In contrast, most TNP non-users did not find the ZYN brand, product, packaging, and flavor variety appealing at all (Table 17). The child-safety lid was the most appealing attribute among both TNP and non-TNP users.

Table 17: Appeal of ZYN Assessed by All Respondents

(b) (4)

(b) (4)

13.4 Results for Secondary Objectives

Descriptive statistical analyses by cohort are presented in [Tables 18–24](#) ([Appendix 16.1](#)). Sensitivity analyses were conducted for every outcome with the outliers removed to determine whether results differed from the full sample analyses (see [Section 11.3](#)).

13.4.1 Secondary Objective 1 – Perceptions of Absolute Risk

13.4.1.1 Pre-exposure Perceptions of Absolute Health Risk

Pre-exposure perceptions of the absolute health risk of smoking cigarettes daily and never having used TNPs were assessed for four health conditions (adult tooth loss, gum disease, mouth cancer, and serious health problems) with response options ranging from a very low to a very high risk of developing these conditions ([Table 18](#) and [Table 19](#)).

Across cohorts, the majority of respondents perceived that a person who smoked only cigarettes daily and no other TNP had a high to very high absolute risk of developing a health condition ([Table 18](#)). The majority of TNP non-users and cigarette smokers with intention to quit perceived higher absolute risks (e.g., respondents answered “high” to “very high”) of developing a health condition for daily cigarette smoking compared with current tobacco users (excluding cigarettes) and cigarette smokers without intention to quit. Across all cohorts, (b) (4) of respondents perceived a very low to low absolute risk of developing a health condition to a person who has never used TNPs ([Table 19](#)).

Table 18: Perceptions of Absolute Risk to a Person who Smokes Cigarettes Every Day but Uses no Other Tobacco Products

(b) (4)

(b) (4)

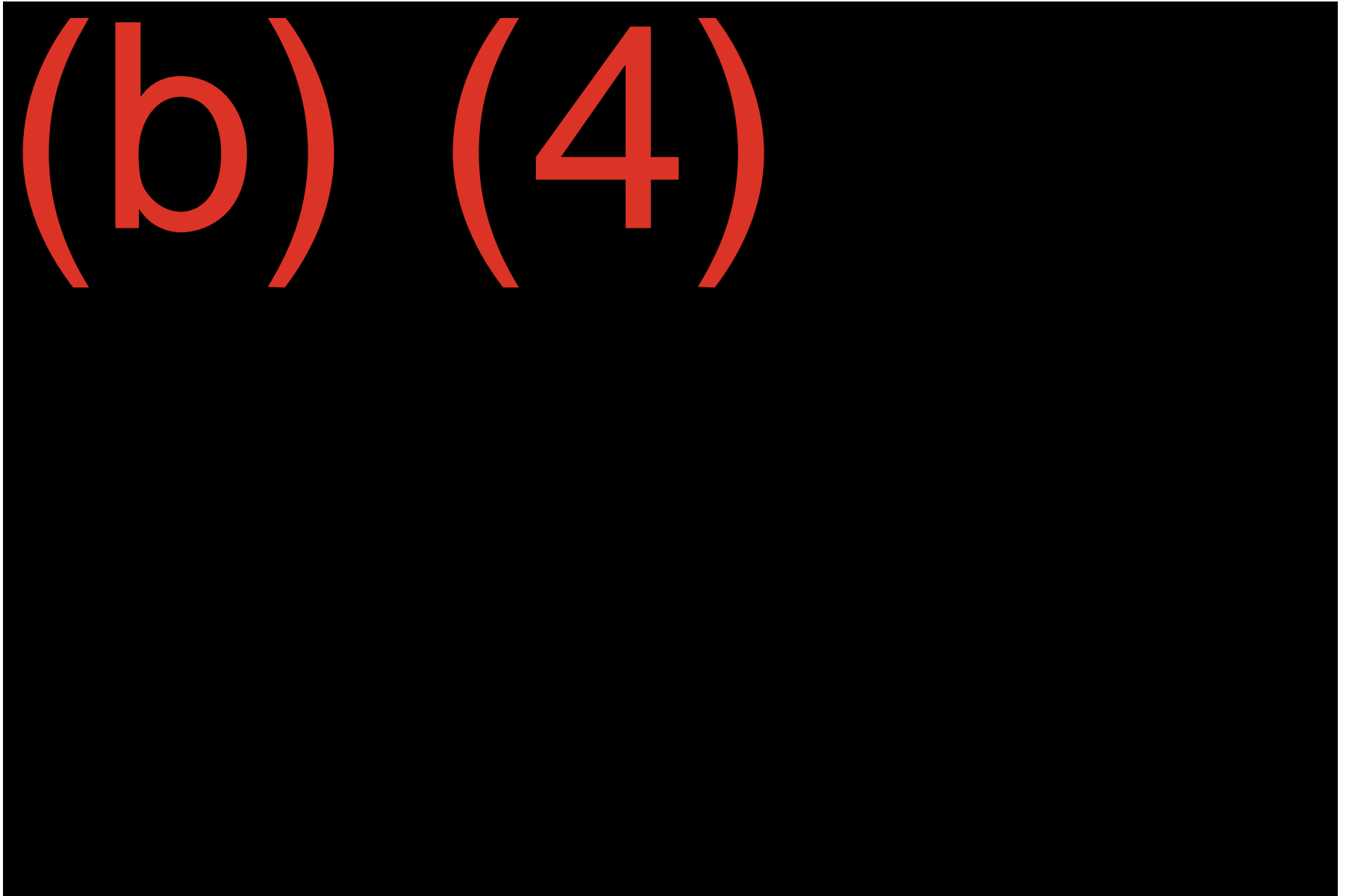
(b) (4)

(b) (4)

Table 19: Perceptions of Absolute Risk Associated with Never Having Used any TNPs

(b) (4)

(b) (4)



(b) (4)

13.4.1.2 Post-exposure Perceptions of Absolute Risk

The perceptions of absolute health risk of the daily use of ZYN and no other TNP was assessed for each of the four health conditions (adult tooth loss, gum disease, mouth cancer, and serious health problems) after exposure to ZYN stimuli (Table 20).

Across cohorts, (b) (4) respondents perceived a moderate to high chance of developing a health condition with daily ZYN use. Less than (b) (4) (range: (b) (4)) of respondents across cohorts perceived a very high absolute risk with ZYN. The perceptions of absolute risk, across conditions, due to the daily use ZYN was similar across TNP never-user age groups. In general, TNP users perceived lower health risks associated with the ZYN product compared with TNP non-users. Cigarette smokers perceived low to moderate absolute health risk, across conditions, of daily use of ZYN. For cigarette users intending to quit, a larger proportion of the legal to 24 years of age population ((b) (4)) perceived moderate risks compared with the older than 24 years of age population ((b) (4)).

When looking across all absolute risk metrics, a consistent pattern evolved. Respondents found that cigarettes presented the greatest risk of harm. Usage of ZYN was associated with some risk of health conditions, but at a lower rate than cigarettes. Never using TNP was generally deemed to carry the lowest risk.

Table 20: Perceptions of Absolute Risk Associated with Using Only ZYN Daily

(b) (4)

(b) (4)

(b) (4)

13.4.2 Secondary Objective 2 – Perceptions of Relative Risk

Across all cohorts, (b) (4) of respondents perceived the daily use of ZYN to carry a lower relative risk (a much lower/lower chance) of developing a health condition than the daily use of only cigarettes, and both cigarettes and ZYN (Table 21-Table 24). Across all cohorts, the daily use of ZYN was perceived to carry the same (range: (b) (4)) or lower (range: (b) (4)) risk relative to moist snuff, chewing tobacco, and snus (Table 21-Table 24). One-third (range: (b) (4)) of respondents across all cohorts perceived the risk associated with daily use of ZYN to be the same as the daily use of aids to help stop smoking (Table 21-Table 24).

Many respondents across all cohorts perceived higher risks for daily use of ZYN relative to quitting all TNP and never using TNP (Table 21-Table 24). In particular, less than (b) (4) of respondents across all cohorts perceived a much higher risk of serious health problems with daily use of ZYN compared with never having used TNP (Table 24). Generally, TNP users compared with TNP non-users tended to perceive lower risks of developing a health condition due to daily use of ZYN relative to other TNPs.

When looking across all relative risk metrics, a consistent pattern evolved. Respondents consistently attributed high risk to the presence of cigarette usage, whether in the presence of ZYN or otherwise. However, the majority of respondents across all cohorts perceived the daily use of only ZYN to carry the same or lower risk of each health condition as cigarettes, both cigarettes/ZYN, moist snuff, chewing tobacco, and snus. Additionally, ZYN was perceived to carry higher risk relative to quitting all TNP and never using TNP.

Table 21: Perceptions of Relative Risk of Adult Tooth Loss

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

Table 22: Perceptions of Relative Risk of Gum Disease

(b) (4)

(b) (4)

(b) (4)

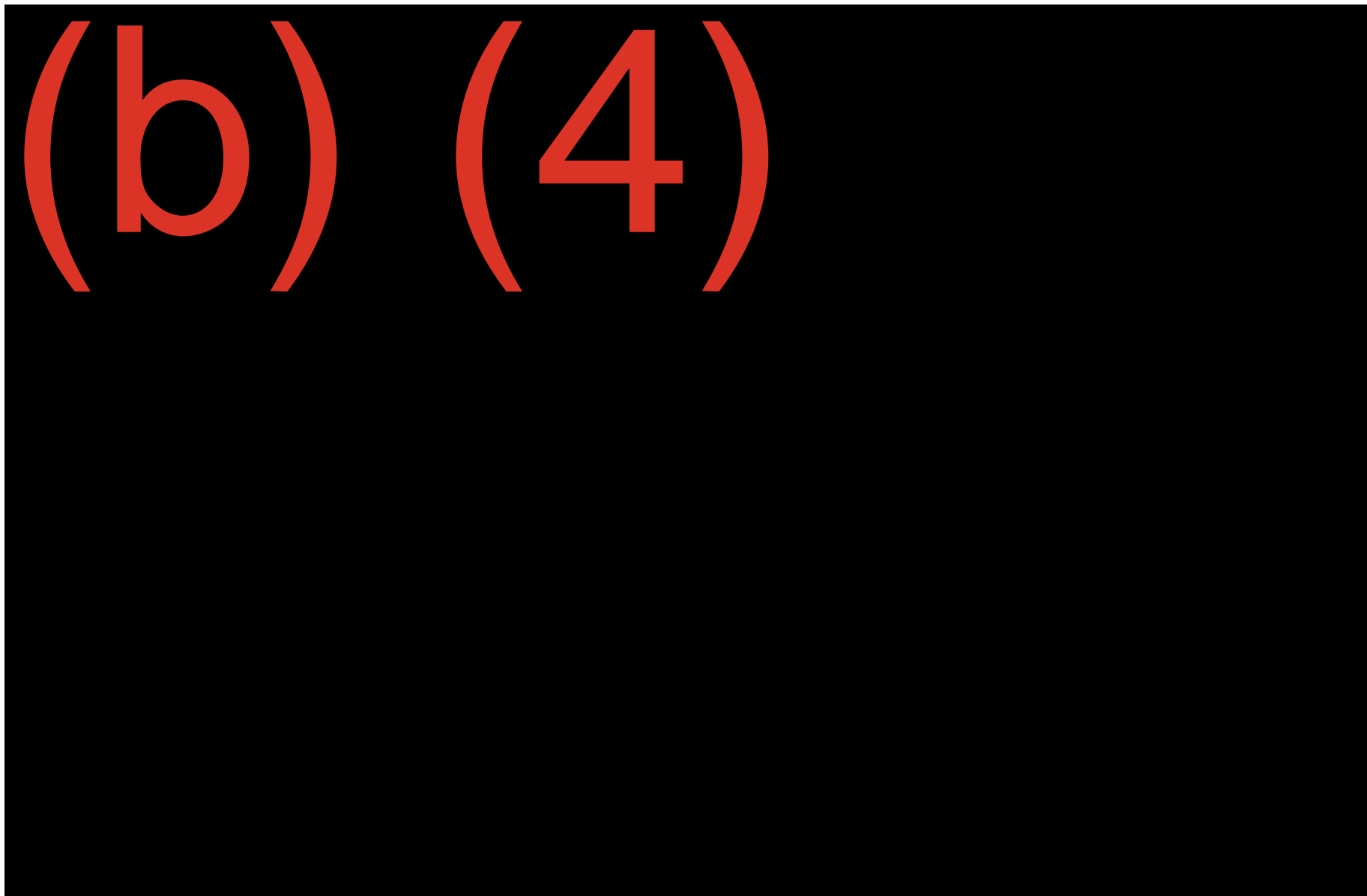
(b) (4)

(b) (4)

Table 23: Perceptions of Relative Risk of Mouth Cancer

(b) (4)

(b) (4)



(b) (4)

(b) (4)

Table 24: Perceptions of Relative Risk of Serious Health Problems

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

13.5 Results for Sensitivity Analyses

Sensitivity analyses were conducted for every outcome with the outliers removed (Sensitivity Tables 11S–24S, Attachment 17.2). The results of the sensitivity analyses demonstrated that the exclusion of the outliers (b) (4) did not affect the original descriptive results in a substantive way.

13.6 Summary of Results

The demographic data were comparable between the seven cohorts in this study. The outcomes associated with each objective revealed how exposure to the ZYN stimuli affected the intentions, behaviors, and perceptions of TNP users and non-users. Respondents demonstrated comprehension of ZYN stimuli.

Primary Objective 1

Among all respondents, assess whether being exposed to ZYN stimuli has an impact on perceptions and intentions related to the use of TNP.

Likelihood to initiate or reinitiate TNP: All TNP non-users and former users were unlikely to buy any kind of TNP in the future, including ZYN. Exposure to ZYN stimuli did not create any interest in the product.

Future intention to buy ZYN among TNP users: After exposure to the ZYN stimuli, the likelihood that cigarette smokers would buy ZYN in the future ranged between (b) (4) points on an 11-point Juster scale (from 0 = no chance, almost none – 10 = certain, practically certain). The mean likelihood that current tobacco users, excluding cigarettes, would purchase ZYN in the future was (b) (4). Notably, cigarette smokers with intention to quit showed higher likelihood to buy ZYN than cigarette smokers without intention to quit.

Current use of TNP and future intention to use current TNP after exposure to ZYN: The majority of TNP users reported smoking cigarettes every day, with the highest frequency among those without intention to quit (b) (4). After exposure to ZYN stimuli, nearly (b) (4) of cigarette smokers with intention to quit and (b) (4) of cigarette smokers without intention to quit reported intending to cut back or quit completely future cigarette smoking.

Current and future intention to quit TNP: The future intention of TNP users to quit TNPs did not change after exposure to the ZYN stimuli. Prior to exposure to the ZYN stimuli, cigarette smokers with intention to quit already had high levels of desire to quit TNP use (mean MTSS scores ranging from (b) (4)), whereas most cigarette smokers without intention to quit (mean MTSS scores ranging from (b) (4)) and tobacco users (mean MTSS scores ranging from (b) (4)) had less desire to quit their TNP use. Scores on MTSS range from 1="I don't want to stop smoking"; 2="I think I should stop smoking but don't really want to"; 3="I want to quit smoking but haven't thought about when"; 4="I really want to stop smoking but I don't

know when I will”, 5=“I really want to stop smoking and hope to soon”; 6=“I really want to stop smoking and intend to in the next 3 months”; 7=“I really want to stop smoking and intend to next month.”

Primary Objective 2

Among all respondents, measure the appeal of various ZYN brand and product attributes after being exposed to ZYN stimuli.

TNP users considered the ZYN brand and its various product attributes (flavor variety, product design, physical product) to be more appealing compared with TNP non-users. In particular, the child-safety lid was the most appealing attribute among both TNP and non-TNP users.

Secondary Objective 1

Among all respondent cohorts, explore variation in perceptions of absolute risk associated with never having used any TNP, smoking cigarettes, and using ZYN.

Across all health conditions (adult tooth loss, mouth cancer, gum disease, and serious health problems), most respondents perceived low absolute risks for never having used any TNPs, moderate absolute risks for using only ZYN daily, and high absolute risks for smoking cigarettes daily.

Secondary Objective 2

Among all respondent cohorts, explore variation in perceptions of relative risk of using ZYN as opposed to using other tobacco products, aids to help stop smoking, quitting all TNP, and never using any TNP.

Respondents consistently attributed high risk to the presence of cigarette usage, whether in the presence of ZYN or otherwise. However, the majority of respondents across all cohorts perceived the daily use of only ZYN to carry the same or lower risk of each health condition as cigarettes, both cigarettes/ZYN, moist snuff, chewing tobacco, and snus. Additionally, ZYN was perceived to carry higher risk relative to quitting all TNP and never using TNP.

14. DISCUSSION AND OVERALL CONCLUSIONS

The principal research questions “How does exposure to the ZYN stimuli affect intentions, behaviors, and perceptions of TNP users and TNP non-users?” and “Does exposure to the ZYN stimuli have a different impact on intentions, behaviors, and perceptions across TNP user and TNP non-user groups?” were addressed in this observational Likelihood of Use study.

14.1 Strengths and Limitations of the Study

This study was conducted following the guidance of the Center for Tobacco Products ([FDA Guidance for Industry, 2011](#)) within the FDA on data for human studies designed to evaluate the risks and benefits to the population, including users and non-users of tobacco products. The Likelihood of Use study relied on relevant statutes, and information obtained from the Tobacco Products Scientific Advisory Committee Meeting to frame the research questions addressed in the General Snus MRTP study ([FDA CTP Response Letter, 2017](#)). The study also benefited from guidance for best practices in consumer research for Tobacco Product Perception and Intention Studies (TPPIS), based on a March 2017 meeting between the FDA and SMNA ([CTP Addendum, 2017](#)).

The study featured many strengths, the first being the extensive number of individuals included in the survey panels, which ensured robustness of findings. The study also benefitted from the use of qualitative cognitive interviews prior to the execution of the quantitative survey, which informed and strengthened the design of the web-based survey. Cognitive interviews ensured that the materials were appropriate and sufficiently clear to respondents. As a result, the questionnaire offered both completeness and simplicity. Additionally, the administration of the web-based survey allowed for improved survey designs and accurate data capture. Importantly, the study results were robust enough to withstand the inclusion of outliers. As the pattern of results were similar in both the full sample analysis and the sensitivity analysis, it appeared that the inclusion of outliers did not have a substantive impact on the findings.

Finally, in virtually all cases survey questions utilized validated scales, or scales directly comparable to studies in literature. In particular, usage of the Juster Scale and Motivation to Stop Scale allowed for simple, justifiable interpretation. Scales used in risk perception questions line up with other tobacco-related research, such as HINTS.

There were limitations to the current study, arguably none of which should draw concern regarding data integrity. The data collected were based on post-exposure responses to stimuli for ZYN. The perceived health risk assessments were intended to simulate real-world perceptions after exposure to real-world information on ZYN, but obviously they did not have the same contextual, social, and emotional consequences of actual decisions. Similarly, one could only expect a limited degree of accuracy and extrapolation while capturing behavioral intentions, as unforeseen factors can impact actual behaviors. Thus, differences may arise between stated and actual choices, and stated and actual behaviors. Potential hypothetical bias may be limited by constructing questions that mimic realistic perceptions and behaviors as closely as possible. In

addition, since data from this study were dependent on respondent self-reporting, subsequently reported variables may also be subjected to recall bias and the inability to confirm actual tobacco use behavior. Self-reported data collection is a standard approach and any potential problems with recall bias were anticipated to be constant across time points.

Every effort was made to approximate the socio-demographic profiles of the adult population enrolled in the PATH study, though it was difficult to recruit the full cohort for current cigarette smokers with intention to quit from legal age to 24 years (cohort 4; (b) (4)), which was under-sampled by over (b) (4) respondents. Although we intended to follow CTP guidance which requires oversampling in vulnerable populations, specifically the young adult population (legal age for tobacco use in their states, to age 24) among current cigarette smokers, due to insufficient numbers of active panel members in the desired age range who also met the precise requirements of being smokers and intending to quit, we were not able to recruit a full cohort as planned. It may be that younger smokers were more likely to have started smoking recently and thus would be less likely to already have intentions to quit smoking. Thus, the population base for sampling this cohort is small relative to older smokers. In the end, the achieved socio-demographic proportions in the current study were within $\pm 20\%$ of the corresponding PATH demographics.

Respondents were recruited based on their membership with an online market research panel. As a result, recruitment could be considered a convenience sample. While multiple panels were used, similar to any other data source used (e.g. random dialing), consumers who were not part of these data sources did not have the opportunity to participate. Further, due to sample selection during recruitment, respondents who were more interested in research, or perhaps healthy enough to participate, may be over-represented, hence the possibility of selection bias. Although these issues raised concerns about the external validity of the findings (e.g., our sample may not be fully generalizable to all consumers), the recruitment plan was designed to mirror the underlying populations. Even with efforts to ensure a representative sample using stratification, the precise proportion of subgroups in the study sample could not be completely controlled.

14.2 Overall Conclusions

Study findings support the conclusion that overall, the introduction of ZYN does not appear to compromise public health in any way, based on likelihood of use and perceptions of risk as assessed in the current study. Specifically, results demonstrated that:

- Respondents who did not use TNPs were not likely to initiate or reinstate TNPs after viewing the ZYN description and packaging label ('stimuli').
- Current tobacco users and current cigarette smokers demonstrated some interest in purchasing ZYN in the future. Additionally, cigarette smokers with intention to quit showed greater interest in purchasing ZYN than cigarette smokers without intention to quit.
- Among TNP users, exposure to the ZYN stimuli did not affect their intentions to quit TNP, as reflected in MTSS scores. However, according to future intention to use TNP, the majority of smokers with intention to quit did report that they would cut back or completely quit the use of cigarettes, moist snuff, cigars/cigarillos/filtered cigars filled with tobacco, and/or pipe tobacco after exposure to the ZYN stimuli.
- Respondents perceived that there are risks of certain health conditions associated with using ZYN, but those risks are 1) the same or lower for cigarettes, both

15. REFERENCE LIST

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16. APPENDICES

16.1 Statistical Tables

Table Number	Title
11	Socio-demographic and Comprehension Check Variables for all study participants
12	Primary Objective 1 - Likelihood to Initiate or Reinitiate TNP
13	Primary Objective 1 - Future Intention to Buy ZYN among TNP Users
14	Primary Objective 1 - Current Use of TNP among TNP Users
15	Primary Objective 1 - Future Intention to Use Current TNP after Exposure to ZYN
16	Primary Objective 1 - Pre-exposure Intention to Quit TNP (MTSS) and Post-Exposure Intention to Quit TNP (MTSS)
17	Primary Objective 2 – Appeal of ZYN Brand and Product Attributes
18	Secondary Objective 1 – Perceptions of Absolute Risk to a Person who Smokes Cigarettes Every Day but Uses no Other Tobacco Products
19	Secondary Objective 1 – Perceptions of Absolute Risk Associated with Never Having Used any TNPs
20	Secondary Objective 1 – Perceptions of Absolute Risk Associated with Using Only ZYN Daily
21	Secondary Objective 2 – Perceptions of Relative Risk of Adult Tooth Loss
22	Secondary Objective 2 – Perceptions of Relative Risk of Gum Disease
23	Secondary Objective 2 – Perceptions of Relative Risk of Mouth Cancer
24	Secondary Objective 2 – Perceptions of Relative Risk of Serious Health Problems

Table 11. Socio-demographic and Comprehension Check Variables for All Study Participants.

(b) (4)

(b) (4)

(b) (4)

(b) (4)

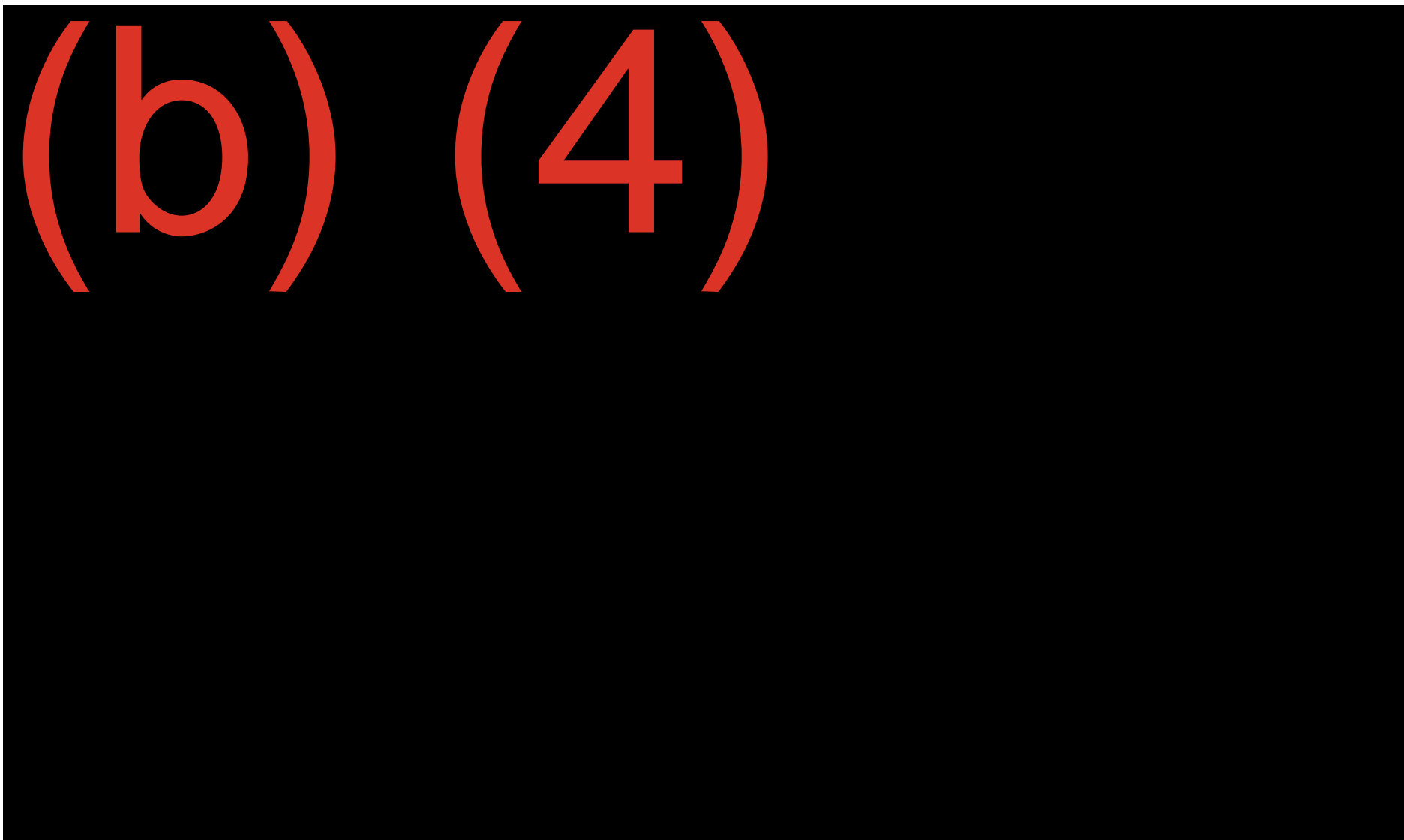
Table 12. Primary Objective 1 - Likelihood to Initiate or Reinitiate TNP.

(b) (4)

(b) (4)

Table 13. Primary Objective 1 - Current Use of TNP among TNP Users.

(b) (4)



(b) (4)

(b) (4)

(b) (4)

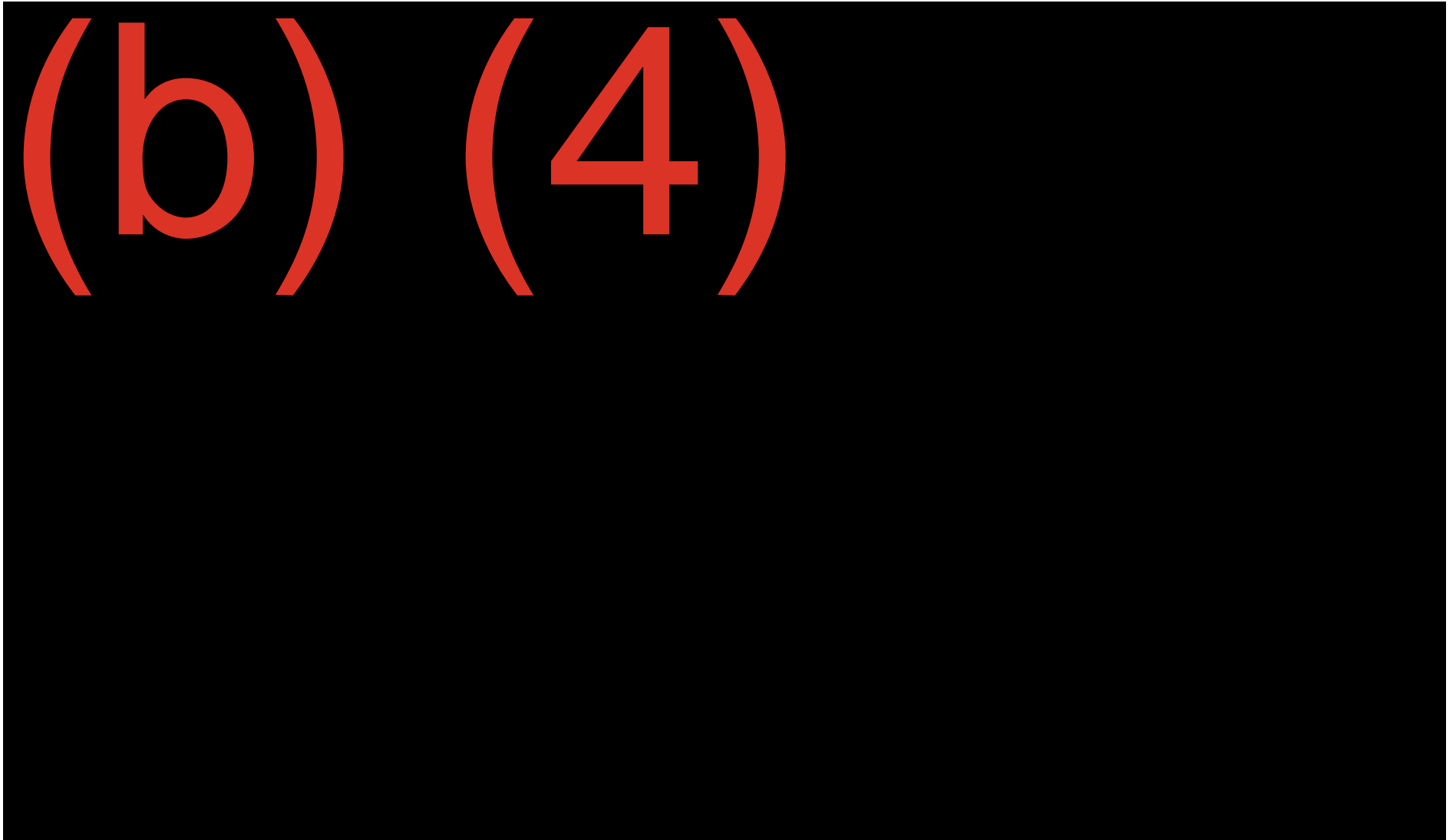
Table 14. Primary Objective 1 - Future Intention to Buy ZYN among TNP Users.

(b) (4)

Table 15. Primary Objective 1 - Future Intention to Use Current TNP after Exposure to ZYN.

(b) (4)

(b) (4)



(b) (4)

(b) (4)

Table 16: Primary Objective 1 - Pre-exposure Intention to Quit TNP (MTSS) and Post-Exposure Intention to Quit TNP (MTSS).

(b) (4)

(b) (4)

Table 17. Primary Objective 2 – Appeal of ZYN Brand and Product Attributes.

(b) (4)

(b) (4)

(b) (4)

Table 18. Secondary Objective 1 – Perceptions of Absolute Risk to a Person who Smokes Cigarettes Every Day but Uses no Other Tobacco Products.

(b) (4)

(b) (4)



(b) (4)

Table 19. Secondary Objective 1 – Perceptions of Absolute Risk Associated with Never Having Used any TNPs.

(b) (4)

(b) (4)

(b) (4)

(b) (4)

Table 20. Secondary Objective 1 – Perceptions of Absolute Risk Associated with Using Only ZYN Daily.

(b) (4)

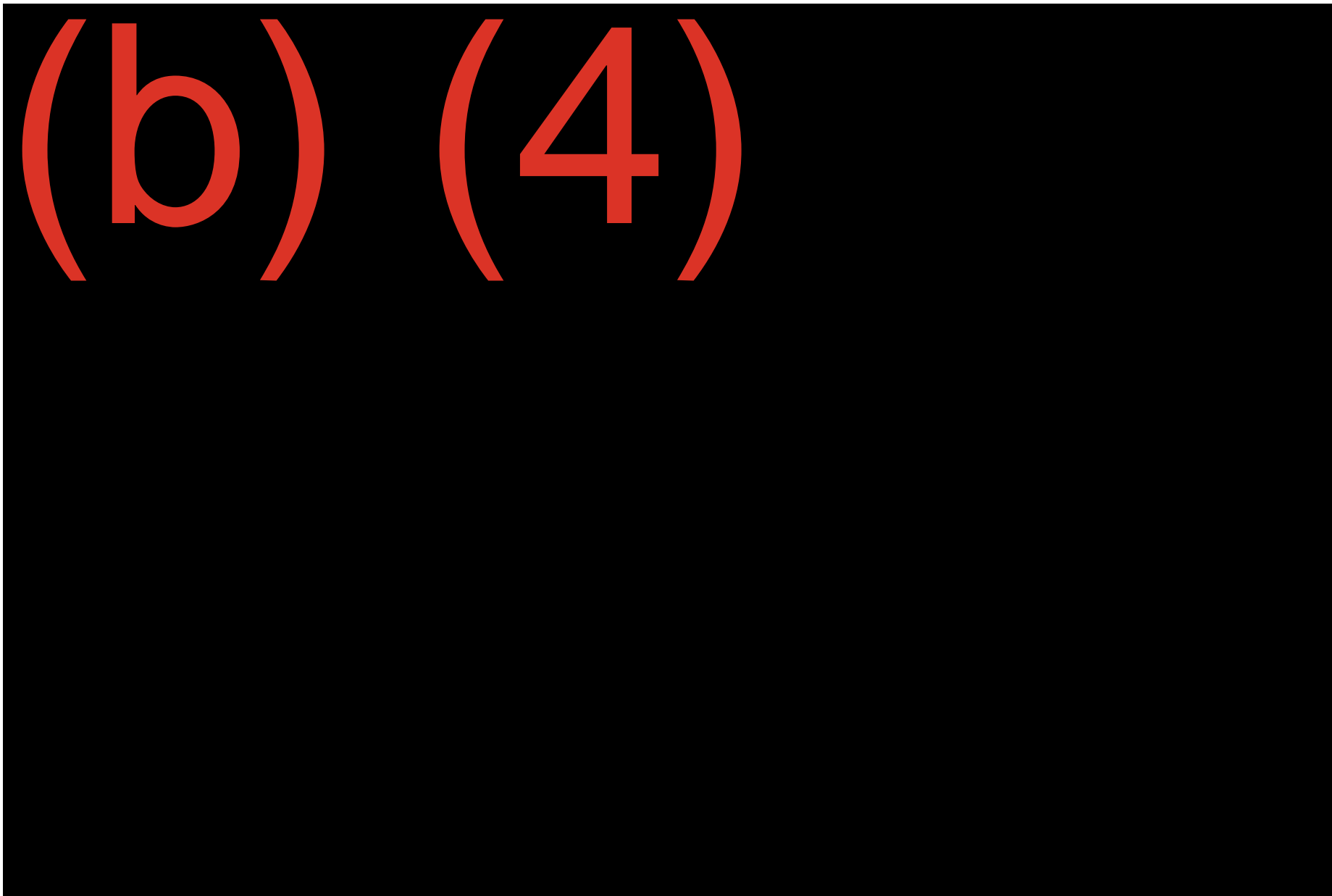
(b) (4)

(b) (4)

(b) (4)

Table 21. Secondary Objective 2 – Perceptions of Relative Risk of Adult Tooth Loss.

(b) (4)



(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

Table 22. Secondary Objective 2 – Perceptions of Relative Risk of Gum Disease.

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

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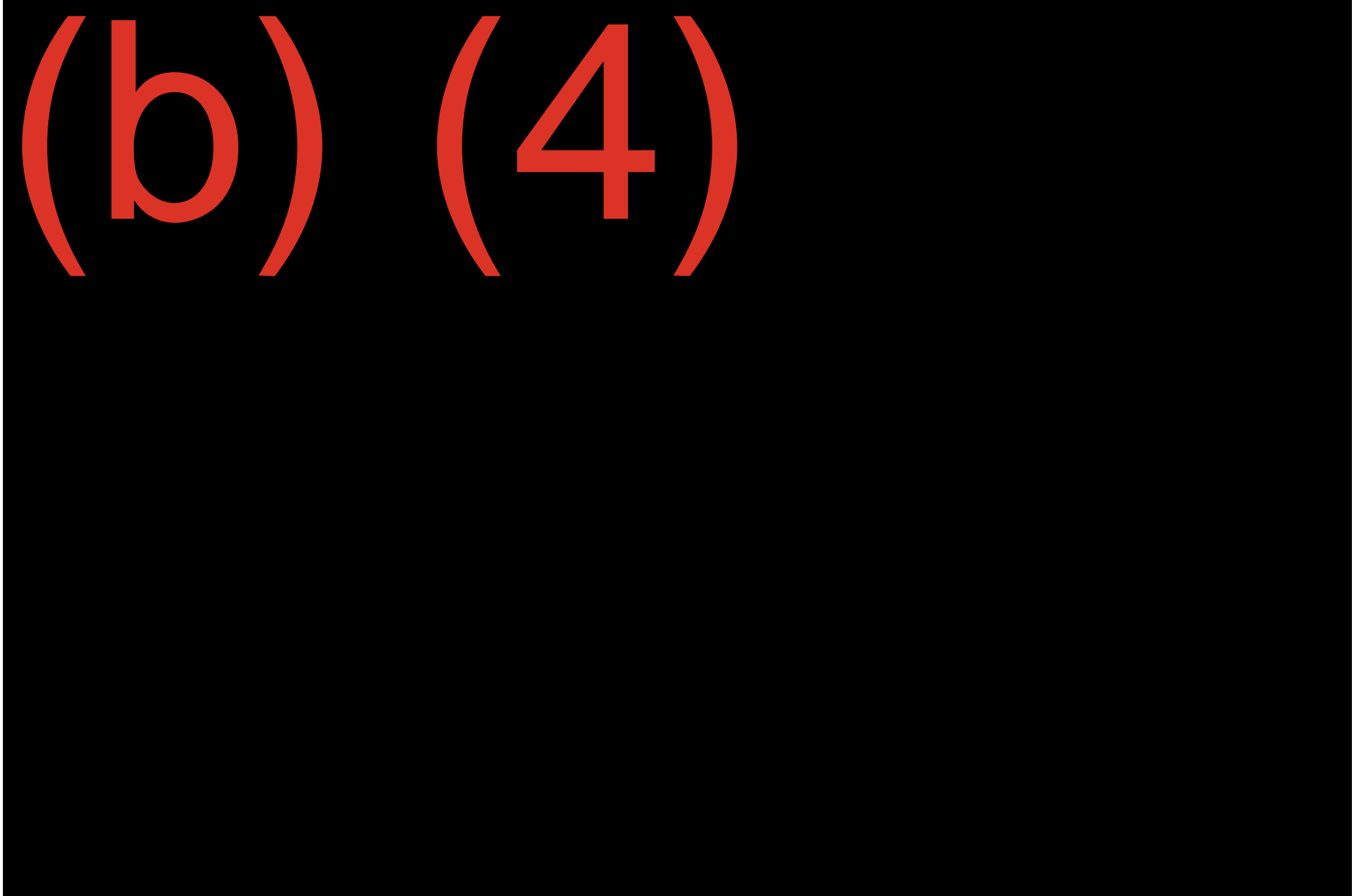
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Table 23. Secondary Objective 2 – Perceptions of Relative Risk of Mouth Cancer.

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Table 24. Secondary Objective 2 – Perceptions of Relative Risk of Serious Health Problems.

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SIGNATURE PAGE

I approve of this ZYN® *Likelihood of Use* final report.

Name (typed or
printed):

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

Institution:

(b) (4)

Signature:

(b) (6)

Date: 6 August 2018

(Day Month Year)

Name (typed or
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Institution:

Swedish Match North America

Signature:

(b) (6)

Date: 6 August 2018

(Day Month Year)