DEPARTMENT OF VETERANS AFFAIRS

Memorandum

Date: December 3, 2025

From: Beverly Ventura, Project Manager for CSP #2016

Subj: CSP #2016, “National Adaptive Trial for PSTD related Insomnia” Informed Consent Document

To: ORD

Informed consent document for the ClinicalTrials.gov record.

Official Title: CSP #2016, “National Adaptive Trial for PSTD related Insomnia” (NAP)

NCT ID Number: NCT03668041

ICF Document Date: 9/10/2024

Participant Name: [PDF Fillable Field]

Title of Study: CSP #2016 **N**ational **A**daptive Trial for **P**TSD related Insomnia (NAP)

Principal Investigator: VA Facility:

Principal Investigator for Multisite Study: John H. Krystal, M.D.

KEY SUMMARY INFORMATION ABOUT THIS STUDY

You are being invited to take part in a research study that is being funded by Department of Veterans Affairs. Before you decide to take part, it is important for you to know why the research is being done and what it will involve. This includes any potential risks to you, as well as any potential benefits you might receive. Taking part in this study is completely voluntary.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

Many veterans with posttraumatic stress disorder (PTSD) have trouble sleeping (insomnia) or frequent nightmares. So far, no medication has been shown to specifically treat the insomnia in PTSD. The purpose of this study is to find out if taking the medications trazodone or eszopiclone can help decrease symptoms of insomnia in patients with PTSD.

You will be assigned to receive trazodone, eszopiclone or placebo. Placebo is a pill that looks like study medication but has no medication in it. The study medication that you will receive will be decided randomly, like the flip of a coin. You will have an equal chance of getting placebo or one of the active study medications. Neither you nor the study team will know which study treatment (trazodone, eszopiclone or placebo) you will be assigned to. At some point during the study, it's possible that one of the active study medications may no longer be evaluated in the study if they don't appear to be working well, but this will not affect the medication you take. No one on the local study team will know if this happens.

You will be in the research study for approximately 23 weeks (about 5 1/2 months), which includes a screening period lasting approximately 4-6 weeks to determine your eligibility. Once you are enrolled in the study, you will come in for 7-8 visits and will be asked to take study medication every night for about 12 ½ weeks. You will also have a phone interview during the screening period which can take up to 4 hours, and another phone interview at 12 weeks, which will last up to 2 hours. You will also be asked to return 4 weeks after the last dose of your study medication for a brief follow-up visit. Data about your condition and events you experience that occur after week 17 will not be collected.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

If you agree to take part in this research study, there may not be a direct benefit to you. Potential benefits to you may include a reduction in your insomnia symptoms. The investigators hope the information learned from this research study will benefit other patients with PTSD and insomnia in the future.

For a complete description of benefits, refer to the Detailed Information section of this consent.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

Each of the medications used in this study have been used with other patients for many years. However, all medications have risks.

You may experience a decreased mental or physical ability to perform tasks that require attention, concentration, memory, or coordination. This side effect most commonly occurs in the hours following a dose of study medication but can sometimes last into the next day following a night's dose.

Other common side effects occurring in people taking trazodone or eszopiclone include drowsiness, dizziness, headache, fatigue, dry mouth, nausea/vomiting, foul or metallic taste in mouth, feeling nervous, or increases in blood pressure.

Rarely, trazodone or eszopiclone can cause serious, life-threatening side effects.

For a complete description of risks, refer to the Detailed Information section of this consent.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of the study is [*insert name of Local Site Investigator*] at the [*insert name of VA facility*]. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study, their contact information is: [*insert LSI contact information*].

DETAILED INFORMATION ABOUT THE STUDY

WHY IS THIS RESEARCH BEING DONE?

Many veterans with posttraumatic stress disorder (PTSD) have trouble sleeping (insomnia) or have frequent nightmares. The purpose of this research study is to find out if taking the investigational medications trazodone or eszopiclone can help decrease symptoms of insomnia (or trouble sleeping) in military veterans with PTSD. There are reasons to think each of these might work for veterans with PTSD, but it hasn't been proven. PTSD is a psychological disorder found in about 30 percent of returning service members. It is a form of intense anxiety which sometimes results from severe trauma, and symptoms may include nightmares, flashbacks, troublesome memories, difficulty sleeping, poor concentration, irritability, anger, and emotional withdrawal.

You will be assigned to receive trazodone, eszopiclone or placebo. Placebo is a pill that looks like study medication but has no medication in it. The study medication that you will receive will be decided randomly, like the flip of a coin. You will have an equal chance of getting placebo or one of the active study medications. Neither you nor the study team will know which study treatment (trazodone, eszopiclone or placebo) you will be assigned to. At some point during the study, it's possible that one of the active study medications may no longer be evaluated in the study if they don't appear to be working well, but this will not affect the medication you take. No one on the local study team will know if this happens.

Trazodone is approved by the Food and Drug Administration (FDA) for treating major depression in adults but is not approved for treating PTSD. Although trazodone has not been approved by the FDA to treat insomnia or PTSD, some doctors have tried it for these purposes. The doses in this study will be lower than the doses used to treat depression.

Eszopiclone is approved by the FDA for treating insomnia, but it's unknown if eszopiclone can help treat insomnia when it's related to PTSD. Some doctors have tried it for this purpose. The doses in this study will be the same as the doses used to treat insomnia. A small study found it to be helpful for treating patients with PTSD.

WHY HAVE YOU BEEN ASKED TO TAKE PART IN THIS RESEARCH STUDY?

You are being asked to participate because you may have trouble sleeping, you are over 18, and you may have Posttraumatic Stress Disorder (PTSD). PTSD is a psychological disorder found in approximately 30 percent of returning service members.

HOW MANY PEOPLE WILL TAKE PART IN THE RESEARCH STUDY?

About 774 people will take part in this study at up to 34 VA sites across the country. VA [*insert local VA hospital*] will have approximately 50 participants.

WHO IS CONDUCTING THE RESEARCH STUDY?

This study is sponsored by the Department of Veterans Affairs. The study is directed by John Krystal, MD, a researcher at the VA Connecticut (West Haven) Medical Center. He is assisted by staff at the Palo Alto VA, the Albuquerque VA, and [*insert local VA hospital*].

HOW LONG WILL I BE IN THE STUDY?

This research study is expected to take approximately 3 years and 4 months. Your individual participation in the project will take approximately 23 weeks (about 5 1/2 months), which includes a screening period lasting approximately 4-6 weeks to determine your eligibility. Once you are enrolled in the study, you will come in for 7-8 visits and receive study medication for about 12 ½ weeks. You will also be asked to return 4 weeks after the last dose of your study medication for a brief follow-up visit. The researcher may decide to take you off the study medication at any time; for example, if the treatment is found to not be in your medical interest or if your condition worsens.

WHAT WILL HAPPEN IF I TAKE PART IN THE STUDY?

This study is not meant to replace visits with your health care provider. We want you to continue seeing your health care provider for ongoing medical care.

The following sections describe the screening process, study procedures and your responsibilities. All the procedures for this study are done only for purposes of this research.

Screening Visit(s)

Before you can begin the study, you will need to be screened to make sure you meet the study criteria and that there is nothing that would make it unsafe for you to be in the study.

To be included in the study you must meet the following criteria: (1) be a Veteran with a current diagnosis of PTSD, (2) be experiencing at least moderate levels of insomnia, (3) agree to take the study medication you are randomly assigned to take, and (4) you must not start any new PTSD treatment while you are receiving study medication.

The screening includes:

- A physical exam including weight, height, temperature, blood pressure, and pulse
- Urine drug test
- A urine test for pregnancy and questions about pregnancy prevention/birth control methods (if you are a woman who can have children)
- An electrocardiogram (ECG) which measures your heart rhythm
- Using a machine (ApneaLink) designed to measure your sleep (if applicable)
- A blood draw (about 1.5 tablespoons total) for routine medical tests
- A review of your medical history, medical records, and current medications
- Interviews and questionnaires about your general health

The interviews will be done by study staff. In the interviews and questionnaires, you will be asked about your life, and relationships. You will also be asked about your use of over-the-

counter and prescription medications, herbal and other dietary supplements, alcohol, nicotine and illicit drugs. You will be asked about any psychiatric symptoms that you are now having or have had in the past. It will take about 1-2 hours to complete these interviews.

In addition, you will have an interview over the phone by a trained assessor in the privacy of your house or in a private room at your local VA or Community Based Outpatient Clinic (CBOC) (if available). You will be asked about your combat exposure and any traumatic experience(s), as well as symptoms of PTSD. You will be asked in-depth questions about your current and past psychiatric symptoms. These interviews will be digitally recorded for training and reliability (to ensure the interviewers are consistently getting the same results across different phone assessments) purposes. Only the Assessment Core Staff will have access to your recordings. The initial phone interview can take up to 4 hours.

During the screening period, you may be asked to wear a device (ApneaLink) while you sleep for 1 night to test whether you have sleep-disordered breathing. The device collects information related to how much and how well you breathe at night. You will insert prongs from a tube into your nostrils, looping tubing around your ears and then connecting the tube to a belt device that is secured around your waist while you sleep. You will also secure one of your fingers to a sensor. You will be asked to remove any finger nail polish or artificial nails on the index finger of your non-dominant hand prior to using ApneaLink. You will also be asked to come in for an in-person visit about 3-7 days after you wear the ApneaLink in order to return the device and have your results read. If this device determines you have sleep apnea, you will be referred for follow-up treatment with your medical provider. You can be re-evaluated for the study after treatment is sought. If the ApneaLink device is unable to collect the needed information, you may be referred to a local sleep lab to assess sleep apnea.

The total time for completing screening can take up to 10-12 hours, which includes everything discussed above, and can be done over 3-4 days. Screening will be scheduled to take place over more than one visit, but it should be completed within 45 days prior to randomization. If any of the screening procedures are not completed within the allocated time windows, they will need to be re-done. At the end of screening, you will be told whether you are eligible for the study.

You cannot be in the study if you have (1) any current psychotic symptoms, (2) active thoughts of hurting yourself (if you have suicidal ideas without intent you will be eligible), (3) current

mania or unstable Bipolar disorder, or (4) current moderate to severe drug or alcohol use. If you are currently dependent on drugs or alcohol you will be informed about where treatment is available and referred to an appropriate clinic. You can be reconsidered for the study one month after you are no longer dependent on drugs or alcohol. Your responses will be kept confidential as explained in the "*HOW WILL MY PRIVATE INFORMATION BE PROTECTED?*" and "*WHAT IS A CERTIFICATE OF CONFIDENTIALITY?*" sections of this consent form. You also cannot be in the study if you are already taking certain medications for sleep or have certain medical conditions. If you decide to discontinue your current sleep medicaion, you may experience some discomfort. You are strongly encouraged to discuss this with your provider first.

Procedures and Assessments During the Study

Once you are determined to be eligible for the study you will be prescribed a study medication. You will be assigned to receive trazodone, eszopiclone or placebo. This will be decided randomly, like the flip of a coin. You have an equal chance of getting placebo or one of the active study medications. At some point during the study, it's possible that one of the active study medications may no longer be evaluated in the study if they don't appear to be working well. This will not affect the study medication you are currently taking. You will take your study medication every night immediately before bedtime, for about 12 ½ weeks. You should not eat grapefruit or drink any grapefruit juice on days that you take the study medication because doing so could make it unsafe to take your study medication.

Changes to the dose of your study medication will ideally occur over the first 3 weeks of the study, based on your side effects. You will then stay on your highest tolerated dose until completing the week 12 visit, unless it is lowered due to side effects. You will need to take 1, 2, or 4 large capsules every night, depending on your dose. After 12 weeks, your dose may be lowered for 3 days. After that, the study medication will be stopped. You will continue to take your usual medications, including any medications you may be prescribed for PTSD, during and after the study.

After you start the study medication, you will be asked to visit the research site at this VA Medical Center at Weeks 1, 2, 3, 6, 9, 12, and 17. If you are unable to come in for an in-person appointment, assessments may be completed over the phone in order to collect as much assessment information as possible. Missed visits may also be scheduled at different time points in order to re-evaluate dose titration and/or obtain research assessments. Study

medication can only be picked up at the local VA Medical Center or mailed to you. You will receive a visit calendar to help keep track of your appointments. Follow-up appointments should be as close as possible to the day that they are due.

- At each visit, the following activities will occur: Study staff will measure and record your vital signs (weight, temperature, blood pressure, and pulse) and check side effects of the study medication
- You will be asked about any over-the-counter medications, prescription medications, and herbal and dietary supplements you have taken
- You will be asked about any changes in your symptoms, mood, thoughts, or behaviors (like depression, problems sleeping, irritability, etc.)
- You will also be asked to complete some questionnaires which will take approximately 20 minutes
- You will be provided with enough pills to last until your next visit (Any extra pills are to be used only if you can't make a scheduled visit, for example, when your visit is 1 or 2 days after the expected date)
- You will be asked to return any leftover pills
- You will be asked to secure any firearms (e.g., keep in safe, lock box, gun case, etc.) in your possession while receiving study medication

Most visits will take about 30 to 60 minutes, but the week 12 visit will take several hours to complete. At 12 weeks, there will be an in-person research office visit lasting approximately an hour and a separate phone interview that will last about 2 hours. This phone interview will also be digitally recorded.

Unless you have significant side effects or require additional changes to your study medication, you will not have study visits during any other weeks. Even if you must stop taking the study medication earlier than expected, the study staff would want you to keep coming to study visits (if you agree). You may also request to withdraw from all study activities including taking study medication and follow-up assessments. In this case, you will be asked, prior to withdrawing, if you are willing to just complete the final assessments, including the phone interview, and allow study staff to access your medical record for 7 more days to obtain information about your safety.

You will speak with several people as part of your research participation, including local study coordinator, local study doctor and telephone interviewer. Study staff, including the researchers and your local study coordinator, will monitor your treatment and whether problems result from your participation. They will also alert you if there is a problem with the study medication. You will see your regular health care providers as usual.

WHAT IS EXPECTED OF ME IF I TAKE PART IN THIS STUDY?

If you decide to participate in the research study, it will be your responsibility to:

- Take your study medication at the same time every night. You will have to take one, two, or four large capsules at night, depending on your dose
- Attend scheduled research visits and contact the study staff to reschedule as soon as you know you will miss the appointment
- Take the study medication as instructed, and if you miss a scheduled dose, simply take the next scheduled dose. Do NOT double your dose.
- Keep the study medication in a safe place, at room temperature, and away from children
- Bring back the blister cards (that contained your study medication) and any left-over pills to each visit
- Not to consume any grapefruit or grapefruit juice on days you take study medication
- Not to consume alcohol starting AT LEAST 3 hours prior to taking study medication and during the 8 hours after taking study medication
- Complete your questionnaires as instructed. You will be free to skip any questions that you would prefer not to answer.
- Agree to have your telephone interviews recorded
- Ask questions as you think of them
- Tell the study staff if you change your mind about staying in the study
- Contact the study staff at [*insert phone number*] before starting any new medication (including over-the-counter medications) or any new psychotherapy
- Report safety concerns, including side effects, immediately to study staff. While participating in this research study, do not take part in any other research without

approval from the investigators. Taking part in other research studies without first discussing it with the investigators of this study may affect your safety and invalidate the results of this research, as well as those of the other studies.

- Agree to secure firearms while taking study medication to prevent accidental discharge while under the influence of study medication.

For women:

- Tell the study staff if you believe you might be pregnant
- If you decide to participate in the study, you must agree to not become pregnant and to not breastfeed for the 13 weeks you are taking study medication
- If you can become pregnant, you must also agree either to not have sex or to use a reliable form of birth control while taking the study medication – reliable forms of birth control include condoms with or without a spermicide, diaphragms or cervical caps with spermicide, intrauterine devices (IUDs), hormone-based birth control pills, or injections (Depo-Provera®).

WHAT POSSIBLE RISKS OR DISCOMFORTS MIGHT I HAVE IF I TAKE PART IN THIS STUDY?

Risks of Trazodone and Eszopiclone

Each of the medications used in this study have been used by other patients for many years. However, all medications have risks. Since you won't know if you are taking trazodone or eszopiclone, or if you are taking a placebo, the possible side effects you may experience from any of these medications are summarized here.

- Side effects that occur in more than 10% of people taking trazodone or eszopiclone:
  - Drowsiness, dizziness, headache, fatigue, dry mouth, nausea/vomiting, foul or metallic taste in mouth, feeling nervous, increases in blood pressure.
  - Confusion or Loss of Coordination (Cognitive or Motor Impairment): You may experience a decreased mental or physical ability to perform tasks that require attention, concentration, memory, or coordination. Make sure that you know how you react to the study medication before you drive or do any activity that requires

alertness. You should not take study medication unless you have at least 7 hours of sleep time ahead of you to decrease impairment during the next day.

- Side effects that occur in more than 1% but less than 10% of people taking trazodone or eszopiclone: Constipation or diarrhea, blurred vision, confusion, weight gain, weakness, tremor, skin rash, changes to sex drive, breast enlargement, abnormal dreams, hallucination, swelling of feet and ankles, congested nose, decrease in coordination. Inability to have or maintain an erection of the penis was noted in some men.

Stopping these medications suddenly can worsen some of their side effects. To avoid this and depending on your dose, your dose of study medication may be gradually decreased before being stopped.

There may also be risks associated with how trazodone and eszopiclone work with your regular medications. This is why it is important to let the study staff know about any medications you are taking and before you start taking new medications.

For women: The effects of trazodone and eszopiclone in pregnant women and nursing mothers has not been established. Consequently, there may be unknown risks to you (or to your embryo or fetus) if you are or may become pregnant. Women of childbearing potential enrolling in this study must (i) must have a negative pregnancy test, and (ii) must agree to use a birth control measure (an intrauterine device (IUD), birth control pills, a condom, diaphragm, or abstinence) for the duration of the study. Women are considered to be of childbearing potential unless they have been surgically sterilized (for example tubal ligation or hysterectomy) or are post-menopausal, that is, no menstrual period for more than 6 months. Nursing mothers may not participate in this study.

If you become pregnant during the study, you should immediately stop taking the study medication and tell study staff because of the possibility that the drugs may affect the unborn child. You will be asked to return any unused medication and to continue with regular study visits, for as long as you are able, so that we can continue to collect study information about you as planned. However, you will not receive any further study medication. If you become pregnant while taking a study medication, we will find out which medication you were given and provide you with this information. If you were on trazodone, you will also be provided information about a pregnancy registry in which you may enroll if you choose. We will continue to collect information about your safety until you complete your study participation by Week 17. The intent

of collecting safety information during this time is part of the study's standard collection of safety information and is not focused on studying the effect of the study medication on pregnancy. However, if you happen to experience a serious safety issue involving your pregnancy during this time, this information will end up being collected since the study requires the collection of all serious safety issues that occur before completing participation. The risks associated with collecting this safety information and the risks of loss of confidentiality of the collected information are very low.

Rarely, trazodone and/or eszopiclone can cause the following serious side effects:

- Worsening of PTSD Symptoms and Suicidal Thoughts and Behavior: Notify your study staff if you notice new or worsening symptoms of anxiety, agitation, panic attacks, or aggressiveness. Any of the study medications can rarely increase your risk for suicidal thoughts, and trazodone specifically has a special warning for increased suicidality in children, adolescents, and young adults. At each study visit we will ask how you are feeling, so we can help you if you experience worsening PTSD or new or worsening suicidal thinking and behavior. The study staff may arrange for further evaluation for your safety.
- Sleep Behaviors: Eszopiclone specifically has a special warning for injury due to sleep behaviors. This may include performing activities while asleep including sleepwalking, sleep eating, or sleep driving. Firearms should be secured in the house while taking the study medication to reduce the risk of accidental discharge. If you suspect that you have been doing any activities while asleep, even if you don't fully remember doing them, notify your site study staff immediately.
- Serious Breathing Problems: If you combine the study medication with opioid medications, you may become confused or disoriented, dizzy or lightheaded, and risk entering a drug-induced deep sleep where your breathing slows or stops, causing death. Others near you may see your lips, fingers, toes and other skin becoming blue-colored. Those with COPD or other lung disease, or are older persons, have greater risk. Do not combine opioid medication or other tranquilizers with your study medication.
- Serious Allergic Reactions: If you notice any symptoms of a serious allergic reaction, including rash, itching/swelling (especially of the face/tongue/throat), and trouble breathing, go to your nearest emergency room or call 911, and tell them you are in a

research study. You will be given a Participant Study ID Card that should be with you all the time in case of an emergency. This card will have information about the study and study staff's contact info.

- Unusual Behaviors and Abnormal Thinking: Notify your study staff if you experience any symptoms of agitation, aggressiveness, or decreased inhibition that seems out of character, or if you experience amnesia or hallucinations.
- Serotonin Syndrome: Serotonin syndrome is a rare but serious drug reaction that is caused by high levels of serotonin, a chemical that transmits messages in the brain and body. Immediately seek medical attention or call 911 if you have any of the following: agitation or confusion, hearing voices or seeing visions, loss of consciousness, or a seizure.
- Changes in Heart Rhythm (QT Prolongation): An ECG will be performed during a screening visit to determine if your heart rhythm is normal. If you experience an irregular or abnormally fast heartbeat, please contact the study staff immediately or go to a nearby clinic or local hospital emergency room for evaluation.
- Erection Lasting Longer than 4 Hours (Priapism): Men can have a painful or prolonged erection lasting 4 or more hours. If this happens seek immediate medical attention at an emergency room. Women can experience clitoral priapism, which is associated with pain, discomfort, and changes in sexual response.
- Low Blood Pressure and Fainting (Hypotension and Syncope): You may experience low blood pressure or feel dizzy or faint when you go from sitting to standing. You may be at higher risk if you are currently treated with a medication for high blood pressure or other medications that can cause low blood pressure.
- Abnormal Bleeding: You may experience unusual bruising or bleeding while you take the study medication. You may have an increased risk of bleeding-related problems if you are also taking NSAIDs (such as ibuprofen or naproxen), aspirin, or other medications that affect blood clotting or bleeding.
- Low Sodium in the Blood (Hyponatremia): Severe symptoms of hyponatremia can include hearing voices or seeing visions, fainting or loss of consciousness, and seizures. The study staff will measure your blood sodium level before you start the study medication.

- Increased Pressure in the Eye (Angle-Closure Glaucoma): If you experience sudden onset of eye pain, headache, blurry vision, or seeing halos around lights, go to your nearest emergency room.
- Drug Abuse and Dependence: The study medication is a controlled substance. Abuse and dependence can occur from taking doses higher than those used in this study. Never take more study medication than the amount instructed by your study team.

Risks from Other Study Activities or Assessments

Medical Evaluations: During screening and throughout the study treatment, you will have tests to monitor your health and to obtain information needed for the research. There is a possibility that a medical condition that you did not previously know about will be found. If so, the result does not necessarily mean that you have a new medical condition. You will be referred to your regular treatment provider for follow-up.

Confidentiality: Every effort will be made to keep the information you provide to us confidential (see "*HOW WILL MY PRIVATE INFORMATION BE PROTECTED?*" and "*WHAT IS A CERTIFICATE OF CONFIDENTIALITY?*" sections of this consent form). There is the possibility that data could be compromised or there could be a need to provide information to other health care providers or authorities in order to try to prevent harm, as required by state and other laws.

Urine Sample: There are minor risks associated with providing a urine sample. The results of a urine drug screen performed during screening will appear in your medical record, where health care staff will be able to see it. We do not recommend that you join the study if you are using illicit drugs. If your urine test is positive, the results will be reviewed by the study doctor to see if your prescription medication is the cause. The study doctor will discuss this with you and you may not be able to enroll in the study.

Blood Draw: Blood draws may cause pain, redness, or bruising at the site of the needle stick. There is also a small possibility of infection at the site of the needle stick. It is also unlikely but possible for your blood pressure to drop when blood is drawn. This may cause lightheadedness or fainting.

Electrocardiogram (ECG): An ECG is a generally safe, non-invasive procedure. There is a minor risk of skin irritation from the electrodes used for the ECG.

Interviews and Questionnaires: When being interviewed or filling out a questionnaire, you will be asked about topics that may make some people feel uncomfortable, for example: memories of past trauma, PTSD symptoms and substance use. Stress and feelings of guilt or embarrassment may arise from thinking or talking about your past experiences. You might find that your symptoms temporarily worsen. Or you may feel that your privacy has been invaded. It is important to remember that you can stop the interview, or refuse to answer any question, at any time.

There is always a chance that any procedure can harm you. The procedures in this study are no different. In addition to the risks described above, you may experience a previously unknown risk or side effect.

Risks of the usual care you receive are not risks of the research. Those risks are not included in this consent form. You should talk with your health care providers if you have any questions about the risks of usual care.

WHAT ARE THE POSSIBLE BENEFITS OF THIS STUDY?

If you agree to take part in this research study, there may not be a direct benefit to you. Potential benefits to you may include a reduction in your symptoms. However, your PTSD symptoms and problems sleeping may get better, get worse, or may not change. The investigators hope the information learned from this research study will benefit other patients with PTSD and insomnia in the future. The knowledge gained from this study will serve to inform future research and clinical care for veterans.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT WANT TO JOIN IN THIS STUDY?

Instead of being in this research study, you have these options:

Your treatment provider may prescribe a medication for insomnia. All drugs used in this study as well as others are available with a prescription from your physician. In addition, there are psychotherapeutic treatments for PTSD insomnia that are also available outside of the study through your mental health or primary care provider, though none of these have been studied and approved by FDA for the treatment of insomnia in veterans with PTSD.

If you have PTSD, you may be eligible for treatment at your local VA or Vet Center based on VA guidelines. If you do not have PTSD, you may contact the mental health clinic at your local VA or Vet Center to discuss your eligibility for other services.

HOW WILL MY PRIVATE INFORMATION BE PROTECTED?

Every effort will be made to maintain the confidentiality of your study records. The data from the study may be published; however, you will not be identified. Your identity will remain confidential unless disclosure is required by law. All data will be identified by code numbers. These data will be stored in locked file cabinets that will be accessible only to study staff. The key listing names and code numbers will be kept in a separate locked filing cabinet or separate secure computer drive. During the study, records will be released only with your written consent and HIPAA authorization to appropriate VA research team members including, if requested and warranted, people from the Food and Drug Administration, the General Accountability Office, the Office of the Inspector General, the VA Office of Research Oversight, the VA Central Institutional Review Board (IRB), the VA Research and Development Committee, and the study monitors. Destruction of all research records pertaining to this study will be in accordance with the Federal Policy of the Department of Veterans Affairs and will be retained for a minimum of 6 years after the end of the study. The electronic recordings of your phone interviews will be uploaded to a password-protected computer file folder behind the VA firewall and deleted from the recorder as soon as the uploading is completed. Only Assessment Core staff will have access to the recordings. Recordings will be maintained in the secure folder in accordance with the Federal Policy of the Department of Veterans Affairs and will be retained for a minimum of 6 years after the end of the study. If applicable, your ApneaLink data and readings will be removed from the ApneaLink device and it will reside in the VA secure network drives managed by your local VA and the VA Cooperative Studies Program (CSP). Your ApneaLink data will not be used by anyone outside of CSP #2016 team unless authorized by you for the purpose of follow-up treatment with your primary providers.

Your information will be combined with information from other people taking part in the study. We will write about the combined information we have gathered. Any talks or papers from this study will not identify you.

If you are a VA patient, you already have a VA medical record. If you are not a current VA patient, we will create a VA medical record for you that requires your Social Security Number

(SSN). Also, your SSN will be required for payment processing and Internal Revenue Service income reporting if necessary (see section below under, "*WILL YOU BE PAID TO PARTICIPATE IN THIS RESEARCH STUDY?*" for more information). You will not be able to participate in this study unless you give us your SSN.

We will put information about your participation in this study into your medical record. This electronic medical record will be kept in accordance with the VA-approved records retention schedule. Authorized users of electronic VA medical records are able to access your medical record.

Other researchers may request to use identifying information about you from this study and other sources, together with your medical records, to do more research. The purpose would be to learn more about health conditions. We will only share your information from this study with other researchers if their research is approved by a committee that protects the rights and safety of patients in research. Identifiers will be removed from any identifiable private information and that, after such removal, the information could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

Under the Privacy Act and Freedom of Information Act there is also a possibility that the study's research records might be inspected and photocopied by other regulatory authorities or legally authorized entities.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

WHAT IS A CERTIFICATE OF CONFIDENTIALITY?

To further protect your privacy, the investigators have obtained a Certificate of Confidentiality from the Department of Health and Human Services (DHHS). With this certificate, the investigators may not disclose information (for example, by court order or subpoena) that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes. A Certificate of Confidentiality does not prevent the sharing

discussed in the section above or you from voluntarily releasing information about yourself or your involvement in this research. Even with the Certificate of Confidentiality, the investigators will report child abuse or neglect and information to prevent you from carrying out any threats to do serious harm to yourself or others. If elder abuse reporting is mandated in your state, the study staff would have to report that as well. If keeping information private would immediately put you or someone else in danger, the investigators would release information to protect you or another person.

WHAT ARE THE COSTS TO ME IF I TAKE PART IN THIS STUDY?

You or your insurance will not be charged for any treatments or procedures that are part of this study. All study treatment is free of charge to study participants. If you usually pay co-payments for VA care and medications, you will still pay these co-payments for VA care and medications that are not part of this study.

WILL YOU BE PAID TO PARTICIPATE IN THIS RESEARCH STUDY?

You will be paid $25 for in-person screening visits (up to 2 visits), $50 for the phone assessment and $25 if assigned to a study medication for a total of $100 for the screening (or $125 if an additional screening visit is done). You will be paid an additional $15 if you are asked to wear the ApneaLink device. You will then be paid $25 if you complete the follow-up visits at weeks 1, 2, 3, 6, 9 and 17, and $25 for completing the final in-person assessment and $50 for the phone assessment at week 12 to compensate you for your time. Therefore, you will be compensated a total of $325 (or $340 if applicable for the ApneaLink device) if you complete all assessments.

If you are asked to come in for a research visit that is not a scheduled visit for safety or any other concerns (e.g., asked to have another EKG done, additional in-person screening appointment) or an additional dose evaluation visit, you will be paid $25 for up to 2 unexpected visits.

In addition, if you are traveling more than 50 miles each way or 100 miles roundtrip from home to attend an in-person study visit, you will be compensated for travel expenses at the rate of $0.55 per mile. A separate payment for transportation costs will be provided to you, if applicable, in addition to the compensation for your study participation as described above.

Payments will be made in the form of gift card or electronic funds transfer. Payments involved for being a part of this research study will count as income and may affect your income taxes.

WHAT WILL HAPPEN IF I AM INJURED BECAUSE OF MY BEING IN THE STUDY?

If you are injured as a result of taking part in this study, the VA will provide necessary medical treatment at no cost to you or your insurance unless the injury is due to non-compliance with study procedures. The Department of Veterans Affairs does not normally provide any other form of compensation for injury. By signing this form, you have not released this institution from liability for negligence.

If you should have a medical concern or get hurt or sick as a result of taking part in this study, call: *[List local site contacts]*

DURING THE DAY:

Dr./Mr./Ms. _____ at _____ and

AFTER HOURS:

Dr./Mr./Ms. _____ at _____.

Emergency and ongoing medical treatment will be provided as needed.

DO I HAVE TO TAKE PART IN THE STUDY?

PARTICIPATION IS VOLUNTARY

It is up to you to decide whether or not to take part in this study. If you decide to take part, you may still withdraw at any time. If you do not wish to be in this study or leave the study early, you will not lose any benefits to which you are entitled. If you are a VA employee, refusal to take part in this study will in no way influence your employment. If you do not take part, you can still receive all usual care that is available to you. Your decision not to take part will not affect the

relationship you have with your doctor or other staff, and it will not affect the usual care that you receive as a patient. If you decide to stop taking study medication you will be asked to come to the remaining visits, but again, this is voluntary and you will not be penalized for declining. If you withdraw completely from the study and discontinue study medication and study follow-ups, data that has already been collected as part of the study can be utilized by the study team.

RIGHT OF INVESTIGATOR TO TERMINATE MY PARTICIPATION

The study staff may end your participation in the study if they believe it is in your best interest or if you are not following study requirements. If so, your study doctor will explain the reasons and arrange for your usual medical care to continue. Termination from the study will not affect the relationship you have with your doctor or other staff, and it will not affect the usual care that you receive as a patient.

WHO DO I CONTACT ABOUT THIS STUDY IF I HAVE QUESTIONS?

If you have any questions regarding this study, if you experience side effects or want to report a research-related injury or illness, or if you have any additional concerns or complaints while you are participating in this study, you can contact the study doctor at [*insert LSI contact information*].

If you have questions about your rights as a study participant or you want to make sure this is a valid VA study, you may contact the VA Central Institutional Review Board (IRB). This is the Board that is responsible for overseeing the safety of human participants in this study. You may call the VA Central IRB toll free at 1-877-254-3130 if you have questions, complaints or concerns about the study or if you would like to obtain information or offer input.

WILL I BE TOLD NEW INFORMATION ABOUT THIS STUDY?

Sometimes during the course of a research study, new information becomes available about the treatments being studied that might change a person's decision to stay in the study. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw from the study, your study doctor will arrange for your medical care to continue. If you decide to continue in the study, you might be asked to sign an updated informed consent form.

Individual research results from this study will not be available and/or disclosed to participants at any time. However, a summary of the overall results will be available at the end of the study in the following website: http://www.ClinicalTrials.gov. In addition, participants will be notified of their treatment assignment when the study ends.

FUTURE USE OF DATA

The information collected about you during the course of the study will be stored in a research database maintained by the VA Cooperative Studies Program until destroyed according to VA regulations. The database will be shared per VA policy and applicable Federal requirements among the researchers involved in this project and others in the future who have a VA-approved agreement to use the study data. Information that discloses your personal identity will not be released without your permission unless required by law. Your personal information will always be kept separate from the research database.

OPTION TO BE CONTACTED FOR OTHER FUTURE RESEARCH STUDIES

[ ] YES [ ] NO Participant Initials _____

I consent to be contacted in the future by affiliated investigators and staff of CSP #2016 (or CSP #2016 site staff) to learn about opportunities to participate in other related VA-approved research studies affiliated with CSP #2016. My consent extends to methods of communication established between myself and VA representatives in the course of current research participation or standard care (i.e., mail, telephone, and/or VA-approved electronic communication formats).

Participant Name: [PDF Fillable Field]

Title of Study: CSP #2016 **N**ational **A**daptive Trial for **P**TSD related Insomnia (NAP)

Principal Investigator: VA Facility:

Principal Investigator for Multisite Study: John H. Krystal, M.D.

AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY

Dr./Mr./Ms._____ [*or indicate a study role that has been delegated by the PI/SC or LSI to obtain informed consent*] has explained the research study to you. You have been told of the risks or discomforts and possible benefits of the study. You have been told of other choices of treatment available to you. You have been given the chance to ask questions and obtain answers.

By signing this document below, you voluntarily consent to participate in this study. You also confirm that you have read this consent, or it has been read to you. You will receive a copy of this consent after you sign it. A copy of this signed consent may also be put in your medical record per local VA policy.

I agree to participate in this research study as has been explained in this document.		
_____ Participant's Name	_____ Participant's Signature	_____ Date

FOR VA CENTRAL IRB USE ONLY

PI/SC Approval Date: September 10, 2024 – *PDF Fill*

LSI Approval Date: NA

LSI Verification Date: NA