Consent to Participate in Research

Title of Research Project:	Low Nicotine Content Cigarettes in Vulnerable Populations: Opioid Dependent Smokers
Principal Investigator:	Stacey C. Sigmon, PhD
Sponsor:	National Institutes of Health and the Food and Drug Administration

Introduction

You are being invited to take part in this research study because you are a smoker, currently receiving buprenorphine or methadone maintenance, and you are not currently seeking treatment for quitting smoking. People invited to participate in this study must be between the ages of 21 and 70 years old, healthy (and if female, cannot be pregnant or breastfeeding, must report using an approved form of birth control if applicable determined by the Project Medical Director, and must have the ability to complete weekly face-to-face video assessments and use a portable smartphone-based device to measure carbon monoxide (CO) which allows us to assess recent smoking. This study is being conducted by the University of Vermont at the UVM Medical Center. A total of 205 individuals may be asked to participate.

We encourage you to ask questions and take the opportunity to discuss the study with anybody you think can help you make this decision.

Key Information to Help You Decide Whether or Not This Study Is Right for You

The purpose of this research study is to find out how much the availability and appeal of electronic cigarettes (e-cigarettes) affects the use of cigarettes with different nicotine contents in people receiving opioid maintenance treatment with buprenorphine or methadone.

The first visit of this study is a screening visit. The screening visit will be split into two parts, conducted in separate visits. The first part will be mostly questionnaires. If you are eligible after the first part of the screening, we will schedule the second part of the screening where we will give you equipment to take your own health measurements with instructions from research staff. We will know whether or not you are eligible to participate in the study after collecting information at both parts of the screening visit.

If you are eligible for the study after the two-part screening visit, you will be required to complete 19 additional visits that will happen about once a week across 19-20 weeks. You will also be required to come to UHC each week to exchange your study provided tobacco product. When you come to UHC, you must pass a COVID19 screening before entering the building. Once you pass the COVID19 screening, we will invite you up to the clinic to exchange

your products. Each visit may last between 1 and 4 hours, with most visits lasting between 45 minutes and 2 hours. After the first two study visits, you will be randomly assigned to 1 of 4 groups. There is a 1 in 4 chance (25%) that you could be assigned to any given group. The groups will vary in the nicotine content of the cigarettes that you are asked to use. You will not be aware of the nicotine content of your assigned cigarette until after the entire study has been completed.

Two of the groups also include an e-cigarette that will be available to you to use. One of the two e-cigarette groups will be assigned an e-cigarette with tobacco flavoring. The other e-cigarette group will be able to select their own flavoring. You will be asked to smoke only your assigned cigarette/e-cigarette for the duration of the study.

Once you are assigned to a group, you will have weekly remote visits for the remainder of the study. The first part of the remote visit will consist of you doing questionnaires online through a link that we send to you via text or email. The second part of the remote visits will be video meetings over Zoom where we will ask you more questions and also have you take physical measurements (for example, breath samples and heart rate) while we observe. We will ask you to show us the monitors or results of the measurements that you have taken so we can read the results. You will also visit the lab weekly to exchange your study product for the remainder of the study. At each visit, we will ask you questions about your smoking, mood, craving for cigarettes, and about the cigarettes/tobacco products that you have been using. You will be asked to provide urine or saliva samples to test for levels of nicotine and other chemicals that are in cigarettes as well as provide breath samples using a device to measure carbon monoxide to measure recent smoking.

If you are a woman, a urine pregnancy test will be done every two weeks. Additionally, we will ask about drug (both your opioid maintenance medication and illicit drug use) and alcohol use and test the urine or saliva samples for illicit drug use. Results of these drug tests may affect your participation in the study, so it is important to try and not use drugs, other than your opioid maintenance medication, during the study.

Potential study risks include harms that come from use of cigarettes and e-cigarettes, potential mood and psychiatric changes, potential discomfort when answering survey questions and providing urine or saliva samples, and risk of elevated blood pressure or heart rate. Risks are explained in more detail later in this consent form.

The information above is only a brief summary of the study. If you are interested in learning more, it is important to read the following pages for additional detailed information about the study. If you decide to take part in the research, you will be asked to provide written consent at the end of this document.

Why Is This Research Study Being Conducted?

The purpose of this study is to learn how the availability of e-cigarettes affects the use of cigarettes with different nicotine contents in people receiving opioid maintenance treatment with buprenorphine or methadone. This research is supported by the National Institutes of Health and the Food and Drug Administration. This research may help

inform the Food and Drug Administration how best to regulate tobacco products in the future with the goal of improving public health. *This is not a treatment program to help you quit smoking.*

What Is Involved in The Study?

This study will last for 19 to 20 weeks. During the study, you will have 20 visits (including the screening visit), described in more detail below. After your third visit, you will be assigned to 1 of 4 groups. The groups vary in the nicotine content of the cigarettes that you are asked to use. Two of the groups also include an e-cigarette that will be available to use. One e-cigarette group will be assigned an e-cigarette with tobacco flavoring and the other group will be assigned an e-cigarette with flavors selected by the participant. At the study visits, we will ask you questions about your cigarette and e-cigarette use, mood, and craving for cigarettes/e-cigarettes.

Identifiable samples and/or identifiable private information collected from you during this study may be used for future research studies or shared with other researchers for future research. The identifiable samples and/or identifiable private information may be used for future research of topics related to tobacco use and associated disorders. If the investigator distributes your samples and/or information to other researchers or institutions, your samples and/or information will be labeled with a research code so that you cannot be identified. No additional consent will be requested for the future research use of your samples or information collected from you during this study. If you have questions about storing samples or would like to request that samples be removed from storage, please let us know. It is not always possible to remove samples from storage or to retrieve samples from which identifiers have been removed and/or that have already been sent to other investigators.

Screening Procedures

Signing this consent form does not mean that you will be able to take part in this study. You will first undergo screening tests to help the study team determine if you are eligible to take part in this study. If you agree to participate in the two-part screening visit, you will be asked to do the following:

During the first part of the screening, we will ask you questions about your medical history, medication use, psychiatric symptoms, and current and past smoking and vaping. This first part of the screening should take between 1-2 hours. We will determine whether you are eligible to move on to the second screening visit after assessing the information collected during the first part of the screening.

If you are eligible to move on, we will schedule you for a second screening visit on a separate day, and this visit will happen over video chat. We will give you equipment that will allow you to take different measurements that we will need to determine whether you are fully eligible. You will be asked to use the equipment you received to take your blood pressure, oxygen saturation, temperature, heart rate, respiratory rate, and breath carbon monoxide. We will

show you how to use the equipment to get each measurement. If the equipment to collect your carbon monoxide results remotely is not available, we will conduct your carbon monoxide test during your visits to the lab for your product exchange. The following steps will occur if curbside breath CO testing needs to be done: A research assistant will bring down the CO monitor when they bring the rest of the equipment to the participant. While maintaining 10 feet of distance and wearing gloves, we will tell you how the breath CO monitor works. Once you are is ready to take the test, we will press a button on the machine and will then set the CO monitor down and back away 10 feet. You will then come to pick up the device and will blow into the monitor. After you complete the test, you will set down the monitor and back up 10 feet and we will retrieve the monitor. After every use, we will wipe down the CO monitor with disinfectant hydrogen peroxide wipes. We will also assign you your own reusable mouthpiece, called a D-piece, to use with the monitor along with the single-use mouthpieces. These D-pieces prevent any air from getting into the monitor itself, and they also filter over 99% of bacteria and over 97% of viruses. As a result, the D-pieces act as a safeguard for contracting illnesses from the monitor. Your personal D-piece will be kept at our lab and will be disinfected after each use. It will be kept in a container separate from other D-pieces. The carbon monoxide device and monitor will also be cleaned and disinfected between each use.

During the second part of the screening, you will also provide a urine or saliva sample in order to identify whether you have recently used illicit drugs (that is, any drugs you are not currently prescribed by a doctor), aside from marijuana and your opioid maintenance medication. If the test indicates that you have used illicit drugs, aside from marijuana and your opioid maintenance medication, we will stop the interview and ask you if you would like to try the part-two screening again on another day. If you attempt a screening a second time and test positive for illicit drugs, aside from marijuana and your opioid maintenance medication, you will not be able to participate in the study. A urine or saliva sample positive for marijuana does not mean you will be excluded. If you seem impaired, we will stop the interview and as you to come back another time if you would like to try screening again. If you come back the second time and seem impaired, you will not be able to participate in the study. You can attempt to screen as many times as you like but you will not be compensated for more than one ineligible screening.

If you are a woman, you will be asked to complete a urine pregnancy test. (If the test shows that you are pregnant, you will not be able to take part in the study.) Next, you will be asked to blow into another small machine that will tell us how much you have been smoking recently. The second part of the screening visit will take anywhere from 1-2 hours.

After we finish with these activities, we will make an initial decision about your eligibility. If you appear eligible, our staff will schedule your first baseline visit. The Principal Investigator of the study determines your eligibility. In the event that the Principal Investigator of the study does not think it is appropriate for you to participate in the study, the research assistant will contact you before the first baseline visit to cancel your appointment. Your participation in this screening interview is voluntary, which means that you can leave at any time if you lose interest or are uncomfortable.

Study Procedures

If after this screening visit you are eligible and you decide to participate in the study, you will be asked to complete 19 additional visits that will take place over 19 to 20 weeks. These visits will occur over video chat. You will also be asked to come to our offices every week at University of Vermont Medical Center (UHC Campus) to exchange your study product. The first 2 visits will last about 2 hours each and will be about a week apart. In these visits, we will ask you questions related to your health, cigarette smoking, e-cigarette use, drug (both your opioid maintenance medication and illicit drug use) and alcohol use, and mood. We will ask you to prepare a urine or saliva sample to check for illicit drug use. If we ask for a saliva sample, you will provide the saliva sample over video chat while the staff observes. If we ask for a urine sample, we will ask that you use the bathroom during the time of your visit, that you bring the urine sample in the cup that we send to you to your phone or computer and test the urine while we are on video chat.

If you are eligible after these screening visits you are eligible and you have decided to participant in the study, you will be asked to complete for 19 additional visits that will take place over 19 to 20 weeks. You will also be asked to come to our offices at University of Vermont Medical Center (UHC Campus) to exchange your product. The first 2 baseline visits after screening will last about 2 hours each and will be about a week apart. In these visits, we will ask you questions related to your health, cigarette smoking, e-cigarette use, drug and alcohol use, and mood. We will also ask you to prepare a urine sample during one of these visits. You are to bring that urine sample to the lab, and we will give you a storage cup for this urine sample. We will test the urine samples for levels of nicotine and other chemicals that are in cigarettes.

At the end of the first baseline visit, we will teach you how to use an automated (computer) phone system. This phone system will call you every day during the study to ask about your tobacco and nicotine product use from the day before. The time of day that you receive these calls will be up to you. On some occasions, we will ask about your mood and nicotine withdrawal symptoms on these daily phone calls. All information you provide during these phone calls will be stored separately from your name and phone number.

At the end of the second baseline visit, you will be randomly assigned to 1 of 4 groups. We will tell you which group you were randomly assigned to and provide details. We will provide you with your study product(s) when you come to the lab at this time as well. The groups will vary in the nicotine content of the cigarettes that you are asked to use. Two of the groups also include an e-cigarette that will be available for you to use. One e-cigarette group will be assigned an e-cigarette with tobacco flavoring and the other group will be able to select their own flavors. You will *not* know the nicotine content of your assigned cigarette until after the entire study has been completed.

You will be asked to use only your assigned cigarette and/or e-cigarette for the remainder of the study. We will give you enough cigarettes to replace the amount that you usually smoke each week. Please try to use only the cigarettes/e-cigarettes we give you. We will work with you to achieve this goal, as it is very important for the study. Additionally, you will need to keep track of the cigarettes, e-cigarette, e-cigarette cartridges/pods, and e-

cigarette charger we give to you and we will talk to you more about how to keep track of these items. Although we want you to use only the cigarettes/e-cigarettes that we give you, you can still be in the study if you smoke other non-study cigarettes or use other non-study nicotine products during the study. However, it is important that you tell us about any non-study tobacco or nicotine products that you use.

Do not share study products with anyone else. We will tell you which group you were randomly assigned to and provide details. We will provide you with your study product(s) at this time as well.

Although this study is not a treatment program, if you choose to stop smoking, you can still participate in the study. We will provide you with information about stopping smoking and referrals to local treatment programs at your request. We will also give you the option of not taking home the study cigarettes/e-cigarettes if you do not want to. Whether or not you take home the study product, you not under any obligation to smoke the study product if you do not want to. If you choose to take study cigarettes/e-cigarettes home, you will still be required to keep track of them and bring them with you each week to the laboratory.

Once you are assigned to a group, you will have weekly video chat meeting for the remainder of the study and will be asked to come to laboratory each week to exchange product for the remainder of the study. During each visit, we will ask you questions about your smoking and e-cigarette use, mood, craving for cigarettes, about the cigarettes/tobacco products that you have been using, and any medication use. We will also ask you to get a breath sample to measure recent smoking and drinking. During all of the visits, we will ask you to provide a urine sample, and we will ask you to test this sample over video chat with our guidance. If you are visibly intoxicated during the visits, we will end the session and reschedule your visit.

During three of these visits, you will be asked to collect a urine sample while at home and bring the sample to us at the lab when you are scheduled to exchange your product. Your supplies will include a urine collection cup that will make it easy to bring with you. This means that at three visits, you will be providing a urine or saliva sample for testing during your video chat session as well as bringing one sample from home to the lab. Urine samples will be tested for illicit drugs, levels of nicotine, and other chemicals that are in cigarettes. Ongoing illicit drug use (other than your opioid maintenance medication and marijuana) may affect your participation in the study, so it is important to try to abstain from drug use during the study.

If you are a woman, you will be asked to complete a urine pregnancy test every two weeks. When you come into the lab each week (after your visit over video chat), we will provide you with your assigned cigarette and e-cigarette cartridges or pods as needed. We will also ask you whether you have had any problems using the cigarettes and/or e-cigarette, and whether you have been using any other nicotine products. Although the study itself is 19 to 20 weeks, you will only have cigarettes/e-cigarettes for 16 weeks.

At the end of the study, you will have one additional visit, which is an abstinence session. We will ask you to not smoke from the time you complete your visit over video chat on the day before until your visit on the following day for the abstinence session. You will not

receive the full visit payment if you do not meet the abstinence requirement, which is a breath measure to confirm you have not smoked. Similar to other study visits, during the abstinence assessment visit, we will ask you questions about your cravings, mood and medication use and ask you to prepare a urine or saliva sample to test for illicit drug use.

One month after the last study visit (i.e., after the Abstinence Assessment Session), we will call you to ask about your smoking since the study ended. We will compensate you with 5 prize tickets (described in more detail below) for completing this call, regardless of your responses on the call. If you report that you are not smoking, we will ask you to have a short visit with us over video chat so we can confirm your smoking status using a breath test. We will pay you $40 for attending this visit, regardless of your breath test results. Similar to prior visits, if you are interested in quitting smoking, we can tell you about treatment programs in the area.

Texting and Other Communication

You will have the option of communicating with the Research staff about your participation via text. The nature of the information included in the texts will include appointment information. We ask that you also only use text messaging to communicate about scheduling your appointments. Should you agree to accept texts, you will still be given the opportunity to opt out of receiving text communication at any time. If you are interested, we can also email you through our study email account (uvmtobaccostudy@uvm.edu).

Variable Incentive Program (VIP) for Compliance, Honesty and Attendance

Beginning at Week 1 (the first session after you've received your study cigarettes/e-cigarettes) you will receive up to 7 tickets each time you come for your scheduled visit. Tickets that are "validated" (explained in more detail below) are eligible to win a cash prize. You will receive tickets through Week 16 and you will also receive 5 tickets for completing the end of study follow-up phone call, approximately one month after completing the study.

Experimental Week Tickets:

Attendance Ticket (1): **This ticket is for attending the visit**. As long as you come to the visit and do your best to answer the questions and complete the tasks, this ticket will be "valid."

Honesty Ticket (1): **This ticket is for accurately reporting when you used study and non-study products**. To test this, we may compare what you tell us to what is in your urine or saliva. If your urine or saliva matches what you tell us, this ticket will become "valid." If you slip and use another product, just tell us. This ticket is for being honest, not for being perfect.

Compliance Tickets (5): **You can earn three compliance tickets for using only the study products and not using other nicotine or tobacco products.** We know this is hard, so we are giving you 3 tickets for doing a good job. We may analyze various measures to find out how much you are using different nicotine and tobacco products,

some of which can stay in your body for days or weeks. The more compliant you are, the more tickets we will "validate." So even if you "slip," try to go back to using the study product as soon as possible.

You can earn two more compliance tickets for bringing back all of your study product at your visits. If you do not bring back all of your unused study product and the used packaging, you may not be eligible to earn these two tickets.

After the Experimental Weeks:

30-Day Follow-Up Call (5): As mentioned before, 30 days after completing the study, we will call you to ask you questions about your nicotine and tobacco product use. If you answer this call, regardless of your answers, we will validate 5 tickets for you and put them in the prize bowl after the call.

Study Cigarettes

The study cigarettes have been obtained through the National Institutes on Drug Abuse. The FDA has reviewed the proposed investigational use of the products as described in the protocol Cigarettes are manufactured in the same way as your usual brand cigarette, but they may be modified to reduce the levels of nicotine.

Electronic Cigarettes (E-cigarettes)

The e-cigarettes, pods, and chargers used are JUUL products or Vuse Solo products, which are brands of electronic cigarettes. JUUL and Vuse products are commercially available as a tobacco product and do not need a prescription. JUUL and Vuse products are regulated by the U.S. Food and Drug Administration (FDA). E-cigarettes for this study are obtained via JUUL Labs, Inc (https://www.juul.com/) or R. J. Reynolds Vapor Co. LLC (https://vusevapor.com/).

What Are the Risks and Discomforts of The Study?

Smoking Study Cigarettes. All cigarettes are harmful to a person's health and can lead to cardiovascular (heart) disease, respiratory (lung) illness, cancer and other health problems. In addition to the above medical problems, you may experience some minor negative health effects such as headaches. You may also experience smoking withdrawal symptoms, which are listed below. In addition, due to the altered nicotine levels, there could be a change in your use of cigarettes including the manner in which you inhale the smoke. Smoking the study cigarette does not necessarily provide any less risk than your usual brand of cigarette and could pose increased health risks.

Using Study E-cigarettes. E-cigarettes are devices that heat nicotine to produce an aerosol. The health effects of e-cigarettes are still unclear, but appear to be less than that for tobacco cigarettes. Most e-cigarette users have lower nicotine levels than when they smoked regular cigarettes. Some e-cigarette users, especially those who use both e-cigarettes and regular tobacco cigarettes as well as youth and young adults can have increased nicotine levels. In some rare cases, these use patterns have been associated with seizures. Whether this would

occur with the concurrent use of very low nicotine cigarettes is unclear. E-cigarettes users very often maintain addiction to nicotine, but this addiction appears to be somewhat less than that from tobacco cigarettes. Abruptly quitting e-cigarettes could cause withdrawal symptoms similar to those from quitting tobacco cigarettes (see below) but slightly less severe. The most common side effects include dry mouth, irritation of the throat and mouth, and mild cough. The e-cigarettes we will be providing have not been well-studied but appear to be of similar risk to other e-cigarettes. You may have heard that e-cigarettes, or "vapes," can explode and seriously injure people. Although they appear rare, these explosions are dangerous. The exact causes of these incidents are not yet clear, but some evidence suggests that battery-related issues may lead to vape explosions. In order to prevent e-cigarette related injuries, keep your e-cig away from other metal objects, never charge your e-cig with a phone or tablet charger, don't charge your e-cig overnight or leave it charging unattended, and stop using the e-cig if the batteries get damaged or wet. Always keep e-cig liquid out of kids' and pets' reach and sight after use. If we learn about additional risks of e-cigarettes during the study, we will inform you of these risks.

The Centers for Disease Control released a notice in August of 2019 stating information about outbreaks of severe pulmonary illness associated with using e-cigarette products. E-cigarettes expose the lungs to a variety of chemicals that are not found in tobacco cigarettes. This may be associated with unique risks including a certain type of pneumonia; however, this is not yet fully understood. As of August 27, 2019, 215 possible cases of severe pulmonary illness have been reported associated with the use of electronic cigarettes. The vast majority (≥80%) of these cases have involved vaping cannabidiol (CBD) or marijuana, or e-liguids purchased in the black market. The available evidence does not currently suggest that an infectious disease is the cause of the illnesses. These investigations are ongoing. CDC will provide updates when more information is available. We will share any such information with you if it indicated an increase in risk for you. The e-cigarettes being used in this study are regulated by the FDA to protect against safety hazards.

Regardless of the ongoing investigation:

- Youth should not use e-cigarette products.
- Women who are pregnant should not use e-cigarette products.
- Adults who do not currently use tobacco products should not start using e-cigarette products.
- If you do use e-cigarette products, you should not buy these products off the street (for example, e-cigarette products with THC or other cannabinoids).
- You should not modify e-cigarette products or add any substances to these products that are not intended by the manufacturer.
- Adult smokers who are attempting to quit should use evidence-based treatments, including counseling and FDA-approved medications. If you need help quitting tobacco products, including e-cigarettes, contact your doctor or other medical provider.

CDC and FDA encourage the public to submit detailed reports of any unexpected health or product issues related to tobacco or e-cigarette products to the FDA via the online Safety Reporting Portal.

Patients who developed the severe pulmonary illness mentioned above have reported symptoms such as cough, shortness of breath, or chest pain, nausea, vomiting, or diarrhea, fatigue, fever, or weight loss. If you are concerned about your health after using an e-cigarette product, you should consult your physician. You can also call your local poison control center at 1-800-222-1222.

Mood and Psychiatric Symptom Changes. You may experience smoking withdrawal symptoms during this study. These symptoms can include anger, anxiousness, craving for a cigarette, depressed mood, difficulty concentrating, frustration, increased appetite, impatience/impulsivity, irritability, restlessness, sleep problems, and weight gain. These feelings can be uncomfortable and can last a couple of weeks, but usually are of minimal risk. In addition, if you have a past history of anxiety, depression, or alcoholism, it is possible withdrawal could cause substantial increases in depression and anxiety symptoms, but this appears to be rare. At each visit, we will ask you how you feel. If you or we think that being in this study is putting your mental health at risk, we may have you meet with an on-site clinician and/or stop participating in the study. Further, if you report thoughts of killing yourself or other indicators of suicidality, a study clinician will come to talk to you. You may also request to see a study clinician if you are in discomfort and would like help and/or referrals for mental health resources.

Risk to Fetus. To avoid risks to a fetus, it is important that you are not pregnant during this study. Avoiding sexual activity is the only certain method to prevent pregnancy. However, if you choose to be sexually active, you should be using prescribed birth control pills, patch, ring, injections, implants or intrauterine device (IUD), or appropriate “double barrier” method of birth control (such as female use of a diaphragm, or contraceptive sponge, in addition to male use of a condom) if applicable determined by the Project Medical Director. If you choose to be sexually active during this study, pregnancy could still result even with the use of these birth control methods.

Survey Questionnaires. This interview will include questions about your medical and psychiatric histories, drug and alcohol use and history, breath tests for cigarette and alcohol use, urine or saliva tests of illicit drug use and pregnancy, and questionnaires about your mood. Answering these personal questions could make you uncomfortable. If you report thoughts of killing yourself or other indicators of suicidality, a study clinician will come to talk to you. You may also request to see a study clinician if you are in discomfort and would like help and/or referrals for mental health resources.

Drug Testing. A breach of confidentiality could occur, and others could learn of your drug use. We test for up to the following drugs: marijuana, cocaine, PCP, opiates, oxycodone, MDMA, methamphetamines, amphetamines, barbiturates, buprenorphine, benzodiazepines, and methadone.

Obtaining Blood Pressure and Heart Rate. The blood pressure cuff may cause minimal discomfort. In obtaining your blood pressure we may find that you have abnormal blood pressure and/or heart rate. If your blood pressure is abnormal, we will inform you of this, you may be advised to see a doctor, and you may also be contacted by our study doctor. Also, smoking and nicotine can affect the cardiovascular system, which may result in changes in

blood pressure and/or heart rate.

What Are the Benefits of Participating in The Study?

There are no benefits for taking part in this study. The information that we get from the study may ultimately help the Food and Drug Administration decide how best to regulate tobacco products with the goal of improving public health.

What Other Options Are There?

We are not offering treatment for smoking in this study. If you are seeking treatment for smoking, please let us know and we will help you to find a treatment program.

Are There Any Costs?

All assessments and study procedures will be provided free of charge. There will be no cost to you other than your time.

What Is the Compensation?

The total amount of money that you could earn for this study is $2,841. This includes $25 for the medical consent, $25 plus a $25 bonus for completing each screening visit on time as scheduled, and $100 for each study visit from Baseline 1 to Week 16. Starting at Experimental Week 1 and ending at Week 15, you will have the opportunity to earn a $20 bonus for every study visit that is completed on time as scheduled. You can receive up to $120 for the abstinence assessment, and up to $306 for completing the daily phone calls. You will also receive $150 at the end of the study for completion of all parts of the study. You may also receive $40 if you are invited for an assessment following your one month follow up call. If you start but do not finish the study, you will only be compensated for the sessions that you do complete.

You will also have a chance to earn additional money through the Variable Incentive Program. As mentioned above, you will have a chance to earn additional incentives each month for compliance, honesty, attendance, and completion of the follow up phone call. Each month, seven tickets will be chosen out of several hundred tickets in the jar. One participant will win $500, one will win $200, and five will win $10.

Your name, social security number and address will be disclosed one time to the University of Vermont's Procurement Services Department for purposes of reimbursing you for participation in this study. Your information will be coded, and this code and the information will be kept under lock and key in a staff-occupied or locked office with only authorized personnel accessing the data. Please note that this compensation earned through the study may be taxable.

Can You Withdraw or Be Withdrawn from This Study?

You may withdraw from the study at any time without penalty. If you wish to end your participation in the study, please tell us right away. Leaving the study early will not stop you from getting regular medical care. Any money earned up to the point you withdraw will still be yours. We also retain the right to withdraw you from the study if we feel that continued participation would not be in the best interests of your physical or psychological health. For example, if your blood alcohol levels are higher than 0.01 g/l on the days of your study visits, we may withdraw you from the study. Failure to bring back all of your study product could also be grounds for withdrawal from the study. Your refusal to participate or early withdrawal from the study will not affect your treatment for any medical condition.

What About Confidentiality of Your Health Information?

What health information will be used and disclosed for this study?
The health information we plan to collect for this study is listed below.

- Information that identifies you, such as your name, address, age, and sex

Who is disclosing your health information for this research study?

- The University of Vermont Medical Center
- Other doctors' offices and hospitals where you may receive medical care while this study is active.

Who will use your health information in this study?
Our research team will use your health information. We may also share it with those who assist with the conduct of the research or oversight of the activities for this study. The representatives from the institutions, organizations, and agencies are listed below.

- The University of Vermont and its Committees on Human Research
- The University of Vermont Medical Center
- Other researchers and centers that are a part of this study, including individuals who oversee research at those sites
- The sponsor of this study, National Institutes of Health and the Food and Drug Administration
- Federal and state agencies that oversee or review research information, such as the U.S. Food and Drug Administration (FDA), the Department of Health and Human Services, the National Institutes of Health, and public health and safety authorities

Future Research. Your samples and data will be stored for future use if you have indicated your permission elsewhere in this consent form.

Your health information is protected by a federal law called the Health Information Portability and Accountability Act (HIPAA). Once your health information is shared outside of the University of Vermont Medical Center, we cannot guarantee that these laws will continue to apply. As a result, your health information could be further disclosed for other purposes. In the absence of a Certificate of Confidentiality, it is also possible for a court or other

government official to order the release of study data. The confidentiality of your health information cannot be guaranteed if you agree it may be used in this study.

How long will your health information be used for research?
Your permission to use your health information will not end until the study is completed. During this study, you will not have access to study data. You may ask for your data once study activities are complete. You have a right to receive a copy of the information in your medical record at any time. Data resulting from this research will be kept for 5 years following publication as is recommended by the American Psychological Association.

What if you decide not to give permission for research use of your health information?
If you decide not to allow the use and disclosure of your health information, you may not take part in this study. Your decision will have no effect on your current or future medical care.

If you choose to stop taking part in this study in the future, you may cancel permission for the use of your health information. You should let the research team know that you are cancelling your permission. A member of the research team will assist you in making your decision effective. The study will continue to use the health information already collected for the study before you cancelled your permission, and you cannot get back information that was already shared with others.

Who can answer your questions about the use and disclosure of your health information?

If you have questions or concerns about the use and disclosure of your health information, you should ask a member of the study team at 802-656-0392 or the Privacy Officer at The University of Vermont Medical Center, Inc, at (802) 847-2667.

Safeguarding Your Health Information

A record of your progress will be kept in a confidential form at the Vermont Center on Behavior and Health (University of Vermont Medical Center, UHC Campus). The security of your record will be maintained by the research team. The results of this study may eventually be published and information may be exchanged between medical investigators, but patient confidentiality will be maintained.

If your record is used or disseminated for government purposes, it will be done under conditions that will protect your privacy to the fullest extent possible consistent with public disclosure of information laws relating and the law-enforcement responsibilities. However, if we think you intend to seriously harm yourself or someone else, or if there is reason to believe that you have committed child or elder abuse or neglect, that information will be shared with the proper authorities.

In order to protect your confidentiality, any information about you obtained as a result of participation in this research will be kept as confidential as legally possible. 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, even by court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. 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 does not prevent the researchers from disclosing, voluntarily, without your consent, Information that would identify you as a participant in the research project under the following circumstances: If you express suicidal thoughts or plans of any type, or express intent to seriously harm others, in the answers to our questions.

You may be requested to provide your name, social security number, and address. This information will be disclosed one time to either the University of Vermont's Procurement Services Department or UVM Medical Center Accounts Payable Department for purposes of reimbursing you for participation in this study. If you are not a US Citizen or Permanent Resident Alien you will be required to complete additional paperwork for payment.

Clinical Trials Registration

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

What Happens If You Are Injured?

If you are injured or become ill as a result of being in this research, The University of Vermont Health Network Affiliate hospital where you are enrolled in this research, will provide reasonable and usual medical care for that injury or illness. There will be no cost to you if the conditions listed below apply to your injury or illness. These conditions are:

1. The investigator, in consultation with the study sponsor, determines that your injury or illness results from the research and not from your underlying condition or its usual treatment.
2. You let the investigator know about the injury or illness when you first notice it; and
3. You follow medical advice about proper treatment options for the injury or illness.

If the above conditions are not met, The University of Vermont Health Network affiliate hospital where you are seeking care may claim payments for your medical treatment from the study sponsor or your insurance company when these payments are allowed. If we bill your insurance for this care, you will be responsible for any associated co-payments or deductibles.

For an injury or illness that results from being in this study, The University of Vermont Health Network affiliate hospital where you are receiving care will not offer you any other payments, such as lost wages or expenses, except for your medical care. Even though you may receive medical care at no cost to you under certain conditions if you are in this study, The University of Vermont Health Network affiliate hospital and the University of Vermont do not admit to any responsibility for an injury or illness that results from being in the study.

If you agree to take part in this study and you sign this consent form, you are not giving up any of your legal rights.

Your Rights and Whom to Contact:

You are free to withdraw from the study at any time. Your refusal to participate or withdrawal will involve no penalty or loss of rights to which you are otherwise entitled.

If you have any problems with or questions about the study procedures, please contact Dr. Stacey Sigmon at 802-656-0392. If you have any questions about your rights as a participant in a research project or for more information on how to proceed should you believe that you have been injured as a result of your participation in this study you should contact the Director of the Research Protections Office at the University of Vermont, at 802-656-5040.

		Compensation Schedule																					
	Med Consent	Screen Visit 1	Screen Visit 2	BSL 1	BSL 2	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12	W13	W14	W15	W16	Abstinence Visit	Total
Visit Payment	$25	$25	$25	$100	$100	$100	$100	$100	$100	$100	$100	$100	$100	$100	$100	$100	$100	$100	$100	$100	$100	Up to $120	$1995
Bonus Payment		$25	$25			$20	$20	$20	$20	$20	$20	$20	$20	$20	$20	$20	$20	$20	$20	$20	420	$150	$500
Follow-Up Visit																							$40
Daily Phone Call (IVRS)																							$306
																						Total	$2841

	Study Schedule																			
	Screening visit 1	Screen Visit 2	BSL 1	BSL 2	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12	W13	W14	W15	W16	Abstinence Visit
Approximate Length of Visit	1-2 hours	1-2 hours	2 hours	2-3 hours	1 hour	1 hour	1 hour	2-3 hours	1 hour	1 hour	1 hour	2-3 hours	1 hour	1 hour	1 hour	2-3 hours	1 hour	1 hour	1 hour	2-3 hours	1 hours

VOLUNTARY CONSENT

All of the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that such future questions will be answered by the researcher listed below. By signing this form, I agree to participate in this research study. A signed copy of this consent form will be given to me.

_____

Signature of Subject Date

_____

Name of Subject Printed

Please check <u>one</u>: □ I would like to **OR** □ I would not like to receive text messages regarding appointments

CERTIFICATION of INFORMED CONSENT

I certify that I have explained the nature and purpose of this research study to the above-named individual, and I have discussed the potential benefits and possible risks of study participation. Any questions the individual has about this study have been answered, and we will always be available to address future questions as they arise. I further certify that the only research component collected prior to signing this consent was prescreening questionnaires and opioid medication information obtained through verbal or electronic consent. All other research components of this study were not begun until after this consent form was signed.

_____

Signature of Principal Investigator or Designee Date

_____

Name of Principal Investigator or Designee Printed

Name of Principal Investigator: Stacey Sigmon, Ph.D.
Address: 1 S. Prospect St. MS 482, Burlington, VT 05401
Telephone Number: 802-656-0392