Medical University of South Carolina
CONSENT TO BE A RESEARCH SUBJECT

TITLE OF RESEARCH: Gender and Sex Hormone Influences on Cannabis Use Disorder Remission

You are being asked to volunteer for a research study. Research studies are voluntary and include only people who choose to take part. Please read this document carefully and take your time making your decision. As the study staff discusses this consent form with you, please ask them to explain any words or information that you do not clearly understand. The nature of the project, risks, discomforts, and other important information about the study are listed below.

The purpose of this study is to explore associations between certain hormones and reactions to cannabis use. The results of this study may provide new information that will help to understand relationships between hormones, behavior, and substance use. If you agree to participate, the study is comprised of eleven visits over the course of five months, in which you will receive eight weeks of computerized Cognitive Behavioral Therapy (CBT), answer questions about your substance use and overall mood, and provide urine and saliva samples.

Cognitive Behavioral Therapy (CBT) is a psychological intervention that focuses on changing thought patterns, improving the regulation of emotions, and the development of coping strategies to help solve problems. The first session of CBT will consist of a brief goal setting session with a clinician in which motivational enhancement strategies will be used and you will be introduced to the online treatment platform. The web-based treatment platform (CBT4CBT) teaches cognitive behavioral skills, such as decision-making, assertiveness, and coping skills, that can help you with CUD to gain control over your use of cannabis. CBT4CBT includes 7 modules with interactive, online exercises illustrating CBT concepts.

There are risks involved with participating in this study, including risks associated with study procedures, cannabis withdrawal, and loss of confidentiality. Although there is no guarantee or promise that you will receive any benefit from participation in this study, you will receive standard substance use disorder treatment in the form of computerized Cognitive Behavioral Therapy, and you may reduce your cannabis use.

You may choose not to participate in this study. If you are interested in learning about treatment for problematic substance use, study staff can provide information about other options or you may choose to follow up with your chosen healthcare provider.

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

A. PURPOSE OF THE RESEARCH

The purpose of this study is to explore associations between certain hormones and reactions to cannabis use. You are being asked to participate in this study because you are an adult aged 18 or older who uses cannabis. We expect to include people with a variety of cannabis use histories.

This research is sponsored by the National Institutes of Health (NIH). The investigator in charge of this study is Dr. Rachel Tomko and Aimee McRae-Clark. Portions of Drs. Tomko and McRae-Clark's and their research team's salaries will be paid by this grant. This study is being conducted at one site, the Medical University of South Carolina, and will involve 225 volunteers.

B. PROCEDURES

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

After consent is obtained, a urine sample will be collected for a pregnancy test (for individuals assigned female at birth) and a urine drug test.

Next, you will be administered questionnaires and assessments that will measure your overall mood and substance use, and you will be asked questions about your past experiences with cannabis. Additional questionnaires and assessments that measure your overall mood and general substance use will have been completed as part of the Entryway or Youth Collaborative intake study in which you recently participated (within the last 30 days). Data collected during that visit will be carried over and included in order to avoid repeating tests. Examples of such data include your answers to completed surveys, health history, urine drug test results, and interview data.

After that, you will be taught how to collect saliva on your own. Saliva is being collected to measure the levels of certain hormones. You will be given supplies for 14 days of saliva sample collection at each visit to ensure that you have plenty of collection tubes available in the event that you miss a visit or need to reschedule your next in-person visit. You will also be provided with a small tube rack and freezer pack for self-storage of samples between visits. During the treatment phase of the study, you will be asked to bring any saliva samples you have completed to each in-person visit.

You will also be taught how to record and upload a video of the process, so that we can verify that you collected your own saliva. You will complete a practice video during this visit. When you upload your videos, you will also be asked a few questions about your cannabis use and mood, which we refer to as "daily diaries." You will receive twice daily text message reminders with a secure link to upload your video and fill out your daily diaries. For your privacy and staff's viewing consideration, please make sure you are appropriately dressed when filming your video. Also, for your safety, when recording your daily videos, we ask that you do not complete them while driving. Should you lack a reliable mobile device for completion of daily diaries and video uploads, one will be loaned to you. If you choose to use a loaned device throughout your participation in the study, you are expected to return to the device upon completion of the research procedures. If an iPhone is loaned to you, you agree that you will only use it for the purposes of completing daily diaries and recording and uploading saliva sample videos.

Please initial your choice below if you agree to return all equipment in good working condition and that you also understand that you will use the equipment appropriately for the purposes as instructed by study staff:

____Yes, I agree to return any loaned equipment in working condition and to use appropriately
____No, I don't agree and will not receive any loaned equipment

If you agree to optional genetic testing, a blood sample will be drawn to be used to determine your DNA. Your genes are made up of DNA, which is short for deoxyribonucleic acid. DNA contains information that determines in part the traits, such as eye color, height, or disease risk, that are passed on from parent to child. In this study, we will examine genes that are associated with how your body metabolizes or breaks down cannabis, known as cytochrome P450 genes (for example, CYP2C9, CYP2C19, and CYP3A4). Your genes can affect how you break down or metabolize substances, such as cannabis, and may be related to how cannabis affects your body and interacts with hormones. You do not have to agree to genetic testing to participate in this study.

You will come to the research office weekly during your 8 weeks of computerized Cognitive Behavioral Therapy. Cognitive Behavioral Therapy (CBT) is a psychological intervention that focuses on changing thought patterns, improving the regulation of emotions, and the development of coping strategies to help solve problems. The first session of CBT will happen in office and will consist of a brief goal setting session with a clinician in which motivational enhancement strategies will be used and you will be introduced to the online treatment platform. The web-based treatment platform (CBT4CBT) teaches cognitive behavioral skills, such as decision-making, assertiveness, and coping skills, that can help you with CUD to gain control over your use of cannabis. CBT4CBT includes 7 modules with interactive, online exercises illustrating CBT concepts.

Prior to beginning CBT, at your first visit in office you will meet with a therapist for a brief discussion of your goals and an orientation to the CBT online platform. This session will last approximately 30 minutes. You will complete a computerized CBT4CBT module between visits on your own time. Each module should take approximately 30 minutes to complete. These lessons each focus on a specific CBT skill (e.g., dealing with craving, challenging negative thoughts), include video demonstrations of the skill in practice, and provide opportunities for practice exercises in-between lessons.

During Weeks 1, 2, 4, 6, and 8, you will provide a urine sample for analysis. If your weekly CBT module has not yet been completed, you will be provided with a quiet space in the clinic to complete the module. If you have missed any of your daily diaries, staff will help you complete them at this time. You will also be asked to bring your saliva samples with you to each visit.

You will answer a few questionnaires and interview questions about your mood and substance use. You will be asked if you are willing to have one of the cannabis-related interviews audio recorded at Weeks 1, 4, 8, 12, 16, and 20. This is not a requirement of participation and is used for our quality control process. A portion of recorded interviews will be reviewed by a second study team member for quality control. *Please initial your choice below for audio recording, or scroll down to the bottom of the screen and initial electronically:*

____Yes, I agree to my brief interview being audio-recorded

____No, I do not agree to audio-recording

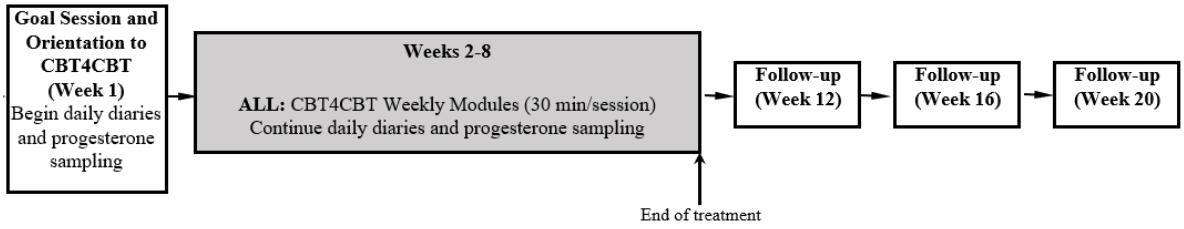
Once the 8 weeks of CBT are complete, you will come to the research office for three follow-up visits four weeks apart.

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 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. Study staff will review these details with you if such a need arises. Your first visit must be completed in the office. If any of the subsequent visits cannot be completed in office, an exception might be made by asking you to complete a partial remote visit via doxy.me or Zoom Pro. During these visits you will complete questionnaires and assessments on your overall mood and substance use. During weeks 4, 8, 12, 16, and 20 you will also be asked to complete a cannabis related interview with a clinician remotely. For these remote visits only, biospecimen collections (e.g. urine, pregnancy test) and vitals will not be collected. If a remote visit is conducted during the treatment phase you will be asked to bring saliva sample collections to the next in office visit. If you run out of saliva sample collection supplies and not able to come into the office to pick up some, staff will ship supplies to you via USPS, UPS, or FedEx.

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 withdraw from the study at any time.

Unscheduled Visit: There is a chance during your study participation or afterwards that you may be asked to return to the office outside of the planned visit schedule. An example of an unscheduled visit would be in the case of a technological issue with the study equipment or surveys that cannot be resolved over the phone or returning to the office for a blood draw.



If you agree to optional genetic testing, a blood sample will be drawn to be used to determine your DNA. Your genes are made up of DNA, which is short for deoxyribonucleic acid. DNA contains information that determines in part the traits, such as eye color, height, or disease risk, that are passed on from parent to child. In this study, we will examine genes that are associated with how your body metabolizes or breaks down cannabis, known as cytochrome P450 genes

(for example, CYP2C9, CYP2C19, and CYP3A4). Your genes can affect how you break down or metabolize substances, such as cannabis, and may be related to how cannabis affects your body and interacts with hormones. You do not have to agree to genetic testing to participate in this study. The blood draw can happen during any study visit, including after your completion of the rest of the study protocol.

C. DURATION

Participation in this study will take 11 visits over the course of 5 months.

D. RISKS AND DISCOMFORTS

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

1. Loss of Confidentiality: Though researchers will take all steps to protect your data, there is a chance that your personal information may not be kept confidential. Some answers you give during the research visits (like whether you use illegal drugs) may put you at risk if other people find out. To keep what you say private, your study records will use a code number instead of your name. We will protect your records to the extent allowed by law by keeping all your materials in locked file cabinets and password-protected servers only available to research staff.

2. Interview/Rating Scales (Questionnaires): The questions that you will be asked may be sensitive in nature and make you feel uncomfortable. You may be asked personal questions that you find distressing. You may refuse to answer any question(s) that you do not wish to answer.

3. Cannabis Withdrawal. You will receive cannabis reduction treatment and may reduce or abstain from cannabis use during the study period. You may experience cannabis withdrawal symptoms and/or discomfort if you make a quit attempt. Cannabis withdrawal symptoms may include: anxiety, depressed mood, irritability, restlessness, sleep difficulty, strange dreams, nausea, headaches, tension, difficulty concentrating and general physical discomfort. You should contact research staff if you feel that your withdrawal symptoms worsen during the study.

4. CBT4CBT Modules: The CBT4CBT modules you will be viewing discuss sensitive topics that can make some people feel uncomfortable. If you find viewing them distressing, you should contact research staff to discuss further.

5. Blood Draw: Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting is possible, although unlikely.

6. Genetic Research: Genetic research studies may present unique risks to human subjects and their relatives. These involve medical, psychosocial, and economic risks, such as the possible loss of confidentiality (private information), loss of insurability and employability, paternity, and social stigmas. Knowledge of one's genetic make-up may also affect one's knowledge of the disease risk status of family members. Genetic research raises difficult questions about informing

you and other participants of any results, or of future results. Some people want to know what is found out about them; others do not.

South Carolina law mandates that your genetic information obtained from any test or from this research, be kept confidential. Our state law prohibits an insurer using this information in a discriminatory manner against your or any of your family in issuing or renewing insurance coverage for you or your family. Our state law further prohibits our sharing your genetic information with anyone except in a few narrow circumstances, one of these being a research project of this type, approved by the Institutional Review Board, and then we must take all steps to protect your identity. You will still be responsible for paying for health care. The Medical University of South Carolina will not be responsible for such costs, even if care is needed for a condition revealed during research or clinical testing.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Be aware that this new federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, nor does it protect you against genetic discrimination by all employers.

E. MEDICAL RECORDS

Information about your study participation will not be in your medical record. This means that neither your research participation nor any of your research results will be included in any MUSC medical record. If you do decide to complete the optional blood draw you will see an appointment with the lab in your MyChart, but no information about the blood draw or the results will be entered in your medical records within MyChart.

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.

This 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.

There are some exceptions to confidentiality. Data can be disclosed as required by federal, state, or local law. Examples of required disclosure include: child abuse and neglect, or harm to self and others, but there could be others.

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.

Information about your study participation will not be in your MUSC medical record. This means that neither your research participation nor any of your research results will be included in any MUSC medical record. 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, or 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

Although there is no guarantee or promise that you will receive any benefit from participation in this study, you will receive standard substance use disorder treatment in the form of computerized Cognitive Behavioral Therapy, and you may reduce your cannabis use.

G. COSTS

There will be no costs to you as a result of participation in this study. If you choose to use your own device for study procedures, your normal cellular and data usage rates will apply.

H. PAYMENT TO PARTICIPANTS

In return for your time and effort, you can earn up to $815 for participation in this study.

- You will be compensated $40 for Week 1 Visit.
- You will be compensated $40 for Weeks 4 and 8 Visits. *Alternatively, you will be compensated $30 for any partial remote visit during these weeks.*
- You will be compensated $40 for Weeks 12, 16, and 20 Visits. *Alternatively, you will be compensated $30 for any partial remote visit during these weeks.*
- You will be compensated $20 for all other visits (Weeks 2, 3, 5, 6, 7). *Alternatively, you will be compensated $10 for any partial remote visit during these weeks*

- You will receive up to a $40 weekly bonus (Weeks 2-8) for completing daily diaries, recording videos of saliva samples, and returning the corresponding samples to the lab at your next visit.
- You will receive up to a $10 weekly bonus (Weeks 9-20) for completing daily diaries post-treatment. The amount of the bonus will be pro-rated if <90% of expected daily diaries, videos, or saliva samples are received.
- All participants will be eligible for an end-of-study data usage or equipment return bonus of $25. If you borrow a phone, this bonus is contingent upon returning the device. For others, this bonus is to offset any data usage charges accrued during their participation.
- You will receive $50 for completing the optional blood draw.

Payment for study visits will be made in cash or 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 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.

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

This study is for scientific purposes only. You have the option of declining to participate in this study. If you choose not to participate in this study and are interested in learning about treatments for substance use disorder, study staff can provide information about other options. Alternative treatment options are available at the Medical University of South Carolina and through other providers in the community. Staff can aid in a referral to MUSC's Center for Drug and Alcohol Programs, and the Charleston Center, as desired or recommended.

J. DATA SHARING

Information about you (including your identifiable private information and/or any identifiable biospecimens) may have all of your identifiers removed and be 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.

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.

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.

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. COLLECTION OF SPECIMENS

Urine will be collected for laboratory tests including urine pregnancy tests for females, urine drug screen, and an analysis of a THC metabolite to determine if you are able to participate in the study. For females, the urine pregnancy test will be done before any other testing, including the urine drug screen. Saliva will be collected for laboratory tests for analysis of the hormone progesterone.

Blood will be taken from a vein in your arm using a needle. The blood sample will be used to, if you consent, to analyze your DNA. We will take no more than about 1.5 tablespoons during the study. If you consent to DNA testing, a portion of your blood sample will be analyzed at MUSC.

You do not have to agree to DNA testing. Please initial your choice below for paper consents, or scroll down to the bottom of the screen and initial electronically:

____Yes, I agree to the analysis of my blood samples for DNA testing
____No, I do not agree to the analysis of my blood samples for DNA testing

As part of this study, we would like to store blood specimens collected from you for future research on cannabis use. This future research may be conducted by Rachel Tomko, Ph.D., or by

other researchers who obtain IRB approval for their research. This research may involve genetic studies. For example, it is possible that future research using your specimen might include whole genome sequencing (i.e., the process of reading the entire genetic code or DNA of an organism).

There are several things you should know before allowing your saliva, urine, and/or blood to be studied or to be stored.

The specimens will be labeled with a code that only study personnel can link back to you. Researchers outside of this study will not be given a link between the code number and your name or any other identifying information. While we hope this will prevent any potential loss of privacy or confidentiality, we cannot make any guarantees.

In addition to your name, other information about you might be connected to your sample. For instance, information about race, ethnicity, sex, your medical history, and so forth might be available to investigators studying your specimen. Such information might be important for research or public health. It is possible that this information (including genetic information) might come to be associated with your racial or ethnic group.

The specimens obtained from you in this research may help in the development of a future commercial product. There are no plans to provide financial compensation to you should this occur. Investigators will not tell you what they find out about you, nor will they contact you if a test becomes available to diagnose a condition you might have or later develop.

You do not have to agree to allow your blood specimens to be stored in order to be part of this study. Please initial your choice below for paper consents, or scroll down to the bottom of the screen and initial electronically:

___ Yes, I agree to allow my samples to be kept and used for future research.
___ No, I do not agree to allow my samples to be kept and used for future research.

P. FUTURE CONTACT

The researcher in charge of this study might like to contact you in the future about other research opportunities. *Please initial your choice below for paper consents, or scroll down to the bottom of the screen and initial 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 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 study 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. Rachel Tomko at 843-792-5447. 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 participant in this study.

I agree to participate in this study. I have been given a copy of this form for my own records and the research study and consent form have been explained to me by:

Signature of Person Obtaining Consent	Date

If you wish to participate, you should sign below for paper consents, or scroll down to the bottom of the screen and sign electronically:

Signature of Adult Participant (18 years or older)	Date

MUSC
Medical University of South Carolina
Changing What's Possible