INFORMED CONSENT FORM

Official title: A Controlled Trial of Topiramate Treatment for Alcohol Dependence in Veterans with PTSD

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Department of Veterans Affairs	**INFORMED CONSENT FORM**
Subject Name:	**Date:**
Title of Study: **A CONTROLLED TRIAL OF TOPIRAMATE TREATMENT FOR ALCOHOL DEPENDENCE IN VETERANS WITH PTSD**	
Principal Investigator: **Steven L. Batki, M.D.**	**San Francisco VAMC**

CONSENT TO PARTICIPATE IN RESEARCH

This is a medical research study funded by the Department of Defense. The principal investigator is Steven L. Batki, MD from the San Francisco VA Medical Center and UCSF Department of Psychiatry. The other researchers are Thomas Neylan, MD and David Pennington, PhD. 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 the information you will need to help you decide if you want to be in this study. Read this form carefully and ask questions about anything you do not understand. Take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. When all your questions have been answered, you can decide if you want to be in this study. If you do decide to be in the study, you will get a copy of this signed and dated form to keep for your records.

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

You are being asked to take part in this study because you have been diagnosed as having posttraumatic stress disorder (PTSD) 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 learn about how the medication topiramate affects a person's use of alcohol and their PTSD symptoms. Topiramate has been shown to help reduce alcohol use in some studies and to possibly reduce certain PTSD symptoms in other studies. Topiramate has not been proven safe or helpful by the US Food and Drug Administration (FDA) for your conditions. Topiramate has been approved by the FDA as therapy for certain types of seizures and for migraine headache prevention. Over 2 million people have been treated to date with topiramate worldwide. It is being studied in several other illnesses.

It is important to know that one-half of the patients will be taking the test drug (topiramate) and one-half will be taking a capsule that looks the same but does not have the drug in it. This is called a placebo or inactive substance. You will be "randomly assigned" to a treatment and there is a 50/50 chance that you will receive the study drug. This is like tossing a coin to see which capsule you will get. A computer program will place you in one of the two groups. Neither you nor your doctor can choose the group you will be in. You will have an equal chance of being placed in either of the two groups.

This study is being funded by the Department of Defense. The investigators in this study do not have any financial interest in the company that manufactures topiramate.

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

Up to 160 patients will be in the study. All patients will receive study capsules (topiramate or inactive substance).

- **If you are in group 1 you will be given topiramate**.
  - The study will last for 17 weeks.
  - You will be asked to take topiramate every day for the 12-week duration of the main phase.
  - You will continue to receive all of your usual treatments for PTSD and substance use in addition to topiramate.
- **If you are in group 2 you will be given a placebo (an inactive substance)**.
  - The study will last for 17 weeks.
  - You will be asked to take the placebo every day for the 12-week duration of the main phase.
  - You will continue to receive all of your usual treatments for PTSD 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 topiramate or other medication for alcohol dependence.
- You are younger than 18 years of age or older than 69 years of age.
- You are already in another alcohol treatment study.
- Certain test results show it is not safe for you to be in the study.
- For women: If you are pregnant or breast feeding, you will not be able to be in this study because we do not know how topiramate will affect your child.

Prior to you starting in the study, we may contact your primary care provider and/or your mental health care provider to make sure it is safe for you to participate in the study.

6. How long will I be in the study?

In total, you will be asked to commit approximately 29 to 41 hours of your time over the course of 17 weeks. The study has 16 visits, and can be divided into the following 3 phases:

- Screening Phase: 3-5 visits over approximately 1 week
- Main Phase: 12 visits over 12 weeks
- Follow-up Phase: 1 visit at week 16, 4 weeks after end of the Main Phase

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 12 weeks, you will take topiramate or placebo, attend weekly research visits, and receive weekly alcohol counseling.

***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 too much alcohol on your breath:

- We will have you wait until the breath alcohol level falls below legal limits or reschedule you for another time.
- You can also be referred to other treatment if you wish.
- If you are legally intoxicated, you will be offered transportation home.
- If your breath alcohol level is above 0.00% you will be asked to wait until it returns to 0.00% or to return at a later date to complete your visit.

- 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. If you have a history of glaucoma or kidney stones, you may not take part in this study.

- **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 11 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, for looking at the possible genetic effects on your response to topiramate, and for measuring the amount of study medication in your blood. 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 specific genes that have been associated with the development of alcohol use disorders and investigate their association with topiramate treatment. These include genes such as GRIK1, COMT, and OPRM1. Since the medical and neuropsychological significance of these genotypes are 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-approved DNA bank, clearly labeled with a numerical code. No personally identifiable information will be linked with this sample in any way. If you have completed the research study and have been asked to return to the Addiction Research Lab for an additional blood drawn, then you will be compensated $25 for your time and effort.

- **You will be asked to give a urine and blood sample (about 3 teaspoons).** The urine sample will be tested for drug use, including illegal drug use and kidney function. The blood sample will be tested for overall health with a focus on kidney and liver function.

- **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 topiramate 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** and asked about psychiatric problems in your family.

- 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 **PTSD** symptoms and about feelings of **anxiety, depression, and suicidal thoughts**.

The procedures and questionnaires listed above will be done over 3 visits of the Screening Phase. Each of the 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 – 12 Weeks *(Titration, Maintenance and Taper 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 topiramate or placebo.

You will be asked to take topiramate or placebo for 12 weeks. The Main Phase is made up of 3 parts:

- Titration Period (5 weeks) – the number of topiramate or placebo capsules will be gradually increased ("titrated") over the course of 5 weeks.
- Maintenance Period (6 weeks) – the number of topiramate and placebo capsules will remain constant for 6 weeks.
- Taper Period (1 week) – The number of topiramate or placebo capsules will decrease ("taper") gradually and then stop over the course of 1 week.

b.1 Titration Period (5 weeks)
The Titration period of the study is 5 weeks during which you will gradually increase the number of capsules you take up to a maximum of 3 capsules (which corresponds to a dose of 300 mg per day), or until you have reached the number of capsules the study doctor determines to be appropriate for you. Your study doctor will give you detailed instructions explaining how to gradually increase the number of capsules per day and may adjust the number as necessary during this period.

Study capsules will be provided in two forms. If taking topiramate, these correspond to 25 mg and 100 mg capsules. 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 (6 weeks)
After you reach the appropriate number of capsules (as determined by the study doctor during the Titration period) you will enter the Maintenance portion of the study. During this period of the study, you will take the same number of capsules daily for 6 weeks.

b.3 Taper Period (1 week)
Upon completion of the maintenance phase you will gradually stop ("taper off") the topiramate or placebo as directed by your study doctor.

The 12-week Main Phase will be followed by 1 Follow-Up Visit at Week 16.

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 that have neurocognitive tests require complete sobriety. This means that at Weeks 4, 8 and 12, your breath alcohol level must be 0.00%. If it is not, you will be asked to wait until it is 0.00% or to 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, PTSD 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 PTSD. You may also continue all other psychotherapy and counseling for your alcohol use disorder. However, in order to be in this study, you may not take other medicines used to treat alcohol use disorders, including disulfiram (Antabuse), naltrexone (Depade, Revia, or Vivitrol), or acamprosate (Campral).
- At the week 6 and 12 visits a small sample of blood (about 6 teaspoons total) will be taken and used for routine medical tests to check your health.
- The study doctor or research staff will also ask for possible side effects. The number of 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 12-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. Please note that sessions may be audiotaped to ensure that you are receiving the same quality of counseling throughout the research project and in comparison to other participants.
- In the rare case that you are not able to attend a study visit at the Ft. Miley campus, the PI may determine that it is safe for you to attend some of the weekly study visits by phone.

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.

8. Table of Study Visits:

The table below shows what will happen during your participation in the study.

Time	What you will do
Screening – 3 visits over 1 week	• Review consent form with study personnel and sign the form if you agree. • Provide information about your medical history, and medications /treatments, time spent in the service and emergency contacts we can call. • Receive a physical examination and blood (up to 3 teaspoons of blood) and urine samples to assess your health. Women will be assessed for birth control and tested for pregnancy. Your urine sample will be tested for substance use. • Provide information about your drug/alcohol use and PTSD and other mental health symptoms. • Take tests to determine your levels of decision-making, risk-taking, and impulsivity. • Learn about the capsules and how to take them on a daily basis. • These 3 visits together take a total of approx. 6.5 to 9 hours to complete.
Week 1,2, and 3 of Main Study	• Let us know if your medication or other treatments have changed since we last saw you • Review topiramate/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 supply of capsules and return all extra capsules from previous week. • This visit should take approx. 1 to 1.5 hours to complete.
Week 4 of Main Study	• Let us know if your medication or other treatments have changed since we last saw you. • Review topiramate/placebo intake and any changes you have noticed in the past week. • Have your breath alcohol concentration and vital signs checked (temperature, weight, heart rate, blood pressure). • Provide a urine sample to be tested for substance use. • Women will be reassessed for birth control method and test for pregnancy. • Provide information about your drug/alcohol use, PTSD symptoms, and sense of well-being. • Participate in a brief alcohol counseling session. • Receive a supply of capsules and return all extra capsules from previous week. • This visit should take approx. 2 to 2.5 hours to complete.
Week 5 of Main Study	• Let us know if your medication or other treatments have changed since we last saw you. • Review topiramate/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 supply of capsules and return all extra capsules from previous week. • This visit should take approx. 1 to 1.5 hours to complete.

Week 6 of Main Study	• Let us know if your medication or other treatments have changed since we last saw you. • Review topiramate/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, PTSD 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 supply of capsules and return all extra capsules from previous week. • This visit should take approx. 3.5 to 5 hours to complete.
Week 7 of Main Study	• Let us know if your medication or other treatments have changed since we last saw you. • Review topiramate/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 supply of capsules and return all extra capsules from previous week. • This visit should take approx. 1 to 1.5 hours to complete.
Week 8 of Main Study	• Let us know if your medication or other treatments have changed since we last saw you. • Review topiramate/placebo intake and any changes you have noticed in the past week. • Have your breath alcohol concentration and vital signs checked (temperature, weight, heart rate, blood pressure). • Provide a urine sample that will be tested for substance use. • Women will be reassessed for birth control method and test for pregnancy. • Provide information about your drug/alcohol use, PTSD symptoms and sense of well-being. • Participate in a brief alcohol counseling session. • Receive a supply of capsules and return all extra capsules from previous week. • This visit should take approx. 2 to 2.5 hours to complete.
Weeks 9,10, and 11 of Main Study	• Let us know if your medication or other treatments have changed since we last saw you. • Review topiramate/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 supply of capsules and return all extra capsules from previous week. • These visits should take approx. 1 to 1.5 hours to complete.

Week 12 of Main Study	• Let us know if your medication or other treatments have changed since we last saw you. • Review topiramate/placebo intake and any changes you have noticed in the past week. • Have your breath alcohol concentration and vital signs checked (temperature, weight, heart rate, blood pressure). • Provide a blood (up to 3 teaspoons of blood) and urine sample to test for alcohol use. • Women will be reassessed for birth control method and test for pregnancy. • Provide information about your drug/alcohol use, PTSD 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. • Return all extra capsules from previous week. • This visit should take approx. 3.5 to 5 hours to complete.
Week 16 Follow-Up Visit	• Review topiramate/placebo intake and any changes you have noticed in the past week. • Have your breath alcohol concentration and vital signs checked (temperature, weight, heart rate, blood pressure). • Provide a urine sample to be tested for substance use. • Provide information about your drug/alcohol use, PTSD symptoms, and sense of well-being. • Participate in a brief alcohol counseling session. • This visit should take approx. 3.5 to 5 hours to complete.

9. Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop your participation safely.

It is important to tell the study doctor if you are thinking about stopping so that you and your doctor can discuss other treatment options.

The study doctor may stop you from taking part in this study at any time if the doctor believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

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

a. Risks of topiramate side effects

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors do not know all the side effects that may happen. Side effects may be mild or very serious. If you are taking topiramate, many side effects go away soon after you stop taking it. You should talk to your study doctor about any side effects you experience while taking part in the study.

Risks and side effects related to taking topiramate include those which are:

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

- Numbness and tingling
- Change in sense of taste
- Fatigue
- Headache

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

- Loss of appetite
- Difficulty with concentration and attention
- Nervousness
- Difficulty with memory and language problems
- Diarrhea
- Dizziness

- Itching
- Sleepiness
- Nausea
- Bloating
- Influenza-like symptoms
- Sinus infection
- Muscle pains

Rare but Serious

- Risk of suicide
- Kidney stones
- Sudden worsening of vision
- Decreased sweating
- Increased levels of ammonia in blood
- Metabolic acidosis (detailed description below)

Metabolic acidosis (decreased bicarbonate in the blood) may be associated with taking topiramate. Metabolic acidosis can cause symptoms such as tiredness and loss of appetite, or more serious conditions including irregular heartbeat (arrhythmia) or coma. Long-term metabolic acidosis can result in thinning of the bones (osteoporosis) with an increased risk for fractures. Metabolic acidosis may increase the risk for kidney stones. We will monitor your blood tests during the study to look for metabolic acidosis.

Risk of suicide:
Like other antiepileptic drugs, topiramate may cause suicidal thoughts or actions in a very small number of people, about 1 in 500.

Call a healthcare provider right away if you have any of these symptoms, especially if they are new, worse or worry you: thoughts about suicide or dying, attempts to commit suicide, new or worse depression, new or worse anxiety, feeling agitated or restless, panic attacks, trouble sleeping (insomnia), new or worse irritability, acting aggressive, being angry, or violent, acting on dangerous impulses, an extreme increase in activity and talking (mania), other unusual changes in behavior or mood.

Do not stop taking your capsules without first talking to a healthcare provider. If you are taking topiramate, suddenly stopping it can cause serious problems. Suicidal thoughts or actions can be caused by things other than medicines. If you have suicidal thoughts or actions, your healthcare provider may check for other causes. Pay attention to any changes, especially sudden changes, in mood, behaviors, thoughts, or feelings. Keep all follow-up visits with your study doctor as scheduled. Call your study doctor, as needed, between visits as needed, especially if you are worried about symptoms. Some patients have had suicidal thoughts or actions.

If you feel a change in your mood or if you feel depressed or feel you may harm yourself, please contact your doctor immediately.

Additionally, you may call the **Veterans Crisis Line** which connects Veterans in crisis and their families and friends with qualified, caring VA responders through a confidential toll-free hotline, online chat, or text. Veterans and their loved ones may call **800-273-8255** and Press 1, chat online, or send a text message to 838255 to receive confidential support 24 hours a day, 7 days a week, 365 days a year.

Kidney stones have occurred in patients taking topiramate. It is recommended for you to drink between 6 and 8 10-ounce glasses of water per day to reduce the risk of developing kidney stones.

A medical condition consisting of **sudden worsening of vision** and an elevation of fluid pressure in the eyes (acute secondary glaucoma) has been described in patients taking topiramate, usually occurring in the beginning of their treatment. If you have sudden, significant worsening of vision, blurred vision, or eye pain you should contact your doctor immediately.

Treatment with topiramate may cause **decreased sweating** (oligohidrosis). Activities such as exercise or exposure to warm temperatures while using topiramate may increase the risk of heat-related side effects, such as heat stroke. Drinking plenty of fluids is recommended while being in the study.

Rarely, increased levels of ammonia in the blood (hyperammonemia) with or without impairment of brain function have been reported with topiramate mainly when it was taken together with valproic acid (Depakote). Please tell your doctor if you are taking Depakote or it is suggested that you being Depakote.

Rare and isolated cases of liver failure/hepatitis and blistering skin rashes (bullous skin eruptions) have been reported.

Topiramate may cause a change (increase or decrease) in the effect of some medications. If you are taking medications during your participation in this study, your doctor will explain whether topiramate may have an effect and if necessary, may adjust the number of capsules you are taking.

Topiramate may reduce the effectiveness of some hormonal birth contraceptives (birth control pills, hormonal implants or hormonal injections) and additional barrier methods, such as condoms or a diaphragm, should be used. If you are taking birth control pills, you should report any change in your bleeding patterns to your study doctor.

It is important to lower the dose of topiramate gradually to reduce the possibility of having seizures when it is stopped. There have been reports of seizures associated with a rapid decrease of topiramate. In situations where rapid withdrawal of it is needed, appropriate medical monitoring is recommended. You should contact your study doctor immediately if you need to stop taking your study capsules.

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 the study capsules.**

You should not share the study capsules with anyone. Keep it out of reach of children and persons not able to read or understand the label.

b. There is a risk that your condition may remain the same or worsen because you are getting a placebo or because topiramate is not effective.

***c. Blood drawing (venipuncture) risks*:** 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).

d. Reproductive risks*:** You should not become pregnant while on this study because the effects of topiramate on a fetus are unknown. **Women of child bearing 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 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.

e. Randomization risks: You will be assigned to a study group by chance, and the capsules you receive may prove to be less effective or to have more side effects than other available treatments.

f. 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.

g. Risk of Relapse to Using Alcohol: You may face the risk of relapse to using alcohol. This risk may be greater if you are assigned to receive placebo as compared to topiramate, although the exact nature of this risk is unknown.

h. Risk of Cessation of Current Alcohol Abuse Medication: You may face the risk of relapse to using alcohol 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 topiramate, although the exact nature of this risk is unknown

i. Risk of Distress/Fatigue due to Psychiatric and Neurocognitive Assessments: Risks related to answering questions about your medical/psychiatric history, reporting of drug use, or 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 assessments, 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.

j. Contraindicated Medications: You may not take any of the following medications because of their possibly harmful interactions with the study medication:

j.1.Alcohol Treatment Medications

- acamprosate (Campral)
- disulfiram (Antabuse, Antabus)
- naltrexone (both oral and injectable for extended release) (Revia, Depade, Vivitrol)

j.2. Topiramate

You will be given a wallet sized card with a list of these medications. Please show this list to your primary care provider and other physicians to make sure that you are not prescribed these medications.

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 PTSD 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 PTSD or alcohol use disorders.

If you do not take part in this you may continue to receive the usual medication treatment for PTSD and for alcohol dependence. The usual medication treatment for alcohol use disorders include disulfiram (Antabuse), naltrexone (Depade, Revia, or Vivitrol), or acamprosate (Campral). It is also possible to receive topiramate (Topamax) off-label.

You may obtain routine treatment for your alcohol use disorder and PTSD symptoms at the SF VAMC Mental Health clinic, outside the context of the study; or pursue such treatment at another VA Mental Health medical clinic. You will also be free to obtain interventions outside the context of the SF VAMC.

13. Will my medical information be kept private?

Participation in research may involve a loss of privacy, but information about you will be handled as confidentially as possible. If you do not already have a medical record at the San Francisco VA Medical Center, one will be created because of your participation in this study.

Some of your research test results, such as the results from your blood tests, reported side effects and other medications you are currently taking, will be included in this record. Therefore, your other doctors in the VA health care system may become aware of your participation. Hospital regulations require that all health care providers treat information in medical records confidentially.

The information that will be collected includes demographic information such as your name, address, age, date of birth, and social security number. Health information that will be collected includes your psychiatric, alcohol and illegal drug use, and medical information. By signing this form, you are giving us permission to use information collected about your health (PTSD, mental health, alcohol and other substance use, and other medical information). This authorization to access and use the information collected **will not expire**. You have the right, at any time, to take back your permission to use your personal health information for research purposes.

Every effort will be made to protect the confidential nature of your identifying information through the use of a unique study identification code, stored in an electronic database on a password-protected secure web server managed through the UCSF Health Research Center at the UCSF School of Medicine available to study staff only. 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 SFVAMC. The log that connects your identification codes to the information you give us will be kept in a file separate from the collected data. This log will have restricted access and stored in locked cabinets when not in use. Data are not transmitted as an attachment to unprotected e-mail messages and data sent via mail or delivery service will be encrypted. Audio recordings of counseling sessions will be stored on a UCSF server/data management system, MyResearch. MyResearch is a secure, HIPAA compliant virtual computer environment.

Organizations that may look at and/or copy your research and medical records for research, quality assurance, and data analysis include:

- Members of the study's Data and Safety and Monitoring Board & Medical Monitor
- UCSF's Committee on Human Research
- The Food and Drug Administration (FDA), involved in keeping research safe for people.
- Department of Defense (DoD)
- Representatives of the U.S. Army Medical Research and Materiel Command
- UCSF's data management systems, REDCap and MyResearch

Complete confidentiality cannot be promised, particularly for 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. 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. However, the Certificate of Confidentiality does not apply to active duty subjects as it pertains to military command authorities.

Exceptions: A Certificate of Confidentiality does not prevent researchers from voluntarily disclosing information about you without your consent. For example, we will voluntarily disclose information about incidents such as child abuse or intent to hurt yourself or others. In addition, the Certificate 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. Finally, the Certificate may not be used to withhold information from the federal government needed for auditing or evaluating federally funded projects or information needed by the FDA.

14. What are the costs of taking part in this study?
You will not be charged for any of the study activities.

15. Will I be paid for taking part in this study?
You will be compensated in return for your time and effort to attend study visits. Payment is also intended to cover, or partially cover, the cost of public transportation/gas/parking.

You will receive:

- $85 total for screening visits. Payment at screening depends on completion of tasks.
- $20 for the briefer weekly visits at weeks 1, 2, 3 ,5, 7, 9,10, 11 (up to $160 for all 8)
- $30 for the longer visits at week 4 and 8 (up to $60 for both)
- $35 for the longest visits, at weeks 6, 12 and the week 16 follow-up visit (up to $105 for all 3)

You will also be compensated an additional $5 at each study visit during weeks 1-12 for returning the medication cap and bottle.

If you attend all study visits, and return the medication cap and bottle at each visit, you will receive the maximum payment of $470.

Payments will be made in cash or check upon the completion of each visit.

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. 3671. 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. 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.

18. 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 3671 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**.

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.

CONSENT

You have been given copies of this consent form and the Experimental Subject'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 procedures by placing your initials on the lines below:

_____ I *agree* to be contacted after this study is done 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.

_____ _____
Date Participant's Signature for Consent

_____ _____
Date Person Presenting this Study and Obtaining Consent