

## ***HRRC PROPOSAL***

To: Mike Ogden  
HRRC Chairperson

Date: February 18, 2009

From: Elaine Round, Mitch Stiles

Subject: Study to Investigate Use of Snus Compared to Smoking Usual-Brand Cigarettes (HRRC Proposal #0902)

- A. *Background*** - RJRT is aggressively pursuing harm reduction efforts in its tobacco products portfolio, including the development and launch of new smokeless products. In early 2008, we developed a new protocol for testing smokers using alternative tobacco products (ATPs) and first tested Tobacco Orbs (Orbs) at that time. That study was successful, but the results suggested changes could be made to improve the information obtained. We revised the protocol in several ways: we required 24-hour urine samples for more accurate biomarker data, we gathered initial serum nicotine profile data following ATP use, we allowed lighter smokers to participate, and we added analysis of an additional biomarker (HPMA) more specific to tobacco combustion. Although the analysis of those studies is not yet complete, an initial look at the data suggests encouraging results. In this study, we propose to test snus with the refined protocol we used to test smokers migrating from cigarette smoking to dual use with Tobacco Strips or Sticks.
- B. *Summary*** - The purpose of this proposal is to obtain approval to recruit and evaluate up to 48 non-RJRT smokers naïve to dissolvable tobacco products and snus as they switch from exclusive use of cigarettes to dual use of snus and cigarettes. Participants will be asked to reduce cigarette use each week to reach a goal of smoking no more than 25% of their initial daily consumption by the end of the study. Participants will be asked to incorporate snus into their daily tobacco-use routine to aid in their cigarette reduction.

Potential participants will be invited to attend a focus group-like orientation session to introduce them to snus. We will provide information about snus, a concept statement developed by Marketing, instructions for use, and an opportunity to try snus before choosing to proceed with the study. For those interested, we will continue that day with discussing study requirements, obtaining informed consent, and providing study supplies for the Visit 1 test session. In addition, participants will be scheduled to receive an oral exam by a medical professional prior to Visit 1 and again at the end of the study.

Participants in this study will be required to attend one test session per week for four consecutive weeks. Tobacco use requirements listed below will be designated by the specific visit, but will also include the week period preceding the designated visit. For example, at Visit 4, participants will have minimized their cigarette smoking and will have been working toward that target for the entire week that started upon completion of Visit 3.

Tobacco use goals throughout the study:

- Visit 1 – smoke usual-brand cigarettes only. (The average daily use for the first week of the study ending on Visit 1 will be calculated and used to determine individual cigarette goals for the remainder of the study.)
- Visit 2 – start incorporation of snus into daily tobacco-use routine and decrease cigarette smoking to 75% of average use in week 1.
- Visit 3 – continue use of snus and decrease cigarette smoking to 50% of average use in week 1
- Visit 4 – continue use of snus and decrease cigarette smoking to no more than 25% of average use in week 1.

Physiological and questionnaire-based measurements will vary at each visit. Physiological measurements will include biomarkers of tobacco exposure in serum, whole blood, breath, 24-hour urine samples, and spot urine samples. Serum nicotine and cotinine levels will be measured to determine nicotine “rise” and estimate total exposure following tobacco use. CO levels in expired breath and percent carboxyhemoglobin (%COHb) in whole blood will be measured to determine carbon monoxide (CO) exposure. NNAL, nicotine plus nine metabolites, and HPMa (used as an additional probe for cigarette smoking) will be measured in 24-hour urine samples and in urine samples collected at study visits (referred to as spot urine samples). Maximum ‘tar’ and nicotine exposure will be estimated from the used cigarette butts (Yield In Use) collected by participants the day before each study visit. In addition, used snus pouches will be collected from participants and analyzed to determine the nicotine and TSNA levels extracted from the pouches as an estimate of maximum nicotine and TSNA exposure from snus (Snus After Use). Questionnaires will capture information on the physical, psychological, and sensory experiences of participants while smoking their usual-brand cigarettes and using snus.

- C. Human Participants** – The physiological and sensory measurements surrounding tobacco exposure require using the blood, urine, expired breath, and questionnaire responses of human smokers; therefore, this study can only succeed by using human smokers as participants.
- D. Product Integrity** – All processes/ingredients related to snus have been approved by Product Integrity Stewardship (see [Attachment 18](#)).
- E. Cigarettes and Snus** – Participants will include smokers of Full Flavor Low Tar (FFLT) cigarettes of any type. Menthol and 100mm cigarette smokers will also be invited to participate, but their inclusion in this study will not surpass the current proportion of U.S. smokers of each type - currently 25% are menthol smokers and approximately 35% are 100s smokers. Smoke yield ranges for FFLT cigarettes using a Cambridge filter method with puffs of 35 mL occurring every 60 seconds and 2 seconds in duration are shown below:

	‘Tar’ mg/cig	Nicotine mg/cig	Carbon Monoxide mg/cig
Usual Brands (range)	7.0 - 13.1	0.56 – 1.04	5.8 – 15.7

[Data taken from TITL Market Sample 51 Final Report, January 27, 2009].

Camel Snus Frost and Camel Snus Mellow will be used in this study. Ingredients in Camel Snus include milled tobacco, salts, buffers, sweeteners, glycerin and glycols as humectants, and flavorings. Snus will be provided to participants in tins containing 15 pouches each. Participants will be permitted to take home only one variety at a time, but may choose to switch varieties at any study visit. Analytical measurements for the Camel Snus to be used in the study are listed in [attachment 1](#).

**F. Procedures for Participant Selection** – Participants will include male and female smokers, ages 21-55, who are smokers of FFLT cigarettes. Bellomy Research of Winston-Salem will conduct smoker recruiting in the area. Participants will have no reported history of heart disease, lung disease, diabetes, liver disease, or kidney disease, no history of drug abuse, neurological disorders, or psychiatric illness and no active oral lesions.

**G. Participant Handling** - Potential participants will be invited to attend a focus group-like orientation session (Visit 0) to introduce them to snus. We will provide information about snus, a concept statement ([Attachment 2](#)) developed by Marketing, instructions for use, and an opportunity for those interested to try snus before choosing to proceed further with the study. For those interested, we will continue that day with a discussion of study requirements to obtain informed consent ([Attachment 3](#)) and distribution of study supplies for Visit 1. A final screening visit will be scheduled in which participants report back to the facility to receive an oral exam by a medical professional (NP, PA, MD, or DO\*). The purpose of this visit is to ensure participants have no oral lesions prior to starting the study procedures. Once enrolled in the study, participants will report to our offsite testing facility one day per week for four consecutive weeks. Each study visit will last 45 to 120 minutes depending on the samples being collected in that visit. Following Visit 4, participants will have a final oral exam. Participants will receive a maximum compensation of \$735 for their time and travel to the orientation and all study visits [Orientation (Visit 0) = \$75, Screening Oral Exam = \$30, Visit 1 = \$200, Visit 2 = \$100, Visit 3 = \$100, Visit 4 = \$200, Final Oral Exam = \$30].

**H. Procedures For Study Visits** – Following the orientation session and oral exam, participants will report to the test facility for one study visit per week for four consecutive weeks (see [Table 1](#) for a condensed study outline). Test sessions will be conducted Monday through Thursday afternoons. During Visit 1, participants will smoke one usual-brand cigarette. Prior to smoking, participants will have a venous catheter inserted into the antecubital area of their arm, and blood samples will be collected at -2, 0, 3, 5, 7.5, 10, 15, 20, 30, 40, 50, 60, 70, 80, and 90 minutes respective to cigarette lighting for measurement of serum nicotine and cotinine levels. Following smoking, participants will complete sensory questionnaires with

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\* nurse practitioner, physician’s assistant, medical doctor, or doctor of osteopathic medicine

regard to the cigarette they smoked. A 25-minute blood sample will be drawn to measure %COHb, and participants will also provide a 25-minute breath sample to measure expired CO levels. Also at Visit 1, participants will return the following to the study staff: completed product use log for the week prior to the study visit, used cigarette butts from the day before the study visit, and a 24-hour urine sample also collected the day before the study visit. A spot urine sample will be collected during the visit for comparison to the 24-hour urine collection results.

Visits 2 and 3 are designed to monitor participants' progress in decreasing cigarette use and including snus in their tobacco-use routine; therefore, blood and urine requirements are reduced in these weeks. During Visit 2 and Visit 3, participants will use snus according to their own use preferences. The duration of snus use will be timed to capture how long each participant uses snus in the lab. Cigarette and ATP questionnaires will be administered. Twenty-five minutes after initiation of snus use, one blood sample will be drawn for %COHb measurement and expired CO will be measured from a breath sample. Participants will return product use logs for the week, used cigarette butts from the day before the visit, and any unused snus to study staff at both visits 2 and 3. In addition, a spot urine sample will be collected. At both Visit 2 and Visit 3, study staff will encourage participants to decrease cigarette smoking according to their goal and continue snus use. At visit 3, participants will also return all their used snus pouches from the previous week.

Visit 4 will follow the same procedures as Visit 1 with a few exceptions. Participants will use snus according to their own use preferences up to a maximum time of 30 minutes. The used snus pouch(es) will be collected and sent for nicotine analysis. Length of snus use will also be timed. Fifteen blood samples will be collected (at -2, 0, 3, 5, 7.5, 10, 15, 20, 30, 40, 50, 60, 70, 80, and 90 minutes with respect to snus use) to measure serum nicotine "rise" and total nicotine absorption for this product, in addition to the whole blood sample that will be drawn at 25 minutes for %COHb measurement. Participants will complete ATP questionnaires and, if participants report smoking any cigarettes during the fourth week of the study, they will also complete the cigarette questionnaires. At Visit 4, participants will return the same materials to the study staff as those returned at Visit 1 with the addition of returning all their used snus pouches from the previous week and any unused snus.

The total amount of blood to be collected in this study is 117 mL, just under 4.0 fluid ounces (or slightly less than half a cup).

Upon completion of the study, participants will be offered three packages of snus in the current market packaging and snus coupons as an additional bonus for participating in the study.

- I. *Forms, Questionnaires, and Written Instructions*** – Forms and questionnaires to be used include: the informed consent form, a demographic information form, thermometer rating questionnaires for usual-brand cigarettes and snus, cigarette and snus attributes questionnaires, cigarette and snus physical impact questionnaires, the Fagerström Tests for Nicotine Dependence for cigarettes and smokeless tobacco, the Minnesota Nicotine Withdrawal Scale, and a snus exit questionnaire. Participants will also be given a calendar to

remind them of which study requirements they should be completing each day of the study, written instructions for the 24-hour urine collection and used butt collection, and a card with phone numbers to call with questions or concerns. (see [Attachments 3 – 17, 19 – 21](#))

- J. *Personal Information*** – Prior to or when they arrive at the test site, Bellomy Research will assign a unique alphanumeric identifier to each participant. All hardcopy or computer data records for each participant will contain only the identifier. The signed informed consent forms will be returned to Bellomy Research and mailed to Telisha Roberts in Product Integrity at RJRT to be archived. At no time following orientation will lab personnel be able to link an identifier with a name.
- K. *Staff Training*** – At least one staff member working at the offsite facility is certified by the American Red Cross to perform CPR. All staff members have been certified by the American Red Cross to properly handle biological samples to protect themselves and others from exposure to blood-borne pathogens. In addition, all staff members will follow Occupational Safety and Health Administration (OSHA) safety guidelines pertaining to Occupational Exposure to Blood-Borne Pathogens when handling biological samples. All biohazard waste generated during this study will be disposed of in accordance with OSHA guidelines.

Piedmont Medical Research Associates will be contracted to provide certified, trained phlebotomists for this study. Certification of the contracted phlebotomists participating in this study will be documented. Training for study-specific procedures will be performed by a certified RJRT staff phlebotomist, and at least one RJRT staff phlebotomist will be on site during study procedures to assist and supervise the contracted phlebotomists.

Piedmont Medical Research Associates will also be contracted to provide oral exams and medical advisory for this study. Oral exams will be performed by a licensed nurse practitioner (NP), physician's assistance (PA), medical doctor (MD), or doctor of osteopathic medicine (DO). Medical advisory will be provided by a licensed MD or DO.

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**Keywords:** Acrolein, ATP, biomarkers, COHb, expired CO, HPMa, NNAL, NNK, serum cotinine, serum nicotine, SAU, snus, snus after use, questionnaires, urine, yield in use, YIU

	<b>Blood Samples</b>		<b>Urine Samples</b>		<b>Breath Sample</b>	<b>YIU</b>	<b>SAU</b>	<b>Product Usage Logs</b>
	15 timed serum samples for nicotine and cotinine measurements	1 whole blood sample for %COHb measurement	24-hr urine collection for nic+9, NNAL, and acrolein measurements	Spot urine collection	1 sample for measurement of expired CO levels	Collection of all butts from cigarettes smoked day before visit	Collection of all snus pouches used for the entire week before visit	
<b>Visit 1</b>	X (a)	X	X	X	X	X		X
<b>Visit 2</b>		X		X	X	X		X
<b>Visit 3</b>		X		X	X	X	X	X
<b>Visit 4</b>	X (b)	X	X	X	X	X	X	X

	<b>Questionnaires</b>									
	FTND - cigarettes	FTND - smokeless tobacco	Cigarette Thermometer	ATP Thermometer	Cigarette Attributes	ATP Attributes	Cigarette Physical Impact	ATP Physical Impact	MN Withdrawal Scale	Snus Exit Questionnaire
<b>Visit 1</b>	X		X	X	X	X	X	X	X	
<b>Visit 2</b>			X	X	X	X	X	X	X	
<b>Visit 3</b>			X	X	X	X	X	X	X	
<b>Visit 4</b>	X*	X	X*	X	X*	X	X*	X	X	X

\* Include these measurements if participants report smoking any cigarettes the week before or day of Visit 4.

**Table 1.** Outline of study protocol broken down by test session.

(a) Time points will include -2, 0, 3, 5, 7.5, 10, 15, 20, 30, 40, 50, 60, 70, 80, and 90 minutes respective to cigarette lighting.

(b) Time points will include -2, 0, 3, 5, 7.5, 10, 15, 20, 30, 40, 50, 60, 70, 80, and 90 minutes respective to initiation of snus use.

# Attachment 1

## Analytical Measurements for Study Snus

Endpoint	Mellow	Frost
	<u>L80I011E</u>	<u>A9VT015D</u>
	as is	as is
pH avg.	7.63	7.79
Moisture % avg.	32.94	32.49
Nicotine % avg.	1.13	1.14
Nicotine, mg avg. per pouch	6.78	6.84
NAB, µg/g avg.	<0.174	<0.180
NAT, µg/g avg.	0.357	0.538
NNK, µg/g avg.	0.281	0.427
NNN µg/g avg.	0.641	0.842
TSNA, µg/g avg. [10]	1.453	1.987
BaP, ng/g avg. [20]	0.785	<0.803
Ars µg/g avg. [0.5]	0.118	0.231
Cad µg/g avg. [1]	0.38	0.42
Chr µg/g avg. [3]	0.64	0.68
Lead µg/g avg. [2]	0.197	0.217
Nick µg/g avg. [4.5]	1.74	1.797
NDMA, ng/g avg. [10]		
Date of Run	2/6/2009	2/6/2009

**SNUS CONCEPT**

Snus is a revolutionary tobacco product that delivers tobacco pleasure that you can enjoy anytime, anywhere. Snus is not Dip. It is pasteurized tobacco that comes in small pouches. Snus comes in two varieties, Frost and Mellow.

To use snus, take one to your mouth, place it under your upper lip, wait a few minutes for a tingle, and enjoy for up to 30 minutes. (No spitting required.)



**INFORMED CONSENT CHECKLIST**

**Study to Investigate Use of Tobacco Snus Compared to Smoking Usual-Brand Cigarettes**

HRRC #0902

February 5, 2009

**Study Sponsor: R.J. Reynolds Tobacco Company**

- \_\_\_\_\_ YOU STATE THAT YOU ARE AT LEAST 21 YEARS OF AGE.
- \_\_\_\_\_ YOU HAVE VOLUNTARILY AGREED TO BE PART OF THIS RESEARCH STUDY. NOBODY HAS PRESSURED YOU TO TAKE PART IN IT.
- \_\_\_\_\_ You are not postponing a decision to quit smoking just to take part in this study.
- \_\_\_\_\_ You should not make other blood donations while taking part in this study.
- \_\_\_\_\_ You understand that you can ask questions at any time if there is something in this form you do not understand.
- \_\_\_\_\_ You are aware of the Surgeon General's warnings concerning cigarette smoking:
- Smoking Causes Lung Cancer, Heart Disease, Emphysema, And May Complicate Pregnancy.
  - Quitting Smoking Now Greatly Reduces Serious Risks to Your Health.
  - Smoking By Pregnant Women May Result in Fetal Injury, Premature Birth, And Low Birth Weight.
  - Cigarette Smoke Contains Carbon Monoxide.
- \_\_\_\_\_ You understand the following warnings concerning use of oral tobacco products:
- This Product is not a Safe Alternative to Cigarettes.
  - This Product May Cause Gum Disease and Tooth Loss.
  - This Product May Cause Mouth Cancer.

- \_\_\_\_\_ All samples collected from you and all data pertaining to you will be identified only by a code number. The link between the code and your identity will be maintained *in strictest confidentiality*. The link will be kept in a unique location not accessible *at any time* after orientation by personnel conducting the study or analyzing the data.

### **WHY THIS STUDY IS BEING DONE**

- \_\_\_\_\_ This research study is designed to examine how smoking your usual brand cigarettes and using snus may or may not affect the levels of various compounds in your body that indicate tobacco use. This study will also examine your personal opinions about the tobacco products tested.
- \_\_\_\_\_ The blood samples to be collected will be analyzed to determine the amounts of carbon monoxide, nicotine, cotinine, and other compounds you have absorbed and/or metabolized as a result of using tobacco products.
- \_\_\_\_\_ The urine samples to be collected will be analyzed to determine the amounts of nicotine and other compounds you have absorbed and/or metabolized as a result of using tobacco products.
- \_\_\_\_\_ The expired breath samples will provide a measure of the amount of carbon monoxide you have absorbed as a result of smoking and other environmental factors.
- \_\_\_\_\_ The cigarette butts to be collected will be analyzed to examine compounds trapped by the filter during smoking.
- \_\_\_\_\_ The snus pouches to be collected will be analyzed to determine the levels of compounds remaining in the pouches following use.
- \_\_\_\_\_ We will attempt to recruit up to 48 participants for this study.

### **YOU UNDERSTAND THE FOLLOWING:**

- \_\_\_\_\_ You state that you smoke at least 7 cigarettes each day and inhale the smoke.
- \_\_\_\_\_ You state that your primary tobacco use is smoking cigarettes.
- \_\_\_\_\_ You will continue to use the same style of usual brand cigarette throughout this study – one example might be Camel Light, king size, non-menthol, hard pack.
- \_\_\_\_\_ You will use only your usual brand cigarettes or the snus provided to you and will not use any other tobacco- or nicotine-containing products during the course of this study. Examples include other cigarettes, pipe tobacco, chewing tobacco, cigars, moist or dry snuff, dissolvable tobacco products, nicotine chewing gum, nicotine lozenges, nicotine spray, or a nicotine patch.

### Attachment 3

- \_\_\_\_\_ You agree to have a brief oral cavity (mouth) examination by a trained medical professional before acceptance into the study and again at the end of the study.
- \_\_\_\_\_ You will report to the research facility (here) for four test sessions that will last about 45 minutes – 2 hours each following the orientation.
- \_\_\_\_\_ You will provide blood sample(s), urine sample(s), an expired breath sample and will complete questionnaires in each test session.
- \_\_\_\_\_ At each study visit you will have a catheter or needle inserted into your arm. The catheter (which will be placed in visits 1 and 4 only) will remain in place throughout the test session.
- \_\_\_\_\_ There may be discomfort when the needle is placed and withdrawn. As with any needle stick or skin breakage, there is a risk of infection, tissue damage, and bleeding. Sterile procedures will be used to limit these risks.
- \_\_\_\_\_ Up to 13 tubes of blood will be collected during the course of each test session. The total volume of blood drawn for the entire study will be approximately 120 mL, just less than 4.0 fluid ounces.
- \_\_\_\_\_ At Visit 1, you will smoke one usual brand cigarette that you will provide to the study staff. At Visits 2, 3, and 4, you will use snus in accordance with your own typical use.
- \_\_\_\_\_ You understand that as with any tobacco product, snus is meant solely for the enjoyment and use of adult tobacco consumers. You understand that snus is meant **only** for **your** use and you take responsibility for keeping it in your possession and control.
- \_\_\_\_\_ You will **not** place snus in a location where it would be available to **minors** at any time.
- \_\_\_\_\_ You will be paid \$75 for the orientation session and \$30 each for the screening and final oral exams, with the following payments during the study: Visit 1 - \$200, Visit 2 - \$100, Visit 3 - \$100, Visit 4 - \$200, making total possible compensation of \$735 for time and travel.
- \_\_\_\_\_ You must follow the study protocol for each week of the study if you decide to participate:
  - The 7 days prior to and including Visit 1 – you will smoke your usual brand (UB) cigarettes only.
  - Leaving Visit 1 up to and including Visit 2 – you will decrease your UB cigarette smoking by 25% and use snus as desired.
  - Leaving Visit 2 up to and including Visit 3 – you will decrease your UB cigarette smoking by an additional 25% and continue to use snus as desired.
  - Leaving Visit 3 up to and including Visit 4 – you will decrease your UB cigarette smoking by an additional 25% and continue to use snus as desired.

### Attachment 3

- \_\_\_\_\_ You will be required to maintain a daily tobacco product usage log throughout the study and to return it at each test session, along with cigarette butts collected the day before each visit and used snus pouches collected throughout the study.
- \_\_\_\_\_ You must honestly and **accurately** record your **actual** tobacco product use patterns throughout the study.
- \_\_\_\_\_ If you do not complete all study requirements - including tobacco use as outlined above, returning the tobacco product log, cigarette butts, used snus pouches, and/or any unused snus specified per visit, and fulfilling visit procedures, including 24-hour urine collections - you will not receive full study payment and may only be paid for test sessions properly completed to date.
- \_\_\_\_\_ You may be dismissed from the study by the study director for various reasons, including but not limited to illness, failure to report to the test session on time, and violations of study protocol (for example, smoking cigarettes other than usual brand, not returning the tobacco product log, collected 24-hour urine, cigarette butts or unused snus).
- \_\_\_\_\_ In the unlikely event of a laboratory accident (such as broken blood tubes or an accidental needle stick of lab personnel), you consent to having another blood sample drawn to test your blood for the Hepatitis B virus surface antigen and antibodies to the Hepatitis C virus and HIV, the virus that causes AIDS. These tests will be to ensure that lab personnel have not been exposed to potential blood-borne diseases. You will be notified of any such requirement and agree to return upon reasonable notice and at a convenient time and place to have further blood testing performed.

Do you have any questions?

YES \_\_\_\_\_ NO \_\_\_\_\_

#### **YOU UNDERSTAND THAT YOUR INVOLVEMENT IN THIS STUDY INCLUDES THE FOLLOWING:**

- \_\_\_\_\_ Below is a list of conditions, symptoms, and behaviors. You should be in generally good health and must **not** participate in the study if you have any of these conditions, symptoms, or behaviors:
- **Any active mouth sores or other oral lesions**
  - **Heart disease, including angina (chest pain)**
  - **Kidney disease**
  - **Liver disease, such as hepatitis**
  - **Stomach ulcers or irritable bowel syndrome**
  - **Any major neurological disease such as fainting spells, epilepsy, or Parkinson's disease**
  - **Any major psychiatric disorder**
  - **Obesity**
  - **Diabetes (blood sugar disease)**
  - **Asthma or any other lung disease**
  - **HIV /AIDS**

Attachment 3

- **Any type of bleeding disorder including hemophilia (tendency for excessive bleeding)**
- **Anemia**
- **Any other “serious” disease such as cancer**
- **Drink more than 14 servings of alcoholic beverages per week – no more than 2 drinks the night before your test sessions (1 drink = 12 oz beer, 6 oz wine, or 1 oz hard liquor)**
- **Use any illegal (including intravenous) or non-therapeutic drugs**

\_\_\_\_\_ You state that you will notify study staff prior to signing this consent form of any other forms of tobacco you use.

\_\_\_\_\_ In signing this consent form and participating in this study, you are stating that to your knowledge, you do not have any of these conditions, symptoms, or behaviors.

\_\_\_\_\_ **You will notify study personnel if you have skin sensitivity to adhesive bandages, rubbing alcohol, chlorhexidine, iodine, or latex.**

\_\_\_\_\_ (WOMEN ONLY) You must not participate in the study if you are breastfeeding, pregnant, or are planning to become pregnant during the course of the study.

\_\_\_\_\_ You will report any medications that you are taking – which may disqualify you from participating in this study – during screening or to the study director.

\_\_\_\_\_ I am going to read you a list of statements. You agree to listen carefully and if any of the statements is **not** true, you agree not to participate in the study. You do not need to identify which statement is **not** true.

1. You do not work in an occupation where you regularly handle tobacco in a hands-on manner.
2. To your knowledge, you do not have AIDS or HIV nor have you had sex with anyone who has AIDS or HIV.
3. To your knowledge, you do not have a sexually-transmitted disease nor have you been treated for such a disease (for example, gonorrhea or syphilis) in the last 12 months, nor have you had sex with anyone who has.
4. You have never been diagnosed as having hepatitis B or C nor had a positive test for hepatitis B or C. You have not had close contact with anyone who has been diagnosed with hepatitis B or C within the last year.

\_\_\_\_\_ You state that **all** of the previous statements are true for you.

\_\_\_\_\_ Whether you can be a part of this study depends upon all the information you have provided in this form.

### Attachment 3

\_\_\_\_\_ You can address any questions you have to the personnel performing the study before signing this form. For questions regarding scheduling, study instructions, product or supplies, call the study staff at pager number 750-5940. For medical concerns related to the study, call Piedmont Medical Research at 768-8062. During your call, please identify yourself as a participant in the RJ Reynolds study. Piedmont Medical Research is located at 1901 S. Hawthorne Rd, Suite 306, Winston-Salem, NC 27103.

\_\_\_\_\_ You are free to withdraw from the study at any time.

\_\_\_\_\_ In signing this consent form, you confirm that you have answered all the questions concerning your health and medical history accurately and you know of no reason why you should not participate in this study.

Do you have any questions?                      YES \_\_\_\_\_                      NO \_\_\_\_\_

\_\_\_\_\_  
Participant (PRINT NAME)

\_\_\_\_\_  
Participant Signature

Date:\_\_\_\_\_

Time:\_\_\_\_\_

\_\_\_\_\_  
Person Administering Consent (PRINT NAME)

\_\_\_\_\_  
Person Administering Consent (Signature)

Date:\_\_\_\_\_

Time:\_\_\_\_\_

**The Fagerström Test – Cigarettes**

1. How soon after you wake up do you smoke your first cigarette?  
  
Within 5 minutes ..... \_\_\_\_\_ (3)  
6 - 30 minutes ..... \_\_\_\_\_ (2)  
31- 60 minutes ..... \_\_\_\_\_ (1)  
After 60 minutes ..... \_\_\_\_\_ (0)
  
2. Do you find it difficult to refrain from smoking in places where it is forbidden e.g. in church, at the library, in cinema, etc.?  
  
Yes ..... \_\_\_\_\_ (1)  
No ..... \_\_\_\_\_ (0)
  
3. Which cigarette would you hate most to give up?  
  
The first one in the morning ..... \_\_\_\_\_ (1)  
Any other.. ..... \_\_\_\_\_ (0)
  
4. How many cigarettes per day do you smoke?  
  
≤ 10. .... \_\_\_\_\_ (0)  
11-20 ..... \_\_\_\_\_ (1)  
21-30 ..... \_\_\_\_\_ (2)  
≥ 31. .... \_\_\_\_\_ (3)
  
5. Do you smoke more frequently during the first hours after waking than during the rest of the day?  
  
Yes ..... \_\_\_\_\_ (1)  
No ..... \_\_\_\_\_ (0)
  
6. Do you smoke if you are so ill that you are in bed most of the day?  
  
Yes ..... \_\_\_\_\_ (1)  
No ..... \_\_\_\_\_ (0)

Reproduced with permission.

Source: Heatherton, T. F., L. T. Kozlowski, et al. (1991). "The Fagerstrom Test for Nicotine Dependence: a revision of the Fagerström Tolerance Questionnaire." Br J Addict **86**(9): 1119-27.

**The Fagerström Test – Smokeless Tobacco**

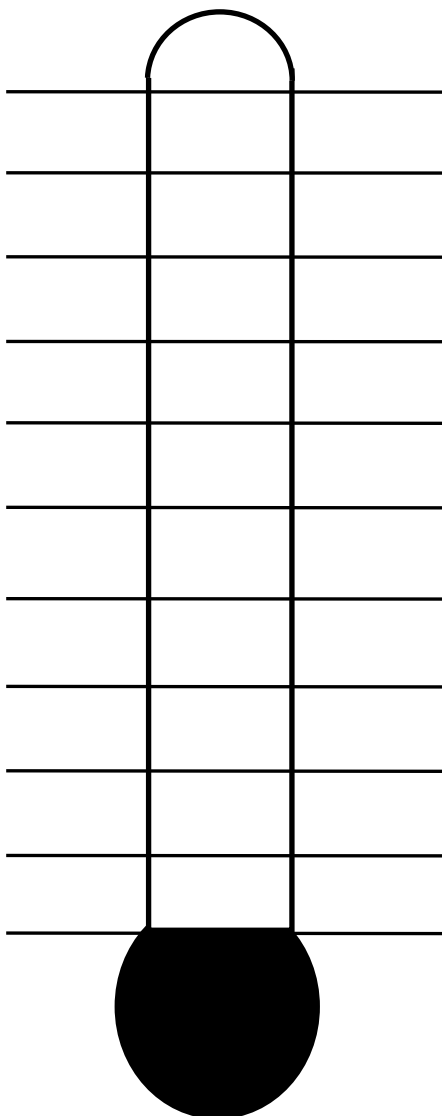
1. How soon after you wake up do you use your first snus pouch?  
Within 5 minutes.....☐3  
6 – 30 minutes.....☐2  
31 – 60 minutes.....☐1  
After 60 minutes.....☐0
2. How often do you intentionally swallow tobacco juice?  
Always.....☐2  
Sometimes.....☐1  
Never.....☐0
3. Which snus would you hate to give up most?  
The first one in the morning.....☐1  
Any other.....☐0
4. How many tins per week do you use?  
More than 3.....☐2  
2 – 3.....☐1  
≤ 1.....☐0
5. Do you use snus more frequently during the first hours after awakening than during the rest of the day?  
Yes.....☐1  
No.....☐0
6. Do you use snus if you are so ill that you are in bed most of the day?  
Yes.....☐1  
No.....☐0

Modified from the original and reproduced with permission.  
Source: Ebbert JO et al. (2006). “The Fagerström Test for Nicotine Dependence-Smokeless Tobacco (FTND-ST).” Addictive Behaviors **31**:1716-1721.

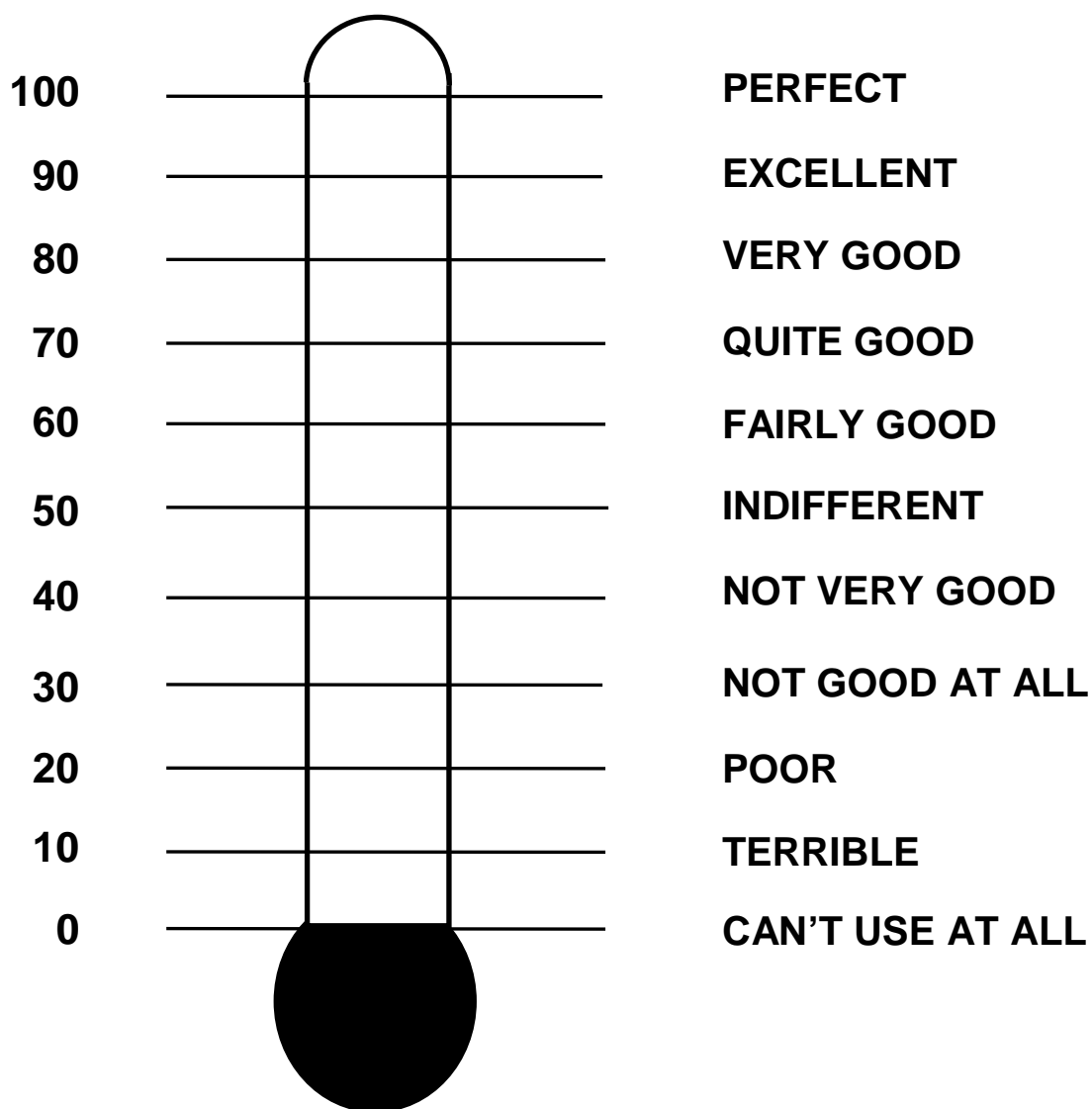


Please circle the number that best describes your opinion of the cigarette you are smoking this week. Circle ONE NUMBER ONLY.

100		THE VERY BEST
90		EXCELLENT
80		VERY GOOD
70		QUITE GOOD
60		FAIRLY GOOD
50		INDIFFERENT
40		NOT VERY GOOD
30		NOT GOOD AT ALL
20		POOR
10		TERRIBLE
0		THE VERY WORST



Please circle the number that best describes your opinion of the oral tobacco product you are using this week. Circle ONE NUMBER ONLY.



**CIGARETTE QUESTIONNAIRE**

Please circle the number you feel best describes the cigarette you are smoking this week. Please circle only one number for each of the following phrases.

**THE CIGARETTE WAS:**

Not strong tasting at all	1	2	3	4	5	6	7	Extremely strong tasting
Extremely easy to get smoke through filter	1	2	3	4	5	6	7	Extremely hard to get smoke through filter
Not harsh at all	1	2	3	4	5	6	7	Extremely harsh
Not smooth at all	1	2	3	4	5	6	7	Extremely smooth
Not satisfying at all	1	2	3	4	5	6	7	Extremely satisfying
Cigarette had: No tobacco taste	1	2	3	4	5	6	7	Extremely strong tobacco taste
Cigarette left: No strong aftertaste	1	2	3	4	5	6	7	Extremely strong aftertaste

## Attachment 9

Snus Evaluation Form

Participant # \_\_\_\_\_ Visit # \_\_\_\_\_ Date \_\_\_\_\_

**Please circle the appropriate rating (number) for each attribute.**

Attribute	Rating Scale							Comments
<b>Sweetness</b>	1	2	3	4	5	6	7	
	Too Little		Just Right			Too Much		
<b>Flavor</b>	1	2	3	4	5	6	7	
	Too Little		Just Right			Too Much		
<b>Tobacco Taste</b>	1	2	3	4	5	6	7	
	Too Little		Just Right			Too Much		
<b>Texture</b>	1	2	3	4	5	6	7	
	Too Slimy		Just Right			Too Coarse		
<b>Bitterness</b>	1	2	3	4	5	6	7	
	None					Extreme		
<b>Mouth Burn</b>	1	2	3	4	5	6	7	
	None					Extreme		
<b>Throat Burn</b>	1	2	3	4	5	6	7	
	None					Extreme		
<b>Side Effects (hiccups, nausea, etc.)</b>	1	2	3	4	5	6	7	
	None					Extreme		
<b>Aftertaste</b>	1	2	3	4	5	6	7	
	Unpleasant					Pleasant		
<b>Overall Taste</b>	1	2	3	4	5	6	7	
	Unpleasant					Pleasant		
<b>Overall Likeability</b>	1	2	3	4	5	6	7	
	Hate it					Love it		

Where did you place the snus in your mouth?

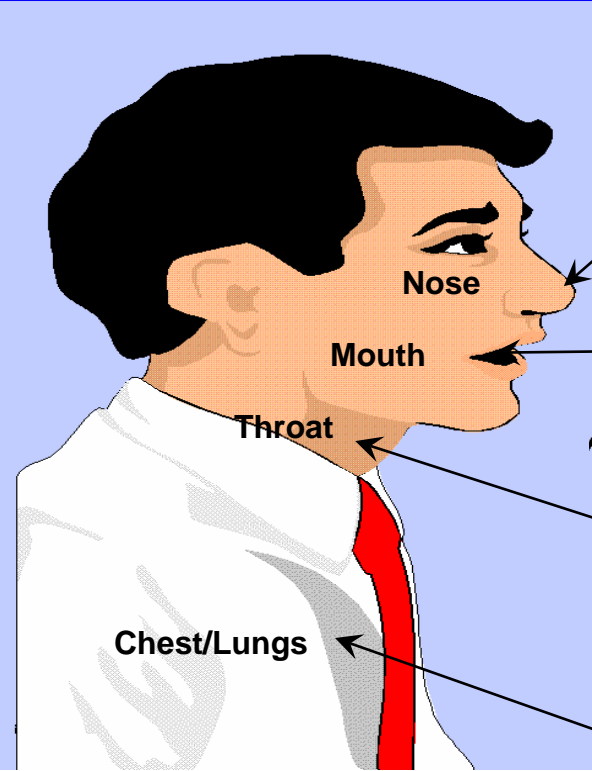
Do you consider this product Acceptable?

(Circle One)

Yes

No

Participant # \_\_\_\_\_  
Visit # \_\_\_\_\_  
Tobacco Product \_\_\_\_\_



The diagram shows a profile of a man's head and neck. Four labels with arrows point to specific scales:

- Nose**: Points to the top scale.
- Mouth**: Points to the second scale.
- Throat**: Points to the third scale.
- Chest/Lungs**: Points to the bottom scale.

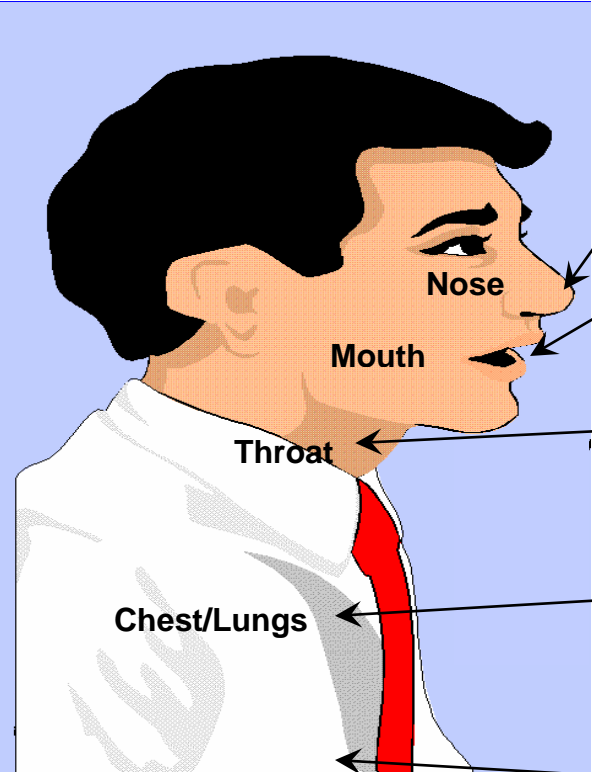
Each scale is a horizontal line with vertical tick marks and numbers 0 through 8. The word "None" is above the 0 and "Extreme" is above the 8.

None	0	1	2	3	4	5	6	7	8	Extreme

With the cigarette you are smoking this week, rate the level of IMPACT you feel (from None to Extreme) in EACH of the areas indicated BY CIRCLING THE NUMBER.

Participant # \_\_\_\_\_  
Visit # \_\_\_\_\_  
Tobacco Product \_\_\_\_\_

	None	0	1	2	3	4	5	6	7	8	Extreme
Nose											
Mouth											
Throat											
Chest/Lungs											
Stomach, Esophagus, GI Tract											



With the oral tobacco product you are using this week, rate the level of IMPACT you feel (from None to Extreme) in EACH of the areas indicated BY CIRCLING THE NUMBER.

## Minnesota Nicotine Withdrawal Scale

**Please rate yourself for the last week:**

**0 = none, 1 = slight, 2 = mild, 3 = moderate, 4 = severe**

1. Angry, irritable, frustrated	0	1	2	3	4
2. Anxious, nervous	0	1	2	3	4
3. Depressed mood, sad	0	1	2	3	4
4. Desire or craving to smoke	0	1	2	3	4
5. Difficulty concentrating	0	1	2	3	4
6. Increased appetite, hungry, weight gain	0	1	2	3	4
7. Insomnia, sleep problems, awakening at night	0	1	2	3	4
8. Restless	0	1	2	3	4
9. Impatient	0	1	2	3	4
10. Constipation	0	1	2	3	4
11. Dizziness	0	1	2	3	4
12. Coughing	0	1	2	3	4
13. Dreaming or nightmares	0	1	2	3	4
14. Nausea	0	1	2	3	4
15. Sore throat	0	1	2	3	4

Original reference (with additions made by the University of Vermont, Department of Human Behavioral Pharmacology):

Hughes, JR and Hatsukami, D (1986). Signs and Symptoms of Tobacco Withdrawal. Arch Gen Psychiatry **43**: 289-94.

Available through public domain.

**CSD STUDY of SNUS**  
**Demographic Information**

**CSD0905**

PARTICIPANT ID \_\_\_\_\_ PARTICIPANT # \_\_\_\_\_ VISIT # \_\_\_\_\_

DATE \_\_\_\_\_ GENDER \_\_\_\_\_ WEIGHT \_\_\_\_\_ HEIGHT \_\_\_\_\_

DATE OF BIRTH \_\_\_\_\_ AGE \_\_\_\_\_ RACE \_\_\_\_\_

USUAL BRAND \_\_\_\_\_ NUMBER SMOKE/DAY \_\_\_\_\_

NUMBER OF YEARS SMOKED \_\_\_\_\_ NUMBER SMOKED TODAY \_\_\_\_\_

**INFORMED CONSENT WAS PROVIDED ON \_\_\_\_\_.**

**GROUP: \_\_\_\_\_**



Participant ID \_\_\_\_\_

Participant # \_\_\_\_\_

**DAILY LOG SHEET – Week 1**

**PLEASE RECORD THE NUMBER OF CIGARETTES YOU SMOKE PER DAY  
FOR THE NEXT EIGHT DAYS.**

**\*\*Remember, you are allowed to smoke ONLY your Usual Brand  
cigarettes until the completion of this study.\*\***

<b>Day 1</b>	<b>Number of cigarettes smoked today _____</b>
<b>Day 2</b>	<b>Number of cigarettes smoked today _____</b>
<b>Day 3</b>	<b>Number of cigarettes smoked today _____</b>
<b>Day 4</b>	<b>Number of cigarettes smoked today _____</b>
<b>Day 5</b>	<b>Number of cigarettes smoked today _____</b>
<b>Day 6</b>	<b>Number of cigarettes smoked today _____</b>
<b>Day 7 (Collect Butts)</b>	<b>Number of cigarettes smoked today _____</b>
<b>* 24-hour urine collection</b>	
<b>Day 8 (Visit 1)</b>	<b>Number of cigarettes smoked today _____</b>

**Comments/Observations concerning the cigarette:**

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Participant ID \_\_\_\_\_

Participant # \_\_\_\_\_

**DAILY LOG SHEET – Week 2**

**PLEASE RECORD THE NUMBER OF TOBACCO PRODUCTS YOU USE PER DAY  
FOR THE NEXT EIGHT DAYS.**

**\*\*Remember, you are allowed to smoke ONLY your Usual Brand  
cigarettes until the completion of this study.\*\***

<b>Day 1 (Test day)</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 2</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 3</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 4</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 5</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 6</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 7 (Collect Butts)</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 8 (Visit 2)</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____

**Comments/Observations concerning the oral tobacco products:**

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Participant ID \_\_\_\_\_

Participant # \_\_\_\_\_

**DAILY LOG SHEET – Week 3**

**PLEASE RECORD THE NUMBER OF TOBACCO PRODUCTS YOU USE PER DAY  
FOR THE NEXT EIGHT DAYS.**

**PLEASE COLLECT ALL SNUS POUCHES USED THIS WEEK.**

**\*\*Remember, you are allowed to smoke ONLY your Usual Brand  
cigarettes until the completion of this study.\*\***

<b>Day 1 (Test day)</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 2</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 3</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 4</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 5</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 6</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 7 (Collect Butts)</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 8 (Visit 3)</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____

**Comments/Observations concerning the oral tobacco product:**

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Participant ID \_\_\_\_\_

Participant # \_\_\_\_\_

**DAILY LOG SHEET – Week 4**

**PLEASE RECORD THE NUMBER OF TOBACCO PRODUCTS YOU USE PER DAY  
FOR THE NEXT EIGHT DAYS.**

**PLEASE COLLECT ALL SNUS POUCHES USED THIS WEEK.**

**\*\*Remember, you are allowed to smoke ONLY your Usual Brand  
cigarettes until the completion of this study.\*\***

<b>Day 1 (Test day)</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 2</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 3</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 4</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 5</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 6</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>Day 7 (Collect Butts)</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____
<b>* 24-hour urine collection</b>		
<b>Day 8 (Visit 4)</b>	<b>No. of snus used today</b> _____	<b>Number of cigarettes smoked today</b> _____

**Comments/Observations concerning the oral tobacco product:**

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## 24-Hour Urine Collection Instructions

**Please read instructions carefully. If you have any questions, please ask!**

1. Consume your usual daily intake of fluids on the day of and the day preceding urine collection.
2. Do not consume more than TWO alcoholic beverages (2 glasses of wine, 2 beers or 2 oz. of liquor) on the day of and the day preceding urine collection.
3. Precisely adhere to the following collection instructions, **keeping urine cold at all times**:

### **Morning of Collection:**

- ❑ **Use the toilet for** your **FIRST** morning void and immediately **RECORD** the Start Time on the collection bottle lid.
- ❑ **COLLECT** your **SECOND** void.
- ❑ Collect **all** urine for the remainder of the day, evening and also through the night.  
\* Again, this is a 24 hour urine collection and it is **EXTREMELY** important that you collect **each void**.

### **The next morning:**

- ❑ When you arise the next morning, **COLLECT** your **FIRST** morning void **ONLY** and immediately **RECORD** the End Time on the collection bottle lid.
  - ❑ **Keep the urine collections cold** and return them to Bellomy at your scheduled session time.
4. Void directly into the brown urine collection container (provided), OR void directly into the small, clean sample container (provided) and immediately transfer the urine directly into the brown urine collection container.
  5. Keep the brown container(s) of urine on ice (ice packs are provided) inside the cooler (provided) at all times or keep refrigerated. Remember to **rotate your ice packs** from the freezer to your cooler as needed in order to keep urine **COLD** at all times (at least 2 to 3 times/day).
  6. Always check the identification number on your brown collection containers to confirm that this is your participant number.
  7. You must turn in two brown containers each designated time, even if only one has been used.

**You will receive the following:**

**1 Ice Cooler**

**4 Ice Packs**

Keep 2 ice packs inside the cooler and 2 ice packs in a freezer, exchanging them as needed.

**2 Brown Urine Collection Containers for each urine sample**

For each collection day, you will receive 2 large containers prior to starting your collections. Please take both containers with you and use both if needed. During each drop-off time, return both containers, whether or not both were used. (For each collection day, you will receive 2 containers and return 2 containers.)

**1 Urine Sample Container**

If using the collection container, immediately transfer the urine into the large brown collection containers. Please ensure that the small collection containers are washed thoroughly with **water only** and dried between each use.

**Please,**

**Collect ALL urine for the designated 24-hour period.**

**DO NOT add water.**

**DO NOT add someone else's urine.**

**KEEP the urine COLD at all times.**

**If you miss a collection, need assistance, or have any problems with the urine collection procedure, please call a study staff member at pager # 750-5940.**

**Thank You!**

## Attachment 16

### Collection of cigarette butts:

On the day before your next visit, you are to collect the butts from all the cigarettes smoked during the day – from the time you get up in the morning, until the time you go to bed at night. You are being provided with a set of numbered vials for the collection of your cigarette butts. Please follow the following instructions for collection:

- \_\_\_\_\_ The cigarettes should be placed in the plastic vials in numerical order.
- \_\_\_\_\_ The smoked cigarette goes into the container lit. Do not put the cigarette out before placing it in a vial.
- \_\_\_\_\_ The cigarette goes into the vial lit end first.
- \_\_\_\_\_ You should bring the set of vials with you wherever you go on the day you are collecting cigarette butts. Do not leave the vials behind. If it is not convenient to carry the entire set of vials with you in certain settings, place enough vials in a plastic bag (provided) to last until you have access to the set of vials.
- \_\_\_\_\_ Safety is important! Do not place cigarettes in the vials while driving although you should bring them with you. Use your car ashtray to put out any cigarettes you smoke when driving. Try to gently remove the coal and keep the cigarette straight when you stub it out.
- \_\_\_\_\_ You should put the lit cigarette directly into the container without extinguishing it first in all situations besides driving.
- \_\_\_\_\_ Please put the cigarettes that you have put out in your car ashtray into the container AS SOON AS YOU CAN.
- \_\_\_\_\_ Put all smoked cigarettes smoked during the day into the vials.
- \_\_\_\_\_ Write the collection date on the vial.

Collection of snus pouches:

In the third and fourth weeks of this study, you will collect all of the snus pouches you use each day. You are to use your snus according to your preferences. You are being provided with a set of numbered jars for the collection of your used snus.

- Beginning at the time you leave your second study visit, immediately after you leave the facility, you are to collect the used pouches from all of the snus used for the remainder of the day. Place the snus pouches in the jar labeled “Week 3 Day 1.” Before you go to bed, place the jar with the used pouches in a freezer.
- On the next day (day 2) through day 7, you are to collect the used pouches from all of the snus used during the day – from the time you get up in the morning, until the time you go to bed at night. Use a new jar each day starting with the jar labeled “Week 3 Day 2” and ending with “Week 3 Day 7. Before you go to bed each day, place the jar with the used pouches in a freezer.
- On day 8, you will return to the facility to turn in the collection jars. You are to collect the used pouches from all of the snus used from the time you get up in the morning, until the time you return to the facility. Use the jar labeled “Week 3 Day 8” to collect these used pouches. You will return all of your collection jars to the facility when you report for your study visit.
- You will follow the same instructions for collecting your used snus pouches for the fourth week of the study.

Please use the following instructions for collection:

\_\_\_\_\_ The snus should be placed in the jar specified for that day’s collection as described above.

\_\_\_\_\_ DO NOT place any other tobacco products in the jars provided for snus collection.

\_\_\_\_\_ Each jar with used snus should be placed in a freezer at the end of each day’s collection. The used snus should be kept frozen until your return visit.

\_\_\_\_\_ DO NOT spit in the collection jar.

\_\_\_\_\_ You should bring the jar specified for that day with you wherever you go during the day when you are collecting used snus pouches. Do not leave the jar behind.

\_\_\_\_\_ Put all snus pouches used during the day into the appropriate jar.

\_\_\_\_\_ Safety is important! Do not place pouches in the jar while driving although you should have the jar with you.

\_\_\_\_\_ Please put the pouches that you use when driving into the jar AS SOON AS YOU SAFELY CAN.



# Inter Office Memo

## *Product Integrity*

### **Stewardship**

**SUBJECT:** Study to Investigate Use of Snus  
Compared to Smoking Usual-  
Brand Cigarettes (HRRC  
Proposal #0902)

**DATE:** February 11, 2009

**TO:** Dr. Mike Ogden, Ms. Elaine  
Round, Mr. Mitch Stiles

**FROM:** Ryan J. Potts

### **Summary**

Stewardship has reviewed a proposal to conduct a study comparing the use of CAMEL Snus to smoking usual brand cigarettes. Based on a review of all available data, Stewardship approves the specific testing detailed in the protocol (HRRC Proposal #0902).

This proposal requires review by the Human Research Review Committee (HRRC). This recommendation does not constitute approval for any other human studies or market launch of this test prototype without further review by Stewardship.

### **Background**

The purpose of the proposed study is to obtain information on CAMEL Snus 'Mellow' and 'Fresh' usage, biomarkers of exposure, and questionnaire-based measurements in 36 study participants over a period of 4 weeks. Participants will include both males and females, ages 21-55, who are current smokers of full-flavor light cigarettes. Participants will be asked to reduce cigarette use and increase Snus use each week to reach a goal of smoking less than 25% of their typical cigarette use by Week 4 of the study.

The CAMEL Snus variants to be tested are current market products. Levels of selected analytes (nicotine, metals, nitrosamines, acrylamide, nitrite and polycyclic aromatic hydrocarbons) were determined for CAMEL Snus in a 2008 market survey (Labstat Project M93); all analytes were within the range of commercially available smokeless tobacco products and below applicable GothiaTek® limits.

Based on a review of all available data, Stewardship approves the specific testing detailed in HRRC Proposal #0902. This proposal requires review by the HRRC. This recommendation does not constitute approval for any other human studies or market launch of this test prototype without further review by Stewardship.

2

cc: C.D. Garner

Pocket Card Contact Phone Numbers

A card will be distributed to each participant with the following information:

**Study Contact Information**

**Questions regarding scheduling, study instructions, product  
and/or supplies - RJRT Pager: 750-5940**

**Study-Related Medical Questions -  
Piedmont Medical Research:  
768-8062**

# March

<i>Sun</i>	<i>Mon</i>	<i>Tue</i>	<i>Wed</i>	<i>Thu</i>	<i>Fri</i>	<i>Sat</i>
<b><u>Study Contact Information:</u></b> Questions regarding scheduling, study instructions, product and/or supplies - RJRT Pager: 750-5940 Study-Related Medical Questions - Piedmont Medical Research: 768-8062						
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>
<b>8</b>	<b>9</b>	<b>10</b>	<b>11</b>	<b>12</b>	<b>13</b>	<b>14</b>
<b>15</b>	<b>16</b>	<b>17</b>	<b>18</b>	<b>19</b>	<b>20</b>	<b>21</b>
<b>22</b>	<b>23</b> <i>Smoke Usual Brand</i> Begin recording # of cigarettes smoked on Daily Log	<b>24</b> <i>Smoke Usual Brand</i>	<b>25</b> <i>Smoke Usual Brand</i>	<b>26</b> <i>Smoke Usual Brand</i>	<b>27</b> <i>Smoke Usual Brand</i> Freeze 4 Ice Packs	<b>28</b> <i>Smoke Usual Brand</i>
<b>29</b> <i>Smoke UB</i> <i>Begin 24-hour Urine Collection</i> & Collect all cigarette butts Today	<b>30</b> <u>Report to Bellomy</u> Return 24-hour urine collection, completed log, & cigarette butts <i>Decrease UB &amp; Incorporate Snus</i>	<b>31</b> <i>Decrease UB &amp; Incorporate Snus</i>				

# 2009

# April

<i>Sun</i>	<i>Mon</i>	<i>Tue</i>	<i>Wed</i>	<i>Thu</i>	<i>Fri</i>	<i>Sat</i>
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**Study Contact Information:**

Questions regarding scheduling, study instructions, product and/or supplies - RJRT Pager: 750-5940

Study-Related Medical Questions - Piedmont Medical Research: 768-8062

			<b>1</b> <i>Decrease UB &amp; Incorporate Snus</i>	<b>2</b> <i>Decrease UB &amp; Incorporate Snus</i>	<b>3</b> <i>Decrease UB &amp; Incorporate Snus</i>	<b>4</b> <i>Decrease UB &amp; Incorporate Snus</i>
<b>5</b> <i>Decrease UB &amp; Incorporate Snus</i> & Collect all cigarette butts <u>Today</u>	<b>6</b> <u>Report to Bellomy</u> Return completed log, cigarette butts, & unused Snus <i>Decrease UB, Continue Snus &amp; Collect all used pouches (Day 1)</i>	<b>7</b> <i>Decrease UB &amp; Continue Snus</i> & Collect all used Snus pouches (Day 2)	<b>8</b> <i>Decrease UB &amp; Continue Snus</i> & Collect all used Snus pouches (Day 3)	<b>9</b> <i>Decrease UB &amp; Continue Snus</i> & Collect all used Snus pouches (Day 4)	<b>10</b> <i>Decrease UB &amp; Continue Snus</i> & Collect all used Snus pouches (Day 5)	<b>11</b> <i>Decrease UB &amp; Continue Snus</i> & Collect all used Snus pouches (Day 6)
<b>12</b> <i>Decrease UB &amp; Continue Snus</i> & Collect all cigarette butts & all used Snus pouches (Day 7)	<b>13</b> <u>Report to Bellomy</u> Return completed log, cigarette butts, used (Day 8) & unused Snus <i>Decrease UB, Continue Snus &amp; Collect all used pouches (Day 1)</i>	<b>14</b> <i>Decrease UB &amp; Continue Snus</i> & Collect all used Snus pouches (Day 2)	<b>15</b> <i>Decrease UB &amp; Continue Snus</i> & Collect all used Snus pouches (Day 3)	<b>16</b> <i>Decrease UB &amp; Continue Snus</i> & Collect all used Snus pouches (Day 4)	<b>17</b> <i>Decrease UB &amp; Continue Snus</i> & Collect all used Snus pouches (Day 5)  <b>Freeze 4 Ice Packs</b>	<b>18</b> <i>Decrease UB &amp; Continue Snus</i> & Collect all used Snus pouches (Day 6)
<b>19</b> <i>Decrease UB &amp; Continue Snus</i> <u>Begin 24-hour Urine Collection</u> & Collect all cigarette butts & all used Snus pouches (Day 7)	<b>20</b> <u>Report to Bellomy</u>  Return 24-hour urine collection, completed log, cigarette butts, used (Day 8)& unused Snus	<b>21</b>	<b>22</b>  36	<b>23</b>	<b>24</b>	<b>26</b>

# 2009



Study No. CSD0905

Participant No. \_\_\_\_\_ Participant ID No. \_\_\_\_\_

## **EXIT INTERVIEW QUESTIONNAIRE SNUS**

For

R.J. Reynolds Tobacco Company  
PO Box 1487  
Winston-Salem, NC 27102

By

Bellomy Research, Inc.  
175 Sunnynoll Court  
Winston-Salem, NC 27106

For office use only: I confirm that this subject has been consented to complete this questionnaire and the questionnaire was received on the following date:

Study Coordinator (or designee): \_\_\_\_\_ Date: \_\_\_\_\_

**Your opinion counts! Please give us your opinion of the study product you used, as well as your feedback on the study. Answer each question by circling the number beside the best answer. Circle only one choice unless indicated otherwise. When completed, please return your questionnaire to the study coordinator.**

- 1) Before participating in this study, had you ever used a smokeless tobacco product? (Circle one)

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

- 2) While participating in this study, what other tobacco products, if any, did you use besides the study-provided Snus smokeless tobacco product? (Circle all that apply)

Cigarettes..... 1  
Moist snuff or dip in a round can..... 2  
Chewing tobacco ..... 3  
Pipe tobacco ..... 4  
Cigars or little cigars ..... 5  
Other (Specify) ..... 7  
None ..... 8 (SKIP TO Q. 6)

**→ IF YOU USED OTHER TOBACCO PRODUCTS BESIDES SNUS OR YOUR USUAL BRAND OF CIGARETTE, PLEASE ANSWER Q. 3 – Q. 5. OTHERWISE, YOU MAY SKIP TO Q. 6.**

- 3) If you used other tobacco products besides Snus or your usual brand of cigarette while participating in this study, during which week(s) did you use them? (Circle all that apply)

Week 1 ..... 1  
Week 2 ..... 2  
Week 3 ..... 3  
Week 4 ..... 4

- 4) If you used other tobacco products besides Snus or your usual brand of cigarette while participating in this study, how much did you use during the study? (Circle one)

Once a week ..... 1  
2-3 times per week..... 2  
4-6 times per week..... 3  
Once a day..... 4  
Several times a day ..... 5

- 5) Why did you use other tobacco products besides Snus or your usual brand of cigarette while participating in this study? (Please be as specific as possible.)

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# Attachment 21

- 6) For weeks 1, 2, 3 and 4 would you say that the number of cigarettes you smoked during the study was less than usual, about the same or more than usual compared to the number of cigarettes you smoked before the study? (Circle one for each week)

	Less than usual	About the same	More than usual	Did not use cigarettes during this week
<b>Week 1</b> (Circle one)	1	2	3	4
<b>Week 2</b> (Circle one)	1	2	3	4
<b>Week 3</b> (Circle one)	1	2	3	4
<b>Week 4</b> (Circle one)	1	2	3	4

- 7) While participating in this study, what nicotine replacement products, if any, did you use? (Circle all that apply)

Nicotine patch ..... 1  
 Nicotine gum ..... 2  
 Nicotine lozenges..... 3  
 Nicotine nasal spray..... 4  
 Nicotine inhaler ..... 5  
 Other (Specify) ..... 6  
 None ..... 7 **(SKIP TO Q. 11)**

- 8) If you used nicotine replacement products while participating in this study, during which week(s) did you use them? (Circle all that apply)

Week 1 ..... 1  
 Week 2 ..... 2  
 Week 3 ..... 3  
 Week 4 ..... 4

- 9) If you used nicotine replacement products while participating in this study, how much did you use during the study? (Circle one)

Once a week ..... 1  
 2-3 times per week..... 2  
 4-6 times per week..... 3  
 Once a day..... 4  
 Several times a day ..... 5

- 10) Why did you use nicotine replacement products while participating in this study? (Please be as specific as possible.)

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- 11) How difficult was it for you to reduce smoking while participating in this study? (Circle one)

Impossible.....1  
 Very Difficult.....2  
 Somewhat Difficult .....3  
 Somewhat Easy.....4  
 Easy.....5

## Attachment 21

- 12) How accurate were you when reporting the number of cigarettes you smoked during the study?  
(Circle one)

I know I recorded every cigarette I smoked.....1  
 I missed a few cigarettes over the 4 weeks .....2  
 I missed a few cigarettes each week .....3  
 I missed one or more cigarettes every day.....4  
 I estimated the number of cigarettes I smoked each day ...5

- 13) Upon starting the study, what were your thoughts about quitting smoking? (Circle one)

Not at all interested in quitting.....1  
 Neither interested nor uninterested in quitting.....2  
 Somewhat interested in quitting.....3  
 Very interested in quitting.....4

- 14) Have you tried to quit smoking before participating in this study? (Circle one)

Yes.....1  
 No.....2 **(SKIP TO Q. 17)**

**→ IF YOU HAVE TRIED TO QUIT SMOKING BEFORE, PLEASE ANSWER Q. 15-16. OTHERWISE, YOU MAY SKIP TO Q. 17.**

- 15) If yes, how many attempts to quit smoking have you made in the past? (Circle one)

One attempt.....1  
 Two to five attempts.....2  
 More than five attempts.....3

- 16) Why did you attempt to quit smoking?

Financial reasons.....1  
 Reduce smoke exposure to family/friends.....2  
 Health reasons/reduce smoke exposure to self.....3  
 Socially unacceptable.....4  
 Inconvenient to smoke/smoking restrictions.....5  
 Other (specify).....6

- 17) About how long did it take you to get used to the study-provided Snus smokeless tobacco product? (Circle one)

1 to 3 days.....1  
 4 to 7 days.....2  
 2<sup>nd</sup> week .....3  
 3<sup>rd</sup> week.....4  
 I never got used to using Snus .....5

- 18) On average, how often did you use the study-provided Snus smokeless tobacco product while participating in this study? (Circle one)

Every day .....1  
 5 or 6 days per week.....2  
 3 or 4 days per week.....3  
 1 or 2 days per week.....4  
 Less than one day a week .....5



## Attachment 21

19) When using the study-provided Snus smokeless tobacco product, how long did you keep it in your mouth? (Circle one)

Less than 5 minutes ..... 1  
 5 to 9 minutes..... 2  
 10 to 30 minutes..... 3  
 31 to 45 minutes..... 4  
 46 to 60 minutes..... 5  
 More than 1 hour..... 6

20) Where did you place Snus in your mouth? (Circle all that apply)

In the front between upper lip and gum ..... 1  
 In the front between lower lip and gum ..... 2  
 On the upper side between cheek and gum ..... 3  
 On the lower side between cheek and gum..... 4  
 Under your tongue ..... 5  
 On top of your tongue ..... 6  
 On the roof of your mouth ..... 7  
 Different places ..... 8  
 Did not use enough to have a pattern..... 9

21) Where did you **most frequently** place Snus in your mouth? (Circle one)

In the front between upper lip and gum ..... 1  
 In the front between lower lip and gum ..... 2  
 On the upper side between cheek and gum ..... 3  
 On the lower side between cheek and gum..... 4  
 Under your tongue ..... 5  
 On top of your tongue ..... 6  
 On the roof of your mouth ..... 7  
 Different places ..... 8  
 Did not use enough to have a pattern..... 9

22) Did you typically move the Snus around or reposition it while you were using it? (Circle one)

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

23) Did you notice any change in mouth feel during or after use of the study-provided Snus smokeless tobacco product? (Circle one)

Yes ..... 1  
 No..... 2 **(SKIP TO Q. 25)**

24) What kind(s) of changes in mouth feel did you notice? (Circle all that apply)

Tingling sensation with lips or gums or tongue .... 1  
 Dried out mouth..... 2  
 Coating sensation in mouth ..... 3  
 Other (Specify) ..... 4

Attachment 21

25) Did you ever try using multiple pouches of Snus at the same time? (Circle one)

Yes ..... 1  
No ..... 2 **(SKIP TO Q. 28)**

26) When you used multiple pouches of Snus, how many did you use at one time? (Circle one)

2 pouches ..... 1  
3 pouches ..... 2  
More than 3 pouches ..... 3

27) What percent of the time would you say you used multiple pouches of Snus at the same time?  
(Circle one)

Less than 25% of the time ..... 1  
25% to 50% of the time ..... 2  
More than 50% of the time ..... 3  
Most of the time ..... 4

28) Did you ever drink a beverage while using the Snus smokeless tobacco product? (Circle one)

Yes ..... 1  
No ..... 2 **(SKIP TO Q. 32)**

29) How often did you drink a beverage while using the Snus smokeless tobacco product? (Circle one)

Infrequently ..... 1  
Occasionally ..... 2  
Often ..... 3  
Most of the time ..... 4

30) Did drinking a beverage while using the Snus smokeless tobacco product increase or decrease your enjoyment of the product? (Circle one)

Increase ..... 1  
Decrease ..... 2  
Did not change ..... 3

31) What type of beverage did you most often drink while using Snus?

Please specify: \_\_\_\_\_

32) How long did it take you to use one container of the study-provided Snus smokeless tobacco product in Week 4? (Circle one)

1 day ..... 1  
2 days ..... 2  
3 days ..... 3  
4 days ..... 4  
5 days ..... 5  
6 days ..... 6  
7 days or more ..... 7

Attachment 21

- 33) Where PRIMARILY did you use the study-provided Snus smokeless tobacco product? (Circle one) Where ELSE did you use it? (Circle all that apply)

	Primarily Used	Other Locations Used
	(Circle one)	(Circle all that apply)
At work	1	1
At home	2	2
In my car	3	3
In a restaurant	4	4
In a bar/club	5	5
Around friends/others	6	6
At a sporting event	7	7
In a plane	8	8
On public transportation (bus/subway)	9	9
Other public areas that ban smoking	10	10
Other (Specify) _____	11	11

- 34) Which varieties of the study-provided Snus smokeless tobacco product did you try? (Circle all that apply) And which ONE variety was your favorite? (Circle one)

	Varieties Tried	Favorite Variety
	(Circle all that apply)	(Circle one)
Mellow	1	1
Frost	2	2

- 35) Did you primarily stick to one variety of the study-provided Snus smokeless tobacco product throughout the study or did you frequently change varieties? (Circle one)

Primarily stuck with one variety ..... 1

Changed varieties throughout study ..... 2

- 36) On a scale from 1 to 10, with 1 being "Not Satisfied At All" and 10 being "Completely Satisfied," how satisfied were you with the study-provided Snus smokeless tobacco product? (Please circle a number from 1 to 10.)

Not Satisfied At All									Completely Satisfied
1	2	3	4	5	6	7	8	9	10

- 37) Did you find using the study-provided Snus smokeless tobacco product to be an enjoyable alternative to smoking a cigarette? (Circle one)

Yes ..... 1

No ..... 2

Attachment 21

38) Did you miss some of the rituals of smoking a tobacco-burning cigarette, such as tapping the ashes? (Circle one)

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

39) Did you notice any change in the study-provided Snus smokeless tobacco product's taste from the first pouch in the container to the last? (Circle one)

Yes ..... 1  
No ..... 2 **(SKIP TO Q. 41)**

40) What, specifically, did you notice? (Please be as specific as possible.)

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41) Did you notice any change in the study-provided Snus smokeless tobacco product's taste throughout the study? (Circle one)

Yes ..... 1  
No ..... 2 **(SKIP TO Q. 43)**

42) What, specifically, did you notice? (Please be as specific as possible.)

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43) Did you notice any change in the study-provided Snus smokeless tobacco product's appearance throughout the study? (Circle one)

Yes ..... 1  
No ..... 2 **(SKIP TO Q. 45)**

44) What, specifically, did you notice? (Please be as specific as possible.)

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Attachment 21

45) Would you say that the study-provided Snus smokeless tobacco product ...? (Circle one)

- Greatly exceeded your expectations ..... 1
- Somewhat exceeded your expectations ..... 2
- Met your expectations ..... 3
- Somewhat failed to meet your expectations ..... 4
- Did not at all meet your expectations ..... 5

46) Taking into consideration everything you know about the study-provided Snus smokeless tobacco product and your experience with the product, what specifically did you **like** about it? (Please be as specific as possible.)

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47) What specifically did you **dislike** about the study-provided Snus smokeless tobacco product? (Please be as specific as possible.)

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48) What change(s), if any, to the Snus smokeless tobacco product would you suggest to make it better? (Please be as specific as possible.)

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49) How well or poorly do you think the study-provided Snus smokeless tobacco product fits into your lifestyle? (Circle one)

- Fits extremely well ..... 1
- Fits somewhat well ..... 2
- Fits neither well nor poorly ..... 3
- Fits somewhat poorly ..... 4
- Fits very poorly ..... 5

50) Have you spoken with any other adult smokers about the study-provided Snus smokeless tobacco product? (Circle one)

- Yes ..... 1
- No ..... 2 (**SKIP TO Q. 52**)

Attachment 21

51) How many adult smokers have you spoken to about the study-provided Snus smokeless tobacco product? (Circle one)

1 to 3 ..... 1  
4 to 6 ..... 2  
7 to 9 ..... 3  
10 or more..... 4

52) Did you offer any of the study-provided Snus smokeless tobacco product to an adult friend who smokes? (Circle one)

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

53) How likely would you be to recommend the study-provided Snus smokeless tobacco product to an adult friend who smokes? (Circle one)

Definitely would recommend..... 1  
Probably would recommend ..... 2  
Might or might not recommend ..... 3  
Probably would not recommend ..... 4  
Definitely would not recommend..... 5

54) How likely would you be to continue using the study-provided Snus smokeless tobacco product if it were available in your local store? (Circle one)

Extremely likely ..... 1  
Very likely..... 2  
Somewhat likely ..... 3  
Not very likely..... 4  
Not at all likely..... 5

55) Why would you continue or not continue using the study-provided Snus smokeless tobacco product if it were available? (Please be as specific as possible.)

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56) If you were to continue to use the study-provided Snus smokeless tobacco product, would you use it in combination with cigarettes or other tobacco products? (Circle one)

Would use in combination with cigarettes only ..... 1  
Would use in combination with cigarettes and other tobacco products..... 2  
Would only use the study-provided Snus smokeless tobacco product..... 3  
Would not continue using the study-provided Snus smokeless tobacco product... 4

## Attachment 21

57) Where would you expect the Snus smokeless tobacco product to be located in a retail store?  
(Circle one)

With the cigarettes..... 1  
With the moist snuff..... 2  
Some other location (Specify) \_\_\_\_\_ 3

58) If the Snus smokeless tobacco product were available in stores, would you expect it to be priced...? (Circle one)

More than your usual brand of cigarettes..... 1  
Less than your usual brand of cigarettes ..... 2  
The same as your usual brand of cigarettes ..... 3

**In these last few questions, we would like your opinion about the study in which you participated.**

59) How did you initially hear about the study? (Circle one)

Through the mail..... 1  
Phone ..... 2  
Responded to a print ad ..... 3  
Online ..... 4  
Word of mouth ..... 5  
Other (Specify) \_\_\_\_\_ 6

60) Did you discuss the study with anyone else and/or encourage them to participate? (Circle one)

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

61) Below is a list of activities that were required of you during the course of the study. On a scale of 1 to 7, with 1 being "Extremely Unappealing," 4 being "Neither Appealing nor Unappealing" and 7 being "Extremely Appealing," how appealing were each of the following activities to you? (Circle one rating for each item.)

	<b>(Circle one rating for each)</b>						
	<b>Extremely Unappealing</b>			<b>Neither Appealing nor Unappealing</b>			<b>Extremely Appealing</b>
Visits every week	1	2	3	4	5	6	7
Travel to and from the site	1	2	3	4	5	6	7
Compensation	1	2	3	4	5	6	7
Length of the study	1	2	3	4	5	6	7
Product you were asked to use	1	2	3	4	5	6	7
Completing questionnaires	1	2	3	4	5	6	7

# Attachment 21

62) How would you rate each of the following characteristics of the study? (Circle one rating for each item.)

	(Circle one rating for each)				
	Poor	Fair	Good	Very Good	Excellent
Convenience of the site location	1	2	3	4	5
Cleanliness of the facilities	1	2	3	4	5
Comfort of the site	1	2	3	4	5
Comfort with the study team members	1	2	3	4	5
Encouragement and motivation by the study team members in helping me achieve my study goals	1	2	3	4	5

63) Why or why not would you consider participating in a similar study in the future? (Please be as specific as possible.)

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64) Would you have found a brief phone call(s) from study staff during each week of the study – in addition to your test session reminder call – to be helpful? The call would include conversation on items like how you're doing with study procedures and what you're thinking about the study product. (Circle one)

- Yes, that would be very helpful..... 1  
Yes, that would be somewhat helpful ..... 2  
That wouldn't make any difference ..... 3 **(SKIP TO Q. 67)**  
No, that would not be helpful ..... 4 **(SKIP TO Q. 67)**  
No, that would be intrusive ..... 5 **(SKIP TO Q. 67)**

65) How many phone calls would you have found helpful? (Circle one)

- One ..... 1  
Two ..... 2  
More than two ..... 3

66) Why or why not would you have found such calls to be helpful? (Please be as specific as possible.)

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Attachment 21

67) Do we have your permission to contact you in the future to ask some questions about your tobacco use at that time? (Circle one)

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

68) Did you enjoy participating in this study? Why or why not? (Please be as specific as possible.)

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69) Do you have any additional comments or suggestions that you would like to share with us about the study or study product? (Please be as specific as possible.)

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**Thank you for your help and your opinions as part of our research!**