DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

PROTOCOL SUBMISSION

FDA Research Involving Human Subjects Committee

RIHSC File Number

Select one of the following submission types.

☒ **New Submission** ☐ **Resubmission** ☐ **Modification** ☐ **Information Supplement**

1. Study Title

Experimental Study on the Presentation of Harmful and Potentially Harmful Tobacco Constituents

2. Brief Synopsis of Study

This experimental study is designed to help inform decisions about how to implement section 904(d)(1) of the Family Smoking Prevention and Tobacco Control Act and to provide information about how consumers understand information about harmful and potentially harmful constituents in tobacco products. The study is an on-line study being conducted by RTI International using the e-Reward on-line panel. The subjects will be adolescents and adults with an estimated total of 3,150 participants.

3. FDA Sponsor

a. Name of FDA Sponsor	b. Center
Laura Shay	Center for Tobacco Products
c. Telephone Number	d. E-mail Address
301-796-0994	laura.shay@fda.hhs.gov

4. Principal Investigator *(If different from above)*

a. Name of Principal Investigator	b. Address
Jon Blitstein	3040 Cornwallis Road PO Box 12194 Research Triangle Park, NC. 27709-2194
c. Telephone Number 919-541-5024	
d. E-mail Address jblistein@rti.org	

5. Will the proposal/protocol be FDA funded? ☐ No ☒ Yes *If Yes, please complete 5.a and 5.b.*

a. Grants/Contracts Office Approval	Date
☒ Approved ☐ Not Approved	06/07/2011

b. Specify funding instrument *(e.g., Contract, Interagency Agreement, Grant)*

Contract

6. Is this project to be conducted under a regulatory application *(i.e., IND/IDE, etc.)*?

☒ No ☐ Yes *If Yes, please provide number (in 6.a), and state the regulatory status of the clinical protocol (in 6.b).*

a. IND/IDE Number	b. Regulatory Status

7. Is this project eligible for an Expedited Review? ☐ No ☒ Yes

Eligibility: *http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.110*

8. Eligible Population

a. Will both sexes be accrued? ☒ Yes ☐ No	*If No, please provide justification.*
b. Will there be an age limitation? ☐ No ☒ Yes	*If Yes, please provide justification.* Anyone under age 13 is not eligible because the study not intended for children.
c. Do the subject selection criteria specifically address the use of special populations *(e.g., minors, pregnant women (fetuses), HIV+ people, minorities, students, prisoners, etc.)*? ☐ No ☒ Yes	*If Yes, please describe the protections in place for vulnerable subjects.* Parental consent and minor assent are required. Minors are not recruited. Only parents of minors receive a recruitment message.

9. Total Number of Subjects to be accrued	10. Proposed Duration of Study *(Including accrual/data analyses)*
3,150	1 month

11. Will subjects be compensated for participation? ☐ No ☒ Yes

12. List the performance site(s) where research will be conducted.
On-line throughout the United States

13. Does this site(s) have an IRB that will be reviewing the protocol (IRB-of-record)? ☐ No ☒ Yes

a. If yes, please provide the name, address, telephone number, federal-wide Assurance number, and name of chair for each IRB *(a separate page may be used)*.

Juesta M. Caddell, PhD, Director
Office of Research Protection
RTI International FWA 3331
Phone: 919-541-6523, x26523
Fax: 919-485-5589, x25589

Note: both the FDA RIHSC and the RTI IRB are reviewing the study.

14. Have all the key personnel been trained in human subject protection rules and regulations. Key personnel include all individuals responsible for the design and/or conduct of the study. ☒ Yes ☐ No

15. *By signing below, I acknowledge that:*

a. I have reviewed and understand my obligations under: The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, 2) the U.S. Department of Health and Human Services (HHS) regulations for the protection of human subjects at 45 CFR part 46, 3) FDA's Federal-wide Assurance and applicable Terms of the FWA, and 4) FDA Internal Standard Operating Procedures for FDA's Institutional Review Board, the Research Involving Human Subjects Committee (RIHSC).

b. I will assure that all IRBs involved have approved the protocol prior to the initiation of the research, including any advertising or recruitment of subjects.

c. I will abide by all determinations of the RIHSC and will accept the final authority and decisions of the RIHSC, including but not limited to directives to terminate participation in designated research activities.

d. I will not initiate changes in the research without prior RIHSC review and approval, except where necessary to eliminate apparent immediate hazards to subjects.

e. I will report immediately to the RIHSC any unanticipated problems involving risks to subjects or others in research covered under this Agreement.

f. I acknowledge and agree to cooperate in the RIHSC responsibility for initial and continuing review, record keeping, reporting, and certification for the research referenced above. I will provide all information requested by the RIHSC in a timely fashion.

g. I acknowledge that I am primarily responsible for safeguarding the rights and welfare of each research subject, and that the subject's rights and welfare must take precedence over the goals and requirements of the research.

Signature of FDA Sponsor	Date
[signature]	7-9-12

15. *By signing this, I assure that all the above information is correct.*

Signature of RIHSC Liaison	Date

Form RIHSC-EXPD

APPLICATION FOR AN EXPEDITED RIHSC REVIEW OF RESEARCH
FDA Research Involving Human Subjects Committee

Sponsoring Office/Center: **Center for Tobacco Products / Office of Science (Laura Shay, PhD, RN)**
Principal Investigator: **Jon Blitstein, PhD of contractor RTI (subcontracted to "Research Now")**

Protocol/Project Title: **Experimental Study on the Presentation of Harmful and Potentially Harmful Tobacco Constituents**

INSTRUCTIONS: Please read Section 1, Applicability, below. If you feel your research could possibly be reviewed using an expedited review procedure, then go on complete the checklist in Section 2 and sign page 2.

Section 1. Applicability

(A) Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the categories in Section 2 below, may POSSIBLY be reviewed by the RIHSC through the expedited review procedure. Any activity listed in Section 2 should not be deemed to be of minimal risk simply because it is included on the list. Inclusion merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

(B) The categories in Section 2 apply regardless of the age of subjects, except as noted. Children are defined in the HHS regulations as persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." 45 CFR 46.402(a).

(C) The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

(D) The expedited review procedure may not be used for classified research involving human subjects.

(E) The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review expedited or convened utilized by the RIHSC.

Section 2. CHECK LIST FOR RESEARCH ACTIVITIES WHICH MAY BE REVIEWED THROUGH EXPEDITED REVIEW PROCEDURES

Minimal risk = the risks of harm anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Yes	No	
X	☐	Can this study be classified as minimal risk, based on the definition above?

If **yes**, continue to questions on page 2. If **no**, project/protocol will require full board review.

By signing below, I assure that the information is accurate:

SIGNATURE (Center/Office Liaison)_____Susan Rudy, MSN, CRNP /s/_____DATE _____7/10/2012_____

Indicate which of these categories apply to your study/project/protocol (more than one may apply)
Once you have completed the checklist on this page, please sign and submit this form with the materials indicated.

THE FOLLOWING 9 CATEGORIES PERTAIN TO BOTH INITIAL AND CONTINUING IRB REVIEW

Yes No
□ X Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

Yes No
□ X Research on medical devices for which (I) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

Yes No
□ X Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows (Circle **a** or **b**, whichever applies):
(a) From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
(b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

Yes No
□ X Prospective collection of biological specimens for research purposes by noninvasive means. Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (I) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

Yes No
□ X Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

Yes No
□ X Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

Yes No
□ X Collection of data from voice, video, digital, or image recordings made for research purposes.

Yes No
X □□ Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

Yes No
□ X Research on individual or group behavior or characteristics of individuals, such as studies of perception, cognition, game theory, or test development, where the investigator does not manipulate subjects□ behavior and the research will not involve stress to subjects.

THE LAST 2 CATEGORIES PERTAIN TO CONTINUING REVIEW ONLY

Yes No
□ □ □□Continuing review of research previously approved by the convened IRB as follows (Circle **a**, **b**, or **c**, whichever applies):
(a) Where (I) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
(b) Where no subjects have been enrolled and no additional risks have been identified; or
(c) Where the remaining research activities are limited to data analysis.

Yes No
□ □ □□Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

SIGNATURE (Center/Office Liaison)_____Susan Rudy, MSN, CRNP /s/_____DATE ___7/10/2012_____

Transmittal Memorandum

TO: Chair, Research Involving Human Subjects Committee

From: Susan Rudy, MSN, CRNP, CORLN
CTP Center/Office RIHSC Liaison

Date: July 11, 2012

Protocol Title: Experimental Study on the Presentation of Harmful and Potentially Harmful Tobacco Constituents

Principal Investigator: Contracted to "RTI" and Subcontracted to "Research Now"

FDA Sponsor (if PI is not from FDA): Laura E. Shay, PhD, RN

New Submission [X] Resubmission [ ] Amendment [ ] Continuing Review [ ]

RIHSC Protocol #_____(to be filled in by RIHSC Office if new submission)

By signing below, I assure that:

A. For protocols applying for RIHSC review:
    1. The protocol/concept, as submitted, has undergone scientific review for technical merit and programmatic relevance by my Center/Office and has been approved by the Center Director/Office Director or designee.
    2. The principal investigators are qualified to do the research.
    3. The FDA sponsor has completed the required training in human subjects protection and understands his/her obligations under the regulations and is qualified to provide adequate oversight of this protocol.
    4. The potential risks to the subjects are appropriate for the potential benefits.
    5. The informed consent document conveys the risks and benefits in a clear, scientifically accurate and balanced manner.
    6. The completed submission form (Form RIHSC-PROT) or continuing review form (Form RIHSC-CR) and, if appropriate, the request for expedited review form (Form RIHSC-EXPD) and supporting information are accurate and have been attached.
    7. An IDE/IND ____is___X____is not required.

B. For protocols requesting exemption from RIHSC review:
    1. The protocol has undergone scientific review for technical merit and programmatic relevance by my Center/Office and has been approved by the Center Director/Office Director or designee
    2. The completed exemption form (Form RIHSC-EXT) and supporting information are accurate, and have been attached.

_Susan Rudy, MSN, CRNP /s/ 7/11/2012
Signature of Center /Office Liaison Date

See Addendum Attached

ADDENDUM to Transmittal Memo: Shay HPHC Experimental Study

Protocol Title: Experimental Study on the Presentation of Harmful and Potentially Harmful Tobacco Constituents

FDA Sponsor: Laura E. Shay, PhD, RN

Request: Expedited Review (Minimal Risk study)

Reason for Addendum

The CTP RIHSC Liaison review of this protocol was limited to human subjects protections issues and identified the need for clarifications. Because the submitted protocol is concurrently under review with OMB under the Paperwork Reduction Act and because CTP is mandated to do this study by section 904(d)(1) of the Food Drug and Cosmetics Act as amended by the Tobacco Control Act (Public Law 111-31) with an imminent statutory deadline, we provide the Sponsor's responses to the identified issues in this cover memo addendum, rather than in a revised or amended protocol.

Executive Summary

This protocol is for an experimental study designed to inform CTP's decisions about how to implement section 904(d)(1) of the Family Smoking Prevention and Tobacco Control Acto and to provide information about how consumers understand information about harmful and potentially harmful constituents in tobacco products. The Sponsor proposes an on-line 30-minute survey of 3,150 participants aged 13 and over. Subjects are current tobacco users and minors who are at risk for becoming tobacco users. Subjects are recruited from a pre-existing panel of members of an online marketing research company, "Research Now," who have supplied identified demographics, interests and activities data upon joining the pre-existing registry. Recruitment is accomplished by sending a general email to potentially eligible members, which identifies the topic of the survey, but not the reason the recipient has been selected for invitation. Minors are recruited only through their parents who are also members of the registry and are enrolled only after parental consent, then minor assent. Survey data specific to this study is collected after electronic informed consent, followed by screening questions to confirm eligibility. Collected survey data is irreversibly unlinked from the respondent at the time of collection. Subjects are rewarded in "e-Rewards" points "currency," equivalent to $7.50.

There is an executed contract in place with Research Triangle Institute ("RTI"), Jon Blitstein, Ph.D., PI, for conduct of the study, and RTI has subcontracted with "Research Now." The RTI IRB is also reviewing and overseeing the study.

This research is not exempt because it involves vulnerable subjects (minors). After considerable interaction between the CTP_RIHSC and the Sponsor, we recommend this research for expedited review and believe that it involves no greater than minimal risk under 45 CFR 46.404. Informed consent complies with 45 CFR 46.117(c) and 45 CFR 46.408.

Review Interaction Summary Log

- Protocol submitted to CTP_RIHSC on 5/4/2012 (This was our first CTP_RIHSC submission).
- Review assigned to S. Rudy, CTP RIHSC Liaison alternate, by I. Chen, Clinical Team Leader on 5/30/2012 (in RIHSC Liaison, Dr. Lacorte's absence).
- CTP RIHSC Liaison alternate, Susan Rudy, CRNP, met with the Sponsor, Laura Shay, on 5/31/2012 for clarifications.
- S. Rudy sent a formal e-mail request to Sponsor for additional information and clarifications on 6/1/2012
- Sponsor submitted responses by email to S. Rudy on 6/5/2012
- S. Rudy sent additional follow-up queries to Greta Tessman, MA, covering for Sponsor on vacation, on 6/8/2012
- I. Chen, Clinical Team Leader, informed Sponsor and Social Sciences team of new CTP form documenting team / office / center sign-off for scientific and technical merit.
- There was a meeting of the social sciences team (Choiniere, Tessman, & Johnson) with the CTP_RIHSC team (Chen & Rudy) on 6/11 for clarifications (see separate minutes).
- S. Rudy met with G. Tessman (covering for Sponsor) briefly, at her request, on 6/19/2012 to discuss data storage (contractors will erase data after passing to next entity) and the issue of personally identifiable information (PII) (none is collected in the Agency survey or received by CTP, documents are being rectified and clarified on this point)
- The Sponsor submitted responses to our 6/8 AI request on 6/29/2012
- S. Rudy met with the Sponsor on 7/2/2012 for additional clarifications
- There was additional email discussion between S. Rudy and the Sponsor 7/3-7/9 to clarify how data is collected such that PII is never linked initially and is never able to be linked intentionally or unintentionally.
- S. Rudy sent second request to Sponsor 7/10/2012 requesting signed memo of CTP Center sign-off for scientific & technical merit.
- Complete package submitted to FDA RIHSC by S. Rudy on 7/12/2012 (OMB / PRA approval still pending).

Sponsor Qualifications

The Sponsor is a full-time FDA / CTP / OS employee, qualified by formal academic training (PhD in Nursing), experience within CTP, and completion of specific training in Human Subject Research Protections on 5/3/2011, expiration 4/20/2014, as offered by the CITI Social and Behavioral Science Course.

Equitable selection of subjects

This study includes minors aged 13 and older as well as adults, with no upper age limit. We have knowledge from clinical practice and published sources that children younger than age 13 participate in both experimentation with tobacco and regular tobacco use. The Sponsor explained that the reason for not sampling children younger than age 13, is that they would not likely be able to independently and reliably complete an online survey of this nature without parental supervision and assistance. It is not feasible within the mandated timeline and budget to sample younger children outside of this online survey contract mechanism.

As an online survey, only people with access to the internet will be sampled and those without access are excluded. With computers being present in schools, workplaces, and public arenas such as libraries, and internet cafés, the majority of the U.S. population has access, whether or not they are skilled or inclined to use computers. Smartphones have additionally increased access. A recent study of 1620 people from low-income adult Supplemental Nutrition Assistance Program Education participants in the Midwest found that approximately 50% had a working computer in their home (Neuenschwander, Abbott, & Mobley, 2012). While the proposed sampling schema may somewhat limit access to lower socioeconomic and elderly participants, it stands a reasonable chance to obtain a representative sample and it is not feasible within the mandated timeline and budget to sample additional strata of the population outside of this online survey contract mechanism.

The study bears no upper age limit for participation and as written makes no requirement for assuring that any elderly subjects will participate. The sampling schema is consistent with the CTP mission, which is weighted toward prevention of smoking initiation and promotion of early cessation. Elderly persons do own and use computers and are members of e-Rewards, available for sampling, and thus the sampling schema bears a reasonable chance to obtain a representative sample, including the elderly. It is not feasible within the mandated timeline and budget to sample additional strata of the population outside of this online survey contract mechanism. In addition, there is an adequate body of published work on issues of particular concern for product labeling in the elderly, such as font size and style, contrast, and layout, as summarized by Rudy (2008).

The age range of the e-Reward panel is 13-85 and above. The percentages of age ranges are listed in the table below. Note that the HPHC information will eventually be publically available on the FDA website. The likelihood that elders without computer access will seek out this information is low. The on-line design of this study helps provide ecological validity of the user population.

Age Range	Percent
13 - 14	0.12%
15 - 17	0.67%
18 - 24	9.53%
25 - 34	23.12%
35 - 44	20.78%
45 - 54	20.38%
55 - 64	17.11%
65 - 74	6.94%
75 - 84	1.15%
85 and above	0.11%
Not Provided	0.11%

References:

- Neuenschwander, L. M., Abbott, A., & Mobley, A. R., (2012). Assessment of low-income adults' access to technology; Implications for nutrition education. J Nutr Educ Behav, 44(1), 60-65. DOI: 10.1016/jneb.2011.01.004

- Rudy, S. F. (2008). Editorial: Aging Eyes. ORL-Head and Neck Nursing, 26(1), 5-7.

Recruitment and rewards for vulnerable subjects

1. Justification for research on vulnerable subjects: This study includes a cohort of minors aged 13 to 17 and asks sensitive questions about illegal and parentally disallowed behavior of smoking cigarettes. The use of cigarettes below age 18 is illegal in some states and the sale of cigarettes to minors is illegal in all states. The protocol adequately justifies soliciting sensitive information from minors. Because the public display of the harmful and potentially harmful constituent (HPHC) information will not be limited to adults, it is important that CTP study youth's reactions to this information.

2. The submitted protocol is unclear on how subjects are recruited and what the incentive reward is.

   All subjects are recruited via a subcontractor, Research Now, an online marketing research company that manages an internet consumer panel called, "e-Rewards." The company independently recruits panels of potential respondents for many types of marketing research based on internet responses to a broad range of questions on demographics, interests and activities. A subpanel of potentially interested and applicable respondents is then invited to participate in specific marketing research (such as the CTP proposed study) as needs arise per contractual arrangements. Respondents who participate in panels and subpanels are rewarded using a points system, so that no reward is linked to participation in a particular study, except by a number of points rewarded for completion of the study. Points earned for completing a study or for a cumulative number of completed studies can then be traded by the participant for a variety of rewards, which include clothing and accessories, food and dining, gifts, magazines, and travel and lodging. The array of potential rewards does not include money. Completion of the ~30-minute electronic survey, nets an e-Rewards "currency" of $7.50 which is nominal and incidental.

Risks and Benefits

Privacy and confidentiality issues for respondents

The primary risk for subjects and the investigators / sponsor in this online questionnaire study is the potential for inadvertent breach of privacy and confidentiality of the data. The protocol includes physical data security, good information management practices and computer processes for data security (e.g., password protections, access granted only per need to know, encryption of transferred data) following DHHS and FDA regulations and policies as well the Council of American Survey Research Organizations® Code of Standards and Ethics for Survey Research. The protocol (p. 6) states that "data coming directly from the survey engine are stored in a proprietary database. While this data is not encrypted, once inside the firewall, they are stored in a relational database protected by several layers of intrusion detection and access control." We understand that stored data should be encrypted and requested the Sponsor to provide additional information about data security for this study.

The protocol states (p. 5) that personal information will not be shared with third parties without the respondent's permission "…unless it is required by law to protect their rights

or to comply with judicial proceedings, court order, or other legal process." However, informed consent documents (Appendix A, p.1) state only that "no one will be able to link your responses to your identity" and do not discuss any mechanism or situation whereby personal information may be shared with a third party.

The privacy promise information that potential respondents see before agreeing to participate and complete the survey is said in the protocol to be available from a particular website link. However, on reviewer testing, the link was "broken" displaying a message that the site is no longer functioning. We asked the Sponsor to provide the functioning web link and / or the content of the privacy information the participants will see.

In several rounds of follow-up communication and clarification the following acceptable clarifications are submitted. Note that the Sponsor had follow-up communications with the contractor, but the CTP_RIHSC reviewer had communications only from the Sponsor:

1. The functioning link to privacy information for participants is now

   http://www.e-rewards.com/privacypolicy.do

   See the privacy statement also as Attachment 1 to this memo and the member agreement as Attachment 2 to this memo. The site does not seek to collect individually identifiable information about children under 18 years of age.

2. E-Rewards participates in the TRUSTe Privacy Seal Program http://www.truste.org/consumers/watchdog_complaint.php.

   E-Rewards provides their physical address as well as electronic contact information to participants.

3. The PII that is collected (i.e., name, address, internet protocol address, cookies and advanced cookies) is never linked to the responses to this FDA / CTP survey by any involved entity at any point in time, even briefly. The following protections are in place to assure privacy and confidentiality:

   a. The email invitation for survey participation issued to a subset of adult e-Rewards members does identify that the survey pertains to tobacco products but does not identify the recipient as a smoker and even if it did, this would not be sensitive information for adult legal smokers.

   b. The email invitation for survey participation issued to a subset of adult parents of minors who are members of e-Rewards and are tobacco users or are at risk to become tobacco users, identifies that the survey pertains to tobacco products, but states the reason for the invitation to be only that a teenager is thought to reside in the household. It does not state or insinuate that the teens are smokers.

   c. E-mail invitations to participate in the survey are not issued directly to minors; they are issued only to adult parents of minors, requiring parental consent before the child can access the survey via their e-Rewards account.

d. Survey computer coding never links the survey responses to the PII during the informed consent process, survey response process or rewards process, and thus it is impossible for e-Rewards technical computer staff, RTI staff, or FDA / CTP Sponsor or OIM staff to connect survey responses to individuals, and likewise hackers would be unable to connect survey responses to respondents.

e. The language aimed at participants in the e-Rewards privacy statement is clear that PII is shared only in anonymous singular summary and aggregate form (both terms are defined and explained) with site Sponsors, reward partners, panel partners, marketing partners, clients (FDA / CTP is a client), and third parties for purposes of marketing and research, with some exceptions. The detailed circumstances under which PII may be shared comply with federal guidelines and standards (e.g., audits, legal queries, etc.) and apply only to the ability to release that a person is a member of e-Rewards. By their computer coding, it is impossible for any involved party to identify what individuals were invited to participate in this FDA / CTP survey, as well as which individuals accepted the invitation, or what specific responses they gave. The demographic information received by RTI and FDA / CTP only includes general, categorical measures of race/ethnicity, sex, education, income, occupation, and city/state (optional). As defined by NIST 800-122 (2010) and OMB (March 22, 2010), this demographic information does not contain PII (https://irb.llnl.gov/pdfs/SOP_14.pdf), http://csrc.nist.gov/publications/nistpubs/800-122/sp800-122.pdf . The data received in FDA / CTP from e-Rewards is not able to be linked back to the e-Rewards participant database.

4. Research Now (a.k.a. “e-Rewards”) encrypts the stored data. After sending the data to RTI, they will delete it completely from storage. After data cleaning and analysis, RTI will pass the raw data to FDA / CTP for storage and will destroy data files after successful transmission. FDA / CTP will store data on its secure servers for at least 3 years. All involved parties comply with the standards and guidelines around data and information systems and security outlined in NIST Special Publication 800-53. Per this publication. “Special Publications (SPs) are developed and issued by NIST as recommendations and guidance documents. For other than national security programs and systems, federal agencies must follow those NIST Special Publications mandated in a Federal Information Processing Standard. FIPS 200 [FIPS Publication 200, 2006] mandates the use of Special Publication 800-53, as amended.”

The last edition of NIST Special Publication 800-53 was published in 2009 (Revision 3) (http://csrc.nist.gov/publications/nistpubs/800-53-Rev3/sp800-53-rev3-final.pdf). The data is categorized as “low” impact level.
RTI security professionals are experienced with all security documentation and processes necessary to obtain an Authority to Operate, and with all applicable Department of Health and Human Services (HHS), Federal Information Security Management Act, Health Insurance Portability and Accountability Act, NIST, and other federal policies and regulations that may apply. RTI project team members and security professionals will ensure that all HHS-related technical and security standards, processes, and procedures are followed.

5. The duration for retention of records by FDA / CTP will initially be 3 years beyond completion of the study, pending further guidance from the CTP Office of Policy.

Informed consent

The submitted (5/4/2012) protocol contains no informed consent language aimed at parents of participating minors, which does not comply with 45 CFR 46.408. The protocol states (p. 7) " e-Rewards' invitation to youth does encourage parents to know about and approve of youth involvement in the panel and surveys. However, no active parental consent is required or requested." The Sponsor clarified verbally on 5/31/2012 that this content pertains to the broad recruitment of youth for any and all studies offered through e-Rewards. We asked the Sponsor to provide the consent language and process for the parents of minor participants in this specific study.

The submitted protocol (5/4/2012) does not detail the informed consent process for any participants and contains language (p. 6) that is unclear as to the timing of informed consent in relationship to participant screening for the study. We asked the Sponsor for full details on informed consent.

The FDA sponsor clarifies that the contractor "e-Rewards" collects a full set of demographic information, along with a profile of interests and activities, as part of enrolling its huge database of members along with a membership agreement. This process is pre-existing and completely outside of the submitted study procedures. A small subset of the total "e-Rewards" membership are invited to participate in the submitted study survey based on their demographics and interests, known to e-Rewards but not to the contractor RTI or to the Sponsor, FDA / CTP.

Informed Consent Process

Eligible adults and parents of minors are sent a recruitment email if they have age and smoking status eligibility per the pre-existing e-Rewards database. Minors are not recruited unless their parents are also members of e-Rewards. The specific recruitment messages sent to adults and to parents of minors is submitted 7/2/2012 in Attachments A & B, and includes the reason for the message.

<u>The informed consent process for minors:</u>

Parents who agree that their child may wish to participate in the survey after reading the recruitment e-mail, proceed by clicking on a hyperlink embedded in the recruitment email. This hyperlink takes them to screens containing the informed consent language. They give parental consent by clicking in the box next to "Yes, I agree to let my child participate in this study" at the bottom of the informed consent screen. When parents thus give consent, this allows the minor to access the survey when next signing on to their e-Rewards account (i.e., no recruitment e-mail is ever sent to the minor). When the minor signs onto the survey, the first screen presented is the "Youth Assent Form for Youth Recruited via Parent and Youth Panels." The minor must select "Yes, I agree to participate in this study" at the bottom of the page before they can access the verification screening questions (e.g., age and smoking status). The verification question responses must confirm their eligibility for taking the survey, and then they are granted access to the survey questions.

The informed consent process for adults:

Adults who wish to participate in the survey after reading the recruitment e-mail, proceed by clicking on a hyperlink embedded in the recruitment email. This hyperlink takes them to screens containing the informed consent language. When they consent by clicking a box indicating consent, they are taken to screens containing two eligibility verification screening questions. If their answers to these two screening questions verify their eligibility, they are next taken to the survey content screens.

The informed consent language provided for adult participants (Attachment A, 7/2/2012 – Replaces Appendix A in the 5/4/2012 protocol), Parents of minors (Attachment B submitted 7/2/2012) and minor assent language (Attachment B submitted 7/2/2012) roughly complies with 45 CFR 46.116 *General requirements for informed consent*. The minor exception is that there is no study contact person named if the subject feels they are somehow harmed or injured by the study (45 CFR 46(a) (7)), which is acceptable, since injury is not anticipated in this study and is extremely unlikely to occur in an electronic survey. In addition, adults are not told how many participants are in the study, which is optional under 45 CFR 46.116 (b) (6).

The permission of just one parent is acceptable for this research because it is minimal risk research under 45 CFR 46.404.

There is no hard copy of such an online consent to be signed, witnessed and filed as required by 45 CFR 46.117. By reading the consent and clicking "accept," then completing the survey questions, the subject is consenting. This mechanism is standard in the industry of online minimal risk surveys and has been used by CTP and previously approved by the FDA RIHSC (e.g., RIHSC Protocol# 10-111TP). The lack of a written / signed informed consent document is acceptable for this research under 45 CFR 46.117(c) because such a written informed consent document would breach subject confidentiality and this is a minimal risk study.

The informed consents contain no exculpatory language.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Center for Tobacco Products
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Experimental Study on the Presentation of Harmful and Potentially Harmful Tobacco Constituents

Laura E. Shay
Center for Tobacco Products
May 4, 2012

Introduction

The Tobacco Control Act (Public Law 111-31) amends the FD&C Act to grant FDA authority to regulate the manufacture, marketing, and distribution of tobacco products to protect the public health and to reduce tobacco use by minors. Section 904(d)(1) of the FD&C Act states, "Not later than 3 years after the date of enactment of the Family Smoking Prevention and Tobacco Control Act, and annually thereafter, the Secretary shall publish in a format that is understandable and not misleading to a lay person, and place on public display (in a manner determined by the Secretary) the list [of harmful or potentially harmful constituents] established under [section 904(e)]" of the Act. Section 904(e) of the FD&C Act directs FDA to establish "a list of harmful and potentially harmful constituents, including smoke constituents, to health in each tobacco product by brand, and by quantity in each brand and subbrand." On January 31, 2011, FDA announced the availability of a final guidance representing the Agency's current thinking on the meaning of the term "harmful and potentially harmful constituent" (see 76 FR 5387). On April 3, 2012, FDA published a notice in the Federal Register establishing a list of the harmful and potentially harmful constituents (HPHCs) in tobacco products and tobacco smoke (see 77 FR 20034).

FDA's Center for Tobacco Products requires data on how consumers may respond to information about HPHCs in order to determine the appropriate format of the HPHC list provided to the public.

Purpose and Use of the Information Collection

FDA's Center for Tobacco Products will conduct an experimental study to help inform decisions about how to implement section 904(d)(1) of the Act and to provide information about how consumers understand information about HPHCs. The established list of HPHCs (see 77 FR 20034) contains complex scientific information that may be difficult for consumers to understand, therefore making the information potentially misleading. Section 904(d)(1) requires a version of this list be made available to the public. The Act states that this list must be "understood and not misleading to a lay person." The research goals are to evaluate the impact of different list formats on the public's ability to understand HPHC information, and to assess the potential impact on consumer behavior from exposure to the list.

The impact of different list formats on comprehension will be evaluated by measuring respondents' understanding of the following concepts: (1) the chemicals come from the tobacco leaf itself and from different parts of a tobacco product such as the tobacco smoke, glues, inks, paper, and additives; (2) for smokeless products, many of the chemicals come from the tobacco leaf itself; for smoked products, many of the chemicals come from burning the tobacco leaf; (3) tobacco

companies are required to test their tobacco products and smoke for the chemicals on the list and report the amounts to the FDA; (4) science has linked the chemicals on these lists to health problems or potential health problems; (5) these lists do not necessarily identify all of the health problems that may be caused by the tobacco product; (6) these lists do not necessarily include all of the chemicals in the tobacco product that may be harmful; (7) the amount of a chemical listed for a specific tobacco product does not necessarily indicate the likelihood of experiencing a health problem; (8) the number of chemicals listed for a specific tobacco product does not necessarily indicate the likelihood of experiencing a health problem; (9) when a chemical is listed without a quantity it may mean: the chemical was not detected or the information is not currently available.

The potential impact of different list formats on consumer behavior will be evaluated by measuring the exposure to a list on susceptibility to initiation of tobacco use, motivation and confidence to quit using tobacco, and risk perceptions about tobacco use.

Methods and Study Population

The respondent universe for the experimental study is (1) current adult smokers aged 25 years old and older, (2) young adult smokers aged 18 to 24 years old, (3) youth smokers aged 13 to 17 years old, (4) adult smokeless tobacco users aged 18 and older, and (5) youth age 13 to 17 years old who may be susceptible to initiation of smoking. The five separate quota samples will be selected from the e-Rewards online member panel, a national opt-in email list sample. Sampled panel members will receive an email inviting them to participate in the study. Panel members who choose to participate will complete the questionnaire (see Appendix A). Completed surveys will be monitored to ensure samples are diverse in terms of age, gender, education, and ethnicity/race. We estimate 3,150 respondents will complete a survey.

For the information collection, e-Rewards will send email invitations to the target audiences using their market research panel. Each invitation will contain the survey title, the length of the survey, incentive amount provided for successful completion of the survey, and instructions for accessing the secure website for the survey. Once a panel member enters the secure web site, a brief introduction will be presented informing the panel member of the confidential and voluntary nature of the survey (see attached). Individuals who consent to participate in the survey will be able to access the survey by clicking on the link to the survey URL. Respondents who access the questionnaire will be randomly assigned to an experimental condition.

This experimental study will be conducted using an Internet panel and a questionnaire designed to measure responses to the HPHC list formats and collect demographic and smoking status information from the participant. Participants will be randomly assigned to an exposure or control condition. Participants in the exposure condition will view one of 6 HPHC list formats (see Appendix B) for a hypothetical brand of cigarettes, smokeless tobacco product, or roll-your-own tobacco product. RTI will analyze information collected from the study, the results of which will inform FDA's implementation of a publicly displayed list of HPHCs by brand and subbrand as required by the Tobacco Control Act.

The proposed design implements the experimental study with each of five target groups: (1) current adult smokers aged 25 years old and older, (2) young adult smokers aged 18 to 24 years old, (3) youth smokers aged 13 to 17 years old, (4) adult smokeless tobacco users aged 18 and older, and (5) youth age 13 to 17 years old who may be susceptible to initiation of smoking. In the

experiment, we are testing 6 HPHC list formats and 1 control condition (no HPHC list seen) for either a hypothetical cigarette, smokeless tobacco product, and roll-you own tobacco product for a total of 63 cells. Half of the formats will contain additional written information and half will not (see Appendix B), Each cell will contain 50 respondents for a total sample size of 3,150 (See Table 1).

Table 1

Product	Population	Information	Format 1 (Full List)	Format 2 (Tested/ not tested)	Format 3 (Tested only)	No List (control)
Cigarettes	Adult smoker (n=350)	Present	50	50	50	50
		Not present	50	50	50	
	Young adult smoker (n=350)	Present	50	50	50	50
		Not present	50	50	50	
	Youth smoker (n=350)	Present	50	50	50	50
		Not present	50	50	50	
	Youth at risk for initiation (n=350)	Present	50	50	50	50
		Not present	50	50	50	
Smokeless	Adult smokeless (n=350)	Present	50	50	50	50
		Not present	50	50	50	
	Youth smoker (n=300)	Present	50	50	50	50
		Not present	50	50	50	
RYO	Adult smoker (n=350)	Present	50	50	50	50
		Not present	50	50	50	
	Young adult smoker (n=350)	Present	50	50	50	50
		Not present	50	50	50	
	Youth smoker (n=350)	Present	50	50	50	50
		Not present	50	50	50	
N=3,150			900	900	900	450

Summary of Protocol

Survey:

- Survey screener – confirm eligibility.
- Random assignment to treatment or control.
- Treatment groups are exposed to one of 6 HPHC list formats for either a cigarette, smokeless tobacco, or roll-your-own tobacco product; Control groups are not exposed to a list.
- Respondents answer questions while being exposed to a HPHC list. The questions assess general comprehension about HPHCs in tobacco products. Additional questions assess susceptibility to initiation of tobacco use (youth high risk non-smokers), motivation and confidence to quit tobacco use, and risk perceptions about tobacco use.

Measures

Key Outcomes

- Comprehension - total correct responses to questions assessing the communication objectives
- Risk Perception
    - Perceptions of harmfulness of the stimulus product (i.e. brand X cigarette)
    - Perceptions of harmfulness of tobacco use
- Unintended consequences
    - Quit intentions
    - Openness to smoking (youth)

Covariates:

Age, gender, race, SES (income and education), health literacy

Analysis plan

Primary analyses

1. Tests of treatment effects on comprehension:

   Hypotheses 1: Exposure to the list of HPHCs will improve comprehension of communication objectives, and thus treatment groups will have higher comprehension scores relative to control groups.

   Hypothesis 2: The presentation of supplemental information will improve comprehension and thus treatment groups presented with information will have higher comprehension scores relative to groups not presented with information.

2. Contrasts between treatment groups: comparison of list formats to ascertain relative effectiveness.

    - For comprehension of communication objectives, contrasts will be made between treatment groups (adjusted for multiple comparisons) to assess group differences in understanding based on list format.

Secondary Analyses

3. Tests for group differences in risk perceptions, quit intentions and susceptibility to initiation, based on list exposure and list format.

4. Test for moderating effects of product type and population: Tests for interaction effects will be used to determine if the impact of list format on key outcomes differs by (a) product type and (b) age group.

The sample design is adequately powered to test the primary research hypotheses:

- Exposure to a list of HPHCs, with supplemental information, will result in better comprehension of the communication objectives.

The experimental design includes three list format conditions (with and without additional information) and a control group, with a total of 3,150 participants. Each list format condition (with and without additional information) includes 900 participants, for a total of 2700 exposure participants, and the control group includes 450 participants. Our primary test compares exposure participants to control participants.

For the purpose of sample size calculations, the proportion of participants who comprehend communication objectives will serve as the outcome. Our calculations assume comprehension is assessed as a binary outcome. Data will be analyzed using a logistic regression model with no covariates. Based on these assumptions, the test statistic will have 80% statistical power to observe a difference of 8.2 percentage points or larger if the comprehension rate among the control group is low (e.g., 50%). If the comprehension rate among the control group is higher (e.g., 75%), the test statistic will have 80% statistical power to observe a difference of 6.7 percentage points or larger. This power analysis also applies to examples of measures that employ Likert scale ratings, as these measures will be dichotomized prior to analysis, e.g., assigning high ratings a value of 1 and low ratings a value of 0. For outcomes based on a continuous measure, the sample design is powered to detect statistically significant differences of 0.17 standard deviation units or greater. For a scale with a range of 0 – 100, a mean value of 50, and a standard deviation of 15, the test will have 80% statistical power can detect a significant difference between the exposure and control conditions of 2.55 points or greater.

Confidentiality

Assurance of Privacy Provided to Respondents

All data will be collected with an assurance that the respondents' answers will remain confidential. The study instrument will contain a statement that responses will be kept Private. Private information is protected from disclosure under the Freedom of Information Act (FOIA) under sections 552(a) and (b) (5 U.S.C. 552(a) and (b)), and by part 20 of the agency's regulations (21 CFR part 20). Identifying information will not be included in the data files delivered by contractors to the agency.

Privacy will be assured by using independent contractors, RTI and e-Rewards, to collect the information, by enacting procedures to prevent unauthorized access to respondent data, and by preventing the public disclosure of the responses of individual participants. The contractors will only share data and/or information with FDA in an aggregated form or format, which does not permit FDA to identify individual respondents.

Neither e-Rewards nor RTI will share personal information regarding panel members with any third party without the participant's permission unless it is required by law to protect their rights or to comply with judicial proceedings, court order, or other legal process. Identifying information will not be included in the data files delivered to the agency. FDA and RTI will receive

data for analysis in aggregate form. Although e-Rewards retains contact information on participants for honoraria purposes, individually identifiable information is not shared with anyone, including FDA and RTI; it is stored separately from the survey data file and is not linked in any way to participant responses.

RTI maintains restricted access to all data preparation areas (i.e., receipt and coding). All data files on multi-user systems will be under the control of a database manager, with access limited to project staff on a "need-to-know" basis only. E-Rewards takes the following security measures to ensure separation between respondents' identity and their survey data. First, the survey instrument has no personally identifying information (PII) on it. No respondent name, address, email address, phone number or any other kind of PII appears on the survey. The only way a survey is identified is with a digital identification number. Second, while the invitation method, whether email, mail or direct mail will inherently have PII information included, this will not be combined with survey responses, so the responses from the survey are not linked to the PII. Third, screener data shall be considered part of the survey data. E-Rewards will provide the results of the screener questions for all panelists, regardless of whether they qualify for the study. However, e-Rewards will not retain responses to screening questions for those who are deemed ineligible for any other purpose outside the scope of this project. Fourth, e-Rewards will retain study records for the duration of the study. Upon final delivery of data files to RTI and completion of the project, e-Rewards will destroy all study records including data files upon request. E-Rewards will not be able to supply or access this information for any reason, even at the request of RTI, once destroyed. Finally, data coming directly from the survey engine are stored in a proprietary database. While this data is not encrypted, once inside the firewall, they are stored in a relational database protected by several layers of intrusion detection and access control. Data files delivered to RTI by e-Rewards will be sent via encrypted files.

All electronic data will be maintained in a manner that is consistent with the Department of Health and Human Services ADP Systems Security Policy as described in DHHS ADP Systems Manual, Part 6, chapters 6-30 and 6-35. All data will also be maintained in consistency with the FDA Privacy Act System of Records #09-10-0009 (Special Studies and Surveys on FDA Regulated Products).

Justification for Sensitive Questions

The public display of the list of HPHC required under section 904(d)(1) is not restricted to adults thus, it is important to understand youth responses to the HPHC information. In order to identify those youth at risk of smoking or already smoking we need to ask the youth potentially sensitive questions about tobacco use. These questions are potentially sensitive because tobacco use among youth under 18 years of age is illegal in a few states and sales to youth under 18 years of age is illegal in all states.

To alleviate any potential concern for the youth, we will take all necessary measures to ensure privacy. Also, no personal identifying information will be attached to the data used for analysis – e-Rewards keeps personal identifying information to invite youth to participate in surveys but this information will not be shared with RTI (this restriction is stated in the sub-contract between RTI and e-Rewards).

E-Rewards has a standing panel of youth ages 13-17 form which our sample will be recruited. The u.talk.back® panel was created specifically to reach children aged 13-17 years old directly, without parental involvement. The Federal law protecting children, Children's Online Privacy Protection Act (COPPA), does not restrict this type of activity for children aged 13 years old and older. No personally identifying information will be released, per the u.talk.back® member and privacy agreements (http://www.utalkback.com/privacypolicy.do). In summary, e-Rewards' activities for this study will be fully compliant not only with the Federal Law, but with the Council of American Survey Research Organizations® (CASRO) Code of Standards and Ethics for Survey Research, a tough, internationally-cited set of standards, which has long been the benchmark for the industry.

E-Rewards' invitation to youth does encourage parents to know about and approve of youth involvement in the panel and surveys. However, no active parental consent is required or requested. For this study, when the youth are invited to join our specific survey, both parental consent and youth assent will be requested and required. In the invitation for our specific study it will be emphasized that youth responses are strictly confidential and that youth will be instructed to NOT take the survey under their parents' supervision nor to share their answers or opinions with their parents. We will emphasize to the youth and parents that will want to encourage honest responses to the questions so that we can measure a valid youth response to the HPHC list formats.

Questionnaire
See Appendix A

Test Stimuli
See Appendix B

Appendix A
Questionnaire

Intro1
[DISPLAY FOR ADULTS]
This study is funded by the U.S. Food and Drug Administration's (FDA's) Center for Tobacco Products (CTP) and conducted by RTI International. This survey asks you about your smoking habits and your opinions about tobacco products. Your participation in this research study is completely voluntary, and you may skip any questions you do not want to answer. No one will be able to link your responses to your identity. This survey will take about 20 minutes to complete.

If you have any questions about this study, you may call Katherine Kosa of RTI at 1-800-334-8571, extension 23901. If you have any questions about your rights as a study participant, you may call RTI's Office of Research Protection at 1-866-214-2043

Intro2
[DISPLAY FOR YOUTH]
This study is funded by the U.S. Food and Drug Administration's (FDA's) Center for Tobacco Products (CTP) and conducted by RTI International. This survey asks teenagers what they think about cigarette smoking and other tobacco products. About 1,700 teenagers will complete this survey. This survey will take about 20 minutes to complete.

Your participation in this research study is completely up to you. As part of the survey, you will view some information related to cigarette smoking and other tobacco products. You've probably read similar information online or in health class. The survey asks questions about your experiences and thoughts regarding cigarette smoking. You may skip any questions you do not want to answer. During the survey, we do not ask for your name; therefore, your name will not be connected to your answers. Additionally, we will not share any information you provide in the survey with anyone outside the research team, including your parents.

To ensure your answers are kept private, please complete the survey in a place where no one can look over your shoulder and view your answers. Also, please complete the survey in one sitting and close the screen when you are done taking the survey.

If you have any questions about the study, you may call Katherine Kosa of RTI at 1-800-334-8571, extension 23901. If you have any questions about your rights as a study participant, you may call RTI's Office of Research Protection at 1-866-214-2043.

S. Screening Questions
S1. What is your age? _____years old
[IF S1 < 13, NOT ELIGIBLE.]

S2. Have you ever smoked a cigarette, even one or two puffs? (Select one.)
1) Yes
2) No

S3. Do you use smokeless tobacco products, such as snuff, dip, or Snus…? (Select one.)

1) Every day
2) Some days
3) Rarely
4) Not at all

[IF 13 ≤ S1 < 18 AND S2 =2 AND S3=4, GO TO S5.]
[IF S2 =2 AND S3≠4 (SMOKELESS ONLY = YES), GO TO SECTION A.]
[IF S1 ≥ 18 AND S2 = 2 AND S3=4 NOT ELIGIBLE.]

S4. During the past 30 days, how many days did you smoke a cigarette? (Select one.)

1) 0 days
2) 1 or 2 days
3) 3 to 5 days
4) 6 to 9 days
5) 10 to 19 days
6) 20 to 29 days
7) All 30 days

[If S1 ≥ 18 AND S4 = 1 AND S3=4 NOT ELIGIBLE.]
[If S1 ≥ 18 AND S4 = 1 AND S3≠4 (SMOKELESS ONLY = YES), GO TO SECTION A.]
[If S1 ≥ 18 AND S4 ≠ 1 GO TO S8.]
[IF 13 ≤ S1 < 18 AND S4 ≠ 1 (CURRENT YOUTH SMOKER=YES) GO TO Section B.]
[IF 13 ≤ S1 < 18 AND S4 = 1 AND S3≠4 (SMOKELESS ONLY =YES) GO TO Section B.]

S5. Do you think you will smoke a cigarette at any time in the next year? (Select one.)

5) Definitely Not
6) Probably Not
7) Probably Yes
8) Definitely Yes

S6. Do you think in the future you might try a cigarette? (Select one.)

1) Definitely Not
2) Probably Not
3) Probably Yes
4) Definitely Yes

S7. If one of your best friends offered you a cigarette, would you smoke it? (Select one.)

1) Definitely Not
2) Probably Not
3) Probably Yes
4) Definitely Yes

[IF S5 = S6 = S7 = 2, 3, 4 (YOUTH SUSCEPTIBLE TO SMOKING = YES). IF S5 = S6 = S7 = 1 NOT ELIGIBLE.]

S8. Have you smoked at least 100 cigarettes in your entire life?
1) Yes
2) No

[IF S1 ≥ 25 AND S8 = 1 (CURRENT ADULT SMOKER=YES). IF 18 ≤ S1 ≤ 24 AND S8 = 1 = 2 (YOUNG ADULT SMOKER=YES). IF S1 ≥ 25 AND S8 = 2 NOT ELIGIBLE.]

SECTION B: TOBACCO USE BEHAVIOR

[FOR B1-B3, EXCLUDE YOUTH SUSCEPTIBLE TO SMOKING AND SMOKELESS ONLY.]

The next set of questions asks about your use and beliefs about tobacco.

B1. On average, in the past 30 days, about how many cigarettes did you smoke a day? (Select one.)
1) Fewer than 5 cigarettes
2) 5-9 cigarettes
3) 10 cigarettes (1/2 a pack)
4) 11-19 cigarettes (more than 1/2 pack but less than 1 pack)
5) 20 cigarettes (1 pack) or more

B2. When you smoke, how often do you use hand-rolled or "roll-your-own" cigarettes? (Select one.)
1) Never
2) Rarely when I smoke
3) Sometimes when I smoke
4) Often when I smoke
5) Always when I smoke

B3. On the days that you smoke, how soon after you wake up do you have your first cigarette? (Select one.)
1) Within 5 minutes
2) 6-30 minutes
3) 31-60 minutes
4) After 60 minutes

[IF S3 ≠ 4, THEN B4-B6; OTHERWISE SKIP.]

The next set of questions asks about your use of smokeless tobacco.

B4. During the past 30 days, how many days did you use a smokeless tobacco product, such as snuff, dip, or Snus…? (Select one.)
1. 0 days
2. 1 or 2 days
3. 3 to 5 days
4. 6 to 9 days
5. 10 to 19 days
6. 20 to 29 days
7. All 30 days

B5. On average, in the past 30 days, about how many times did you use smokeless tobacco a day? *(Select one.)*
1. Once a day
2. 2 to 3 times a day
3. 4 to 5 times a day
4. More than 5 times a day

B6. On the days that you use smokeless tobacco, how soon after you wake up do you place your first dip? *(Select one.)*
1. Within 5 minutes
2. 6-30 minutes
3. 31-60 minutes
4. After 60 minutes

SECTION A: COMMUNICATION OBJECTIVE QUESTIONS
[RANDOMLY ASSIGN R TO TREATMENT AND STIMULI or CONTROL.]
[IF TREATMENT GROUP, DISPLAY TEXT AND RANDOMLY SELECT AND DISPLAY STIMULI IN POP-UP WINDOW. KEEP STIMULI VISIBLE THROUGHT SECTION A.]

Please click on the icon here to display a list of chemicals that are in [smokeless tobacco products such as snuff, dip, or Snus / cigarettes / roll-your-own cigarettes]. Please take a moment to look over this list. You can keep the list open while you complete the survey and can click on the icon at any time to view the list.

Please use information provided on the list to answer the following questions.

A1. Do chemicals in cigarettes come from…? *(Select one for each item.)* **[RANDOMIZE LIST.]**

	Yes	**No**
1. The tobacco leaf		
2. Tobacco smoke		
3. The cigarette carton		
4. Glues, inks, and paper		
5. The filter		
6. Additives		

[CONTROL & TX=CIG & RYO.]

A2. How many of the chemicals in cigarettes come from the tobacco leaf and the smoke? (*Select one*.)

1) None of the chemicals
2) A few of the chemicals
3) Many of the chemicals
4) All of the chemicals

[CONTROL & TX=SMK.]

A3. How many of the chemicals in smokeless tobacco products come from the tobacco leaf? (*Select one*.)

1) None of the chemicals
2) A few of the chemicals
3) Many of the chemicals
4) All of the chemicals

A4. For each question, please answer YES or NO. *(Select one for each question.)*
[RANDOMIZE LIST.]

	Yes	**No**
1. Imagine one tobacco product has a greater number of chemicals than another tobacco product. Can you tell which of these products is more likely to cause a tobacco-related health problem?		
2. Formaldehyde has been linked to cancer. Now imagine one brand of tobacco product has more formaldehyde in it than another brand. Can you tell which of these brands of tobacco product is more likely to cause cancer?		

A5. Who tests tobacco products for harmful chemicals? (*Select one*.)

1) Tobacco farmers
2) Federal government
3) State and local health departments
4) Tobacco companies
5) No one
6) None of the above

A6. For each of the following statements, please select True or False. *(Select one for each statement.)* **[RANDOMIZE LIST.]**

	True	False
1. Researchers have linked some of the chemicals from tobacco products to health problems.		
2. Researchers have discovered all of the health problems that may be caused by harmful chemicals from tobacco products.		
3. Researchers have discovered all of the harmful chemicals that come from using tobacco products.		
4. All tobacco products contain chemicals that may cause harm.		
5. Research is ongoing to find out which chemicals cause harm.		
6. Nicotine causes cancer.		
7. Nicotine is one reason why people have trouble quitting tobacco products.		

A7. For each question, please answer YES or NO. *(Select one for each question.)* **[RANDOMIZE LIST.]**

	Yes	No
1. Can you tell a tobacco user's chance of developing a tobacco-related health problem by counting the **total number** of chemicals in his/her tobacco product?		
2. Can you tell a tobacco user's chance of developing a health problem by looking at the **amount** of a harmful chemical in his/her tobacco product?		

[IF TX GROUP]

A8. For each of the following statements, please select True or False. (Select one for each statement.) **[RANDOMIZE LIST.]**

	True	False
1. When a chemical is listed without an amount it may mean the chemical was not detected.		
2. When a chemical is listed without an amount it may mean the information is not currently available.		

SECTION C: DESIRE TO QUIT / STAGE OF CHANGE

[FOR C1-C3, EXCLUDE YOUTH SUSCEPTIBLE TO SMOKING AND SMOKELESS ONLY.]

C1. Are you seriously considering stopping smoking within the next 6 months? (Select one.)
1) Yes
2) No

C2. Are you planning to stop smoking within the next 30 days? (Select one.)
1) Yes
2) No

C3. On a scale from 1 to 5 with 1 being "not at all" and 5 being the "a lot," how much do you want to quit smoking? (Select one.)
1) Not at all
2) .
3) .
4) .
5) A lot

[IF S3 ≠ 4]

C4. Are you seriously considering stopping using smokeless tobacco products such as snuff, dip, or Snus within the next 6 months? (Select one.)
1) Yes
2) No

[IF S3 ≠ 4]

C5. Are you planning to stop using smokeless tobacco products such as snuff, dip, or Snus within the next 30 days? (Select one.)
1) Yes
2) No

[IF S3 ≠ 4]

C6. On a scale from 1 to 5 with 1 being "not at all" and 5 being the "a lot," how much do you want to stop using smokeless tobacco? (Select one.)
6) Not at all
7) .
8) .
9) .
10) A lot

SECTION D: RISK PERCEPTION

D1. On a scale of 1 to 5 with 1 being **not harmful at all** and 5 being **extremely harmful**, how harmful to someone's health is…? *(Select one for each statement.)* **[RANDOMIZE 1-3.]**

	not at all harmful 1	**2**	**3**	**4**	**extremely harmful 5**
1. Smoking cigarettes					
2. Smoking roll-your-own tobacco					
3. Using smokeless tobacco					
4. **[TX = CIG. SHOW STIMULI.]** Smoking this brand of cigarettes					
5. **[TX = RYO. SHOW STIMULI.]** Smoking this brand of roll-your-own tobacco					
6. **[TX = SMK. SHOW STIMULI.]** Using this brand of smokeless tobacco					

D2. How strongly do you agree or disagree with the following statement? There is no safe tobacco product. *(Select one.)*

1) Strongly agree
2) Somewhat agree
3) Somewhat disagree
4) Strongly disagree

[FOR D3-D7, EXCLUDE YOUTH SUSCEPTIBLE TO SMOKING AND SMOKELESS ONLY.]

D3. How likely do you think *you* are to get a disease from smoking cigarettes? *(Select one.)*

1) Very unlikely
2) Somewhat unlikely
3) Somewhat likely
4) Very likely

D4. Do you think your smoking has affected your health? *(Select one.)*

1) Yes
2) No

D5. How concerned are you that your smoking could affect your health? *(Select one.)*

1) Not at all concerned
2) Only slightly concerned
3) Fairly concerned
4) Very concerned

D6. Do you think that your smoking has affected the health of someone else (e.g. spouse, partner, child, grandchild)? *(Select one.)*

1) Yes
2) No

D7. How concerned are you that your smoking could affect the health of someone else? *(Select one.)*

1) Not at all concerned
2) Only slightly concerned
3) Fairly concerned
4) Very concerned

[IF S3 ≠ 4]

D8. How likely do you think *you* are to get a disease from using smokeless tobacco? *(Select one.)*

1) Very unlikely
2) Somewhat unlikely
3) Somewhat likely
4) Very like

[IF S3 ≠ 4]

D9. Do you think your use of smokeless tobacco has affected your health? *(Select one.)*

1) Yes
2) No

[IF S3 ≠ 4]

D10. How concerned are you that your use of smokeless tobacco could affect your health? *(Select one.)*

1) Not at all concerned
2) Only slightly concerned
3) Fairly concerned
4) Very concerned

SECTION E: YOUTH BELIEFS/ATTITUDES ABOUT TOBACCO USE

[IF YOUTH SUSCEPTIBLE TO SMOKING]

E6. On a scale of 1 to 5 with 1 being **strongly disagree** and 5 being **strongly agree,** how much do you agree or disagree that cigarette smoking is…? *(Select one for each item.)* **[RANDOMIZE LIST.]**

	strongly disagree 1	**2**	**3**	**4**	**strongly agree 5**
1. Glamorous					
2. Rebellious					
3. Cool					
4. Disgusting					
5. Foolish					

SECTION E: HEALTH LITERACY

The remaining questions are not about tobacco. These questions are to help us get a better sense of who you are and how you make decisions about your health. The information below is from the back of a container of a pint of ice cream. Please use this information to answer the following questions.

Nutrition Facts

Serving Size	½ cup
Servings per container	4
Amount per serving	
Calories 250	Fat Cal 120
	%DV
Total Fat 13g	20%
Sat Fat 9g	40%
Cholesterol 28mg	12%
Sodium 55mg	2%
Total Carbohydrate 30g	12%
Dietary Fiber 2g	
Sugars 23g	
Protein 4g	8%

*Percentage Daily Values (DV) are based on a 2,000 calorie diet. Your daily values may be higher or lower depending on your calorie needs.

Ingredients: Cream, Skim Milk, Liquid Sugar, Water, Egg Yolks, Brown Sugar, Milkfat, Peanut Oil, Sugar, Butter, Salt, Carrageenan, Vanilla Extract.

F1. If you eat the entire container, how many calories will you eat?
_____ Calories
[ENTER NUMBER]

F2. If you are allowed to eat 60 grams of carbohydrates as a snack, how many cups of ice cream could you have?
_____ Cups
[ENTER NUMBER]

F3. Your doctor advises you to reduce the amount of saturated fat in your diet. You usually have 42 g of saturated fat each day, which includes one serving of ice cream. If you stop eating ice cream, how many grams of saturated fat would you be consuming each day?
_____ Grams
[ENTER NUMBER]

F4. If you usually eat 2,500 calories in a day, what percentage of your daily value of calories will you be eating if you eat one serving?
_____ %
[ENTER NUMBER]
For the next few questions, pretend that you are allergic to the following substances: penicillin, peanuts, latex gloves, and bee stings.

F5. Is it safe for you to eat this ice cream?
1) Yes
2) No

[If F5 = 1 GO TO G1]

F6. Why isn't it safe to eat this ice cream? (Select one)
1) It is high in calories
2) It contains peanut oil
3) It is high in fat
4) The ice cream container is coated with latex
5) People who are allergic to penicillin should not eat ice cream

CLOSING QUESTIONS

G1. What is your sex? *(Select one.)*
1) Male
2) Female

G2. Are you Hispanic or Latino? *(Select one.)*
1 Yes
2 No
99 I do not wish to answer

G3. What is your race? *(Select all that apply.)*

1 American Indian or Alaska Native
2 Asian
3 Black or African American
5 Native Hawaiian or Other Pacific Islander
6 White
99 I do not wish to answer

[ADULTS ONLY]

G4. What is the highest level of school you completed or the highest degree you received? *(Select one.)*

1 Never attended school
2 Grades K through 8 (Elementary or grade school)
3 Grades 9 through 12 (Some high school)
4 Grade 12 (High school graduate) or GED
5 Some college
6 College graduate
7 Postgraduate/masters/doctorate/law/MD
99 I do not wish to answer

[YOUTH ONLY]

G5. What grade or year of school are you currently in? *(Select one.)*

1 4th grade
2 5th grade
3 6th grade
4 7th grade
5 8th grade
6 9th grade
7 10th grade
8 11th grade
9 12th grade or GED
10 Not currently in school
11 Graduated high school or GED
99 I do not wish to answer

[ADULTS ONLY]

G6. What was your annual household income from all sources in 2011? Was it…? *(Select one.)*

1 Less than $25,000
2 Between $25,000 and $49,999
3 Between $50,000 and $74,999
4 More than $75,000
99 I do not wish to answer

[ADULTS ONLY]

G7. Which statement best describes your current employment status? *(Select one.)*

1. Working full time as a paid employee
2. Working full time, self-employed
3. Not working, on temporary layoff from a job
4. Not working, looking for work
5. Not working, retired
6. Not working, disabled
7. Not working, other

G8. Please enter your 5-digit zip code **–OR–** your city and state.

5-digit zip code: _____

–OR–

City: _____

State (2 letter abbreviation): _____

99 I do not wish to answer

Thank you for completing today's survey. You will be awarded XX for completing this survey. If you would like to learn more about the dangers of smoking or to get information about quitting smoking, please visit www.smokefree.gov.

Appendix B

Test Stimuli

Attached are the list formats for smokeless tobacco. The same formats will be tested for cigarettes and roll-your own tobacco.

Tobacco Product: Brand X Smokeless Tobacco

Tobacco Amount Per Gram	CHEMICAL	CA	HB	RP	AD
0.97 – 72.3 µg	Acetaldehyde	■			■
0.1 – 3.5 µg	Arsenic	■	■	■	
1.1 – 57.3 ng	Benzo[a]pyrene	■			
0.1 – 3.1 µg	Cadmium	■		■	
0.5 – 19.4 µg	Crotonaldehyde	■			
0.2 -72.3 µg	Formaldehyde	■			
0.1 – 1.6 µg	4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	■			
11.3 – 26.7 mg	Nicotine			■	■
0.9 – 6.9 µg	N-Nitrosonornicotine (NNN)	■			

There are many other chemicals that have been linked to the health problems on this list. The information on these chemicals is not currently available.

A machine is used to test for these chemicals. The amount of chemical that gets into the body may be higher or lower depending on how a person uses the tobacco product. Companies may use different tests to measure these chemicals. Results may vary.

KEY

Chemicals have been linked to:

- **CA** Cancer
- **HB** Heart and Blood Vessel Problems
- **RP** Reproductive Problems
- **AD** Addiction

- **ND** Not Detected
- ✦ The information is not currently available

mg= milligram
µg = microgram
ng = nanogram
pg= picogram

Tobacco Product: Brand X Smokeless Tobacco

Tobacco Amount Per Gram	CHEMICAL	CA	HB	RP	AD
0.97 – 72.3 µg	Acetaldehyde	■			■
0.1 – 3.5 µg	Arsenic	■	■	■	
1.1 – 57.3 ng	Benzo[a]pyrene	■			
0.1 – 3.1 µg	Cadmium	■		■	
0.5 – 19.4 µg	Crotonaldehyde	■			
0.2 -72.3 µg	Formaldehyde	■			
0.1 – 1.6 µg	4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	■			
11.3 – 26.7 mg	Nicotine			■	■
0.9 – 6.9 µg	N-Nitrosonornicotine (NNN)	■			

The information is not currently available on the following chemicals.

Tobacco Amount Per Gram	CHEMICAL	CA	HB	RP	AD
✦	Aflatoxin B1	■			
✦	Ammonia				
✦	Anabasine				■
✦	Benz[a]anthracene	■	■		
✦	Benzo[b]fluoranthene	■	■		
✦	Benzo[k]fluoranthene	■	■		
✦	Beryllium	■			
✦	Chromium	■		■	
✦	Chrysene	■	■		
✦	Coumarin (banned in food)				
✦	Dibenz[a,h]anthracene	■			
✦	Ethyl carbamate (urethane)	■		■	
✦	Indeno[1,2,3-cd]pyrene	■			
✦	Lead	■	■	■	
✦	Mercury	■		■	
✦	Naphthalene	■			
✦	Nickel	■			
✦	N-Nitrosodiethanolamine (NDELA)	■			
✦	N-Nitrosodimethylamine (NDMA)	■			
✦	N-Nitrosomorpholine (NMOR)	■			
✦	N-Nitrosopiperidine (NPIP)	■			
✦	N-Nitrosopyrrolidine (NPYR)	■			
✦	N-Nitrososarcosine (NSAR)	■			
✦	Nornicotine				■
✦	Polonium-210	■			
✦	Selenium				
✦	Uranium-235	■			
✦	Uranium-238	■			

A machine is used to test for these chemicals. The amount of chemical that gets into the body may be higher or lower depending on how a person uses the tobacco product. Companies may use different tests to measure these chemicals. Results may vary.

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Chemicals have been linked to:

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Tobacco Product: Brand X Smokeless Tobacco

Tobacco Amount Per Gram	CHEMICAL	CA	HB	RP	AD
0.97 – 72.3 µg	Acetaldehyde	■			■
✦	Aflatoxin B1	■			
✦	Ammonia				
✦	Anabasine				■
0.1 – 3.5 µg	Arsenic	■	■	■	
✦	Benz[a]anthracene	■	■		
✦	Benzo[b]fluoranthene	■	■		
✦	Benzo[k]fluoranthene	■	■		
1.1 – 57.3 ng	Benzo[a]pyrene	■			
✦	Beryllium	■			
0.1 – 3.1 µg	Cadmium	■		■	
✦	Chromium	■		■	
✦	Chrysene	■	■		
✦	Coumarin (banned in food)				
0.5 – 19.4 µg	Crotonaldehyde	■			
✦	Dibenz[a,h]anthracene	■			
✦	Ethyl carbamate (urethane)	■		■	
0.2 -72.3 µg	Formaldehyde	■			
✦	Indeno[1,2,3-cd]pyrene	■			
✦	Lead	■	■	■	
✦	Mercury	■		■	
0.1 – 1.6 µg	4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	■			
✦	Naphthalene	■			
✦	Nickel	■			
11.3 – 26.7 mg	Nicotine			■	■
✦	N-Nitrosodiethanolamine (NDELA)	■			
✦	N-Nitrosodimethylamine (NDMA)	■			
✦	N-Nitrosomorpholine (NMOR)	■			
0.9 – 6.9 µg	N-Nitrosonornicotine (NNN)	■			
✦	N-Nitrosopiperidine (NPIP)	■			
✦	N-Nitrosopyrrolidine (NPYR)	■			
✦	N-Nitrososarcosine (NSAR)	■			
✦	Nornicotine				■
✦	Polonium-210	■			
✦	Selenium				
✦	Uranium-235	■			
✦	Uranium-238	■			

KEY

Chemicals have been linked to:

CA Cancer

HB Heart and Blood Vessel Problems

RP Reproductive Problems

AD Addiction

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mg= milligram
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A machine is used to test for these chemicals. The amount of chemical that gets into the body may be higher or lower depending on how a person uses the tobacco product. Companies may use different tests to measure these chemicals. Results may vary.

Tobacco Product: Brand X Smokeless Tobacco

All tobacco products contain chemicals.

The purpose of this list is to provide information about the chemicals in this tobacco product that researchers have linked to health problems. Research is on going to find out which chemicals in tobacco and tobacco smoke cause harm.

There may be other health problems and chemicals that have not been discovered yet.

Tobacco companies test their tobacco for these chemicals and report the amounts to the FDA.

Please note: There is no safe tobacco product. Based on what we currently know, you can not tell your chance of developing a health problem by the number of chemicals or the amount of a chemical in a tobacco product.

Amount Per Gram	CHEMICAL	Cancer	Heart and Blood Vessel Problems	Reproductive Problems	Addiction
0.97 – 72.3 µg	Acetaldehyde	■			■
0.1 – 3.5 µg	Arsenic	■	■	■	
1.1 – 57.3 ng	Benzo[a]pyrene	■			
0.1 – 3.1 µg	Cadmium	■		■	
0.5 – 19.4 µg	Crotonaldehyde	■			
0.2 -72.3 µg	Formaldehyde	■			
0.1 – 1.6 µg	4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	■			
11.3 – 26.7 mg	Nicotine			■	■
0.9 – 6.9 µg	N-Nitrosonornicotine (NNN)	■			

There are many other chemicals that have been linked to the health problems on this list. The information on these chemicals is not currently available.

KEY

Chemicals have been linked to:

- Cancer
- Heart and Blood Vessel Problems
- Reproductive Problems
- Addiction

ND Not Detected

✦ The information is not currently available

Where do these chemicals come from?

Many of these chemicals come from the **tobacco leaf**. The rest come from additives and the pouch if one is present.

mg= milligram
µg = microgram
ng = nanogram
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A machine is used to test for these chemicals. The amount of chemical that gets into the body may be higher or lower depending on how a person uses the tobacco product. Companies may use different tests to measure these chemicals. Results may vary.

Tobacco Product: Brand X Smokeless Tobacco

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11.3 – 26.7 mg	Nicotine			■	■
0.9 – 6.9 µg	N-Nitrosonornicotine (NNN)	■			

The information is not currently available on the following chemicals.

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✦	Aflatoxin B1	■			
✦	Ammonia				
✦	Anabasine				■
✦	Benz[a]anthracene	■	■		
✦	Benzo[b]fluoranthene	■	■		
✦	Benzo[k]fluoranthene	■	■		
✦	Beryllium	■			
✦	Chromium	■		■	
✦	Chrysene	■	■		
✦	Coumarin (banned in food)				
✦	Dibenz[a,h]anthracene	■			
✦	Ethyl carbamate (urethane)	■		■	
✦	Indeno[1,2,3-cd]pyrene	■			
✦	Lead	■	■	■	
✦	Mercury	■		■	
✦	Naphthalene	■			
✦	Nickel	■			
✦	N-Nitrosodiethanolamine (NDELA)	■			
✦	N-Nitrosodimethylamine (NDMA)	■			
✦	N-Nitrosomorpholine (NMOR)	■			
✦	N-Nitrosopiperidine (NPIP)	■			
✦	N-Nitrosopyrrolidine (NPYR)	■			
✦	N-Nitrososarcosine (NSAR)	■			
✦	Nornicotine				■
✦	Polonium-210	■			
✦	Selenium				
✦	Uranium-235	■			
✦	Uranium-238	■			

A machine is used to test for these chemicals. The amount of chemical that gets into the body may be higher or lower depending on how a person uses the tobacco product. Companies may use different tests to measure these chemicals. Results may vary.

KEY

Chemicals have been linked to:

- Cancer
- Heart and Blood Vessel Problems
- Reproductive Problems
- Addiction

ND Not Detected

✦ The information is not currently available

Where do these chemicals come from?

Many of these chemicals come from the **tobacco leaf**. The rest come from additives and the pouch if one is present.

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µg = microgram
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Tobacco Product: Brand X Smokeless Tobacco

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✦	Benz[a]anthracene	■	■		
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✦	Benzo[k]fluoranthene	■	■		
1.1 – 57.3 ng	Benzo[a]pyrene	■			
✦	Beryllium	■			
0.1 – 3.1 µg	Cadmium	■		■	
✦	Chromium	■		■	
✦	Chrysene	■	■		
✦	Coumarin (banned in food)				
0.5 – 19.4 µg	Crotonaldehyde	■			
✦	Dibenz[a,h]anthracene	■			
✦	Ethyl carbamate (urethane)	■		■	
0.2 -72.3 µg	Formaldehyde	■			
✦	Indeno[1,2,3-cd]pyrene	■			
✦	Lead	■	■	■	
✦	Mercury	■		■	
0.1 – 1.6 µg	4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	■			
✦	Naphthalene	■			
✦	Nickel	■			
11.3 – 26.7 mg	Nicotine			■	■
✦	N-Nitrosodiethanolamine (NDELA)	■			
✦	N-Nitrosodimethylamine (NDMA)	■			
✦	N-Nitrosomorpholine (NMOR)	■			
0.9 – 6.9 µg	N-Nitrosonornicotine (NNN)	■			
✦	N-Nitrosopiperidine (NPIP)	■			
✦	N-Nitrosopyrrolidine (NPYR)	■			
✦	N-Nitrososarcosine (NSAR)	■			
✦	Nornicotine				■
✦	Polonium-210	■			
✦	Selenium				
✦	Uranium-235	■			
✦	Uranium-238	■			

A machine is used to test for these chemicals. The amount of chemical that gets into the body may be higher or lower depending on how a person uses the tobacco product. Companies may use different tests to measure these chemicals. Results may vary.

KEY

Chemicals have been linked to:

- Cancer
- Heart and Blood Vessel Problems
- Reproductive Problems
- Addiction

ND Not Detected

✦ The information is not currently available

Where do these chemicals come from?

Many of these chemicals come from the **tobacco leaf**. The rest come from additives and the pouch if one is present.

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µg = microgram
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