Title: Zonisamide Treatment of Alcohol Use Disorder: an Evaluation of Efficacy and Mechanism of Action

NCT #: NCT02900352

Document date: July 10, 2020

Document Type: Informed Consent

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE: Zonisamide Treatment Of Alcohol Use Disorder: An Evaluation Of Efficacy And Mechanism Of Action

VCU IRB NO: HM20014185

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SPONSOR: **National Institute on Alcohol Abuse and Alcoholism (NIAAA)**

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. If any information contained in this consent form is not clear, please ask the study doctor or study staff to explain any information that you do not fully understand. 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 to not 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

The purpose of this research study is to test the safety, tolerability, and effectiveness of Zonisamide and to learn whether this drug will help people cut down or stop their excessive alcohol drinking. Having an alcohol problem is common, with almost a third of our country having such a problem at one point in their life, and it can cause many health risks. Excessive alcohol intake is amongst the leading preventable causes of death in the USA. Better treatments are needed to help people cut down their drinking. You are being asked to participate in this study because you would like to cut down or stop drinking.

Zonisamide has been approved by the U.S. Food and Drug Administration (FDA) for the treatment of seizures, but has not yet been approved for treatment of Alcohol Use Disorder (AUD). For this reason, it is considered an investigational drug. In this study, Zonisamide will be compared to placebo (sugar pill). You will be randomly assigned (like the flip of a coin) to either the Zonisamide (Group A) or placebo (Group B). You will have a 50% chance (one in two) of being in either group A or group B. In this study, neither you nor your study doctor will know which group you are in nor which medication you will be receiving. However, a member of the research staff can get this information if needed for emergency purposes. You will take the study medication once a day.

You may not personally be helped by taking part in this study. However, if the study medication (zonisamide) is found to reduce drinking, your participation may lead to a new treatment for patients with alcohol dependence.

Before starting the study, you may be referred to an alcohol detoxification program to stop drinking under medical supervision if clinically necessary. Also you should NOT be taking any other alcohol treatment medications such as disulfiram, acamprosate or naltrexone at the time of study enrollment.

You will be asked to do the following things:

1. Visit VCU Institute for Drug and Alcohol Studies (IDAS) a minimum of 12 times for study visits, however the PI may discuss with you that more visits may be needed pending your labwork or ability to complete all tasks at individual visits or your personal medication titration schedule.
2. Have your blood drawn (total of 10 tablespoons). From time to time, repeat bloodwork may be needed in order to monitor your health, so you may be asked to have additional blood drawn if determined necessary by the study doctor. You may also be asked to give a saliva sample.
3. Females will take pregnancy tests
4. Keep a drinking diary at home
5. Take cognitive/behavioral assessments and questionnaires about personal and family history of alcohol use, personal psychiatric questionnaires, life stressors, substance use history.
6. You may be asked to participate in, and complete Stress lab sessions where you will do a mental imagery technique which will examine your response to stress and have saliva samples collected to assess for the presence of hormone that are related to stress.
7. Have your medical history collected and a physical exam performed.
8. Laboratory testing (see Consent Addendum page for testing schedule)
9. Give permission for the researchers to collect information about health history, including psychiatric history from your medical records.
10. Have genetic testing done and give permission to the researchers to your data and/or samples for future research studies about the cause of alcohol addiction or studies related to understanding which populations respond better in various treatments

If determined eligible after screening, your participation in this study would last up to 4-5 months of consecutive visits and 1 follow-up visit approximately 3 months later. Approximately 160 individuals will participate in this 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.*

Please note that collecting a DNA sample is a necessary part of this study and if you do not wish to have your DNA sample collected, then you will not be able to proceed with the main portion of the study.

If you decide not to enter this study, you can receive the standard medical practice that you would receive even if you were not in the study. *We will provide you with information for treatment centers,* or *you may be referred for either inpatient or outpatient services under the guidance and*

recommendation of the study doctor. The study doctor will discuss with you these options and other FDA approved medications available for treating your condition. You do not have to participate in this study to be treated for substance abuse.

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.

Most Common Risks and Discomforts	**Benefits to You and Others**
Zonisamide Risks: 1. There is a risk that study drug may not be as good as the usual approach for your alcohol problem. 2. There is also a risk that you could have side effects from taking study drug. Below are some of the most common side effects: • Numbness or tingling • Upset stomach • Tiredness 3.There may be some risks to you that the study doctors do not know about yet, so we will let you know of any new findings. 4. Procedural Risks: • Blood draws may cause pain, bleeding, and/or bruising. You may faint and could develop an infection at the site where blood is drawn. • The study questionnaires ask personal questions that are sensitive in nature and may make you feel uncomfortable. 5. Confidentiality 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.	1. There is some evidence that zonisamide is effective in treating alcohol problems. However, it is unlikely that it will work with everyone, and we cannot promise that it will help you. This study may help the study doctors learn things that may help other people in the future. 2. There is no guarantee that you will receive any medical benefits from being in this study. However possible benefits include reducing or stopping your drinking. We hope the information learned from this study will provide more information about alcohol problems.

In general, we will not give you any individual results from the study. However, if we find something of medical importance to you, we will inform you, although we expect this to be a rare occurrence. Once the study has ended, you may contact us if you want us to send you a summary of all the results of the study and what they mean.

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.

WHAT WILL HAPPEN IF I PARTICIPATE IN THE STUDY?

Visit 1 (Screening visit):

We will ask you some brief questions about your medical, mental health, alcohol and drug use history, demographic information (personal and family history of alcoholism, marital status, education, occupation, and ancestry) to determine if you qualify for the study. A physical exam will be performed. We will ask detailed questions about your drinking habits and patterns of use. You will be expected to have a Breath Alcohol Level under the legal limit (.08) at each visit, or else your visit may be rescheduled and you may not receive compensation that day.

You will be asked to provide a locator's (a person who we can contact if our efforts to reach you are unsuccessful) information. We will also collect information from your medical records about your personal health history, including psychiatric history. Medical record information will be collected during your participation in the study and for 5 years after you finish taking the study drug.

The following laboratory tests will be done:

- Urine sample for drug screen
- Females will have a urine pregnancy test done
- Blood drawn (2 tablespoons)
- ETG/ETS test, an indicator that a person has consumed an alcohol beverage
- PEth test, detection of alcohol use over the previous 3-4 weeks
- GGTP test, checks the health of your liver
- DNA, 2 tablespoons of blood or saliva 2 mL collect by spit into a tube

Visit 2 (Baseline and Stress Lab 1):

This visit will take place after Visit 1. The first stress reactivity lab session occurs after screening but prior to starting medication. The second stress reactivity lab session occurs after being on the target dose for at least 2 weeks. You will complete a packet of questionnaires and research nurse will train you on how to record your daily alcohol consumption, medication administration, and other daily variables such as daily mood and alcohol use and attitudes toward alcohol use using an automatic IVR (Interactive Voice Response) system. At this visit, you will also complete a Stress Lab and the session last up to 4-6 hours.

You will be given the study drug and instruction on how to take the study drug. You will be randomly assigned (like the flip of a coin) to either the Zonisamide (Group A) or placebo (Group B). You will have a 50% chance (one in two) of being in either group A or group B. In this study, neither you nor the study doctor will know which study drug you are receiving. This information is available to the study doctor if needed in an emergency. This is called blinding, and it is done so that a fair evaluation of results may be made.

You will have Medical Management (MM) counseling, an orientation intervention on AUD symptoms, advise on how to reduce or stop drinking, and instructed on the importance of daily medication compliance. You will be given a medication bottle at each visit that tells you how you should take your study medication. We will review with you how you should take your study medication at each visit. You should keep all medication bottles out of the reach of children.

Before the start of Stress Lab, your impulsivity (a tendency to act on a whim, displaying behavior characterized by little or no forethought, reflection, or consideration of the consequences) risk-taking will be measured with BART and BIS assessments (computer program and paper questionnaires). You will do a mental imagery technique, which will examine your responses to stress. Research staff will assist you in developing six scripts 5-minute long that are read and audiotaped in preparation for you to listen to them and have your response recorded in another phase of the stress lab. Each audiotape will consist of a script that is based off your initial verbal responses during the script development phase and these scripts will be read by the staff. The scripts topics are about 2-very stressful events in your life, 2-neutral events, and 2-pleasant alcohol-related events. You will sit in an isolation booth and listen to the audiotapes while your psychological measures are recorded. We will not tell you in advance the order in which the script will be played to you. You will have ten minutes relaxing between each listening session. Throughout the imagery sessions you will repeatedly complete computer tasks and questionnaires that ask about how you are feeling after completing the session and your current craving for alcohol. At several points, you will be given a cotton swab to put in your mouth for a few minutes so that we can collect a sample of your saliva to look for hormones that are related to stress. Between weeks, 8-16 of being on the study drug this lab session is repeated.

Medication Dosing:

During the course of the study, you will be asked to take your study medication once a day. You will be started on one pill daily (100 mg or placebo), then increased over 7 weeks to a target dose of five pills daily (500 mg total or placebo). If needed, the dose may be adjusted within the range recommended by the manufacturer in order to improve your response and reduce side effects. You will continue on the study medication for another 9 weeks (after you get to the full dose). If you and the study doctor feel that you would benefit from an additional pill each day (600 mg/day) you will have the option to increase your dose after two weeks on 5 pills (500 mg OR placebo) daily. At the end of 16 weeks, we will help you gradually reduce the medication over a two-week period and you will return for a visit at week 18. It is important to decrease the amount of medication you are taking gradually, and not just stop the drug suddenly, because this could cause withdrawal symptoms.

Treatment visits (*weeks 1, 3, 5, 7, 9, 11, 13 and 16*):

At these visits, the study nurse will repeat the MM counseling. You will be interviewed about the belief of your treatment completing the MED-Q (Medication Questionnaire) and complete other questionnaires assessing your mood, life events, alcohol use and cravings, and response to study medications.

The following laboratory tests will be done:

- Breathalyzer test, which involves blowing into a tube to estimate your blood alcohol level
- Urine sample for drug screen
- Blood drawn (2 tablespoons) at initial screening, then again at weeks 5, 9 and 16, and additional labwork will be drawn if necessary (for example, if your labwork shows a concerning result or lab error and requires a redraw for verification)
- Females will have a urine pregnancy test done
- ETG/ETS test, an indicator that a person has consumed an alcohol beverage
- PEth test, detection of alcohol use over the previous 3-4 weeks
- GGTP test, check on the health of your liver

Treatment visits (*weeks 2, 4, 6, 7, 8 10, 12, 15 and 17*):

At these weeks, you will be asked to complete daily phone calls to the IVR system that will briefly ask you a few questions about your drinking and feelings about drinking. You will be performing daily IVR assessments throughout the study and unless otherwise directed you will not attend any clinic visits during these weeks.

Stress lab session 2:

This "stress lab" will take place after you have reached the target dose of the medication in the last 8 weeks of the study (between weeks 8 and 16). The same procedures you had in Session 1 will be repeated in this session. We will not tell you in advance the order in which the script will be played to you. This session will last about 3-4 hours.

We ask that you tell the study staff of any appointments you need to miss or change, or if your contact information (e.g., phone number) changes while you are in the study. There will be times during the study when the research staff will need to contact you by telephone (for example, to reschedule an appointment).

Follow-up (3-month after treatment):

The follow-up visit will be scheduled with a research staff member following the completion of the 16-weeks active phase of the study. Blood (2 tablespoons) will be drawn at this visit. At this visit, you will also be asked to complete many of the screening forms you completed during your baseline visit, a urine drug screen, vital signs, weight and a breathalyzer test

During the study, your visits will include regularly scheduled sessions (approximately 60-90 minutes) to monitor your status over the 16 weeks of study medication use. During these sessions, we will review how the study is going for you, complete assessments, and address any questions you may have. The initial weekly sessions will begin within 1 week after your baseline visit. We may make a voice recording of some of your weekly sessions in order to make sure that important topics are being covered by the Research Staff.

WHAT RISKS AND DISCOMFORTS COULD I EXPERIENCE FROM BEING IN THE STUDY?

Zonisamide:

The most common adverse events are tiredness, decreased appetite, dizziness, headache, nausea, irritability, a sensation of numbness and tingling, or prickling in parts of the body, a distorted sense of taste, difficulty concentrating or remembering, vomiting, trouble sleeping, and kidney stones. We recommend you drink plenty of water while taking Zonisamide. This may reduce the risk of kidney stones. Some potentially serious but unlikely side effects include blood and immune system reactions such as "aplastic anemia" (this is a condition where bone marrow does not make enough new blood cells), and severe allergic or toxic reactions, which could result in death. Depression and mood problems have also been reported with Zonisamide treatment. Some patients have had suicidal thoughts or actions.

You should not take Zonisamide if you have a history of allergic reaction to sulfonamide medications (i.e., sulfa drugs), penicillin, or a serious reaction to any other medication.

Sometimes Zonisamide may cause a condition known as "metabolic acidosis" in some patients, which is a dangerous change in the acid and base balance of the blood. Generally, Zonisamide will cause this

condition early in treatment if it is going to occur at all, but it may develop at any time during treatment. Symptoms of metabolic acidosis are breathing fast (hyperventilation), fatigue, and loss of appetite. More severe symptoms and risks of this condition include an irregular heartbeat, unconsciousness, and death.

Due to the possibility of dizziness or drowsiness, you must be cautious when operating a vehicle or heavy equipment while in this study, until you have experience-taking Zonisamide, and know how your body will react.

You should discuss taking any medication other than the study medication with the research staff. This includes prescription drugs and over-the-counter medications such as cough and cold remedies, pain relievers, and antacids.

There is a risk that your condition may not improve or may worsen because the study medication is not effective for you.

Blood Drawing:
The blood draws will involve the insertion of a small needle into your arm. Blood drawing can result in pain, bruising, and rarely infection, blood clots, dizziness and possibly fainting. You should not donate blood during the study or for one month after the study.

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. This study will ask you questions, interview you, and ask you to complete questionnaires about personal topics that are sensitive in nature and might be embarrassing to talk about. You may refuse to answer any question that makes you feel uncomfortable. The multiple imagery sessions will require you to talk about and/or imagine stressful, traumatic, and alcohol related events. These procedures are expected to cause a moderate degree of anxiety, psychological discomfort, and alcohol craving. Clinically trained research staff will guide you through relaxation techniques if your symptoms become too severe. If necessary, you may be referred for further evaluation and/or treatment.

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:
Zonisamide involves risks that are currently unknown or unforeseeable. 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.

Reproductive Risks:

As the study procedures might injure an unborn child, pregnant women may not participate. Women who might become pregnant should use a medically accepted form of birth control such as total abstinence, birth control pills, an IUD, diaphragm, progesterone injections or implants, or condoms plus a spermicide. Methods of birth control other than total abstinence are not 100% effective, and should a women become pregnant there is a risk of injury to an unborn child. For similar reasons, women who are nursing an infant may not participate.

WHAT ARE THE COSTS OF BEING IN THE STUDY?

There are no costs for participating in this study other than the time you will spend on the study visits. There will be no charge for care received as part of your participation in this study.

WILL I BE PAID TO PARTICIPATE IN THE STUDY?

You can earn up to $1110 for your participation during the entire study. This payment is for the time and effort associated with study assessments and procedures outlined are in Table A below. If you do not have a cell phone to complete the calls study staff will discuss with you options to help you complete the required phone calls during the study. If a study phone is made available to you, it is solely for study-related calls, and the phone must be returned when you are finished. Payment for your participation will be given in the form of cash, check, gift card or clincard at the time of your participation. You will be responsible for transportation to each study visit. In the event that safe transportation is needed for the return trip, please notify study staff and we will discuss available options with you to help you coordinate safe transport.

Total payments within one calendar year that exceed $600 will require the University to annually report these payments to the IRS and you. This may require you to claim the compensation 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.

Please be aware that the investigators team and the University may receive money for the conduct of this study

Table A: Visit and payment overview

Visit title	VISIT #	Weeks of completed medication	Payment ($)
Screening	1		50
Baseline	2	0	65
Weekly treatment visit	3	1	25
Biweekly treatment visit	4	3	40
Biweekly treatment visit	5	5	40
Biweekly treatment visit TARGET DOSE achieved (500mg)	6	7	40
Biweekly treatment visit- **midpoint assessments**. Subjects eligible to	7	9	45

go to 600mg daily.			
Biweekly treatment visit	8	11	40
Biweekly treatment visit	9	13	40
Endpoint visit	10	16	80
Two weeks post endpoint visit follow up (end of medication taper)	11		15
3 month follow up visit	12		30
Total	**12**		**510**
Additional compensation			
Stress script session			40
Stress lab 1			100
Stress lab 2			100
Stress Lab Computer tasks			Up to 40 (up to $20 per session)
IVR phone calls			Up to 320 ($2 per completed phone call plus $6 for each week where 6 or more calls are completed (up to $20/week for 16 weeks))
Maximum Total compensation for all visits, labs, and phone calls			**1110**

WHAT HAPPENS IF I AM INJURED OR BECOME SICK BECAUSE I TOOK PART IN THE STUDY?

If you are injured or become ill as a direct result of your participation in this research study, you should contact the study doctor immediately. Medical treatment is available at VCU Health System. Your study doctor will arrange for short-term emergency care at VCU Health System 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's very important to follow all study directions.

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, we ask that you contact the PI and complete an Early Termination Form and you will be asked to taper the medication. Stopping the study drug early may result in an increased risk for seizures.

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

- the study doctor thinks it necessary for your health or safety
- You have not followed study instructions
- The sponsor has stopped the study or
- Administrative reasons that require your withdrawal
- Another provider requiring that you take a contraindicated concomitant medication

If you wish to discontinue the study medication for any reason, either by your own decision or the decision of the study team, you may be given the option to complete a few additional visits. Depending on where you are in the study, these visits may be necessary to help you safely taper off the medication.

HOW WILL INFORMATION ABOUT ME BE PROTECTED?

VCU and the VCU Health System have established secure research databases and computer systems to store information and to help with monitoring and oversight of research. Your information may be kept in these databases but are only accessible to individuals working on this study or authorized individuals who have access for specific research related tasks.

Identifiable information in these databases are not released outside VCU unless stated in this consent or required by law. Although results of this research may be presented at meetings or in publications, identifiable personal information about participants will not be disclosed.

Personal information about you might be shared with or copied by authorized representatives from the following organizations for the purposes of managing, monitoring and overseeing this study:

- The study Sponsor, representatives of the sponsor and other collaborating organizations
- Representatives of VCU and the VCU Health System
- Officials of the Department of Health and Human Services or the Federal Food and Drug Administration

This study is a clinical trial and uses the investigational pharmacy at VCU Health, because of this it may be necessary to place a note in your electronic health record at VCU Health if required by their guidelines. This information is protected just as any of your other health records are protected.

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 Website will include a summary of the results. You can search this Web site at anytime.

If you tell us that you may hurt yourself or someone else, the law says that we must let people in authority know.

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.

Future Research Studies
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.

Certificate of Confidentiality
To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

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

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

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under the following circumstances: We will disclose this information in the event of a severe adverse event wherein knowledge of the identity of the study drug and your participation is necessary for effective emergency treatment of the event or if there is concern for potential harm to yourself or others.

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 NIH
- Health Care Providers at VCU Health
- Data Coordinators
- Institutional Review Boards
- Research Collaborators
- Government/Health Agencies
- Data Safety Monitoring Boards
- Others as Required by Law

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.

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 deidentified data sets in a registry/repository to be available for other research studies in the future. No identifiable personal information is kept in the deidentified data sets. We keep raw data that has identifying factors such as name or age and this is kept for 5 years, and is kept 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. 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.

Genetic studies (DNA sample):

The use of your blood or saliva for genetic testing raises special issues of confidentiality, because it is conceivable 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.

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 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 only be stored using procedures described above to protect your confidentiality, unless information has become completely stripped of information that could identify you.

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, 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.

Permission to Store Data and/or Samples for Future Research Studies

Please circle your answer and initial: I agree that my blood, DNA, tissue, and other data may be stored and used for future research as described above.

Initials:_____YES NO

WHO SHOULD I CONTACT IF I HAVE QUESTIONS ABOUT THE STUDY?
The investigators of this study will be glad to answer any further questions at any time.
If you have any questions, complaints, or concerns about your participation in this research, 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, you may contact:

Office of Research
Virginia Commonwealth University
800 East Leigh Street, Suite 3000
Box 980568
Richmond, VA 23298
Telephone: (804) 827-2157
Email: orsp@vcu.edu

Contact this number for general questions, concerns, or complaints about research. You may also call this number if you cannot reach the research team or if you wish to talk to someone else. General information about participation in research studies can also be found at http://www.research.vcu.edu/irb/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.

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

CONSENT FORM ADDENDUM

1. PARTICIPANT EXAMPLE TAKE-HOME SCHEDULE

This calendar is an example only and may be modified at any time depending on which parts of the study you participate in and the need for labwork or other participation needs as determined by the PI.

Week	Brief description
Screening Clinic Visit	Consent forms, Screening forms, Labwork/blood draw
Baseline Clinic Visit (within 3 weeks of Screening) clinic visit	Baseline Assessment forms, Labwork/blood draw as needed, Begin Medication/daily IVR
1 (1 week from Baseline) clinic visit	Assessment forms Labwork as needed
2	Visit – Titration phase (medication dosage change) phone call: no In-Person Visit
3 clinic visit	Visit - Assessment forms Labwork as needed
4	Phone call: No In-Person Visit
5 clinic visit	Visit – Assessment forms, Labwork/blood draw as needed
6	Phone call: No In-Person Visit
7 clinic visit	Visit - Assessment forms Labwork as needed
8	Phone call: No In-Person Visit
9 clinic visit	Visit – Assessment forms, Labwork/blood draw as needed
10	Phone call: No In-Person Visit
11 clinic visit	Visit - Assessment forms Labwork as needed
12	Phone call: No In-Person Visit
13 clinic visit	Visit – Assessment forms, Labwork/blood draw as needed
14	Phone call: No In-Person Visit
15	Phone call: No In-Person Visit
16 clinic visit	Visit –Endpoint – Endpoint Assessment forms, Labwork/blood draw as needed
17 titration down	Titration Down Phase (medication dosage decrease) Phone call: No In-Person Visit
18 titration down – clinic visit	Visit - Titration Down Phase (medication dosage decrease), Assessment forms Labwork
28 clinic visit	Follow up visit Follow-up Assessment forms Labwork/blood draw as needed