Informed Consent Document

Acute Effect of Lemborexant on CSF Amyloid-Beta and Tau

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INFORMED CONSENT DOCUMENT

Project Title: Acute Effect of Lemborexant on CSF Amyloid-Beta and Tau

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This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights and responsibilities as a research participant.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We invite you to participate in this research study because you are 60-80 years old in general good health.

The purpose of this research study is to find out the effect of a medication, lemborexant, in individuals who are poor sleepers and whether this medication has an effect on certain proteins in the brain (Amyloid-beta and Tau) that are known to be associated with Alzheimer's disease.

Lemborexant is approved by the U.S. Food and Drug Administration (FDA) at 5 mg and 10 mg doses for the treatment of insomnia (trouble falling asleep or staying asleep). However, in this study we will use a dose of 25 mg, which is higher than what is currently FDA approved. The use of lemborexant is considered investigational in this study.

If you participate in the study, you will be randomized to take lemborexant or a placebo (an inactive substance) for two nights.

WHAT WILL HAPPEN DURING THIS STUDY?

Participants that screen fail may be invited back to rescreen at a later date.

Visit 1: This visit will occur at the Neurology Clinical Research Unit (NCRU) and at the Clinical Translational Research Unit (CTRU). At this visit, we will ask you about your medical history and the medications you are taking. You will be asked to complete questionnaires about your sleeping habits, and you will be tested on your memory. We will also ask questions about your mental health, including if you have ever had any suicidal thoughts or behaviors. You are free to skip any questions that you would prefer not to answer.

If you tell us that you are thinking about hurting yourself or others, the research staff may give you referrals for treatment or work with you to contact your personal doctor or therapist to discuss your thoughts of harming yourself. We may need to work with you on a plan that might include getting you to a medical facility for safety. We also want to provide you with contact information for available resources, should you decide you need assistance at any time. You can call the toll-free 24-hour National

Suicide Prevention Lifeline at 1-800-273-TALK (1-800-273-8255) or St. Louis Behavioral Health Response at 1-800-811-4760 (https://bhrstl.org/crisis-hotline).

Vital signs (including your height and weight), a physical exam, a neurological exam, and an electrocardiogram (ECG) will be performed. An ECG is a tracing test that measures electrical signals from your heart. We may also measure your neck size. You will be asked to complete a medical records release form at this visit so we can obtain medical records from your physician.

We will also perform a blood draw for routine laboratory tests, genetic testing and an amyloid-beta test, which will measure how much amyloid-beta protein is in your blood. Approximately 90 mL of blood will be collected at this visit (approximately 6 tablespoons).

The amyloid-blood test will determine how much amyloid-beta is present in your blood.

- If you had previously participated in certain studies at the Alzheimer's Disease Research Center (ADRC), you will be asked to repeat this blood test.
- If you participated in SEABIRD study (HRPO 201902081), you have already completed the amyloid-beta blood test. This test will not need to be repeated.

You will be asked to complete a questionnaire about your concerns about Alzheimer's disease and how you feel about receiving results about your amyloid status.

At the end of your visit, you will be given a sleep diary to complete for two weeks. You will return the diary to the study team once completed. You will also be given a medication log to record any changes in your medications throughout your participation in the study.

ADRC Data Request
If you previously participated in any ADRC studies, we may request data from the ADRC. This includes markers for Alzheimer's disease gathered from blood draws (including genetic test results) and CSF, results from questionnaires, memory and thinking tests, imaging data, neurological exams, vital signs (including height & weight), health history, and medications you took during the study. Additional data may be shared with the study team.

Amyloid Status Disclosure:
You will be provided information about your amyloid blood test. This will likely occur over the phone, but you may be asked to come in for a visit to get these results. We encourage you to have someone with you at this visit. If you have a positive or elevated amyloid result, this does not mean you will have amyloid plaques in your brain or will experience cognitive impairment. A positive test does not mean that you will develop Alzheimer's disease dementia. The amyloid blood test is done for research purposes for this study. You will not receive a copy of your results, and results will not be added to your medical record.

Visit 2: If you qualify to continue with the study, you will undergo a polysomnogram (attended sleep study) at the Washington University Sleep Medicine Center.

After admission, vital signs will be taken and approximately thirty electrodes will be applied to your head and body to monitor your sleep overnight. Eight wires will be affixed to your head with paste to measure brainwave activity. These wires will be removed with water the following day. The rest of the

wires will be placed on your face and body with tape. These wires measure eye movements, muscle tone, breathing, oxygen levels, ECG, and leg movements.

You will be video recorded during this study. The video recording will document your body position while you sleep and will record any movements that might be associated with any sleep disorders.

You will have the option to have the sleep study recording results added to your medical record. If you choose not to add the sleep study results to your medical records, you will still receive a letter informing you of any findings. The letter will only contain very general information, stating if there was an elevated number of breathing events or leg movements present during the study.

Your sleep study may contain identifying information including your name and date of birth. A paper copy of you sleep study report will be filed with your research records.

As part of this study, you will undergo polysomnography (attended sleep study). You may choose to have the results added to your medical record.

Do you agree to allow us to add sleep study results to your medical record?

_____ Yes **_____ No**
Initials **Initials**

Visit 3: This visit will occur one week prior to your three-night stay at the CTRU. During this visit, we will obtain your weight, review any changes to medications or medical conditions, and blood will be collected for a routine laboratory test.

If you are taking any medication that affects sleep, we may ask that you speak with your health care provider about stopping that medication prior to, or during, the study. Also, if you take a daily aspirin, we will ask that you speak with your health care provider about stopping it one week prior to the lumbar catheter placement (Visit 4).

You will be given a sleep diary to complete at home. You will be asked complete the sleep diary until the day you are discharged from the CTRU. You will also receive instructions for your stay at the CTRU.

Visit 4: You will be admitted to the Clinical CTRU for a three-night stay. Questionnaires will be administered at admission and prior to discharge, and you will be asked to perform psychomotor vigilance testing (PVT) for alertness. PVT requires you to use a small electronic device for 10 minutes to record reaction times where you press a button once a numerical counter has started.

You will be randomly assigned to receive either a placebo (does not contain active ingredient(s)) or lemborexant at bedtime for the first two nights that you are in the CTRU. The study treatment you receive will be determined purely by chance, like flipping a coin. You will have a 2-to-1 chance of receiving lemborexant. That means for every two participants who receive lemborexant, one participant will receive placebo. You will not be told what group you have been placed into.

During this study, we are asking you to have approximately 30 thin wires applied to your head and face to monitor sleep. Up to 21 wires will be glued to your scalp and will be removed with acetone at the end of the study. The remaining electrodes will be applied to your face with tape. The wires will monitor

brain waves, (which is called electroencephalography or EEG), eye movements, and muscle tone during the same time as the CSF (fluid that surrounds the brain and spinal cord) and blood sampling hours. You will have these wires on the entire time you are at the CTRU.

You are asked to allow the use of video monitoring during your admission to monitor sleep-wake behavior and for safety monitoring. The video monitor will be on for the duration of the CSF collection, as explained below, but this video will not be recorded.

The nursing staff will monitor you throughout your stay and vitals (blood pressure for example) may be taken periodically. Upon admission, you will have one or two IV catheters placed in each arm. An IV catheter is a small, flexible tube placed into a vein to draw blood or administer medications or fluids. For this study, one IV will be used to collect blood samples during your visit and the other will be used to administer an amino acid called leucine. Your body naturally has amino acids and they combine to form proteins such as the proteins we are studying, amyloid-beta and tau. The amino acid that you will receive will be labeled (tagged) with carbon-13, an atom that occurs naturally in the body and in the food we eat. The purpose is to make the amino acids heavier to help with their measurement.

Cerebrospinal fluid (CSF) samples will be analyzed in a device called a mass spectrometer which sorts molecules by their weight. The carbon-13 will allow researchers to view how much amyloid-beta, a protein naturally found in the body, is in each CSF sample.

While admitted to the CTRU, all meals will be provided, and a specific diet must be followed. The CTRU staff will contact you before your visit to discuss meal options. All food and water consumed will be recorded by nursing staff.

After the IVs are in place, you will have a lumbar catheter placed in your lower back by a specially trained physician. A lumbar catheter is a small flexible tube that is placed through the skin into a fluid filled space in the spinal canal. This tube will be used to collect CSF (fluid that surrounds the brain and spinal cord). This catheter is similar to the epidural catheters used for an epidural block during child delivery. You will be asked to sit in a special chair or lie down on one side of the bed. Your lower back will be cleaned with a solution and allowed to dry. A medicine to numb your skin will be injected into the skin. The spinal needle will then be inserted and directed towards the spinal canal. A flexible tube is inserted through the needle. The needle is withdrawn, and the tube is held to the lower back with a bandage.

It may take more than one attempt to place the catheter. 6 ml (a little over one teaspoon) of CSF will be collected every 2 hours through this catheter. CSF will be collected 25 times over a 48-hour period (about 1 teaspoon every 2 hours) for a total CSF collection of 30 teaspoons or about 10 tablespoons. Your body makes more than three teaspoons of CSF an hour and will replace the samples taken. At the end of the study, an additional 2 ml sample of CSF will be collected and sent to the local lab to check for any signs of infection.

Blood and CSF are collected to measure biomarkers related to Alzheimer's disease, such as amyloid-beta and tau proteins. At the start of the study, blood will be collected at 0, 5, 10, 15, and 30 minutes after the lumbar catheter placed. Then, blood will be collected every 30 minutes until hour 4. After hour 4, blood will be collected every 2 hours for the remainder of the 48-hour collection period. 1-3 teaspoons of blood will be collected at 34 time points over 48 hours.

During the infusion of the carbon-13 labeled amino acid (leucine) and collection of CSF and blood, you will be asked to sleep as you are able after taking either placebo or drug.

You will be asked to stay at least 8-12 hours after the study is completed for observation to ensure you have tolerated the procedure and do not develop a spinal headache. A physical exam will be performed prior to discharge. Before you leave, you will repeat the PVT to assess if your level of alertness has returned to baseline. When you leave, you will be given the beeper number of the physician performing the procedure in order to contact him/her in the event a problem arises after leaving the research center. In addition, the physician or a member of his/her research staff will contact you by phone 24 and 48 hours after discharge.

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Table 1: Study Schedule

Procedures	Visit 1	Visit 2	Visit 3	Visit 4			
				Admission	48 Hours Sampling	8-12 Hour Observation	Discharge
Medical History/Medication Review	X						
Questionnaires	X			X		X	
Amyloid-Beta Blood Test*	X						
Physical Exam	X						X
Neurological Exam	X						
Medication Review	X		X	X			X
Vital Signs	X	X		X	X	X	
Height	X						
Weight	X		X	X			
Lead ECG	X						
Routine Blood Test(s)	X						
Blood Collection (Blood Clotting Tests)			X				
Blood Draw (genetic testing)	X						
Attended PSG		X					
Unattended PSG				X	X	X	
Video Recording		X					
Lumbar Catheter Placement				X	X		
Leucine Infusion				X			
Study Drug Administration (2 nights)					X		
CSF/Blood Catheter Sampling					X		
PVT				X		X	
CSF Safety Labs					X		
Asses for Adverse Events	X	X	X	X	X	X	X
24-Hour Phone Follow-Up							X
48-Hour Phone Follow-Up							X

* Not required if referred by the SEABIRD study

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GENETIC & BIOMARKER RESEARCH

Blood samples will be collected from you for genetic and biomarker research. Biomarkers are molecules in the body that may be used to see if there is increased risk of disease and/or follow how well the body responds to a treatment.

Genes are a unique combination of molecules (called DNA) that we inherit from our parents. There are millions of tiny differences in our genes. These differences may make us more or less likely to develop certain diseases or conditions or to have certain characteristics. Genetic research involves studying the differences in genes and DNA between individuals. This type of testing creates information that is as unique to you as your fingerprint.

Previous studies have shown that a gene called apolipoprotein E ("APOE") may influence the rate of disease progression or a person's response to treatment. We will test your blood to see what form of the APOE gene you have. **This genetic testing is not optional.**

The results of these tests will be maintained in scientific databases for this research study. These results are important only for research - not for helping to care for you. For this reason, the results will not be released to you or your family.

No information regarding your genetic or biomarker results will be entered into your regular medical record. If you are concerned about a potential genetic disorder, you should discuss this with your primary care doctor. You and your doctor may choose to test specifically for it, but this would require additional blood samples and would not be part of this research project.

Data from your genetic or biomarker tests will not be revealed to your family members, insurance companies, employers, or other individuals or organizations.

Although the study researchers will have access to coded individual data, any information gained from this research will be reported in publications in an anonymous summary form. Data will be stored in a locked file, and in a computer with restricted access.

Only the research team will have access to the original research data.

Will you save my samples or research data to use in future research studies?

As part of this study, we are obtaining data, DNA, blood, and cerebrospinal fluid samples from you. The data, blood, and cerebrospinal fluid samples we are obtaining in this study may be made available for studies going on right now as well as studies that are conducted in the future. These studies may be done by researchers at Washington University, other research centers and institutions, or private companies involved in research.

We may also share your research data with large data repositories (a repository is a database of information) for use by others, such as the research community, institutions, private companies and the general public. If your individual research data is placed in one of these repositories, your name and other identifying information will be removed. All reasonable precautions will be taken to protect your privacy and confidentiality. Necessary approvals will be obtained to use the data. Certain summary

information may be available to the general public.

These future studies may provide additional information that will be helpful in understanding Alzheimer's disease, or other diseases or conditions, including research to develop investigational tests, treatments, drugs or devices that are not yet approved by the U.S. Food and Drug Administration. Should this occur, there are no plans to provide financial compensation to you. There are no plans to provide financial compensation to you should use of your data, DNA, blood and cerebrospinal fluid occur. It is unlikely that what we learn from these studies will have a direct benefit to you. By allowing us to use your data, DNA, blood and cerebrospinal fluid, you give up any property rights you may have in the data, DNA, blood and cerebrospinal fluid. We will protect the confidentiality of your information to the extent possible.

If you participated in the SEABIRD or ADRC studies, only data collected before you take study drug will be shared with their study team prior to the study completion. Specifically, we will share amyloid status, markers for Alzheimer's disease at the initial draw of cerebrospinal fluid (hour 0) and testing for memory and thinking (Mini-Mental State Exam). Additional data may be shared after the study is completed.

If you change your mind and do not want us to store and use your data, blood, DNA, and cerebrospinal fluid samples for future research you should contact the research team member identified at the top of this document. They will no longer be used for research purposes. However, if some research with your data, blood, DNA, and cerebrospinal fluid samples has already been completed, the information from that research may still be used. Also, if the data, blood, DNA, and cerebrospinal fluid samples has been shared with other researchers it might not be possible to withdraw the data or samples to the extent it has been shared.

Shared data will not include your name but may be linked by a global unique identifier (GUID) number. This ID number will allow us to share data without using your personal information. In order to generate the ID number, you will be asked to provide information that is unique to you, such as your date of birth and place of birth.

Audio Recording/Video Recording

One aspect of this study involves making video recordings of you during a sleep study that is part of the screening process to determine eligibility for the study. The video recording of your sleep will be performed at the sleep center. The recording will be used to determine body position while you sleep and to record movements that might be associated with any sleep disorders. Only the sleep center and research team will have access to your sleep study video recording. Recording video during a sleep study is standard practice and will be mandatory for this study. If you do not wish to have the video recorded, you may not be able to participate in the study.

During your 3-night stay at the CTRU, a video and audio monitor will be on, but will not be recording. This will be done for safety monitoring.

HOW MANY PEOPLE WILL PARTICIPATE?

About 30 people will take part in this study conducted by investigators at Washington University.

HOW LONG WILL I BE IN THIS STUDY?

Your participation in this study is expected to last approximately 4 ½ weeks of total participation, although spread out over several months depending on the timing of scheduling each visit.

You will come in for a total of four visits. Two of your study visits include overnight stays. Your overnight stay at the sleep center will last approximately 12 hours. Your CTRU admission visit will last approximately 72 hours. You will be called 24 and 48 hours after discharge.

You will also be contacted by phone and may be asked to come in for a visit to discuss your amyloid status.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition, there may be unknown risks, or risks that we did not anticipate, associated with being in this study. Some risks described in this consent document, if severe, may cause death.

Risks associated with lemborexant:

- Sleepiness/drowsiness is the most common side effect (at least 5 people out of 100) and has been reported to be generally mild to moderate in severity.
- Decreased alertness and motor coordination may occur, including impaired driving
- Because lemborexant can cause drowsiness, patients, particularly the elderly, are at a higher risk of falls
- Unusual dreams may occur
- Headache
- Urinary tract infection (UTI)
- Fatigue/tiredness and/or weakness
- Worsening of depression/suicidal thoughts
- Sleep paralysis, which is a brief inability to move or speak, typically lasting for a few seconds to a few minutes, and usually occurring either while initially falling asleep or when waking up.
- Seeing and/or hearing things that are not there (hallucinations) while sleeping and awakening
- Sleep-walking and/or sleep-driving
- Sudden loss of muscle tone, usually triggered by emotions and an emotional behavior such as laughing. If you experience symptoms like these, be sure to inform your study doctor immediately.
- There is a potential for abuse, misuse and addiction with medications used to treat insomnia.

As with any drug, it is possible that you could have an allergic reaction to the study drug, such as itching, skin rash, facial swelling, or a severe or sudden drop in blood pressure. The sudden drop in blood pressure may lead to shock with loss of consciousness and/or possible seizures, including the possibility of death. If you have any of the above symptoms in the research clinic/hospital, you will receive prompt medical attention. If you have any of the above symptoms after being discharged from the research clinic, you should seek medical attention right away.

Lemborexant may interact with certain medications. Please notify the study team of any current medications or before you start taking new medications to prevent any interactions. You will be monitored closely to guard against these interactions and will be constantly under nursing care, including video monitoring. We are also screening for medical problems that could be made worse by lemborexant. You may not participate if you have any of these conditions.

The study will be stopped and you will be allowed to sleep if you experience any significant or serious side effects from lemborexant.

We will tell you of any new risks with the study drug.

Risk of Intravenous (IV) catheter placement and blood draws:

- Small amount of discomfort, pain, and/or bleeding
- Dizziness or feeling faint
- Bruising, bleeding, and swelling may occur at the IV/blood draw site
- Infection (rare) at the IV/blood draw site

Leucine IV Infusion:

Leucine is an amino acid found in foods and your body.

- There are no risks associated with Leucine.
- IV infiltration (fluid leaking outside of the vein into surrounding tissue) which could cause temporary swelling or discomfort. If this were to happen, the IV is removed and re-inserted into a new vein

CSF Sampling:

Likely/Common:

- Catheter placement may cause discomfort
- Brief cramping and/or pain in a leg
- Minor pain, bruising, or swelling
- Dizziness or feeling faint
- Feeling lightheaded, dizzy, or woozy upon standing after 60 hours of bed rest. With the assistance of a nurse, you will be encouraged to get up slowly out of bed, sit up at the side of the bed, stand, and walk as you feel able to ensure you do not have any feelings of lightheadedness. All participants are up for 2 hours prior to discharge.

Less likely:

- Ringing in the ears
- Nausea and vomiting. If severe, you may be given medication to help with the nausea.

Rare:

- Nerve damage. Only physicians experienced in performing lumbar catheters will perform this procedure.

- Allergic reaction to the local anesthetic (lidocaine 1%) used. An allergic reaction could cause swelling and a rash on your skin where the anesthetic was injected. Please tell us if you have ever had a reaction to local anesthetic before (such as when you were visiting the dentist).

Very Rare:

- In individuals with problems of blood clotting, a lumbar catheter may cause a large amount of bleeding and lead to complications such as subdural (spinal) bleeding. This is extremely rare and completely preventable through screening for problems with blood clotting.
  The needle may introduce pathogens internally, leading to infection. This is very rare if the proper sterile technique is used, as we will during this study. At the end of the study 2 additional ml (~1 tsp) of CSF will be sent to the lab to check for any signs of infection

Risk of Headache

Participants may have a headache following placement of a lumbar catheter, due to the decreased amount of CSF. Post-lumbar catheter headache occurs frequently (50-80% of participants) and can be mild to moderate in severity. For most individuals, the headache goes away once the catheter is removed.

Occasionally (30% or less), a headache may continue after removal of the catheter and requires treatment. If headaches occur during or following CSF removal, they are usually mild and last 0-2 days. However, they can be severe and last up to a week or longer if not treated with a local injection into your back of your own blood ("blood patch") which usually stops the headache within hours.

If you have a severe headache after the study, we recommend that you receive a blood patch to resolve the headache as soon as possible. We will provide the patch at the CTRU at no charge. If you receive a patch or other medical care from another institution, we will not pay for any charges or be able to protect your confidentiality.

All precautions will be taken to minimize these risks. If you have travelled from out of town we will have you stay another 24 hours. This means from the time the catheter is removed you will have a rest and recovery period of 8-12 hours.

Risks of ECGs

- There is no pain or discomfort during an ECG; however, removing the pads may cause some irritation to your skin.

Risks of Testing and Questionnaires

- You might feel frustrated when completing the memory assessment.
- You may experience emotional discomfort when answering some questions. You have the right to refuse to answer any questions.
- Some of these surveys ask about depression. If you have thoughts of suicide, the study physician will perform a thorough evaluation and appropriate medical care will be provided. You can obtain further help by calling the National Suicide Prevention Hotline at 1-800-273-8255 or the Behavioral Health Response Crisis Hotline at 314-469-6644

Risks of Polysomnography:

- You might find some of the wires uncomfortable and may experience skin irritation from the electrodes and the tape or paste used to secure them
- Worse sleep quality is common and mild. People usually do not sleep as well in an unfamiliar environment. Therefore, participants may be more tired than usual the next day.

Women Capable of Becoming Pregnant

If you are a woman capable of becoming pregnant, we will ask you to have a pregnancy test during the study. You must use effective birth control methods and try not to become pregnant while participating in this study. If you become pregnant, there may be unknown risks to your unborn child, or risks to your unborn child that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to an unborn child. You must tell the doctor if your birth control method fails while you are on the study. If you believe or know you have become pregnant while participating in this research study, please contact the research team member identified at the top of this document as soon as possible. Please discuss with the research team how long you need to wait before becoming pregnant after completing the treatment or procedures on this study.

Risks to pregnant women, fertility, unborn, or breastfeeding infants

Taking the study drug may involve risks to a pregnant woman or unborn baby that are currently unknown.

There is some evidence that the study drug can harm the developing fetus in certain animal studies. The relevance of this finding to humans is unknown. The study drug should not be taken by pregnant women or by women who are attempting to become pregnant.

If you are a woman who is able to have children, you must use a highly effective method of contraception for at least 28 days before the study and you must agree that you will continue to use a highly effective method of contraception during the entire study period and for 28 days after your taking part in the study. Your study doctor will advise you on what methods of contraception are considered highly effective methods.

Data from a clinical lactation study show the presence of trace quantities of lemborexant in human milk. However, there are no data on the effects of lemborexant on the breastfed infant, or the effects on milk production. Infants exposed to the study drug through breastmilk should be monitored for excessive sedation.

Genetic Research

There may be information obtained from the genetic testing that indicates that you, or potentially a family member (since we inherit genes from our parents, and pass genes on to our children) are at risk for a particular disease or condition. For example, genetic sequencing may indicate that an individual is more prone to develop certain types of cancer or other types of diseases, (e.g. Alzheimer's or other inherited diseases).

While the data developed for this study are being stored without traditional identifiers (stored only with coded ID numbers, no names), there may be ways of linking the genetic materials back to you. Because your DNA is unique to you, it is possible that someone could look at the information in the DNA database and compare it to information in another database and use that to identify you. This is difficult to do and is very unlikely to happen.

If made available to persons or agencies outside of our research group, information about genetic test results could affect your employment or insurance. For instance, employers, insurers, or others may use this information when making decisions about you or your family members regarding employment, insurance, or other benefits.

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

Breach of Confidentiality
One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure. Please see the section in this consent form titled *"How will you keep my information confidential?"* for more information.

WHAT ARE THE BENEFITS OF THIS STUDY?
You will not benefit from being in this study.

However, we hope that, in the future, other people might benefit from this study because we will learn if it is possible to decrease the levels of amyloid-beta in the brain and possibly prevent or treat Alzheimer's disease.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?
You will not have any costs for being in this research study.

You and/or your medical/hospital insurance provider will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?
You will be paid for being in this research study. You will be asked to provide your social security number (SSN) in order for us to pay you. You may choose to participate without being paid if you do not wish to provide your social security number (SSN) for this purpose. You may also need to provide your address if a check will be mailed to you. You should receive your payment within 6-8 weeks of completing the study. If your social security number is obtained for payment purposes only, it will not be kept for research purposes.

If you complete all study visits, you may be compensated up to $925 for your participation in this study.

- You will be paid $25 total for screening visit one if you complete all visit assessments including questionnaires, physical examination, blood draw, and ECG.
- You will be paid $100 for completing the attended sleep study.
- You will be paid $800 by check after the CSF and blood collection procedures are completed for 48 hours. If samples cannot be collected during the procedure, you will still receive $300 payment for at least two attempts at CSF collection and for the time and inconvenience involved in participating.
    - **48 Hour Collection-Can be up to 72 hours total**
        - $300 for CSF catheter placement
        - $300 for four 12 hour CSF/blood collection periods
        - $200 for 8-12 hour post-catheter removal rest period

For people who previously consented into this study but were determined to be ineligible: If you are asked to repeat Visit 1 screening procedures, you will be paid $25 for completing the office visit

WHO IS FUNDING THIS STUDY?

Eisai Inc. is funding this research study. This means that Washington University is receiving payments from Eisai Inc. to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from Eisai Inc. for conducting this study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

Washington University investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator Dr. Lucey and/or the Human Research Protection Office at 1-(800)-438-0445.

Decisions about whether payment for medical treatment for injuries relating to your participation in research will be made by Washington University. If you need to seek medical care for a research-related injury, please notify the investigator as soon as possible.

HOW WILL YOU KEEP MY INFORMATION CONFIDENTIAL?

Other people such as those listed below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you. We will keep your participation in this research study confidential to the extent permitted by law.

- Government representatives, (including the Office for Human Research Protections) to complete federal or state responsibilities
- The U.S. Food and Drug Administration
- Eisai Inc., the company funding the study
- Your primary care physician if a medical condition that needs urgent attention is discovered
- National Institute of Health
- Hospital or University representatives, to complete Hospital or University responsibilities
- Information about your participation in this study may be documented in your health care records and will be available to anyone with access to your health care record, including your health

insurance company. This information may also be released as part of a release of information request.

- Data Safety Monitoring Committee
  The last four digits of your social security number may be used in hospital or University systems to track billing information for research procedures
- Washington University's Institutional Review Board (a committee that oversees the conduct of research involving human participants.) The Institutional Review Board has reviewed and approved this study.

Any report or article that we write will not include information that can directly identify you. The journals that publish these reports or articles require that we share your information that was collected for this study with others to make sure the results of this study are correct and help develop new ideas for research. Your information will be shared in a way that cannot directly identify you

To help protect your confidentiality, we will implement the following measures. All paper questionnaires, blood samples, and cerebrospinal fluid samples will be labeled with an ID number and not your name. There will be a master list that is behind two locks in the research office at Washington University School of Medicine that links the participant's name to the ID number. Only study team members will have access to the list. All questionnaires and other forms will be transported only by a member of the research team from a clinic office, NCRU, or the CTRU to a secure, locked room in Dr. Lucey's office or Washington University School of Medicine that is dedicated only to research. Paper records will be stored in a dedicated research office at Washington University School of Medicine or Dr. Lucey's office for the duration of the study. Paper records that contain your name, such as this document and your sleep study report, will be filed separately from the other research documents.

Electronic records, such as your sleep studies and a database with information from paper forms, will be stored on computers with access to the Washington University Department of Neurology server. The computers will be password-protected and only the study team will have access to these files. Your sleep study will also be stored at the Washington University Sleep Medicine Center.

The research team will send study results to Eisai. Information sent to Eisai will use a coded number and not your name. Trial data will be used for research purposes and to guide future studies for potential commercial use. In the future, Eisai may continue to use your health information that is collected as part of this study. For example, Eisai may combine information from this study with the results of other studies to re-analyze the safety and effectiveness of the study medication to evaluate other products or therapies, to develop a better understanding of a disease, or to improve the design of future research studies. Eisai may also share information from the study with regulatory agencies in foreign countries.

If you receive Medicare benefits, are injured as part of your participation in this research study and medical treatment relating to this injury is paid by anyone other than you or your insurance company, that payer will need to collect personal information about you. This information includes your name, date of birth, gender, social security number, Medicare identification number and information related to this research study. The payer will report this information to the Centers for Medicare & Medicaid Services (CMS), the federal agency that oversees the Medicare program, during your participation in the study and for as long as the payer is required by CMS to report this information. If you do not want to

release your personal or treatment related information you have the right to refuse reimbursement by the payer for any research injury. The payer will not use this information for any other purpose.

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.

You have the right to share your information or involvement in this study with anyone at any time. You may also give the research team permission to disclose your information to a third party or any other person not connected with the research.

Are there additional protections for my health information?

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form. The research team will follow state and federal laws and may share your health information with the agencies and people listed under the previous section titled, "How will you keep my information confidential?"

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form or as permitted or required by law. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University's Privacy Officer at 866-747-4975.

Although you will not be allowed to see the study information, you may be given access to your health care records by contacting your health care provider.

If you decide not to sign this form, it will not affect

- Your treatment or the care given by your health provider.
- Your insurance payment or enrollment in any health plans.
- Any benefits to which you are entitled.

However, it will not be possible for you to take part in the study.

If you sign this form:

- You authorize the use of your PHI for this research
- This authorization does not expire.
- You may later change your mind and not let the research team use or share your information (you may revoke your authorization).
    - To revoke your authorization, complete the withdrawal letter, found in the

Participant section of the Human Research Protection Office website at hrpo.wustl.edu or you may request that the Investigator send you a copy of the letter.

- **If you revoke your authorization:**
  - The research team may only use and share information already collected for the study.
  - Your information may still be used and shared as necessary to maintain the integrity of the research, for example, to account for a participant's withdrawal from the research study or for safety reasons.
  - You will not be allowed to continue to participate in the study.

Can we contact you by email?

We would like to contact you by email for the purposes listed below. Some of these emails may contain health information that identifies you.

- Appointment scheduling
- Study education

Only the research team will have access to your email communications. We will only communicate by email to send you the information listed above. If you have any questions, wish us to stop sending these messages or need to contact us for an urgent or emergent situation, please contact the research team member identified at the top of this document.

You should be aware that there are risks associated with sending your health information via email.

- There is always a risk that the message could be intercepted or sent to the wrong email address. To avoid sending messages to the wrong email address, the first email we send you will be a test message to ensure we have the correct email address.
- When using any computer you should be careful to protect your username and password. Make sure you log-out before getting up from the computer.
- If you share a home computer with other family members, and do not want them to know you are participating in this study make sure you provide an email address that only you can access.
- Your employer will have access to any email communications sent or received on any electronic devices used for work or through a work server.
- If you lose your phone, others may be able to access the messages that we send.

Do you agree to allow us to send your health information via email?

_____ Yes **_____ No**
Initials **Initials**

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed.

If you decide not to be in this study, or if you stop participating at any time, you will not be penalized or lose any benefits for which you otherwise qualify.

What if I decide to withdraw from the study?
You may withdraw by telling the study team you are no longer interested in participating in the study or you may send in a withdrawal letter. A sample withdrawal letter can be found in the Participant section of the Human Research Protection Office website at hrpo.wustl.edu.

If you decide to withdraw from the study after the lumbar catheter procedure, we will ask that you stay for observation to monitor for a headache. We may also call you 24 and 48 hours after you leave to discuss any physical complaints you may experience after the lumbar catheter. If you leave the morning after taking the study drug, you may be asked to complete the PVT to measure your alertness before discharge.

Will I receive new information about the study while participating?
If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can someone else end my participation in this study?
Under certain circumstances, the investigator might decide to end your participation in this research study earlier than planned. This might happen for no reason or because the study has been determined to not be safe for you, or because you are pregnant, or because funding for the research study has ended.

WHAT IF I HAVE QUESTIONS?
We encourage you to ask questions. If you have any questions about the research study itself, please contact Christine Bear at 314-362-7263 or 314-703-7150. If you experience a research-related injury, please contact the research coordinators at 314-362-7263 or 314-703-7150.

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office at 1-(800)-438-0445, or email hrpo@wustl.edu. General information about being a research participant can be found on the Human Research Protection Office web site, hrpo.wustl.edu. To offer input about your experiences as a research participant or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study. As a participant you have rights and responsibilities as described in this document and including:

- To be given enough time before signing below to weigh the risks and potential benefits and decide if you want to participate without any pressure from the research team or others.
- To understand all of the information included in the document, have your questions answered, and receive an explanation of anything you do not understand.
- To follow the procedures described in this document and the instructions of the research team to the best of your ability unless you choose to stop your participation in the research study.

- To give the research team accurate and complete information.
- To tell the research team promptly about any problems you have related to your participation, or if you are unable to continue and wish to stop participating in the research study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

Do not sign this form if today's date is after EXPIRATION DATE: 12/06/23.

_____

(Signature of Participant) (Date)

_____

(Participant's name – printed)

Statement of Person Who Obtained Consent

The information in this document has been discussed with the participant or, where appropriate, with the participant's legally authorized representative. The participant has indicated that they understand the risks, benefits, and procedures involved with participation in this research study.

_____ _____

(Signature of Person who Obtained Consent) (Date)

_____

(Name of Person who Obtained Consent - printed)