PROJECT 4: CLINICAL TRIAL METHODS FOR ASSESSING A TOBACCO PRODUCT
Consent Form

You are invited to be in a study looking at the health effects of snus and smoking. The study product is Camel Snus, a currently marketed, spitless oral tobacco that comes in a pouch. Please read this form and ask questions before you agree to participate.

This study is conducted by Dorothy Hatsukami, Ph.D., and Sharon Allen, M.D. of the Tobacco Research Programs at the University of Minnesota. The study is also being conducted at Ohio State University and Roswell Park Cancer Center. The study is funded by the National Cancer Institute.

Study Purpose

The purpose of this study is to determine if you like or dislike the snus and will look at health effects of cigarette smokers substituting a snus pouch for a cigarette. This study has two phases, the **Sampling Phase** where you may use the snus for 1 week and a **Clinical Trial Phase** where eligible participants use the product for 8 weeks and are followed for 6 months. You were selected as a possible participant because you meet several criteria such as being in good general health, willing to try the snus and attend clinic visits at the University of MN.

Sampling Phase

Your participation in the **Sampling Phase** will be 2 visits about 1 week apart. If you agree to be in the **Sampling Phase** of the study, you will use the study product for one week and attend 1 more visit.

At today's visit, we will review your medical, emotional and smoking history to verify that you are eligible. You will be asked about marital status, education, income, tobacco use history and dependence, smoking patterns, tobacco satisfaction, and your thoughts about health risks of tobacco use. If you are a woman of child-bearing potential, we also will ask about your use of birth control and you will provide a urine sample for a pregnancy test. If you are pregnant you will not be able to participate in the study. If you have a low carbon monoxide level or if you do not smoke many cigarettes per day, we will ask you for a urine sample to test for by products of nicotine to verify your smoking status.

If you are eligible, you will be able to try a pouch of the snus. First, you will smell the product, choose between the two flavors and then answer questions about the product. You will place the pouch between your lip and gum for 5 minutes and afterward, you will answer more questions about what you think about the snus. If you are interested in using the product for 1 week, you will receive 4 tins of the snus. You may use as much or as little of the snus as you like. Should you want more snus within the week, you may stop by the clinic and we will provide up to 10 additional tins. You will keep track of your use of the snus and cigarettes by a daily telephone diary. You will receive daily calls and be asked questions and how much you have used and how many cigarettes you have smoked. After using the snus for 1 week, you will return to the clinic and

complete several forms asking about your experience with the product. Some participants will be asked if they want to continue into the Clinical Trial Phase of the study.

At both visits, you will have your blood pressure and pulse taken and provide a breath sample. Breath samples will measure your carbon monoxide level to determine your rate of smoking. Breath samples are taken by having you exhale into a carbon monoxide monitoring device.

Clinical Trial Phase

The purpose of the **Clinical Trial Phase** of the research study is to understand how the method of using a tobacco product may affect your tobacco use pattern and the product's health effects. This study will specifically look at the influence of different sets of instructions on how to use Snus. The study will examine how each method affects smoking behavior and tobacco related health effects. The health measures examined include exposure to tobacco toxins and related cancer-causing agents, nicotine levels and heart disease risk factors in your blood and urine. The study will also evaluate how using snus and/or smoking impacts withdrawal symptoms, mood and what you think about the study product, such as tobacco satisfaction.

You will be selected as a participant if you meet certain criteria during the Sampling Phase and you are willing to attend 8 more clinic visits and 1 follow-up visit and complete two follow-up phone calls over a 32 week period at the Tobacco Research Programs.

Study Procedures

If you agree to be in this study, you will be interviewed or asked to complete questionnaires that ask personal questions such as medication use, nutritional supplements, family and friends smoking behavior, exposure to tobacco smoke, mood and emotional history, use of alcohol and illegal drugs, tobacco use history and dependence, smoking patterns, tobacco satisfaction, and your thoughts about health risks of tobacco use.

Over the first two visits, we will gather "baseline" information while you are still smoking your regular cigarette at your normal rate. At the end of the second visit, you will be randomly assigned (like the roll of the dice) to 1 of 5 groups. You may be assigned to 1 of 4 different methods instructing you how to use the snus. Two of the methods require you to stop smoking and only use the snus, two of the methods allow you to smoke your own cigarettes and use the snus. If you are assigned to the 5th group you will continue smoking your usual brand of cigarette. This is called a "control group" and it allows us to compare usual smoking to the methods of using snus and cigarettes and if you would like, you will be offered the snus after the 8-week Clinical Trial Phase. If you decide to use the snus, you will attend 3 or more visits to receive more snus as needed for up to 8 weeks and answer some questions about your use of the product.

At the end of the Clinical Trial Phase, you will discontinue using the study products. You will come into the clinic for a follow-up visit 3 months after stopping use of the study snus. We will follow-up by telephone at 1 and 6 months after ending use of the study product. We will ask about your tobacco use and health since your last visit.

It is important that you avoid the use of any recreational drugs while participating in this study. Use of these drugs can increase your carbon monoxide level and will have an affect on the other urine and blood sample analysis.

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Clinic visit procedures:

You will attend 9 clinic visits for the over the next 38 weeks.

At every clinic visit, the following procedures will take about one hour:

- Complete forms asking about tobacco use, withdrawal symptoms, mood, health, desire to smoke, satisfaction with snus or cigarettes, and current medication use and health status.
- Vital signs (blood pressure, pulse, oxygen level and weight) will be taken.
- Breath samples will be taken to measure your carbon monoxide (CO) level to determine your rate of smoking.
- If you are not smoking, you may be asked to provide a spot urine sample. A non-smoker's CO is usually less than 6. If your CO is 6 or more your sample may be analyzed for toxins related to smoke and can confirm you are not smoking.
- Supportive counseling will be provided to assist your efforts to follow the study product use instructions. These counseling sessions may be recorded so that they can be randomly monitored to insure quality and consistency across all participants. All information will remain confidential.

At several visits, the following additional measures will take an additional 30-60 minutes:

- Blood samples will be taken at five visits to look at markers for risk of heart disease and your exposure to nicotine and tobacco toxins.
- Samples of the cells in your mouth will be obtained at three visits. To do this, you will be provided with a toothbrush and be asked to brush your teeth. After 20 minutes, you will have cells collected by having a small brush rubbed on the inside of your cheeks. These cells will be analyzed for changes related to tobacco use.
- Used pouches of snus and/or cigarette butts will be collected the day before two of your appointments. We will provide containers for this collection.
- At seven visits, you will bring in a urine sample from the first time you urinate in the morning after waking up. This sample will be analyzed for nicotine, tobacco toxins and cancer-causing agents and their breakdown products. This sample may be used to confirm that you have used the assigned product.

Phone Diary

You will keep a daily diary of the number of cigarettes you smoke and snus pouches you use throughout the study. The diary uses your home telephone or a cell phone to collect information. We will give you instructions on how to complete the daily calls. You will receive the phone calls every evening for the time you are in the Sampling Phase and for another 10 weeks while you are in the Clinical Phase of the study. You will enter the amount of tobacco you have used. These phone calls will take less than 3 minutes. On certain weeks,

you will complete additional questions about your experience with the study product. The phone calls with the additional questions will take less than 5 minutes.

You may withdraw from the study at any time prior to completing it. However, you will be asked to attend an exit visit. In addition, the study doctor may stop your participation without your consent. This could happen if you develop medical problems, experience serious adverse events, or do not comply with the study requirements or appointment schedule.

Risks of Study Participation

The side effects of the snus would be similar to the use of other oral tobacco products. You could experience an increased risk for mouth sores, gum disease and tooth loss, nausea or stomach aches, vomiting, or high blood pressure. Smokeless tobacco products may have an increased risk for cancer, particularly oral and pancreatic cancer. However, these risks are less than the health risks you are exposed to as a cigarette smoker. Use of both cigarettes and snus may result in an increase in your nicotine and tobacco related toxin levels.

There is a risk of breach of confidentiality or a loss of privacy if other people find out about your participation. All efforts are made to keep your information confidential, but confidentiality is not absolute.

Tobacco use is harmful to a fetus, and it is important that you are not pregnant during the study. You will be asked to use an acceptable birth control method to avoid pregnancy including abstinence, “double barrier” method (such as female use of a diaphragm, contraceptive sponge, in addition to male use of a condom) intrauterine device (IUD), or “birth control” pills, injections, or implants.

A total of 4 tubes of blood (about 2 tablespoons) will be drawn at 5 blood draw visits. A total of 8 tablespoons of blood will be drawn over 10 weeks. Your blood will be drawn by trained personnel using standard blood drawing techniques. Potential complications of blood drawing include slight bruising, soreness, redness, or swelling near the puncture site. In addition, some people occasionally experience dizziness, nausea or fainting. If you have recently donated blood (within the past week), it is important to tell the investigator. A decision must be made about your participation, or a delay can be imposed before you enter the study.

Benefits of Study Participation

You will receive no direct benefit from your participation in this study.

Alternatives to Study Participation

This is not a quit smoking treatment program. Methods for treatment instead of this study include standard tobacco cessation clinics and consulting your own physician, or using an over-the-counter or prescription nicotine replacement or non-nicotine medication.

Study Compensation
Sampling Phase

You will receive $5 at your next visit to help with your travel, $5 for the telephone diary and $40 for trying the snus for 1 week and completing all of the questionnaires for a maximum of $50.

Clinical Trial Phase

You will receive $5 per visit to help with your travel for the visits ($40 total). You will receive additional payment at the end of the study and **only** if you follow study procedures (verified by diaries, breath CO, and potentially urine). Once we confirm you have been following the study procedures during the Clinical Trial Phase, your visit payment will increase by $10 starting at Week 1 using the snus. (see Study Schedule on page 9 & 10). If you are unable to follow the study instructions, your visit amount will drop back down to $10 and you will start the increase all over again. You will receive a check for the amount you have earned after you have completed the Clinical Trial Phase. You will receive $40 for the follow-up visit at three months and $10 for the follow-up calls at one and six months after finishing the Clinical Trial Phase.

If you decide to drop from the study early and have followed the study procedures throughout that time, you will receive the amount you had earned.

You should be aware that the income you receive from being in the study may need to be reported to the IRS on your income tax return. If you receive more than $600 from the University of Minnesota in a calendar year, the income will be reported to the IRS and an IRS Form 1099 will be sent to you.

Study Costs

You will not be charged for any study costs. Neither you nor your insurance carrier will not be charged for any laboratory tests. If you are assigned snus, you will be provided the product throughout the study period without charge.

Research Related Injury

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner to you or your insurance company. If you think that you have suffered a research related injury, let Dr. Hatsukami know right away.

Confidentiality

The records of this study will be kept private. In any publications or presentations, we will not include any information that will make it possible to identify you as a subject. Your record for the study may, however, be reviewed by the funding agency and by departments at the University of Minnesota with appropriate regulatory oversight. No information from this study will be placed in your medical record. To these extents, confidentiality is not absolute. Study data will be encrypted according to current University policy for protection of confidentiality.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This Web site will not include information that could identify

you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

The risks to you and your family from genetic research are very low. Your samples will be identified only with your study code number. In the event of an unexpected breach of confidentiality, a recent federal law (Genetic Information Non-Discrimination Act, GINA) will help protect you from health insurance or employment discrimination based on genetic information obtained about you through research such as this. If you have questions about GINA or the risks of research on genetic information, please ask study staff.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of Federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

The Certificate of Confidentiality will not be used to prevent disclosure of certain communicable diseases, child abuse or neglect or harm to self or others to state or local authorities as required.

Sharing Information within the Tobacco Research Programs

I understand that information regarding my participation in this study may be shared within the Tobacco Research Program staff to ensure my continued eligibility.

Protected Health Information (PHI)

Your PHI created or received for the purposes of this study is protected under the federal regulation known as HIPAA. Refer to the attached HIPAA authorization for details concerning the use of this information.

Voluntary Nature of the Study

Participation in this study is voluntary. Your decision whether or not to participate in this study will not affect your current or future relations with the University. If you decide to participate, you are free to withdraw at any time without affecting those relationships.

Contacts and Questions

The principal researcher conducting this study is Dorothy Hatsukami, PhD. You may ask any questions you have now, or if you have questions later, **you are encouraged to** contact her at 612-626-2121.

If you have any questions or concerns regarding the study and would like to talk to someone other than the researcher(s), you are encouraged to contact the Fairview Research Helpline at telephone number 612-672-7692 or toll free at 866-508-6961. You may also contact this office in writing or in person at Fairview Research Administration, 2344 Energy Park Drive, St. Paul, MN 55108

You will be given a copy of this form to keep for your records.

Statement of Consent

I have read the above information. I have asked questions and have received answers. I consent to participate in the study.

_____ _____
Signature of Subject Date

_____
Print Name

_____ _____
Signature of staff member obtaining consent Date

BIOBANK SAMPLES

If you consent to the storage of your blood and urine samples, they will be kept in our biobank to be used for future analysis as new tests are found that examine tobacco harm or for assay development. These samples may be tested to determine if your genes may influence your response to tobacco products or nicotine. These samples will be kept until they are used up, no longer usable or you contact us and ask that they be destroyed. These samples will be kept in the biobank at the Tobacco Research Programs or at the Masonic Cancer Center. Only appropriate laboratory staff will have access to them. Only your study ID number will be on the sample; no identifying information will be on these samples. If you decide you do not want these samples stored after you have signed this consent form, you may contact the study investigator, Dorothy Hatsukami at 612-626-2121 or send your request in writing to Tobacco Research Programs, 717 Delaware St. SE #260, Minneapolis, MN 55414. If these samples have not been used up at the time of your request, they will be destroyed.

Please sign and date below if you agree to storage of your samples.

Signature:_____ Date: _____

STUDY SCHEDULE

VISIT	***At this visit***	***Sampling Phase Procedures***	***Travel***	***IVR Calls***	***Compensation***
Sampling Phase	Smoking at your normal rate and using snus	Sign consent form Vital signs and carbon monoxide level (CO) Complete questionnaires Start daily phone calls	$0		$0 clinic visit
Sampling Phase	Smoking at your normal rate and using snus	Sign consent form Vital signs and carbon monoxide level (CO) Complete questionnaires Return snus and review use Determine if eligible for Clinical Trial Phase	$5	$5	$40 clinic visit
Clinical Trial Phase (If eligible for Clinical Trial Phase)					
VISIT	***At this visit***	***Visit Procedures***	***Travel***	***IVR calls***	***Compensation***
Baseline 1	Smoking at your normal rate	Bring morning urine sample Vital signs Carbon monoxide level (CO) Complete questionnaires	$5	$5	$10 clinic visit
Baseline 2	Still smoking at your normal rate until the day after this visit	Bring morning urine sample Vital signs and CO Complete questionnaires Blood draw – Mouth cell sample Bring cigarette butts	$5	$5	$10 clinic visit
START SNUS (if assigned)					
Week 1	Use study product as instructed	Vital signs and CO Complete questionnaires Return snus and review use	$5	$10	$20 clinic visit
Week 2	Use study product as instructed	Bring urine sample Vital signs and CO Blood draw Complete questionnaires Return snus and review use	$5	$15	$30 clinic visit
Week 3	Use study product as instructed	Vital signs and CO Complete questionnaires Return snus and review use	$5	$20	$40 clinic visit
Week 4	Use study product as instructed	Bring urine sample Vital signs and CO Blood draw Mouth cell sample Complete questionnaires Bring used snus and/or butts Return snus and review use	$5	$25	$50 clinic visit

VISIT	***At this visit***	***Clinical Trial Phase Procedures***	***Travel***	***IVR calls***	***Compensation***
Week 6	Use study product as instructed	Bring urine sample Vital signs and CO Complete questionnaires Return snus and review use	$5	$30	$60 clinic visit
Week 8	Stop using study products	Bring urine sample Vital signs and CO Complete questionnaires Blood draw – Mouth cell sample Bring used snus and/or butts Return snus and review use Daily calls end	$5	$35	$70 clinic visit
Week 12 (1 month)	FOLLOW-UP Phone call	Complete questionnaires Review tobacco use	$0	$0	$10 phone call
Week 20 (3 month)	FOLLOW-UP Clinic Visit	Bring urine sample Vital signs and CO Blood draw Complete questionnaires Review tobacco use	$0	$0	$40 clinic visit
Week 32 (6 month)	FOLLOW-UP Phone call	Complete questionnaires Review tobacco use	$0	$0	$10 phone call
		SAMPLING PHASE **TRANSPORTATION** **TOTAL FOR FOLLOWING PROCEDURES AT VISIT** **IVR CALLS** **FOLLOW-UP VISIT AND CALLS**	***$5*** ***$40***	***$ 45*** ***$290*** ***$145*** ***$60***	
		TOTAL			***$585***