Medical University of South Carolina-
CONSENT TO BE A RESEARCH SUBJECT

A prospective trial of varenicline and incentives for tobacco cessation in adults

The purpose of this study is to better understand tobacco outcomes using a commonly prescribed stop smoking medication (varenicline) and financial incentives with tobacco users. We are also interested in how cannabis/marijuana and tobacco interact during a tobacco quit attempt. You are being asked to participate in this research study because you are between the ages of 18-40 and are a tobacco user.

If you agree to participate you will undergo a screening/initial visit, to see if you are eligible for the study. You will be asked general questions about your substance use (tobacco, alcohol, cannabis/marijuana, and other drugs), overall mood, and craving. You will complete a psychiatric and medical interview. During the psychiatric interview you will be asked structured questions about times you were sad, happy, anxious, your past and current substance use, and other mood symptoms. During this visit and all others, you will also be asked to provide a urine sample. We will test this urine sample for drugs, cotinine (a by-product of nicotine), and pregnancy (females only, during Day 0, weeks 4, 8, 12, or as needed). You will be asked to provide a breath sample using a breathalyzer that measures the amount of carbon monoxide in your lungs. Also, at this visit, we will check your pulse, blood pressure, and weight (vitals). Vitals will be collected at Day 0, weeks 4, 8, 12, or as needed. At the end of this visit you will be set-up to receive a daily diary, which will ask you to report on cigarettes, other tobacco, other drugs and alcohol used during the previous day. These will be sent to your phone or study phone. This visit will take approximately 2.5 to 3 hours to complete.

If you are eligible and you wish to continue, you will be asked to return for a second visit, known as the Training Visit. At that time, you will receive brief quit smoking counseling to prepare you for your target quit date and be trained on how to complete medication videos during the study on your phone or study phone. This visit should take approximately 30 minutes.

You will then return for your Day 0 visit, where you will be given study medication (varenicline). You will be given instructions on how to start using varenicline. You will be asked to take videos of yourself twice-daily taking medication during the study. You will complete questionnaires, much like prior visits. This visit should last approximately 1 hour. The target quit date will begin on Day 8, which will occur after seven days of medication.

You will then continue to attend weekly visits (week 1 – week 12), a brief phone call visit on week 16, and a follow-up visit (week 26). During these weekly visits, your completion of study procedures will be assessed along with medication adherence (1 pill, twice a day). You will continue to receive brief cessation counseling and will have the ability to earn extra compensation (incentives) for quitting smoking. You will also complete questionnaires about how you are feeling and your use of substances. These visits should last between 30 – 45 minutes.

As an alternative, you may choose not to participate in this study. If you are interested in learning about other alternative treatment options for tobacco use, study staff can provide information about other options or you may choose to follow-up with your chosen healthcare provider. There may be no direct benefit for participating in this study. There is the potential for risks and discomforts such as the following: side effects of varenicline, loss of confidentiality, some questions may be of a sensitive nature, and other unknown risks.

If you are interested in learning more about this study, please continue to read below.

A. PURPOSE OF THE RESEARCH

Please read this consent form carefully and take your time making your decision. As study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand.

The purpose of this study is to better understand tobacco outcomes using a well-known quit smoking medication, varenicline and financial incentives with tobacco users. We are also interested in how cannabis and tobacco interact during a tobacco quit attempt. You are being asked to participate in this study because you are an adult cigarette smoker between the age of 18 and 40. The study will take approximately 6 months to complete and will include 17 study visits. The study is sponsored by the National Institute of Health. The investigator in charge of this study at MUSC is Dr. Erin A. McClure. Study procedures will take place at MUSC Charleston, Behavioral Health Services of Pickens County (BHS), and MUSC Florence. Approximately 208 people will take part in this study.

B. PROCEDURES

If you agree to be in this study, the following will happen:

Screening Visit (2.5 - 3 hrs.): After you have read this Informed Consent and all your questions have been answered, you will decide if you want to participate. If so, you will be asked to sign this form before any other procedures are completed. The Informed Consent process may take place electronically and you may sign electronically. You will be given a paper or electronic copy of this form to keep.

You will then be asked basic demographic questions and about your smoking history. A psychiatric and medical interview will be completed, and urine will be collected for laboratory tests. If you are a patient at MUSC, our medical clinician will have access to your medical record and will check for current health issues or medications that may affect safety. A urine sample will be collected for a urine drug test, pregnancy test (females only), and cotinine test (a by-product of nicotine). The pregnancy test will be completed before the drug testing. Females testing positive or those planning to become pregnant will not be able to participate in the study. We will also do a carbon monoxide breathalyzer test at every visit, where you will blow into a machine, to determine your recent smoking or use of combustible products. We will also check your pulse, blood pressure, and weight (vitals). If you also use marijuana/cannabis, you will be asked to weigh out typical amounts of cannabis used in joints, blunts, etc. using a surrogate (imitation) substance in the clinic. You will also complete questionnaires about your general

substance/tobacco use, mood, and cravings. At the screening visit, you will be trained how to complete daily diaries on your mobile phone or study phone. The daily diary will ask you to report on cigarettes smoked, other tobacco use, other drug use, and alcohol used during the previous day. We will ask you to begin completing daily diaries after today's visit through your week 12 visit.

The research team will use several methods of contact to keep in touch with you. We will ask you to provide us with phone numbers, e-mail addresses, current home address, and contact information of family and friends who may know how best to reach you. If it is determined that you are eligible for the study and you wish to continue, you will be scheduled for a Training Visit.

Training Visit (30 minutes): At this visit, you will be counseled, and the target quit date for cigarette smoking will be set. A urine sample will be collected for a urine drug test and cotinine test. You will also be trained on how to complete medication videos on your phone or study phone during the study. You will have the chance to practice medication videos at home before you start taking medication.

Day 0 (1 hr.): During this visit you will be given study medication (varenicline) and given instructions on how to take it. You will receive brief counseling in preparation for your target quit date. You will be asked to take a video of you taking your medication (twice a day) during the treatment phase (12 weeks). You will also answer questionnaires about your cigarette use, cravings and other substance use, much like at the screening visit. A urine sample will be collected for a urine drug test, pregnancy test (females only), and cotinine test. We will also check your pulse, blood pressure, and weight (vitals).

Weekly Visits (30 – 45 minutes): You will be asked to return to the clinic for weekly visits for the next 12 weeks. Your target quit date for cigarette smoking will be set for your week 1 visit, after seven days of medication. A urine sample will be collected for a urine drug test, pregnancy test (females only; at weeks 4, 8, 12, or as needed), and cotinine test. Self-report questionnaires will be administered (e.g., craving, withdrawal, etc.). You will receive the next week's medication and continue to take two pills twice a day. We will also check your pulse, blood pressure, and weight (vitals) at weeks 4, 8, 12, or as needed.

Week 16/Follow-up Phone (15 minutes): This follow-up visit will be remote. During the call, you will be asked about your overall health and complete a questionnaire about your general mood. Daily use of cigarettes, other substances, alcohol, and other tobacco will be gathered.

Week 26/Follow-up (1 hour): During this final follow-up visit, you will be given self-report questionnaires (e.g., craving, withdrawal, etc.). Daily use of cigarettes, other substances, alcohol, and other tobacco will be gathered.

Unscheduled Visit*:* There is a chance that during study participation you may be asked to return to the office for an unexpected need that is outside of the planned visit schedule. An example would be in the case of an issue with the study equipment or medication that cannot be resolved over the phone. We expect these to occur very rarely, and such a visit would likely take 15 minutes or less to complete.

At-home Procedures: Remote procedures will be used when necessary and as needed for all visits. We may request that you come to our office for certain in person procedures (i.e., urine capture, CO capture, medical interview, etc.). You may be able to complete at home urine testing (cotinine, urine drug screen, and pregnancy [females only] tests). You will be given all appropriate supplies and instructions to complete tests at home. You will be instructed to video conference with the study team to ensure proper testing and results.

If you have an unexpected conflict with attending a visit (for example, transportation issue or travel), please notify staff immediately so we can determine if there are any alternatives available. You may have an opportunity to complete a visit remotely with study staff and provide the urine sample with "at home collection". Study staff will review these details with you if such a need arises.

It is important that you come to your appointment without impairment from substance use, so that you can think clearly and reliably provide informed consent, or the ability to understand and willingly participate in the research for which you are volunteering. It is also important for the research and data collected that you are not under any influence or impairment. If the research team determines that you appear impaired from substance use, your study visit will not be completed, and your visit will be rescheduled.

For your safety and that of others, we ask that you avoid substance use before any self-travel/transportation to your scheduled study visit. If you arrive to a study visit and appear to be under the influence, staff cannot allow you to leave the office to drive your vehicle.

You will have the options to:

1. Call a friend or relative to pick you up.
2. Call a cab or ride share service (e.g., Uber/Lyft).
3. Remain in the clinic until a clinician has decided that you are safe to leave following an evaluation.

Should you leave the building and drive from the parking lot, we will be obligated to notify public safety entities. The intent of this policy is to provide you with the best possible care and to help assure your personal safety and that of others.

You may be withdrawn from this study without your consent if the researchers believe it is in your best interest or if you fail to follow study procedures.

You may change your mind and drop out from the study at any time. If you decide to stop participating in the study, you are encouraged to talk to study staff first so that stopping can be done safely. Another reason to tell study staff that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful to you.

Should you or the researchers determine that leaving the study is the best choice, an Early Termination (ET) visit will be completed. This visit will be important to collect any study equipment and medication from you.

Optional Study: A subset of participants who use both tobacco and cannabis (N=48) will be asked to participate in an additional study. Participation in this additional study is optional and will not

affect your participation in the parent study. If you are interested and eligible for the additional study, you will be asked to sign a separate consent document.

C. DURATION

Participation in this study will include 17 visits over the course of 6 months. Taking part in the additional study mentioned above will not add any time to your study participation.

D. RISKS AND DISCOMFORTS

There are risks involved with participating in this study, including risks associated with Varenicline, study procedures, and loss of confidentiality.

1. Varenicline (brand name Chantix®, Apo-varenicline, or varenicline): You may experience some side effects from the study medication. The most common adverse reactions are nausea (upset stomach), abnormal (e.g., vivid, unusual, or strange) dreams, constipation, flatulence, vomiting, and headache.

   Varenicline has been approved by the US Food and Drug Administration (FDA) since 2006 (brand name Chantix® in the US, varenicline from Par Pharmaceuticals and Glenmark). Apo-varenicline is a generic version that has been approved in Canada and is now authorized for use in the US. During post-marketing use of varenicline (after FDA approval), depressed mood, agitation, changes in behavior and/or mood, hostility, suicidal ideation, suicidal attempts, and suicide have occurred in patients trying to quit smoking with varenicline. Not all patients had known pre-existing psychiatric illness and not all had discontinued smoking. The role of varenicline in these reports is unknown as smoking cessation, with or without treatment, is associated with nicotine withdrawal symptoms and may exacerbate pre-existing psychiatric illness. **Immediately report ANY changes in mood and behavior to study staff, medical clinicians, or other study personnel. These changes may include anxiety, nervousness, tension, depressed mood, hostility, unusual behaviors and thinking about or attempting suicide. These symptoms may occur during varenicline treatment or following withdrawal of varenicline therapy.**

   Although rare, reports of serious skin reactions, including rash, swelling, redness, and peeling of the skin have been reported with varenicline. Some of these skin reactions can become life-threatening. **Stop taking your study medication and get medical help right away if you have any of the following symptoms**:
   - Swelling of the face, mouth (tongue, lips, and gums), throat or neck trouble breathing
   - Rash with peeling skin
   - Blisters in your mouth

   If you have cardiovascular disease (heart or blood vessel problems), taking varenicline may increase your risk of certain cardiovascular adverse events. Contact the medical clinician on this study if you experience new or worsening symptoms of cardiovascular disease while taking varenicline, for example:

- Shortness of breath or trouble breathing
- New or worsening chest pain
- New or worsening pain in legs when walking

You should stop taking study medication and immediately report any such symptoms to the study staff and be sure to make known any history of psychiatric illness prior to beginning treatment.

In July 2021, a voluntary recall of certain lots of Chantix® was issued because of higher than acceptable levels of impurities in the medication. All recalled medication was removed from the supply at that time. The pharmacy at MUSC and study team will monitor our drug supply and any new recalls to do our best to ensure you are not being given recalled drug. We will alert you to any new information.

2. Risk of Loss of Confidentiality: There is a risk of loss of confidentiality regarding the information obtained during the initial assessment. Information about you, as well as your image, will be kept in password-protected databases and computers and will only be accessible by the principal investigator and research staff. To ensure confidentiality, all participant information (questionnaires and identifying information) will be identified with a number (when possible) or name and kept under lock and key and in password-protected databases.

3. Nicotine Withdrawal: You may experience nicotine withdrawal symptoms and/or discomfort during your quit attempt. Nicotine withdrawal symptoms may include: anxiety, depressed mood, irritability, restlessness, sleep difficulty, strange dreams, increased appetite, headaches, tension, difficulty concentrating and general physical discomfort. If you feel that your withdrawal symptoms worsen, please contact the research staff immediately.

4. Interview Questions: The questions that will be asked may be sensitive and make you feel uncomfortable. You may refuse to answer any question(s) that you do not wish to answer, but we may be unable to determine eligibility.

5. Pregnancy (females only): During the study, you will be tested for pregnancy at certain visits or as needed. If you were to become pregnant during the study, please alert staff as soon as possible and discontinue study medication immediately. If you were to become pregnant, you will be withdrawn from the study.

6. Unknown Risks: Unknown risks may occur during the study. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

E. CERTIFICATE OF CONFIDENTIALITY

This research is covered by a Certificate of Confidentiality from the Federal government. This means that the researchers may not disclose information or biospecimens that may identify you,

even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, nor can the information or biospecimens be used as evidence, unless you have consented to this disclosure. Information or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research unless you have consented to the disclosure. More specifically, identifiable information or biospecimens will not be shared with your medical providers who are not involved in this research unless you authorize the study to disclose information to them, or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The medication prescription for this study will be added to your MUSC medical record and will state that medication is for a research study. If you do not have an MUSC record, one will be created with your name and date of birth. No other information about your study participation or data collected through the study will be in your MUSC medical record. We will make every effort to keep confidential all research information in the medical record that identify you to the extent allowed by law. Information in your MUSC medical record will be visible to the study's medical clinician and will be used to help us determine if you are a good fit for this study. A Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must authorize the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law. Examples of required disclosure include: child abuse and neglect, threat of harm to self and others, but there could be others.

Finally, a Certificate may not be used to withhold information from the Federal government needed for auditing or evaluating Federally funded projects or information needed by the FDA.

F. BENEFITS

There may be no direct benefits to you for participating in this study.

G. COSTS

There may be additional costs to you for the use of cellular data and text messaging fees, if you are using a personal smartphone for this study. There will be no other additional costs to you as a result of participation in this study.

H. PAYMENT TO PARTICIPANTS

In return for your time and effort, you will be paid for every visit you complete. You will be compensated $40 for the Screening visit and $30 per visit for Training, Day 0, and other weekly visits (13 visits or ET visit if applicable). You will be compensated $50 for the end-of-treatment visit (Week 12), and $50 for the 6-month follow-up visit (Week 26). All study procedures must be completed to receive the full visit payment. Partial payment may be given in cases when not all procedures have been completed.
You are also eligible to receive up to $20 per week during treatment period (starting at week 2)

for negative cotinine values (shows that you have quit smoking). You will also be eligible for compensation at weekly visits during the treatment phase for the completion of daily diaries and twice-daily medication videos. This compensation will be based on completion of procedures. You may earn a total of $1,050 for study participation and completion of all study procedures.

Payment for study visits will be made using a pre-paid debit card, called a ClinCard. It works like a bank debit card and you may use the card to purchase goods or services everywhere Debit MasterCard is accepted. You will be given or mailed a ClinCard at the beginning of the study. Each time you receive payment for participation in this study, the money will be added to the card, as outlined in the payment schedule above. Details of the debit card system are explained on an additional sheet.

Should you be asked to return to the study office for an Unscheduled Visit, you will receive a payment of $10 for completing the visit.

You are also invited to participate in the recruitment of other participants for this study. You may choose to tell people of your participation in the study and suggest that they call the study team if they are interested in participating in the study. These individuals will not be identified unless they contact the study office themselves. If any of your referrals result in successful scheduling and completion of a Day 0 visit, you will receive $30 for each one. Participation in this process is completely voluntary, and if you elect not to participate, your participation in this study will not be affected in any way.

Payments that you receive from MUSC for participating in a research study are considered taxable income per IRS regulations. Payment types may include, but are not limited to: checks, cash, gift certificates/cards, personal property, and other items of value. If the total amount of payment you receive from MUSC reaches or exceeds $600.00 in a calendar year, you will be issued a Form 1099.

I. ALTERNATIVES

Your alternative is to not participate in this study.

J. DATA SHARING

Information about you (including your identifiable private information and/or any identifiable biospecimens) may have all of your identifiers removed and used for future research studies or distributed to other researchers for future research without additional informed consent from you or your legally authorized representative.

K. DISCLOSURE OF RESULTS

If there are significant new findings during the course of the study, you will be notified. Also, if you would like your medical records released to anyone other than the investigators, you will be asked to sign an additional release of information form.

L. AUTHORIZATION TO USE AND DISCLOSE (RELEASE) MEDICAL INFORMATION

As part of this research study, your study doctor and his/her research team will keep records of your participation in this study.

The health information MUSC may use or disclose (release) for this research study includes information in your medical record, results of physical exams, medical history, lab tests or certain health information indicating or relating to your condition.

Your study doctor and his/her research team will use and disclose (release) your health information to conduct this study. The health information listed above may be used by and/or disclosed (released) to the following, as applicable:

- The sponsor of the study including its agents such as data repositories or contract research organizations monitoring the study;
- Other institutions and investigators participating in the study;
- Data Safety Monitoring Boards;
- Accrediting agencies;
- Clinical staff not involved in the study whom may become involved if it is relevant;
- Parents of minor children if less than 16 years old. Parents of children 16 years old or older require authorization from the child; or
- Health insurer or payer in order to secure payment for covered treatment;
- Federal and state agencies and MUSC committees having authority over the study such as:
    - The Institutional Review Board (IRB) overseeing this study; Committees with quality improvement responsibilities; Office of Human Research Protections; Food and Drug Administration; National Institutes of Health or Other governmental offices, such as a public health agency or as required by law.
- MUSC Pharmacy/Pharmacies
- MUSC Electronic Health Record (EPIC)
- MUSC Hollings Cancer Center (HCC)
- Behavioral Health Services of Pickens County (BHSPC)

Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them. You do not have to sign this consent form. If you choose not to sign, it will not affect your treatment, payment or enrollment in any health plan or affect your eligibility for benefits. However, you will not be allowed to be a participant in this research study.

You will be given a copy of this consent form. Your authorization will expire at the conclusion of this study or, if you are participating in a study designed for the development of a drug or device, your authorization will remain in effect until the drug or device is approved by the FDA or until the company's application to study the drug/device is withdrawn. You have the right to withdraw your agreement at any time. You can do this by giving written notice to your study

doctor. If you withdraw your agreement, you will not be allowed to continue participation in this research study. However, the information that has already been collected will still be used and released as described above. You have the right to review your health information that is created during your participation in this study. After the study is completed, you may request this information.

Your health information will be used or disclosed when required by law. Your health information may be shared with a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury or disability and for conducting public health surveillance, investigations or interventions. No publication or public presentation about the research study will reveal your identity without another signed authorization from you.

If you have questions or concerns about this Authorization or your privacy rights, please contact MUSC's Privacy Officer at (843) 792-8740.

Regulations require that you be given a copy of the MUSC Notice of Privacy Practices (NPP) describing the practices of MUSC regarding your health information. One can be found at the end of this form.

M. STUDENT PARTICIPATION

Your participation or discontinuance will not constitute an element of your academic performance, nor will it be a part of your academic record at this Institution.

N. EMPLOYEE PARTICIPATION

Your participation or discontinuance will not constitute an element of your job performance or evaluation, nor will it be a part of your personnel record at this Institution.

O. FUTURE CONTACT

The researcher in charge of this study might like to contact you in the future about other research opportunities. Please initial by your choice below for paper consents, or scroll down to the bottom of the screen and initial by your choice electronically*:*

____Yes, I agree to be contacted

____No, I do not agree to be contacted

Results of this research will be used for the purposes described in this study. This information may be published, but you will not be identified. Information that is obtained concerning this research that can be identified with you will remain confidential to the extent possible within State and Federal law. The investigators associated with this study, the sponsor, and the MUSC Institutional Review Board for Human Research will have access to identifying information. All records in South Carolina are subject to subpoena by a court of law.

In the event that you are injured as a result of participation in this study, you should immediately go to the emergency room of the Medical University Hospital, or in case of an emergency go to the nearest hospital, and tell the physician on call that you are in a research study. They will call your study doctor who will make arrangements for your treatment. If the study sponsor does not pay for your treatment, the Medical University Hospital and the physicians who render treatment to you will bill your insurance company. If your insurance company denies coverage or insurance is not available, you will be responsible for payment for all services rendered to you.

Your participation in this study is voluntary. You may refuse to take part in or stop taking part in this study at any time. You should call the investigator in charge of this study if you decide to do this. Your decision not to take part in the study will not affect your current or future medical care or any benefits to which you are entitled.

The investigators and/or the sponsor may stop your participation in this study at any time if they decide it is in your best interest. They may also do this if you do not follow the investigator's instructions.

Volunteers Statement

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have any more questions about my participation in this study or study related injury, I may contact Dr. Erin A. McClure at 843-792-7192. I may contact the Medical University of SC Patient and Family Care Liaison 843-792-5555 concerning medical treatment.

If I have any questions, problems, or concerns, desire further information or wish to offer input, I may contact the Medical University of SC Institutional Review Board for Human Research IRB Manager or the Office of Research Integrity Director at (843) 792-4148. This includes any questions about my rights as a research subject in this study.

I agree to participate in this study. I have been given a copy of this form for my own records.

Please sign below for paper consents or scroll down to the bottom of the screen and sign electronically.

Signature of Participant	Date	Name of Participant
Signature of Person Obtaining Consent	Date	