

HRRC PROPOSAL

To: Mike Ogden
HRRC Chairperson

Date: May 18, 2009

From: Elaine Round, Mitch Stiles

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

- 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 36 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. Whole blood will also be used for the development of biomarkers of tobacco effect. 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 to be used in this study is current market product and 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.

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 1](#)) 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, and will obtain informed consent ([Attachment 2](#)), medical history information ([Attachment 3](#)) and will distribute study supplies for Visit 1. An additional 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 \$845 for their time and travel to the orientation and all study visits [Orientation (Visit 0) = \$85, Screening Oral Exam = \$30, Visit 1 = \$250, Visit 2 = \$100, Visit 3 = \$100, Visit 4 = \$250, 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 Tuesday through Friday 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. Three blood samples will be collected prior to smoking: two will be used for the development of biomarkers of tobacco effect and one will be used to measure %COHb. Blood samples will also be collected at -2, 0, 3, 5, 7.5, 10, 15, 20, 30, 40, 50, 60, 70, 80, and

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

90 minutes respective to cigarette lighting for measurement of serum nicotine and cotinine levels. A 25-minute blood sample will be drawn to measure %COHb. Participants will also provide two breath samples for measurement of expired CO levels: one sample will be provided prior to cigarette smoking and the other at 25 minutes after cigarette lighting. Following smoking, participants will complete sensory questionnaires with regard to the cigarette they smoked. 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. Before leaving Visit 1, participants will be given their first supply of study snus.

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. Prior to snus use, one blood sample will be drawn for %COHb measurement and expired CO will be measured from a breath sample. An additional expired CO measurement will be taken at 25 minutes after the start of snus use. Also at Visits 2 and 3, 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. New supplies of snus will be given at each visit. 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 samples that will be drawn prior to snus use and at 25 minutes for %COHb measurement and biomarker development. 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 183 mL, slightly more than $\frac{3}{4}$ of 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 medical history 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 and snus collection, and a card with phone numbers to call with questions or concerns. (see [Attachments 2 – 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 and medical history forms will be retained in a secure location at the offsite testing facility. At the conclusion of the study the records will be transferred to secure records retention for archival purposes. All information contained on the informed consent and medical history forms will remain confidential.
- K. *Staff Training*** – At least one staff member working at the offsite facility is certified 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 bloodborne pathogens. In addition, all staff members will follow Occupational Safety and Health Administration (OSHA) safety guidelines pertaining to Occupational Exposure to Bloodborne Pathogens when handling biological samples. All biohazard waste generated during this study will be disposed of in accordance with OSHA guidelines. RJRT study staff has been trained to properly maintain the confidentiality of study participants, including their personal identity and all personal health information.

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.

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

	Blood Samples			Urine Samples		Breath Sample	YIU	SAU	Product Usage Logs
	15 timed serum samples for nicotine and cotinine measurements	Whole blood sample(s) for %COHb measurement	Two whole blood samples for biomarker development	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	
Visit 1	X (a)	X (c)	X	X	X	X	X		X
Visit 2		X (d)			X	X	X		X
Visit 3		X (d)			X	X	X	X	X
Visit 4	X (b)	X (c)	X	X	X	X	X	X	X

	Questionnaires									
	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
Visit 1	X		X		X		X		X	
Visit 2			X	X	X	X	X	X	X	
Visit 3			X	X	X	X	X	X	X	
Visit 4	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.
- (c) Two whole blood samples will be taken: one prior to product use and one at 25 minutes after initiation of product use.
- (d) One whole blood sample will be taken prior to start of product use.

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 #0902A

March 18, 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.

Attachment 2

- _____ 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 confidence*. Documentation that contains your identity, including this consent form and medical history information, will be kept in a secure location with access limited to study staff and the medical practitioners contracted for this study. Any reports or publications resulting from the data collected in this study will not identify you by name.

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 36 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 2

- _____ You agree to provide the study staff with an accurate medical history and list of medications you are currently taking. It is important that you provide information about your health that is accurate and true. Failure to provide important medical information or not truthfully reporting medical information could put you at risk if you were selected to participate in this study. We encourage you to be honest about all pertinent medical information. Study staff will review with you the information you provide for accuracy.
- _____ 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.
- _____ This study is for research purposes and is not intended to treat any medical condition.
- _____ 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 19 tubes of blood will be collected during the course of each test session. The volume of blood drawn at study visits 1 and 4 will be approximately 88.5 mL, which is equivalent to 3 fluid ounces. The total volume of blood drawn for the entire study will be approximately 183 mL, slightly more than 6 fluid ounces, which is about $\frac{3}{4}$ of a cup.
- _____ 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 \$85 for the orientation session and \$30 each for the screening and final oral exams, with the following payments during the study: Visit 1 - \$250, Visit 2 - \$100, Visit 3 - \$100, Visit 4 - \$250, making total possible compensation of \$845 for time and travel.

Attachment 2

- _____ 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. |
- _____ 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:

- _____ You state that you will notify study staff prior to signing this consent form of any other forms of tobacco you use.
- _____ You state that you do not use any illegal (including intravenous) or non-therapeutic drugs.

Attachment 2

- ____ You state that you do not drink more than 14 servings of alcoholic beverages per week. (1 serving = 12 oz beer, 6 oz wine, or 1 oz, hard liquor)
- ____ You state that you will not drink more than 2 servings of alcoholic beverages the night before your test session.
- ____ (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 do not work in an occupation where you regularly handle tobacco in a hands-on manner.
- ____ Whether you can be a part of this study depends upon all the information you have provided in this form and the medical history information you will provide if you consent to participate in this study. You will not be officially accepted for participation in this study until your medical history has been reviewed and approved by a medical professional.
- ____ 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 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: _____

RJRT Clinical Studies Division
StudyCSD0905

Participant # _____
Participant ID _____
Date _____
YOB _____ **Age** _____

CONFIDENTIAL MEDICAL HISTORY QUESTIONNAIRE

Please answer each question with a check in the appropriate column.

MEDICAL HISTORY Does your history include any of the following?					
	Yes	No		Yes	No
1 Headaches (Migraine, Sinus)			21 Arthritis		
2 Allergy, Asthma, or Hay fever			22 Back or Neck Problems		
3 Head Injury, Unconsciousness			23 Joint Pain		
4 Fainting or Dizzy Spells			24 Swelling of Feet or Hands		
5 Seizures or Convulsions			25 Insomnia		
6 Skin Diseases or Rashes			26 Mental Illness		
7 Frequent Cold or Bronchitis			27 Panic Attacks, Depression		
8 Lung Disease			28 Sugar, Protein, or Blood in Urine		
9 Shortness of Breath			29 Diabetes (Sugar)		
10 Heart Condition			30 Kidney or Bladder Trouble		
11 Heart Murmur			31 Operations/Surgeries		
12 Irregular Heart Rhythm			32 Illness Requiring Hospitalization		
13 High Blood Pressure			33 Alcohol or Drug Addiction		
14 Chest Pain or Angina			34 Medical Care in the Last Year		
15 Ulcers or Frequent Heartburn			35 Allergy to Medications, Latex, Food		
16 Stomach or Intestinal Problem			36 Weakness or Fatigue		
17 Hepatitis, Jaundice			37 Lymph Node Swelling or Anemia		
18 Cancer or Tumors			38 Recent Gain or Loss in Weight		
19 HIV/AIDS			39 Oral Lesions or Mouth Sores		
20 Bleeding disorder, hemophilia			40 Other Health Concerns		

Attachment 3

RJRT Clinical Studies Division
Study CSD0905

Participant # _____

Participant ID _____

Date _____

To be completed by study staff:

Medical Conditions:

Medical Condition	Severity as participant reports: Circle one	Date of Onset	End Date	Con Med? Y/N	Frequency/Comments
	Mild Moderate Severe				
	Mild Moderate Severe				
	Mild Moderate Severe				
	Mild Moderate Severe				
	Mild Moderate Severe				
	Mild Moderate Severe				
	Mild Moderate Severe				
	Mild Moderate Severe				
	Mild Moderate Severe				
	Mild Moderate Severe				
	Mild Moderate Severe				
	Mild Moderate Severe				
	Mild Moderate Severe				
	Mild Moderate Severe				
	Mild Moderate Severe				
	Mild Moderate Severe				

Allergies to medications, latex, or food:

Medication/Latex/Food	Severity as participant reports: Circle one	Date of Onset	Reaction
	Mild Moderate Severe		
	Mild Moderate Severe		
	Mild Moderate Severe		
	Mild Moderate Severe		

RJRT Clinical Studies Division
Study CSD0905

Participant # _____
Participant ID _____

Hospitalizations or Surgeries:

Hospitalization or Surgery	Date

Other Comments: _____

I certify that to the best of my knowledge the information provided is true and accurate and that I have disclosed all pertinent medical history. I understand that this information is for confidential research use only and will not be shared with or released to unauthorized persons without my knowledge or consent.

PARTICIPANT NAME: (Print) _____

PARTICIPANT SIGNATURE: _____ **DATE:** ____/____/____

REVIEWED WITH PARTICIPANT BY: _____ **DATE:** ____/____/____

MEDICAL ADVISOR SIGNATURE: _____ **DATE:** ____/____/____

UPDATES TO MEDICAL HISTORY:

Reason	Date	Medical Advisor Initials	Participant Initials	Staff Initials

Attachment 3

RJRT Clinical Studies Division
Study CSD0905

Participant # _____
Participant ID _____
Date _____

Concomitant Medications:

Medication	Dose	Start Date	Stop Date	Condition

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.

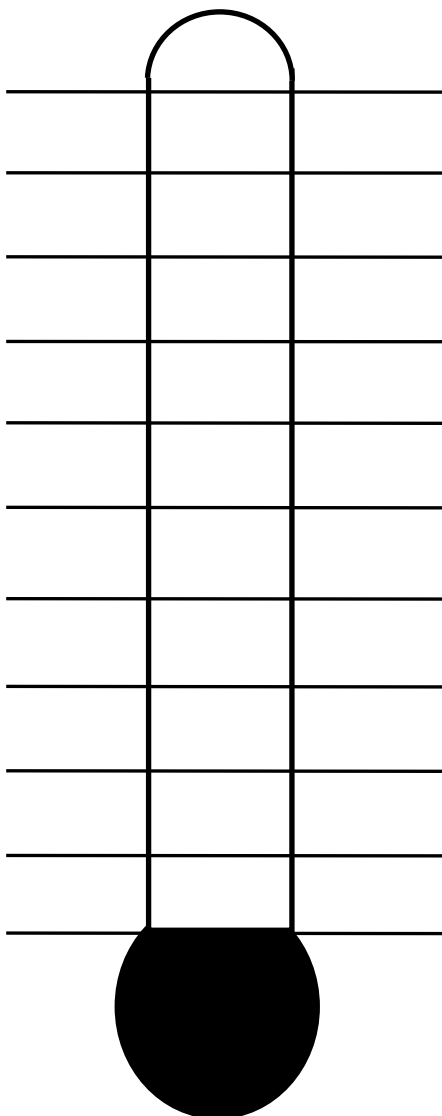
The Fagerström Test – Smokeless Tobacco

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.

100		PERFECT
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		CAN'T USE AT ALL

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

Where did you place the snus in your mouth?

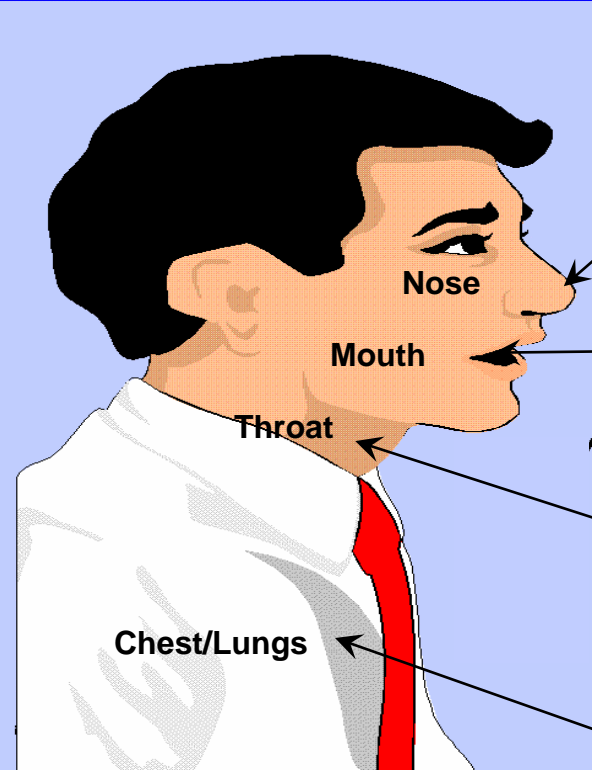
Do you consider this product Acceptable?

(Circle One)

Yes

No

Participant # _____
Visit # _____
Tobacco Product _____



The diagram shows a profile of a man's head and neck. Four arrows point from specific areas to corresponding impact scales:

- Nose:** An arrow points from the tip of the nose to the first scale.
- Mouth:** An arrow points from the mouth to the second scale.
- Throat:** An arrow points from the throat area to the third scale.
- Chest/Lungs:** An arrow points from the chest area to the fourth 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.****

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

Comments/Observations concerning the cigarette:

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.****

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

Comments/Observations concerning the oral tobacco products:

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.****

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

Comments/Observations concerning the oral tobacco product:

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.****

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

Comments/Observations concerning the oral tobacco product:

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**

May


Attachment 20

Group A - Tuesday

<i>Sunday</i>	<i>Monday</i>	<i>Tuesday</i>	<i>Wednesday</i>	<i>Thursday</i>	<i>Friday</i>	<i>Saturday</i>
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					1	2
3	4	5 <i>Smoke Usual Brand</i> Begin recording # of cigarettes smoked on Daily Log (Day 1)	6 <i>Smoke Usual Brand (Day 2)</i>	7 <i>Smoke Usual Brand (Day 3)</i>	8 <i>Smoke Usual Brand (Day 4)</i>	9 <i>Smoke Usual Brand (Day 5)</i> Freeze 4 Ice Packs
10 <i>Smoke Usual Brand (Day 6)</i>	11 <i>Smoke UB (Day 7)</i> <u>Begin 24-hour Urine Collection</u> & Collect all cigarette butts <u>Today</u>	12 <u>Report to Bellomy</u> Return 24-hour urine collection, completed log, & <u>cigarette butts</u> <i>Decrease UB & Incorporate Snus (D1)</i>	13 <i>Decrease UB & Incorporate Snus (Day 2)</i>	14 <i>Decrease UB & Incorporate Snus (Day 3)</i>	15 <i>Decrease UB & Incorporate Snus (Day 4)</i>	16 <i>Decrease UB & Incorporate Snus (Day 5)</i>
17 <i>Decrease UB & Incorporate Snus (Day 6)</i>	18 <i>Decrease UB & Incorporate Snus (Day 7)</i> & Collect all cigarette butts <u>Today</u>	19 <u>Report to Bellomy</u> Return completed log, cigarette butts, & <u>unused Snus</u> <i>Decrease UB, Continue Snus & Collect all used pouches (Day 1)</i>	20 <i>Decrease UB & Continue Snus & Collect all used Snus pouches (Day 2)</i>	21 <i>Decrease UB & Continue Snus & Collect all used Snus pouches (Day 3)</i>	22 <i>Decrease UB & Continue Snus & Collect all used Snus pouches (Day 4)</i>	23 <i>Decrease UB & Continue Snus & Collect all used Snus pouches (Day 5)</i>
24 <i>Decrease UB & Continue Snus & Collect all used Snus pouches (Day 6)</i>	25 <i>Decrease UB & Continue Snus & Collect all cigarette butts & all used Snus pouches (Day 7)</i>	26 <u>Report to Bellomy</u> Return completed log, cigarette butts, used (Day 8) & unused <u>Snus</u> <i>Decrease UB, Continue Snus & Collect all used pouches (Day 1)</i>	27 <i>Decrease UB & Continue Snus & Collect all used Snus pouches (Day 2)</i>	28 <i>Decrease UB & Continue Snus & Collect all used Snus pouches (Day 3)</i>	29 <i>Decrease UB & Continue Snus & Collect all used Snus pouches (Day 4)</i>	30 <i>Decrease UB & Continue Snus & Collect all used Snus pouches (Day 5)</i> Freeze 4 Ice Packs
31 <i>Decrease UB & Continue Snus & Collect all used Snus pouches (Day 6)</i>			37		<div>2009</div>	

June

<i>Sunday</i>	<i>Monday</i>	<i>Tuesday</i>	<i>Wednesday</i>	<i>Thursday</i>	<i>Friday</i>	<i>Saturday</i>
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						
	1 <i>Decrease UB & Continue Snus</i> <i>Begin 24-hour Urine Collection</i> & Collect all cigarette butts & all used Snus pouches (Day 7)	2 <u>Report to Bellomy</u> Return 24-hour urine collection, completed log, cigarette butts, used (Day 8) & unused Snus	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30				

	Study No. CSD0905
Participant No. _____ Participant ID No. _____	

EXIT INTERVIEW QUESTIONNAIRE SNUS

For

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

By

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

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)

Yes1
No2

- 2) While participating in this study, what other tobacco products, if any, did you use besides the study-provided Camel snus and your usual brand of cigarette? (Circle all that apply)

Cigarettes other than your usual brand.....1
Moist snuff or dip in a round can.....2
Chewing tobacco.....3
Pipe tobacco.....4
Cigars or little cigars5
Other (Specify)6
None.....7 (SKIP TO Q. 6)

→ IF YOU USED OTHER TOBACCO PRODUCTS BESIDES SNUS AND 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 the study-provided Camel snus and your usual brand of cigarette while participating in this study, during which week(s) did you use them? (Circle all that apply)

Week 11
Week 22
Week 33
Week 44

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

Once a week1
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 the study-provided Camel snus and your usual brand of cigarette while participating in this study? (Please be as specific as possible.)

- 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
Week 1 (Circle one)	1	2	3	4
Week 2 (Circle one)	1	2	3	4
Week 3 (Circle one)	1	2	3	4
Week 4 (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 11
 Week 22
 Week 33
 Week 44

- 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.)

Attachment 21

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
- Easy5

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 weeks2
- 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
- No2 (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? (Circle all that apply)

- 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 Camel snus? (Circle one)

- 1 to 3 days1
- 4 to 7 days2
- 2nd week.....3
- 3rd week4
- I never got used to using Snus.....5

Attachment 21

18) During the last 3 weeks of the study, how often did you use the study-provided Camel snus? (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

19) When using the study-provided Camel snus, 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 Camel 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 Camel 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 Camel snus around or reposition it while you were using it? (Circle one)

- Yes.....1
- No2

23) Did you ever spit while using the study-provided Camel snus? (Circle one)

- Yes.....1
- No2 (SKIP TO Q.26)

Attachment 21

24) How often did you spit? (Circle one)

Always spit.....1
 Usually spit.....2
 Spit roughly half the time.....3
 Infrequently spit.....4

25) During which weeks(s) of the study did you spit? (Circle all that apply)

Week 21
 Week 32
 Week 43

26) Did you notice any change in mouth feel during or after use of the study-provided Camel snus?
 (Circle one)

Yes.....1
 No2 (SKIP TO Q. 28)

27) What kind(s) of change(s) 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

28) Did you ever try using multiple pouches of study-provided Camel snus at the same time? (Circle one)

Yes.....1
 No2 (SKIP TO Q. 31)

29) When you used multiple pouches of Camel snus, how many did you use at one time? (Circle one)

2 pouches1
 3 pouches2
 More than 3 pouches3

30) What percent of the time would you say you used multiple pouches of Camel snus at the same time?
 (Circle one)

Less than 25% of the time.....1
 25% to 50% of the time2
 More than 50% of the time.....3
 Most of the time.....4

31) Did you ever drink a beverage while using the study-provided Camel snus? (Circle one)

Yes.....1
 No2 (SKIP TO Q. 35)

Attachment 21

32) How often did you drink a beverage while using the study-provided Camel snus? (Circle one)

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

33) Did drinking a beverage while using Camel snus increase or decrease your enjoyment of the product? (Circle one)

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

34) What type of beverage did you most often drink while using Camel snus?

Please specify: _____

35) How long did it take you to use one container of the study-provided Camel snus 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

36) Where PRIMARILY did you use the study-provided Camel snus? (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

- 37) Which varieties of the study-provided Camel snus 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

- 38) Did you primarily stick to one variety of the study-provided Camel snus throughout the study or did you frequently change varieties? (Circle one)

Primarily stuck with one variety.....1
 Changed varieties throughout study.....2

- 39) 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 Camel snus? (Please circle a number from 1 to 10.)

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

- 40) Did you find using the study-provided Camel snus to be an enjoyable alternative to smoking a cigarette? (Circle one)

Yes.....1
 No2

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

Yes.....1
 No2

- 42) Did you notice any change in the taste of the study-provided Camel snus from the first pouch in the container to the last? (Circle one)

Yes.....1
 No2 (SKIP TO Q. 44)

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

Attachment 21

44) Did you notice any change in the taste of the study-provided Camel snus throughout the study?
(Circle one)

Yes.....1
No2 (SKIP TO Q. 46)

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

46) Did you notice any change in the appearance of the study-provided Camel snus throughout the study? (Circle one)

Yes.....1
No2 (SKIP TO Q. 48)

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

48) Would you say that the study-provided Camel snus ...? (Circle one)

Greatly exceeded your expectations1
Somewhat exceeded your expectations2
Met your expectations3
Somewhat failed to meet your expectations4
Did not at all meet your expectations5

49) Taking into consideration everything you know about the study-provided Camel snus and your experience with the product, what specifically did you like about it? (Please be as specific as possible)

50) What specifically did you dislike about the study-provided Camel snus? (Please be as specific as possible.)

51) What change(s) would you suggest, if any, to make Camel snus better? (Please be as specific as possible.)

52) How well or poorly do you think the study-provided Camel snus 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

53) Have you spoken with any other adult smokers about Camel snus? (Circle one)

- Yes.....1
- No2 (SKIP TO Q. 55)

54) How many adult smokers have you spoken to about Camel snus? (Circle one)

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

55) Did you offer any of the study-provided Camel snus to an adult friend who smokes? (Circle one)

- Yes.....1
- No2

56) How likely would you be to recommend Camel snus 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

57) How likely are you to continue using Camel snus knowing it is 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

58) Why would you continue or not continue using Camel snus? (Please be as specific as possible.)

59) If you were to continue to use Camel snus, 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 Camel snus.....3
 Would not continue using Camel snus.....4

60) Where do you expect the Camel snus to be located in a retail store? (Circle one)

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

61) How do you expect Camel snus 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.

62) 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

Attachment 21

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

Yes.....1
No2

64) 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.)

	(Circle one rating for each)						
	Extremely Unappealing			Neither Appealing nor Unappealing			Extremely Appealing
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

65) 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

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

Attachment 21

- 67) 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. 70)
 No, that would not be helpful.....4 (SKIP TO Q. 70)
 No, that would be intrusive.....5 (SKIP TO Q. 70)

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

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

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

- 70) 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

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

- 72) 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.)

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