STUDY TITLE: Rapid Determination of the Clinical Utility of Perampanel for the Treatment of Alcohol Dependence
VCU INVESTIGATOR: Albert J. Arias, MD **(203) 800-1928**

SPONSOR: National Institute on Alcohol Abuse and Alcoholism/ NIH/ DHHS

NOTE: In this consent form, "you" always refers to the research participant.

ABOUT THIS CONSENT FORM

You are being invited to participate in a research study. **It is important that you carefully think about whether being in this study is right for you and your situation.**

This consent form is meant to assist you in thinking about whether or not you want to be in this study. **Please ask the study doctor or the study staff to explain any information in this consent document that is not clear to you.** You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

Your participation is voluntary. You may decide not to participate in this study. If you do participate, you may withdraw from the study at any time. Your decision not to take part or to withdraw will involve no penalty or loss of benefits to which you are otherwise entitled.

AN OVERVIEW OF THE STUDY AND KEY INFORMATION

Why is this study being done?

The purpose of this research study is to test the safety, tolerability, and effectiveness of the drug Perampanel when used in persons who drink alcohol - specifically to understand how a person responds to the medication while they are receiving alcohol intravenously (through an IV). This medication is currently used to treat seizure disorders, and is currently not U.S. Food and Drug Administration (FDA) approved to treat alcohol use disorders. For this reason, it is considered an investigational drug. In this study, the medication is compared to a placebo (a look-alike inactive substance, a "sugar pill"). You will be randomly assigned (like the flip of a coin) to receive either the medication or a placebo. You have an equal chance of being assigned to any one of the groups. There is evidence that anticonvulsants (medications used to treat seizures) can be effective in the treatment of alcohol use disorders. Perampanel is an anticonvulsant.

DESCRIPTION OF THE STUDY INCLUDING PROCEDURES TO BE USED.

This study has two parts. Part 1 includes the preliminary screening, and Part 2 includes three test days. During each test day you will be given an intravenous (IV) alcohol infusion along with the study medication or a placebo. The medication or placebo is given as a pill to take by mouth. We will also give you a small dose of the medication or placebo to take each day for a week prior to each test day. Only the study participant can take the study drug. It must be kept out of the reach of children and persons who may not be able to read or understand the label. All subjects must complete the preliminary screening, which is completed prior to the test days and takes approximately 4 hours. Approximately 75 people will be recruited for the study.

Your participation in this study will include a screening visit (lasting approximately 4 hours), 3 outpatient visits to pick up your study medication (lasting approximately 30-60 minutes) and 3 test days (which will be at least 21 days apart and last approximately 7 hours each day). The total time to complete the study is 28 hours, spread out over a period of approximately 52 days.

What will happen if I participate?
Part 1. Preliminary Screening:
If you agree to participate in this study, you will complete an initial screening that includes a medical history, physical examination, blood test, urine screening (toxicology), and electrocardiogram (EKG) to ensure that you are medically healthy. Female subjects will have a blood pregnancy test performed at screening and a urine pregnancy test performed on each test day. To your knowledge, you are not pregnant at this time. You also agree to avoid becoming pregnant. If you change your mind about becoming pregnant we ask that you tell us immediately. You will also complete a psychiatric evaluation. You will receive a payment of $50 for this initial screening. Based on the results of these evaluations, we will determine whether you may be eligible to participate in Part 2 of the study. Usually the screening can be completed in 1 visit, although sometimes you might have to come back for a second appointment to finish everything. Once all of your screening information is reviewed and if it is determined that you are eligible, you will be asked to come in for a short visit (30-60 minutes) where you will complete several surveys and you will also be given a week (7 day) supply of a low dose of the study medication (perampanel) or placebo to take prior to your scheduled test day. A study nurse or Research Assistant will contact you by phone once between days 2-4 and once between days 5-7 to ask you about any side effects you might be noticing. You may be asked to come to the research center for evaluation if there are any concerns about your safety.

You will be asked to provide a blood sample for DNA analysis. This is not optional, but we will only collect this sample when we are sure that you are eligible to participate in the study. In most cases, we will draw the blood sample when you come in to pick up your first set of take-home medication. The sample will be used to see if common (and some less common) variations in genes affect the response to the medication and alcohol. It may also be used to see if those genetic variations affect drinking and other behaviors measured in the study.

This study will use your samples to sequence all or part of your DNA.

Deoxyribonucleic acid (DNA) is the "blueprint" or "recipe" that gives the body's cells instructions on how to do their jobs. Scientists can use a test called whole genome sequencing to determine the order of all or part of the molecules that make up your DNA, like reading all the letters in a book. Sequencing is usually done to look for changes in the molecules of DNA that may cause health problems.

Part 2. Test Days:
We will ask you to refrain from using illicit drugs while you are enrolled in the study. We will also ask you to refrain from using caffeine, alcohol, and cannabis for 12 hours before each test day. You will also be instructed to not eat after midnight before the session. The morning of test days, you should report to the Clinical Research Services Unit (CRSU) at VCU Health (North 8). On your test days, when you first arrive before testing can proceed, we will check your blood pressure and pulse, perform a urine toxicology (drug screen), urine pregnancy test (females only), breathalyzer and we will look for signs of alcohol withdrawal. If your breathalyzer reading is over 0 (meaning that you have recently used alcohol), you appear to be in significant alcohol withdrawal, or your urine drug screen shows that you have used illicit drugs, you will likely be rescheduled for a later time or we may discontinue you from the study at our discretion and you may not receive payment for this day. If you are rescheduled, you may be asked to continue the study medication, or we may ask you to stop and then restart the medication again later. If your results are satisfactory to the study criteria, the research nurse will then insert an IV line. We will take a blood sample to check your blood count levels as well as the levels of study medication in your blood. You will then be asked to complete several brief questionnaires asking about your mood, smoking habits, and alcohol use**.** You will receive either a high, low, or placebo dose of the test

medication (perampanel) to take orally (by mouth). About 45 minutes later, we will ask you to fill out some forms about alcohol, drugs, and your mood. Approximately 15 minutes later you will be provided with breakfast. About 30 minutes after that, you will receive the infusion. We will ask you to fill out some forms about alcohol, drugs, and your mood.

Your breath alcohol concentration (BrAC) will be kept at a certain level using a small pump to regulate the flow of alcohol into a vein in your arm. The infusion pump rate will be adjusted every few minutes, based on the results of the breathalyzer tests. On each test day you will be following the same procedures, and the target levels of intoxication will be the same on each test day. During the highest level of alcohol administration, your BrAC level may be as high as approximately 0.10. Your heart rate and blood pressure will be monitored throughout the infusion.

An hour and a half after taking the dose of study medication, you will start the IV alcohol infusion. You will begin with a low dose of alcohol (about what is associated with one to two (1-2) 12 oz cans of beer in an hour for a man or one 12oz can of beer for a woman).Then, 30 minutes later, we will administer more alcohol to bring your blood level up to a moderate dose of alcohol (about what is associated with four (4) 12 oz cans of beer in an hour for a man or three (3) 12oz. cans of beer for a woman).Then, 30 minutes after that we will add more alcohol to bring your blood alcohol level to a higher level of alcohol(about what is associated with five to six (5-6) 12 oz cans of beer for a man or five (5) 12 oz cans of beer for a woman; you will feel "drunk" at this point). You will be asked about your experience with the alcohol (e.g., how much you enjoy it, etc.) at each of these three levels of alcohol administration.

You will complete the same questionnaires and tests six times on each test day. This will take about three hours and will be completed before your provided lunch. We will ask you to measure how rewarding you think the alcohol is and to complete a computer challenge called the "Balloon Analogue Risk Task." The balloon task gives you a chance to win some additional money (up to an additional $30 per lab session). The alcohol infusion will end and you will rest in the lab while you sober up from the alcohol.

At the end of the test day you will be debriefed by our study staff. A healthcare provider will examine you before you are allowed to go home. Prior to each test day you will need to make plans to be driven home. You will not be allowed to drive yourself home. If you can't find a ride, we will arrange a taxi (within a 20 mile radius) for you. This is to avoid any difficulties with driving due to any residual sedation. You will not be allowed to leave until your breathalyzer is at or below (≤) 0.02 and a healthcare provider has evaluated you to detect any signs of intoxication that would impair you. If you feel uncomfortable for any reason, you will be allowed to stay overnight at the CRSU at VCU Health. If you are deemed unsafe to leave due to intoxication, you may be not allowed to leave until deemed safe. This procedure will be repeated for your second and third test days.

In-between lab visits:
After each test day, we will give you two days of low dose study medication (perampanel) to taper off the medication. You are asked to avoid driving, swimming, or baths (showers are ok) for 48 hours after the lab visit. These are important safety measures in case you have a seizure (convulsions). You will then begin a 14-21 day washout period (to allow blood levels of study medication to decrease) prior to your next visit. You may require a brief visit during this time to check the medication level by a blood sample. At the next visit, you will briefly come in to receive one week of medication (low dose perampanel or placebo) to lead up to the next test session day. You will also be asked to complete several surveys. During the 7 days you are taking the medication at home a study nurse will contact you by phone once between days 2-4 and once between days 5-7 to ask you about any side effects you might be experiencing. You may be asked to come to the research center

for evaluation if there are any concerns about your safety. This will be repeated until you have completed all three lab sessions.

Follow-up: After you have completed the 3 test days, you will be contacted for 1 follow up phone interview: approximately 1 month, after your last test day. In the interview you will be asked about how you have been doing since the last test day. The phone questionnaire will last approximately 5 minutes.

What alternative treatments or procedures are available?
This is not a treatment study. Your alternative is not to participate. If you are interested in alcohol abuse treatment, we will help you to find a treatment program(s).

What are the risks and benefits of participating?
There are both risks and benefits of participating in research studies. We want you to know about a few key risks right now. We will give you more information in the "WHAT RISKS AND DISCOMFORTS CAN I EXPECT FROM BEING IN THE STUDY?" section.

Risks and Discomforts	Benefits to You and Others
There is a risk that you could have side effects from taking study drug. Below are some of the most common side effects: Dizziness Mood changes (irritability, aggression) Nausea or abdominal pain Fatigue or change in memory Change in ability to balance which may result in decreased coordination, or falls Rash or bruising There may be some risks that the study doctors do not know about yet, so we will let you know of any new findings. Blood draws may cause pain, bleeding, and/or bruising. You may faint and could develop an infection at the site where blood is drawn. Mild to moderate physical activity may cause sore or pulled muscles, heart problems, physical discomfort, and/or accidental injuries such as falling. You may also experience some physical discomfort such as increased heart rate, chest pain, shortness of breath, headache, nausea, and/or fatigue. The study questionnaires ask questions that are personal and sensitive in nature and may make you feel uncomfortable.	There is some evidence anticonvulsants may be effective in alcohol use disorder because of how they affect the brain. Perampanel is an anticonvulsant. This study may help the study doctors learn things that may help other people in the future. This is not a treatment study, and you are not expected to receive any direct medical benefits from your participation in the study. The information from this research study may lead to a better treatment in the future for people with alcohol dependence.

Participation in research might involve some loss of privacy. There is a small risk that someone outside the research study could see and misuse information about you.	

Now that you have a general overview of the study, we want to provide the details about what your participation involves. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask the study staff.

WHY IS THIS STUDY BEING DONE?
The purpose of this study is to test the effects of a medication called perampanel on how you feel while receiving alcohol intravenously. You have been invited because you are a frequent drinker of alcohol. Perampanel is currently approved to treat seizures. For the purposes of this study, it is an investigational drug, which means it has not been approved by the U. S. Food and Drug Administration (FDA) for the way it is being used in this study.

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?
You may not personally be helped by taking part in this study, but your participation may lead to knowledge that may help others who are seeking treatment for alcohol dependence.

WHAT RISKS AND DISCOMFORTS COULD I EXPERIENCE FROM BEING IN THE STUDY?
The Intravenous Lines and Blood Drawing: Blood drawing may cause pain, bruising, and rarely fainting or infection. There is a chance of swelling, redness, bruising or a blood clot forming at the site of blood sampling. Approximately 1/2 tablespoon of blood will be drawn during your initial screening. In addition, blood will be sampled on all 3-test days to provide information about your blood alcohol levels and you may be asked to have an additional sample drawn to check the medication level in between lab sessions. We will also routinely check bloodwork to monitor you for safety. Therefore, the total amount of blood drawn will be about 3 tablespoons per test day, and about ½ tablespoon to check the medication level (if needed), and about 2 tablespoons on repeat labwork days, for a total of 12 tablespoons (6 ounces) for the entire study. Although this amount is less than a typical blood donation (16 ounces), you should not donate blood eight weeks before and after testing.

Study Procedures: During the experimental session, you may not leave the test room. You will not be able to smoke while you are in the test room. If you are a regular smoker, you may experience some withdrawal from nicotine. You may feel irritated or anxious because of this. If you are a regular coffee drinker, you may not consume caffeine for 12 hours prior to the lab sessions, which could cause you to feel irritated, tired, or a headache. If you are a cannabis user, we ask that you abstain from cannabis use 12 hours prior to the lab sessions. At the end of the test session, you will remain in the CRSU until we are satisfied that you are in good health and your Breathalyzer is at or below (≤) 0.02. You will not be allowed to drive yourself home. If you can't find a ride, we will provide a taxi (within 20 mile radius) for you. During the study, you will be asked questions related to your mental health and drug use history which may make you feel uncomfortable or sad. If, in the opinion of the study doctor(s), you are no longer a good fit for the study, your participation may be discontinued, without regard to your wishes. This would apply if you do not comply with the requirements for participation. For example, if you fail to abstain from illicit drugs prior to lab sessions, you may be dropped from the study. Your participation may also be discontinued if it becomes medically unsafe for you to continue, if the study is stopped by a sponsor, or if the VCU IRB withdraws approval.

EXPECTED RISKS OF STUDY:

Alcohol Effects: Possible effects of consuming alcohol are blurred vision, nausea, vomiting, flushing, headache, and lightheadedness. These effects should reach their peak during the infusion and decline thereafter. The administration of alcohol intravenously may result in more intense alcohol effects than you would experience with regular consumption; however, you will be under the constant supervision of medical professionals to intervene if any of these effects become serious. There is a potential for people to abuse alcohol. It is unclear whether exposure to alcohol in the laboratory can result in problems with alcohol abuse or alcoholism. If you are worried about this possibility you should not participate in this study. Drinking more than 2 drinks per day in healthy men and 1 drink per day in healthy women can be hazardous to your health. If at any point after completing this study you become concerned about abusing alcohol, you may contact us. We will refer you to an appropriate treatment facility if necessary. For your safety, you will need to make arrangements to be driven home after each test day. If you do not feel comfortable and do not want to continue participating in the lab session, or the research staff feels that you are at risk, the test day will be discontinued.

Risks due to the study medication (perampanel):

This medication is approved by the U.S. Food and Drug Administration (FDA) for the treatment of Epilepsy. The most common side effects seen with perampanel have been, dizziness, somnolence (drowsiness), irritability, headache, fall, and problems with coordination. Dizziness and somnolence were common in epilepsy trials (more than10% of subjects). Side effects occurring in 1-10% of subjects in epilepsy clinical trials were appetite changes, aggression, anger, anxiety, confusion, irritability, difficulty with coordination, double vision, blurred vision, nausea, back pain, room-spinning dizziness, difficulty walking and falls. You will be monitored closely for rare potential side effects such as violent or homicidal ideation, as these symptoms have been reported (though rarely) in epilepsy trials with the medication. You will be monitored regularly for suicidal ideation (thoughts), as this can be a risk with all anticonvulsants. Serious or life threatening psychiatric and behavioral adverse reactions, including aggression, hostility, irritability, anger, and homicidal ideation and threats have been reported in patients taking perampanel. Because perampanel is newly FDA approved, all the side effects may not yet be known. However, we will work to anticipate possibilities for additional side effects known to occur with similar medications, such as problems producing blood cells in the right amount. The US Drug Enforcement Agency (DEA) has determined that there is some potential for people to abuse perampanel. Post marketing data and case reports have shown less than 1% of: Acute psychosis, delirium, DRESS syndrome, hallucination, increased serum triglycerides, suicidal ideation. You should not take ketoconazole (a common antifungal) while taking perampanel, and perampanel can decrease the efficacy of birth control.

Risks due to the combination of alcohol and perampanel:

The combination of alcohol and perampanel was studied by the company that markets the drug, and they noted that perampanel impaired performance on a simulated driving task, and it basically impaired control of the body more so than just with alcohol alone. You will be informed of any new risks that become known with regard to combining the two. There is the possibility that alcohol and perampanel, when combined, could make you feel tired, or you may have difficulty driving a car. You will be asked to avoid driving or drinking alcohol while on the study medication. Additionally, you will be asked to see how you react to the initial perampanel 2mg dose on day 1 of each phase before driving or operating heavy machinery.

FOR WOMEN: Because alcohol has adverse effects on the fetus, and some medications like perampanel can be harmful to a fetus, you will not be able to participate in this study if you are pregnant or breastfeeding. If you

are pregnant or become pregnant, this research may have a bad or unforeseen effect on a fetus and should not be done during pregnancy. To your knowledge, you are not pregnant at the present time and you agree to avoid becoming pregnant by using two reliable forms of birth control (one method must be non-hormonal, such as using condoms or spermicide, or you may take other precautions against becoming pregnant, etc.) during this study. If you are a woman, you will be screened for pregnancy before and during your participation in the study. You will not be allowed to participate if you are pregnant or breastfeeding.

Perampanel may lower your oral contraceptive's ability to prevent pregnancy if your oral contraceptive contains levonorgestrel. Because of this, women will be asked to use at least two forms of contraception, such as condom with spermicide, and at least one form must be non-hormone based such as a barrier method like a condom. If you change your mind about becoming pregnant we ask that you tell us immediately. You will receive a blood pregnancy test at the initial screening appointment and a urine pregnancy test on each test day. You will be excluded (dropped) from the study if you become pregnant**.** The study staff will either call you to notify you if you test positive for being pregnant during the study or will tell you, in person, if the result is available before you leave the research center when and where the sample was given.

NON-PHYSICAL RISKS
Participation in research might involve some loss of privacy. There is a small risk that someone outside the research study could see and misuse information about you.
Questionnaires may contain questions that are personal or sensitive in nature. You may refuse to answer any question that makes you feel uncomfortable.

This study will ask you questions about personal topics that might be embarrassing to talk about and that could affect your family relationships if this information were to become known outside of the study. You will also be asked about illegal activities, which could have legal and financial consequences if this information were to become known outside of the study.

Genetic Risks:
If known to employers or insurance companies, the results of genetic tests might affect a person's ability to obtain a job or health or life insurance. If this information were released, it could be misused. Such misuse could be distressing, and it could cause you or your family members to have difficulty obtaining insurance coverage and/or a job.

A federal law called the Genetic Information Nondiscrimination Act (GINA) makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. However, this legal protection still may not keep someone from trying to discriminate against you in this way.

Unknown or Unforeseeable Risks:
The researchers will let you know about any significant new findings (such as additional risks or discomforts) that might make you change your mind about participating in the study. Perampanel involves risks that are currently unknown or unforeseeable.

WHAT ARE THE COSTS?
Study drug will be provided by the sponsor at no cost to you. You will not be charged for any study visits, tests, or procedures.

You and your insurance plan will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. This includes:

- The extra blood draws in this study done at every study visit
- The hospital visit for the laboratory sessions

WILL I BE PAID TO PARTICIPATE IN THE STUDY?

You will receive $50 for the completed initial screening, $15 for your first outpatient visit, and $25 for your second and third outpatient visit where you will receive your take home study medication (3 visits total), and $315 for each test day in which you participate (3 sessions). If there is need to do repeat labwork to confirm screening lab results, you will receive an additional $10 for a total of (1) extra payment. If you are asked to return to the clinic for an additional visit between days 7-10 post-lab sessions to check your medication levels, you will earn $20. You may also earn up to an additional $90 over the course of the study depending on how you score on one of the tasks during the lab sessions (maximum $30/session). Since there are three separate test days, the total amount you could earn during this study is $1200. This payment is for the time and effort related to study assessments and procedures. All payments will be made in cash or check.

Total payments within one calendar year that exceed $600 will require the University to report these payments annually to the IRS and you. This may require you to claim the payment you receive for participation in this study as taxable income. VCU is required by federal law to collect your social security number. Your social security number will be kept confidential and will only be used to process payment.

There are no plans to provide compensation for disability or other losses occurring over the long term or if an injury becomes apparent after your participation in the study has ended. However, by agreeing to participate in this research study, you are not waiving or giving up any legal rights to seek compensation.

If you are injured by, or become ill, from participating in this study, please contact your study doctor immediately. Medical treatment is available at the Virginia Commonwealth University Health System (VCU Health). Your study doctor will arrange for short-term emergency care at the VCU Health or for a referral if it is needed.

Fees for such treatment may be billed to you or to appropriate third party insurance. Your health insurance company may or may not pay for treatment of injuries or illness as a result of your participation in this study. To help avoid research-related injury or illness, it is very important to follow all study directions.

Please be aware that the investigative team and the University may receive money for the conduct of this study. There are no plans to share any money or profits with you if the use of your sample(s) results in inventions or discoveries that have commercial value.

CAN I STOP BEING IN THE STUDY?

You can stop being in this research study at any time. Leaving the study will not affect your medical care, employment status, or academic standing at VCU or VCU Health. Tell the study staff if you are thinking about stopping or decide to stop.

If you leave the study before the final regularly scheduled visit, you may be asked to taper your medication schedule and have an additional follow-up visit if determined necessary by the study PI. Stopping the study drug early without tapering may result in withdrawal or side effects including an increased risk for seizure.

Your participation in this study may be stopped at any time by the study doctor without your consent. The reasons might include:

- the study doctor thinks it necessary for your health or safety
- you are found to not be eligible for the study
- the sponsor has stopped the study
- you have not followed study instructions
- administrative reasons require your withdrawal

If you withdraw from the study, data that has already been collected about you will remain part of the study database and may not be removed.

HOW WILL INFORMATION ABOUT ME BE PROTECTED?

Participation in research may involve a loss of privacy. Your research records will be kept as confidential as possible. Only a code number will identify your research records. The code number will not be based on any information that could be used to identify you (for example, social security number, initials, birth date, etc.). The master list linking names to code numbers will be kept separately from the research data.

All research information will be secured in locked files. Your identity will not be revealed in any reports or publications resulting from this study. Only authorized people will have access to the information gathered in this study. Authorized persons may include regulatory agencies such as the Food and Drug Administration (FDA), NIAAA, as well as members of the VCU IRB (when conducting reviews). Therefore, if you participate in this study, a medical record will be created if you do not already have one. Notes from your visits, procedures, and laboratory tests will be included in this record. In addition to the research team, and the VCU Health Staff who provide clinical services, other researchers may be granted approval to access this information in the future. Federal laws and regulation that protect privacy of medical records will apply to your health record. Your name, address and social security number will be provided to the VCU Business Office in order to process your payment for participating in this study. VCU will also provide you with an IRS 1099 form reporting the amount of money paid to you.

It will be noted in your protected electronic health record at VCU Health that you are in this study. Information about the study will be included in the record. This information is protected just as any of your other health records are protected.
In general, we will not give you any individual results from the study. If we find something of medical importance to you, we will inform you, although we expect that this will be a very rare occurrence.

Your blood sample will also be tested for hepatitis. Virginia state law requires the study staff to report the results of positive tests for hepatitis to a local health agency.

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.

HOW WILL MY RESEARCH RESULTS BE USED?

You and your physician will be informed of any important discoveries made during this study which may affect you, your condition, or your willingness to participate in this study. If suicidal intent or other major clinical findings are detected during clinical or research assessments, the study physician will be notified immediately.

You may be not allowed to leave until deemed safe or until you are judged to no longer be considered a threat to yourself or to others.

Any identifying information will be kept in locked files. These records will be kept indefinitely. Only research staff will have access to your files. If results of this study are reported in medical journals or at meetings, you will not be identified by name, by recognizable photograph, or by any other means without your specific consent. Your medical records will be maintained according to VCU Health requirements. However, there is a possibility that the Food and Drug Administration may inspect the records.

We will use some of the blood we draw to obtain DNA which we will study to try to identify genes that might be related to your diagnosis or behavior, or genes important to determining brain structure or function. Therefore, your sample or cell line may be used for research purposes unrelated to the study for which it was collected.

We may also study other genes, and will store the DNA for study in the future. At some point we may create permanent cell lines from cells in your blood, to provide a continuous supply of DNA. Also, your sample and/or cell line may be shared with investigators not associated with this project. If so, your identity will not be shared with these researchers**.** You will not receive any payment if your cells are used for permanent cell lines, even if they are supplied to other researchers commercially.

DNA will be obtained from your blood and used for genetic testing. Your DNA will be kept in the laboratory indefinitely (as long as possible) and may be used for many laboratory tests. The blood samples and the DNA will be labeled with a number only. Your name will not be attached to the samples in the laboratory. This measure is taken to protect your confidentiality, as explained in more detail below.

DNA PROTECTION OF PRIVACY

The use of your blood for genetic testing raises special issues of confidentiality, because it is possible that information about your genes could be used against you if this information became known to the wrong people. For example, an insurance company could try denying benefits, or an employer could try to deny employment, if it became known that you carried certain genes. To reduce this possibility, the following specific measures will be taken to protect your confidentiality:

1) The genetic testing of your DNA is for research purposes only. No results of genetic testing from this study will appear in your medical record.

2) Genetic test results will not be made available to you, your doctors, your other clinicians or any other clinical staff. We do not expect that the genetic testing done in this study to become part of treatment for alcohol problems at any time during this study or in the next few years to come.

3) To protect the confidentiality of computer records related to you or your family members, information that could be used to identify you individually will be stored only on a protected VCU server.

Thus, even if a "hacker" breaks into the laboratory computer system, there will be no information stored there that can identify you as an individual. All paper records containing your identity, will be stored in locked cabinets, and will be available only to authorized research staff.

4) Information about your genes will be stored in the in the Psychiatric Genetics Lab, located at the address below, using procedures described above to protect your confidentiality, unless information has become completely stripped of information that could identify you.

Virginia Commonwealth University
Virginia Institute for Psychiatric and Behavioral Genetics
Biotech 1, 800 E Leigh St.
Suite100, Rm 1-110
Richmond, VA 23298-0424 USA

5) There is a federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans, and most employers, except those with less than 15 employees, to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

While all efforts are aimed at protecting and guarding your blood and/or DNA samples, there remains the possibility that VCU could be compelled by a court or a law enforcement agency to produce such samples. In more than six years of collecting DNA samples at VA Connecticut, where similar studies were previously run, in which many hundreds of samples have been collected, no outside agency has ever tried to gain access to any research participant's blood or DNA samples. Dr. Arias believes that the risk of this happening to your sample is extremely small.

Certificate of Confidentiality Statement
To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. This certificate will offer the protections described here. A Certificate of Confidentiality helps the researchers keep your information private. For example, researchers can refuse to give out your information in a court case. Researchers may have to give your information if the study is audited, or if the information is required by the Food and Drug Administration (FDA).

The researchers may share information about you or your participation in the research project without your consent if there is voluntary disclosure of harm to self or others, or abuse towards others.

The researchers cannot prevent you or others, for example a member of your family, from sharing information about you or your involvement in this research. If you give an insurer, employer, or other person permission to receive research information, then the researchers may not use the Certificate to withhold that information.

OPTIONAL STORAGE FOR FUTURE RESEARCH STUDIES
To advance science, it is helpful for researchers to share information. They do this by putting data or samples into one or more scientific databases (called registries or repositories), where it is stored along with information from other studies. Researchers can then study the information in other ways and combine information from many studies to learn even more about health and disease.

As part of this study, we would like to keep the information and/or samples that you provide, along with your de-identified data sets in a registry/repository to be available for other research studies in the future. No identifiable personal information is kept in the de-identified data sets. We keep data that has identifying

information such as name or age secured per institutional policy. Your information and samples would be stored at VCU by Dr. Albert Arias and could be used for other research studies about any topic. In the future, identifiers might be removed from the information and samples you provide in this study, and after that removal, the information/samples could be used for other research studies by this study team or another researcher without asking you for additional consent. Your data/samples will be protected, but there is always a possibility that information could be accessed by individuals without authorization. There is no limit on the length of time we will store your information/samples.

Your samples, genomic data and/or health information will be stored by VCU in one or more scientific databases, and shared with other researchers. The samples and information will be available for any research question, such as research to understand what causes certain diseases (for example heart disease, cancer, or psychiatric disorders), development of new scientific methods, or the study of where different groups of people may have come from. This information will not be labeled with your name or other information that could be used to easily identify you. However, it is possible that the information, when combined with information from other public sources could be used to identify you, though we believe it is unlikely that this will happen.

Your individual genomic data and health information will be put in a controlled-access database at the National Institutes of Health. This means that only researchers who apply for and get permission to use the information for a specific research project will be able to access the information. Your genomic data and health information will not be labeled with your name or other information that could be used to identify you. However, it is possible that the information from your genome, when combined with information from other public sources could be used to identify you, though we believe it is unlikely that this will happen. Researchers approved to access information in the database will agree not to attempt to identify you.

In the future, if you decide that you don't want to be part of this registry, you can request that your information/samples be removed and destroyed by contacting the PI, Dr. Albert Arias. However, information that has already been shared with other researchers will continue to be used.

In addition, identifiers will only be kept for 5 years following study conclusion. After that time, withdrawal will no longer be an option because the individual specimens will no longer in any way be linked to the person from which they were originally drawn.

Permission to Store Data and/or Samples for Future Research Studies
I agree that my blood, DNA, tissue and other data may be stored and used for future research as described in this document. I understand that by choosing "NO", I will be unable to participate in this study and am opting out.

Please circle your answer and initial:

YES NO Initials _____

HOW WILL MY HEALTH INFORMATION BE USED AND SHARED DURING THIS STUDY?
As part of this research study, we will ask you to share identifiable health information with us and/or permit us to access existing information from your healthcare records. New health information may also be created from

study-related tests, procedures, visits, and/or questionnaires. This type of information is considered "Protected Health Information" that is protected by federal law.

What type of health information will be used or shared with others during this research?
The following types of information may be used for the conduct of this research:

☒ Complete health record
☒ Diagnosis & treatment codes
☒ Discharge summary

☒ History and physical exam
☒ Consultation reports
☒ Progress notes
☒ Laboratory test results
☒ X-ray reports
☒ X-ray films / images
☐ Photographs, videotapes
☐ Complete billing record
☐ Itemized bill
☒ Information about drug or alcohol abuse
☒ Information about Hepatitis B or C tests
☒ Information about mental health
☒ Information about sexually transmitted diseases
☐ Other physical or mental health information (specify):

Who will use or share protected health information about me?
VCU and VCU Health are required by law to protect your identifiable health information. By consenting to this study, you authorize VCU/VCU Health to use and/or share your health information for this research. The health information listed above may be used by and/or shared with the following people and groups to conduct, monitor, and oversee the research:

- Principal Investigator and Research Staff
- Study Sponsor
- Health Care Providers at VCU Health
- Institutional Review Boards
- Government/Health Agencies
- Others as required by law
- Data Coordinators
- Research Collaborators
- Data Safety Monitoring Boards
- NIH

Once your health information has been disclosed to anyone outside of this study, the information may no longer be protected under this authorization.

When will this authorization (permission) to use my protected health information expire?
This authorization will expire when the research study is closed, or there is no need to review, analyze and consider the data generated by the research project, whichever is later.

STATEMENT OF PRIVACY RIGHTS
You may change your mind and revoke (take back) the right to use your protected health information at any time. However, even if you revoke this authorization, the researchers may still use or disclose health information they have already collected about you for this study. If you revoke this Authorization, you may no longer be allowed to participate in the research study. To revoke this Authorization, you must write to the Principal Investigator at the address listed below.

RESEARCH SUBJECTS' RIGHTS
I have read or have had read to me all of the above and I voluntarily consent to participate in this study. The study has been explained to me and my questions have been answered. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me.

I understand that I do not have to take part in this study, and my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss other benefits to which I am entitled. I will receive a signed copy of this consent form.

The results of this study may be published, but my records will not be revealed unless required by law.

In case there are medical problems, a research related injury or complaints, concerns, or pertinent questions about the research at any time, I have been told I can contact

Dr. Albert Arias
Institute for Drug and Alcohol Studies
203 E Cary St, Richmond, VA 23298
860-558-2273 or (804) 828-5793
Email: albert.arias@vcuhealth.org

If you have general questions about your rights as a participant in this or any other research, or if you wish to discuss problems, concerns or questions, to obtain information, or to offer input about research, you may contact:

Virginia Commonwealth University Office of Research
800 East Leigh Street, Suite 3000
Box 980568 Richmond, VA 23298
Telephone:(804)827-2157; https://research.vcu.edu/human_research/volunteers.htm

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

Conflict of Interest Disclosure: A Conflict of interest occurs when a member of the research team including the principal investigator, sub-investigator(s), and/or study coordinator(s), has a significant financial interest or other personal involvement that may compromise, or have the appearance of compromising, his or her professional judgment or integrity while conducting this study.

All members of the local research team who are conducting this study are required to report any potential Conflicts of Interest. Dr. Arias have no reported conflicts relevant to the conduct of this study.

You may speak with Dr. Arias at any time should you have questions regarding these investigator interests. Virginia Commonwealth University has no financial interest in the study drug (perampanel) being used in this research study. You may also choose to seek the opinion of another doctor not related with Virginia Commonwealth University before enrolling in this research study. More importantly, you are not under any obligation to participate in this research study and you may withdraw at any time.

STATEMENT OF CONSENT

I have been provided with an opportunity to read this consent form carefully. All of the questions that I wish to raise concerning this study have been answered. By signing this consent form, I have not waived any of the legal rights or benefits to which I otherwise would be entitled. My signature indicates that I freely consent to participate in this research study. I will receive a copy of the consent form for my records.

Signature Block for Enrolling Adult Participants

_____	
Adult Participant Name (Printed)	
_____	_____
Adult Participant's Signature	Date
_____	
Name of Person Conducting Consent Discussion (Printed)	
_____	_____
Signature of Person Conducting Consent Discussion	Date
_____	_____
Principal Investigator Signature (if different from above)	Date