Official title: N-acetylcysteine Treatment of Alcohol Use Disorder in Veterans with TBI

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Department of Veterans Affairs	**INFORMED CONSENT FORM**
Subject Name:	**Date:**
Sponsor: Department of Defense/ Institute of Translational Neuroscience	
Title of Study: N-ACETYLCYSTEINE TREATMENT OF ALCOHOL USE DISORDER IN VETERANS WITH TBI	
Principal Investigator: Steven L. Batki, MD	**San Francisco VAMC**

CONSENT TO PARTICIPATE IN RESEARCH

This is a medical research study funded by the Department of Defense via the Institute of Translational Neuroscience. The principal investigator is Steven L. Batki, MD from the San Francisco VA Medical Center and UCSF Department of Psychiatry. The other researcher is David Pennington, PhD from the Addiction Research Program at the San Francisco VA Medical Center and UCSF Department of Psychiatry. One of the study staff, supervised by these researchers, will explain the study to you.

1. What is an Informed Consent?

Medical research studies include only people who choose to take part. You are being asked to be in a research study. The purpose of this form is to give you information about the study. Signing it will give your permission to take part in the study. The form describes the purpose, procedures, benefits, risks, discomforts and precautions of the study. You should take part in the study only if you want to. You may decide to not join the study. If you start the study, you may leave it at any time. There is no penalty for leaving and you will not lose any benefits to which you are otherwise entitled. You may decide to not join the study without penalty. Some risks of this study are known. Not all possible risks are known.

Please read this form carefully; you can take as much time as you need. This consent form may contain words you do not understand. Please ask the study doctor or the study staff to explain words or procedures that you do not understand. Please ask as many questions as you need to. The study staff or study doctor can explain anything you do not understand. You should not sign this form if your questions have not been answered to your satisfaction.

You will be given a copy of this form to take home. You may want to talk with family or friends before deciding if you will participate in this study. The decision to join the study is entirely yours to make; participating is strictly voluntary

2. Why am I being asked to take part in this study?

You are being invited to take part in this research study because you have a traumatic brain injury (TBI) and because you use alcohol in amounts that may pose a risk to your health. You have indicated a desire to stop drinking or reduce the amount of alcohol you drink with a possible long term goal to stop.

3. Why is this study being done?

The purpose of this study is to discover how a naturally occurring amino acid, n-acetylcysteine, affects a person's use of alcohol and their TBI symptoms. N-acetylcysteine (NAC) is a compound that may have the potential to regulate brain molecules associated with impulse control but this is not yet known.

NAC has been shown to help reduce cocaine use, cannabis use, nicotine use, pathological gambling and other habits marked by impulsivity/compulsivity. There is some preliminary evidence that suggests it might help reduce alcohol use, too. Additionally, NAC is a neuroprotective (protects the nerves), anti-inflammatory (reduces inflammation) compound which results in anti-oxidative (protect cells from damage) benefits which may also result in improved neurobiological recovery from traumatic brain injury.

NAC has not been proven safe or helpful by the US Food and Drug Administration (FDA) for your conditions. NAC in the injection form has been approved by the FDA to treat acetaminophen overdose and cystic fibrosis. It is being studied in several other illnesses.

This study is being funded by the Department of Defense and the Institute for Translational Neuroscience at UCSF. The investigators in this study do not have any financial interest in the company that manufactures n-acetylcysteine (NAC).

4. How many people will take part in this study?

About 30 veterans will be enrolled in the study. All participants will receive study capsules (NAC or inactive substance (Placebo). It is important to know that one-half of the study participants will receive the active study capsules (NAC) and the other one-half will receive the inactive study capsules (Placebo). You will be randomly assigned to a group, which means that there is a 50/50 chance that you will receive the active compound (NAC). Once you are assigned a group at the beginning on the study, you will stay in that group for the remainder of the study. Neither you nor your doctor will choose the group you will be in; only the research pharmacist will know to which group you have been assigned. You will have an equal chance (50/50) of being placed in either of the two groups.

- **If you are in group 1 you will be given NAC**.
  - The study will last for 13 weeks.
  - You will be asked to take NAC every day for the 8 week duration of the main phase.
  - You will continue to receive all of your usual treatments for TBI and substance use in addition to NAC.

- **If you are in group 2 you will be given Placebo**.
  - The study will last for 13 weeks.
  - You will be asked to take the placebo every day for the 8 week duration of the main phase.
  - You will continue to receive all of your usual treatments for TBI and substance use in addition to the placebo.

5. Are there some people who should not be in this study?

The study doctor or a member of the study staff will talk with you about the requirements to be in this study. It is important that you are truthful with them about your history. You should not be in this study if you do not meet all the qualifications.

You should not be in this study if:

- You are currently receiving NAC or other medication for alcohol dependence, including disulfiram (Antabuse), naltrexone (Depade, Revia, or Vivitrol), or acamprosate (Campral).
- You are younger than 18 years of age or older than 69 years of age.
- You are already in another alcohol treatment study or study involving a medication as a treatment.
- You have had a previous allergic reaction to n-acetylcysteine.
- For women: If you are pregnant or breast feeding, you will not be able to participate in this study because we do not know how NAC will affect your child.

6. How long will I be in the study?
In total, you could be asked to commit approximately 23 to 33 hours of your time over the course of 12 weeks.

7. What will happen if I take part in this study?
After completing the screening phase, if you are eligible to participate, you will begin the main phase. Over a period of 8 weeks, you will take NAC or Placebo, attend weekly research visits, and receive weekly alcohol counseling.

The study can be divided into the following 3 phases:

- **Screening Phase:** 3-5 visits over approximately 1 week
- **Main Phase:** 8 visits over 8 weeks
- **Follow-up Phase:** 1 visit at week 12, 4 weeks after the end of the Main Phase

a. Screening Phase: 3 visits over approximately 1 week
To see if you are eligible to participate in the study, the following will take place during the Screening Phase. Information will be kept confidential (as detailed later in this Consent Form).

- The study will be discussed with you, and you will be asked to sign this **consent form**.

- First, a **breath alcohol** ("breathalyzer") test will be done. If you have ANY alcohol on your breath as measured by the breathalyzer, you will be asked to wait until you have no alcohol on your breath or complete your visit at another time.
    - You can also be referred to other treatment if you wish.
    - If you are legally intoxicated, you will be offered transportation home.

- You will be asked to provide your **contact information**, names and phone numbers to be called in case you miss a study appointment. Research staff will confirm your personal contact information, as well as that of your alternate contact, before you can continue in the study.

- **Medical History and Physical exam:** A study doctor will take your medical history and review the medications you use. You will also have a physical examination, all procedures similar to those done for regular medical care.

- **Medical chart review:** Your medical chart will be reviewed by the study doctors.

- **Blood drawing (venipuncture):** You will be asked to give a blood sample for routine laboratory tests to check your health. Approximately 3 teaspoons of blood will be drawn by inserting a needle into a vein in your arm for these tests. Blood will be taken for routine medical tests, and for looking at the possible genetic effects on your response to NAC. The results of these tests are for the purpose of this research study only and will be kept strictly confidential.

- **Genetic Testing**: Some of this blood will be used to determine variants of several of your genes that may influence the development of alcohol use disorders. We will look at a specific gene, called rs6465084, that has been associated with the development of alcohol use disorders and investigate their association with NAC treatment if that is the arm of the study to which you are assigned. Since the medical and neuropsychological significance of this genotype is not known at this time, the results will not be given to you. All blood samples will be kept up to 50 years. If you decide later that you do not want your blood samples to be used for future research, you will notify the Principal Investigator and any remaining identifiable samples will be destroyed. If you

do not want your blood sample used for genetic testing, you will indicate so on the last page of this document. Your sample will be stored at a VA, clearly labeled with a numerical code. No personally identifiable information will be linked with this sample in any way. Material from your sample will be sent for specific genetic testing to a genetics laboratory at UCSF's facilities.

- **You will be asked to give a urine sample.** The urine sample will be tested for drug use, including illegal drug use and alcohol.

- **Women only: If you are a woman of child bearing potential, an additional urine sample will be taken for a pregnancy test.** Because the effect of NAC upon a fetus is unknown, the **pregnancy test must be negative** for you to continue in the study. Additionally, you may not be breastfeeding. Pregnancy tests will be done monthly throughout your participation in the study to assure that you are not pregnant.

- You will be evaluated for current and previous **medical and psychiatric diagnoses.**

- You will be asked to report your use of alcohol and other substances (cigarettes, marijuana, cocaine, etc).

- You will be asked to complete **questionnaires about your military experience, education, work**, and other aspects of your life.

- You will also be asked questions about the type, frequency, and intensity of your **TBI** symptoms and about feelings of **anxiety, depression, and suicidal thoughts**.

The procedures and questionnaires listed above will be done over approximately 3 visits of the Screening Phase. Each of the 3 Screening visits takes approximately 1 ½ to 2 hours to complete (total time, approximately 6 ½ to 9 hours total over the 3 days).

b. Main Phase – 8 visits over 8 Weeks *(Titration and Maintenance Periods)*
After the Screening tests have been reviewed by the study doctor, if you continue to meet the eligibility requirements, you will enter the Main Phase of the study. You will be "randomly assigned" to receive NAC or Placebo.

You will be asked to take NAC or Placebo for 8 weeks. The Main Phase is made up of 2 parts:
- Titration Period (1 week) – the number of NAC or Placebo capsules will be gradually increased ("titrated") over the course of the first week.
- Maintenance Period (7 weeks) – the number of NAC or Placebo capsules will remain constant for the next 7 weeks.

b.1 Titration Period (1 week)
The Titration period of the study is one week. This means that every participant will begin taking the study capsules at 1200 mg per day- half of what previous studies have considered the effective dose- for 3 days, and then continued at a dose of 1200 mg orally twice per day (2400 mg per day) for 4 days.

Capsules will not be packaged in child-resistant bottles but in special research bottles. It is important that you follow your study doctor or his/her staff's instructions on when and how to take the capsules.

b.2 Maintenance Period (7 weeks)
Starting at week 2, all participants will take study capsules at a dose of 3600 mg per day. If you experience unwanted side effects, the study doctor can lower the dose in 600 mg increments as needed.

c. Follow-Up Phase – 1 Visit

One month after your last visit of the main phase, you will return for one follow-up visit.

At each weekly visit and the follow-up visit, the following will take place:

- A breathalyzer test will be performed. If your breathalyzer test is above 0.025%, a study physician will assess whether or not you may complete the study visit. You may be asked to wait until your breathalyzer test is lower, or you may be asked to complete your visit at another time. Visits at Weeks 4, 8 and 12 have neurocognitive tests that require that you have no alcohol on your breath. This means that at Weeks 4, 8 and 12 if you have ANY alcohol on your breath as measured by the breathalyzer, you will be asked to wait until you have no alcohol on your breat h or complete your visit at another time.

- In addition to the breathalyzer test, at each study visit you will be examined and asked questions about possible alcohol withdrawal symptoms. If your symptoms are severe enough, the study doctor will examine you further and make a decision about whether you need to go to the emergency room and also whether you need to stop your participation in the study.

- Your blood pressure, pulse, and temperature will be recorded. Your weight will be measured monthly.

- You will be asked how you are feeling and if you have started taking any new medications since your last visit.

- You must return all capsules and bottles whether they are empty, partially filled, or completely filled at each visit. Your unused capsules from the previous visit will be collected and counted and new capsules will be dispensed at every visit.

- During every visit, you will be asked about drinking and substance use, TBI symptoms, mood, and sleep. You will also be asked whether or not you currently feeling suicidal. The number of questionnaires will vary from visit to visit.

- If you are a female of childbearing potential, a urine pregnancy test will be performed on a monthly basis. The test must be negative to continue in the study.

- You will continue to receive all of your usual medicines and treatments for your medical illnesses and TBI. You may also continue all other psychotherapy and counseling for your alcohol use disorder.

- At the week 4, 8, and 12 visits a small sample of blood (about 1 teaspoon total) will be taken and used for routine medical tests to check your health. At the week 12 visit, 5 drops of blood will be collected, using the fingerstick method, to test for drug use.

- The study doctor or research staff will also ask for possible side effects. Your weekly dose of study capsules may be adjusted according to your status.

- You will also meet with a member of the study staff for alcohol counseling called “Medical Management,” to discuss your questions about the medication and your weekly goals with regard to your alcohol treatment. Medical Management is a 8-session, supportive therapy which has

been chosen as the counseling manual for this study. It is designed to increase problem recognition, enhance motivation to change drinking patterns, and further engage you in alcohol treatment. Additionally, it serves to promote medication adherence and track any negative side effects you may experience in this study. A Medical Management session lasts about 15 to 30 minutes and will be administered by a medical professional.

When you are finished taking the study medication: You may continue any treatments you are currently receiving, as well as resume any treatments you are being asked to discontinue due to study requirements.

Study location: All study procedures will be done at the San Francisco VA Medical Center.

Table of Study Visits: The table below shows what will happen during your participation in the study.

Time	What you will do
Screening- 3 to 5 visits	• Review consent form with study personnel, ask any questions you may have, and sign the form if you agree to participate. • Provide information about your medical history, current and past medication and treatments, your demographic information, and emergency contacts we can call. • Receive a physical examination, and measurements of your heart rate, blood pressure and body temperature (vitals). • Provide blood (about 3 teaspoons) and urine samples to assess your health. Women will be assessed for birth control and tested for pregnancy. Your urine sample will also be tested for substance use. • Take tests to determine your levels of decision-making, risk-taking, and impulsivity. • Participate in interviews and complete questionnaires about your drug/alcohol use and TBI and other mental health symptoms. • Learn about the study capsules and how to take them on a daily basis, then receive one week's supply of study capsules. • **These visits together should take approximately 6.5 to 9 hours to complete**
Weeks 1, 2, and 3	• Let us know if your medication or other treatments have changed since we last saw you. • Review NAC/Placebo intake and any changes you have noticed in the past week. • Have your breath alcohol concentration and vital signs checked (temperature, heart rate, blood pressure). • Provide a urine sample to be tested for alcohol use. • Provide information about your sense of well-being and drug/alcohol use in the past week. • Participate in a brief alcohol counseling session. • Receive a week's supply of capsules and return all extra capsules from previous week. • **These visits should each take approx. 1 to 1.5 hours to complete.**

Week 4	• Let us know if your medication or other treatments have changed since we last saw you. • Review NAC/Placebo intake and any changes you have noticed in the past week. • Have your breath alcohol concentration and vital signs checked (temperature, heart rate, blood pressure). • Provide a blood sample (about 1 teaspoon) to assess your health. • Provide a urine sample to be tested for substance use. • Provide information about your drug/alcohol use, TBI symptoms, and sense of well-being. • Take tests to determine your levels of decision-making, risk-taking, and impulsivity. • Participate in a brief alcohol counseling session. • Receive a week's supply of capsules and return all extra capsules from previous week. • **This visit should take approx. 3.5 to 5 hours to complete.**
Weeks 5, 6, and 7	• Let us know if your medication or other treatments have changed since we last saw you. • Review NAC/Placebo intake and any changes you have noticed in the past week. • Have your breath alcohol concentration and vital signs checked (temperature, heart rate, blood pressure). • Provide a urine sample to be tested for alcohol use. • Provide information about your sense of well-being and drug/alcohol use in the past week. • Participate in a brief alcohol counseling session. • Receive a week's supply of capsules and return all extra capsules from previous week. • **These visits should each take approx. 1 to 1.5 hours to complete.**
Week 8	• Let us know if your medication or other treatments have changed since we last saw you. • Review NAC/Placebo intake and any changes you have noticed in the past week. • Have your breath alcohol concentration and vital signs checked (temperature, heart rate, blood pressure). • Provide a blood sample (up to 3 teaspoons of blood). • Provide a urine sample to be tested for substance use. • Provide information about your drug/alcohol use, TBI symptoms, and sense of well-being. • Take tests to determine your levels of decision-making, risk-taking, and impulsivity. • Return all extra capsules from previous week. • **This visit should take approx. 3.5 to 5 hours to complete.**
Week 12	• Let us know if your medication or other treatments have changed since we last saw you. • Have your breath alcohol concentration and vital signs checked (temperature, heart rate, blood pressure). • Provide a blood sample by blood draw (about 1 teaspoon) to assess your health. Provide 5 drops, using the fingerstick method, to test for drug use. • Provide a urine sample to be tested for substance use. • Provide information about your drug/alcohol use, TBI symptoms, and sense of well-being. • Take tests to determine your levels of decision-making, risk-taking, and impulsivity. • **This visit should take approx. 3.5 to 5 hours to complete.**

8. Can I stop being in the study?

Yes. You can decide to stop participating in the study at any time. Study participation is entirely voluntary. There is no penalty for not participating, and there is no penalty for choosing to leave the study after you decide to participate.

If you decide to leave the study, it is important that you tell the study staff and study doctor. The study doctor will tell you if there are any potential risks of leaving the study, and he or she will explain those risks to you.

If you leave the study completely, you may be asked to return to the clinic for tests so that you can leave the study safely.

You may be withdrawn from the study at any time even if you do not wish to leave. The study physician may decide to withdraw you from the study at any point. You may be withdrawn from the study for any of the following reasons (or other reasons not listed):

- You tell the study doctor you do not want to be in the study.
- It may be harmful for you to stay in the study.
- You need to take or do take a drug or receive medical treatment that is not allowed in the study.
- You do not follow study instructions.
- You become pregnant.
- You are no longer eligible for study participation.
- The sponsor or the FDA stops the study for any reason.

It is important to know that you may be withdrawn from the study for other reasons not listed here. Please ask the study staff or doctor if you have any questions about something you think might result in your withdrawal from the study. If you are withdrawn from the study, you will be asked to complete an end-of-study visit and a final follow-up visit. A physical exam and other tests at this final visit may be done to make sure it is safe for you to leave the study.

Please ask study staff or doctors any questions you have about leaving the study.

9. What are my responsibilities as a study participant?
As a participant in this study, your responsibilities are as follows:

- Following the instructions given to you by the study staff and study doctor.
- Attending all study visits as scheduled.
- Communicating with study staff if you will not be able to attend a study visit as scheduled.
- Reporting any side effects, injuries, or other changes in your health to the study doctor.
- Reporting all medicines, vitamins, recreational drugs, herbal products, supplements, or over-the-counter products you use during the study.
- Storing your study capsules as directed.
- Reporting any lost or stolen study capsules to the study staff as soon as possible.
- Bringing any remaining study capsules and the study capsule containers with you to study visits.
- Speaking with the study doctor if you decide to stop taking the study capsules.
- For women, using contraceptives to prevent pregnancy.

IMPORTANT: We request that you abstain from driving to the VA Medical Center for study visits if you have been drinking. If you do drive and your breath alcohol is above a 0.08, then a clinician will assess your safety before you will be allowed to leave. This is a VA protocol established to ensure your safety.

NEW INFORMATION ABOUT THE STUDY DRUG
If important or new information about the study drug (good or bad) is learned while you are in the study, you will be told. You will be asked for your consent to continue in the study with the new information. You are free to leave the study at any time without penalty.

10. What side effects or other risks can I expect from being in the study?

The study visits and procedures are designed to limit risks to your health and limit your discomfort as much as possible. These procedures closely monitor your safety throughout the study.

You may have side effects while in the study. Everyone taking part in the study will be watched carefully for any side effects. Side effects may be mild or moderate.

Please report any side effects, illness, or other changes to your health that you notice. It is important to report these changes even if you do not think they are related to the study drug. If you have any serious or long-lasting side effects from the study drugs, the study doctor can remove you from the study.

NAC is not known to have any serious side effects. Below, we have listed side effects that have been known to occur when NAC is administered orally up to 8000 mg. The max dose that you would receive in this study is 2400 mg:

Likely (occurs in greater than 20% or 1 out of every 5 people)

- There are no known risks that occur in greater than 20% of people who take NAC.

Less Likely (occurs in less than or equal to 20% of people)

- Flushing
- Itching
- Rash
- Hives
- Nausea
- Vomiting
- Upset stomach
- Bloating
- Low blood pressure
- Rapid heart rate

Rare but Serious

- Allergic reaction that is rapid in onset
- Rapid swelling of skin

Randomization Risks: There is a risk that your condition may remain the same or worsen because you are getting a placebo or because NAC is not effective. Participants will be assigned to a treatment program by chance, and the treatment received may prove to be less effective or to have more side effects than other available treatments.

Risk of Relapse or Increased Alcohol Use: You may face the risk of relapse or to increased alcohol use. This risk may be greater if you are assigned to receive Placebo as compared to NAC, although the exact nature of this risk is unknown.

Risk of Cessation of Current Alcohol Abuse Medication: You may face a risk if you decide to stop your current alcohol abuse medication to enroll in this study. This risk may be greater if you are assigned to receive Placebo as compared to NAC, although the exact nature of this risk is unknown.

Risk of Distress/Fatigue due to Psychiatric and Neurocognitive Assessments: Risks related to answering questions about your medical/psychiatric history, reporting of drug use, taking part in

neurocognitive assessment may include fatigue and distress. You are free to decline to answer any questions or to stop the assessments at any time. Neurocognitive assessment, interview sessions, and computer training will include breaks. In the event that you appear to be under undue strain, the session will be immediately discontinued.

Blood Drawing (Venipuncture) Risks: Participation in the study requires you to have your blood drawn 4 different times over the course of 12 weeks. Having blood drawn may cause pain (common), fainting/passing out (not very often), a bruise where the needle goes in (not very often), and infection at the same place (rare).

Reproductive Risks: There are no adequate and well-controlled NAC studies in pregnant women. This drug should be used during pregnancy only if clearly needed for clinical care. **Women of childbearing potential will be asked to use *at least 2 forms of birth control*.** Acceptable methods include condom AND spermicide, diaphragm AND spermicide, or not having sex.

If you are of child-bearing potential, pregnancy tests will be done monthly throughout your participation in the study to assure that you are not pregnant. If you become pregnant during the study, study treatment will be discontinued. If you are practicing abstinence, you must agree to continue abstinence or use an acceptable method of birth control, should you become sexually active.

Unknown Risks: You may experience side effects that we do not know about yet. You should call the study doctor or research staff if you have any symptoms or reactions. The researchers will let you know if they learn anything that might make you change your mind about participating in the study. For more information about risks and side effects, ask the study doctor.

Contraindicated Medications: The following medications have been reported to have adverse drug-drug interactions with NAC and should not be taken while participating in the study – carbamazepine and nitroglycerin.

11. Are there benefits to taking part in the study?

Taking part in this study may or may not make your health better. You may respond favorably to the study capsules and reduce your drinking and TBI symptoms, but there is no guarantee that this will happen. Others may benefit from the overall conclusions drawn from the results of this study.

12. What other choices do I have if I do not take part in this study?

You do not have to be in this study to be treated for traumatic brain injury (TBI) and/or alcohol use disorder. You can seek non-research treatment services if that is your choice. You have the right to continue with any ongoing treatment as long as it not an exclusion factor for this study. You may also choose to participate in another study targeting TBI and/or alcohol use disorders if you decide not to participate in this research study.

You can obtain FDA approved medications for alcohol use disorder through the clinical programs at the VA, the Addition Recovery Treatment Services (ARTS), as an alternative to study participation, or should you wish, after you complete study participation. You have the option of requesting clinical treatment for alcohol use disorder instead of study participation. You also have the opportunity to participate in non-medication forms of clinical addiction treatment alongside your participation in the study. You are also free to seek treatment outside the context of the SFVAMC. You may also choose to seek no treatment for TBI and/or alcohol use disorder.

13. Will my medical information be kept private?

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total privacy. Some information from your medical records will be collected and used for this study. If you do not have a San Francisco VA Medical Center medical record already, one will be created for you by the study staff.

The information that will be collected includes demographic information (for example: name, address, age, date of birth, social security number) and health information (psychiatric information, alcohol and drug use, and medical information). By signing this form, you are giving the study staff permission to use the information collected about your health (TBI, mental health, alcohol and other substance abuse, and other medical information). This authorization to access and use the information will not expire. You have the right, at any time, to take back your authorization and end the study staff's access to your personal information.

Every effort will be made to protect the confidential nature of your identifying information by assigning you a unique identification code during the study. All information and data collected by the study staff during this study will contain this identification code instead of any identifying personal information. This identification code will be stored in an electronic database on a password-protected, secure web server managed through the SFVAMC. The data manager will download study data from the server that will be needed for analysis and store it in a password-protected database, stored on a VA server behind a secure VA firewall at the SFAVMC. The written log that connects your identification code to the demographic information you give us will be kept in a file separate from the collected data. This log will have restricted access and will be stored in locked cabinets when not in use. Any data sent via email messages or delivery service will be encrypted and password-protected.

Your doctors and other providers in the VA health care system may become aware of your study participation. Hospital regulations require that all health care providers treat information in medical records confidentially. Also, people involved with your future care and insurance may become aware of your participation in the study and of any study-related information added to your medical record. Progress notes related to your participation in this study indicate that you have been in enrolled in a research study, any details that affect your clinical care, and the name and contact information for the investigator conducting the study. Details like urine drug test results, the study name or number will not be included in the progress notes.

Study tests that are performed by non-VA research labs and information gathered directly from you by the study staff will be part of your research study records but will not be added to your medical record. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are a number of regulatory organizations that may look at and/or copy your research and medical records for research, quality assurance, and data analysis. These organizations include:

- Members of the study's Data and Safety and Monitoring Board and Medical Monitor
- University of California
- University of California, San Francisco Institutional Review Board (UCSF IRB)
- The Food and Drug Administration (FDA)
- Department of Defense (DoD)
- Representatives of the U.S. Army Medical Research and Material Command
- Department of Veterans Affairs
- Institute for Translational Neuroscience (ITN)

- Office for Human Research Protections (OHRP)
- Research Advisory Panel of California (RAPC)

Complete confidentiality cannot be promised, particularly for active military personnel, because information bearing on your health may be required to be reported to appropriate medical or command authorities. In this study, you will be asked questions about illegal drug use and your urine will be tested for illegal drugs. The researchers will keep information about you as confidential as possible, but complete confidentiality cannot be guaranteed. On rare occasions, research records have been subpoenaed by a court.

14. What are the costs of taking part in this study?

There will be no direct cost to you if you take part in this study. The study will pay for the study capsules and study procedures (for example: blood tests). Study participation will be free to you. You may need to pay an indirect cost of transportation to the San Francisco VA Medical Center in order to complete study visits.

15. Will I be paid for taking part in this study?

You will be paid for completed study visits only via cash or check. (Please note that if you choose to be paid via check, you will need to provide your home address and social security number in order to receive payment.) You will be paid immediately after completing each study visit. You will not be paid for any missed visits. If you complete all study visits and procedures, you will be paid as follows:

Week	Attend study visit	Return MEMS cap	Attend all study visits	Total per visit
Screening Visits	$85*			$85
Week 1	$20	$5		$25
Week 2	$20	$5		$25
Week 3	$20	$5		$25
Week 4	$35	$5		$40
Week 5	$20	$5		$25
Week 6	$20	$5		$25
Week 7	$20	$5		$25
Week 8	$35	$5		$40
Week 12	$40		$50	$90
POTENTIAL TOTAL AMOUNT PAID				$405

*Payment for screening visits depends on the completion of tasks at each visit. You will earn up to $85 total if you complete all screening measures.

You will also be compensated an additional $5 at each study visit during weeks 1-8 for returning your medication cap and bottle. If you attend and complete all possible study visits, you will receive an end-of-study bonus in the amount of $50. **If you attend all possible study visits, return the medication cap and bottle each week, and receive the end-of-study bonus, you will receive the maximum possible payment of $405.**

16. What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, Dr. Batki, if you feel that you have been injured because of taking part in this study. You can tell Dr. Batki in person or call him at 415-221-4810, ext. 23671. In the case of an emergency, Dr. Batki can be reached 24 hours a day by pager at 415-313-6537.

Treatment and Compensation for Injury: If you are injured as a result of being in this study, VA will ensure that treatment is made available at a VA medical facility. If you are eligible for veteran's benefits, the costs of such treatment will be covered by the Department of Veterans Affairs. If you are not eligible for veteran's benefits, the costs of treatment may be billed to you or your insurer just like any other medical costs, or covered by the Department of Veterans' Affairs or the University of California, depending on a number of factors. The Department of Veterans Affairs and the University do not normally provide any other form of compensation for injury. For further information about this, call the VA Regional Counsel at (415) 750-2288 or the office of the UCSF Committee on Human Research at (415) 476-1814.

17. Clinical Trial Registry Data Bank

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.

18. What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from the Department of Veterans Affairs health care system.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

19. Who can answer my questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study. At San Francisco VA, please contact your study doctor Steven L. Batki, M.D. at 415-221-4810, ext 23671 or page him at 415-313-6537.

For questions about your rights while taking part in this study, call the office of the **Committee on Human Research**, UCSF's Institutional Review Board (a group of people who review the research to protect your rights) at **415-476-1814**.

CONSENT OF RESEARCH PARTICIPANT

You have been given copies of this consent form and the Experimental Participant's Bill of Rights to keep.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

Optional Procedures: Please indicate if you agree to participate in the following optional procedure by placing your initials on one of the lines below

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_____I *agree* to be contacted after this study is done and/or to be asked to be in other studies.

_____I do not agree to be *contacted after this study* is done or to be asked to be in other studies.

_____I *do* want my blood to be used for genetic testing.

_____I *do not* want my blood to be used for genetic testing.

If you wish to participate in this study, you should sign below.

_____

Signature of Participant **Date**

_____

Printed Name of Participant

_____

Signature of Person Obtaining Consent **Date**

_____

Printed Name of Person Obtaining Consent