If appropriate for this study, a scanned copy of the signed consent form should be uploaded to the participant's Epic/EMR record.

Patient I.D. plate

RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: **Medical Management of Sleep Disturbance During Opioid Tapering**

Application No.: **IRB00198426**

Sponsor/Supporter/Funded By: **National Institute on Drug Abuse**

Principal Investigator: **Andrew Huhn, Ph.D.**
5510 Nathan Shock Drive
Baltimore, MD 21224
Phone: 410-550-1971

You are being asked to join a research study. Participation in this study is voluntary. Even if you decide to join now, you can change your mind later.

1. Research Summary (Key Information):

The information in this section is intended to be an introduction to the study only. Complete details of the study are listed in the sections below. If you are considering participation in the study, the entire document should be discussed with you before you make your final decision. You can ask questions about the study now and at any time in the future.

The purpose of this study is to evaluate whether an FDA-approved medication for insomnia, suvorexant (Belsomra®), can help treat sleep disturbance in patients with opioid use disorder (OUD) who are going through supervised opioid withdrawal in a residential treatment facility.

The study consists of a screening visit, an 11-day residential stay at Johns Hopkins Bayview Medical Center, and a follow-up visit 5-10 days later. You will be stabilized on buprenorphine (Subutex) either during your screening visit or on the day you are admitted for your residential stay. During your stay, you will be maintained on buprenorphine/naloxone (Suboxone) for a 2-3 day period before being tapered off of Suboxone over a 4-day period. We will ask you to stay on the unit with us for an additional 4 days after your final Suboxone dose so we can monitor any withdrawal you may be experiencing. It is expected that you will experience some level of opioid withdrawal as part of this study. Symptoms of opioid withdrawal include nausea, diarrhea or stomach cramping, muscle aches and pains, yawning, sweating, pupil dilation, minor increases in blood pressure, and runny nose/tearing eyes.

You will be asked to take the study drug during the opioid taper and after the opioid taper. The study drug will either be suvorexant (Belsomra®) or placebo (an inactive material that does not contain any active drug). The risks associated with suvorexant (Belsomra®) are side-effects that could include sleepiness/drowsiness (7% of people), headache (7%), dizziness (3%), diarrhea (2%), dry mouth (2%), upper respiratory infection (2%), abnormal dreams (2%), and cough (2%). Serious adverse effects could include sleep paralysis (7%), somnolence (7%), and worsening of depression or suicidal ideation.

There is no cost to you for participating in the study.

2. Why is this research being done?

This research is being done to evaluate whether a study drug called suvorexant (Belsomra®) may help improve sleep in people who are tapering off of opioids.

Belsomra® works differently from other sleep medications. Most other sleep medications help you sleep by sedating you. Belsomra helps you sleep because it stops your natural "wake" cycle from being turned on. We think this may be a better way to help people sleep when they are withdrawing from opioids. Because of these differences, we also think that Belsomra will produce fewer negative side effects than those other medications.

Are there any investigational drugs/devices/procedures?

The use of Belsomra in this research study is investigational. The word "investigational" means that Belsomra is being used in a way that is not yet approved for marketing by the Food and Drug Administration (FDA). Specifically, although Belsomra is being administered to treat sleep, which is its approved indication, this study will administer Belsomra at doses that are higher than what the FDA has approved. The FDA is allowing us to administer Belsomra in this study.

This study is designed to determine which dose of Belsomra increases sleep better than a placebo in patients who want to stop using opioids.

Who can join this study?

Only participants who are physically dependent on opioids and are interested in tapering off of them, and who are at least 18 years old, may join this study.

How many people will be in this study?

About 60 people will be enrolled into the study.

3. What will happen if you join this study?

If you agree to be in this study, we will ask you to do the following things:

Screening Visit

- You will be completing the screening visit today at the Behavioral Pharmacology Research Unit (BPRU). We will ask you to complete several questionnaires to determine whether you are eligible to join the study. The questionnaires will ask about things like your mood, emotional wellbeing, opioid use and withdrawal, drug use, and sleep. We will also ask you to provide a blood sample (no more than 2 tablespoons) that will be used to determine whether it will be medical safe for you to participate in our study and to provide a urine sample that will be tested for study eligibility, recent drug use, and pregnancy (if applicable).

- You may also complete an electrocardiogram (ECG) to make sure your heart is healthy.
- At some point either today or during on Study Day 1, we will also ask you to meet with a medical staff member to complete a medical history and physical examination, and to ensure you have an opportunity to ask a medical team member any questions you may have about the study drug.

Buprenorphine Induction

If you are eligible for the study, we will need to induct you onto buprenorphine (Subutex) and transition you to buprenorphine/naloxone (Suboxone). In order to complete the induction, we will need you to arrive to the study in opioid withdrawal- we will not be able to administer the first dose of Subutex until you have started withdrawing from other opioids. You know your body best, so please time your final dose of opioids so that you will be experiencing mild-moderate withdrawal when you come into the clinic. During the induction, we will give you smaller doses of Subutex throughout the day. This is done to make sure you do not experience any negative side effects of Subutex. Because of this procedure, the induction may take a few hours, but we will aim to bring your withdrawal under control as quickly as possible.

Ideally, we will complete this induction on the day that you are scheduled to be admitted into the residential clinical research unit that is described below. However, sometimes it may not be possible for you to be immediately admitted into that unit. In those cases, we will be able to induct you onto Subutex, following the same procedures described above, and then provide you with some Suboxone to take yourself until you can be admitted into the unit. If this happens, we will provide you with a blister package that contains daily doses of Suboxone for you to take. You will need to come into the clinic weekly to pick up a new package. You will not receive more than 3 weeks' worth of packages, and we will aim to have you admitted into the clinical research unit as soon as possible.

Residential Stay Period

If you are eligible to be in the study, you will be admitted to the residential clinical research unit that is located on our same campus for 11 days (10 nights). During this time, if you are a smoker, you will be allowed to smoke cigarettes.

During your stay, if you have not already been transitioned onto Suboxone then you will complete the induction described above. If you receive Suboxone from us before being admitted and have a dose higher than 16mg, then your dose will be reduced to 16mg on admission day. You will continue to take Suboxone for 2-3 days before beginning a Suboxone taper, which will be spread out over a 4-day period. We will ask you to staying on the unit with us for an additional four days after your final Suboxone dose so we can monitor any opioid withdrawal you may be experiencing.

Study Days 1-3:

- Beginning on Study Day 1 (the day you are admitted onto the residential unit), will ask you to begin wearing an accelerometer (also known as an Actigraph) on your non-dominant wrist (the wrist you do not write with) all day. This device is the size of a watch and is used to measure sleep and daily activity. You will begin completing questionnaires and provide a saliva sample to measure your stress hormones several times a day each day.

- Beginning on Study Day 1, we will also ask you to wear a wireless EEG monitor on your forehead every study night. The EEG monitor is the size of a deck of cards and is used to measure sleep quality overnight. It works by placing self-adhesive sensors on your forehead, which are secured with a strap that goes around your head. We will show you how to use the EEG monitor and nursing or research staff will be available to help you put it on at night as needed.

- At some point during Study Days 1 – 3, you will meet with a staff member to learn more about ways to help you sleep better. You will also complete a brief educational session about opioid-related overdose.

- One Study Day 1 we will collect a blood sample from female participants that will be analyzed for hormone levels, and we will collect a blood sample from all participants on three study days (spread throughout the entire study) that will be used to analyze your stress hormone levels.

Study Days 4-11:

- Beginning on Study Day 4, your Suboxone dose will begin to decrease every day during Study Days 4-7, and you will not receive any Suboxone on Study Days 8-11.

- Beginning on Study Day 4, you will also begin receiving the study drug (either Belsomra or placebo), which will be administered in 2 capsules that you will swallow. Neither you nor the study staff working with you will know whether you are taking Belsomra or placebo.

- Your capsules will consist of one of 3 potential options: a low dose of Belsomra, a high dose of Belsomra, or a placebo. The study drug you receive will be determined randomly (by chance, with a method similar to drawing numbers from a hat). The study drug will not change throughout your participation, and is designed to help you sleep while you are tapering off of opioids. If you are uncomfortable with the study drug, you can speak to a study team member about reducing your dose, otherwise you will continue to take the study drug until the last night of the study (Study Day 10).

- Since the study drug is designed to help you sleep, you should take it 30-60 minutes before you expect to go to sleep at night. The study drug will become available for you to take at 8:30 PM and you will need to ask the nurse for the study drug when you think you may go to sleep soon. If you have not yet started trying to sleep or asked for the study drug by 11:00 PM, then we will ask you to take the study drug at that time.

- Through Study Days 4-11, additional medicines to help you manage symptoms of withdrawal will also be available to you. These medications are commonly used to help reduce some symptoms of opioid withdrawal (for example, Motrin) - to use them you will just need to ask the nurse to provide them to you.

- At the end of the study and before discharge, we will provide you with a referral to additional treatments for opioid use disorder and an intranasal version of the medication naloxone (Narcan®) that is used to reverse opioid-related overdoses, which we will instruct you on how to use.

Follow-up Session:

- You will be asked to come back to the research unit about 5-10 days after your residential stay for a brief follow-up session. Prior to the follow-up visit, we will ask some questions about your mood and drug use behaviors since leaving the unit over the phone. During the follow-up we will ask additional questions related to your mood since leaving the unit and ask you to provide a urine sample.

Will research test results be shared with you?
It is uncertain if the research tests will produce results that would be relevant for your clinical care, so we will not share these results with you unless we identify a clinically significant result. If that happens, we will provide you with the information you need to consult a medical professional.

How long will you be in the study?
You may receive buprenorphine from us for up to 3 weeks while we are scheduling your stay in the residential unit, and once you are admitted onto the unit then you will stay there for 11 days and 10 nights. There will be a brief follow-up session about 5-10 days after your residential stay.

4. What happens to data and biospecimens that are collected in the study?

What testing or procedures may be done with your biospecimens?
Your biospecimens may be used for a variety of research purposes. The specific testing that will be part of this study includes blood, urine, and saliva, which may be tested for hormone levels, pregnancy, and drugs/medications. Most biospecimens contain DNA, which is the genetic code for each person.

Johns Hopkins and our research partners work to advance science and public health. The data and biospecimens we collect from you are important to this effort.

We would also like to collect an optional genetic sample from all study participants. This will be collected as a saliva sample and will be stored for future genetic testing. The goal of this sample will be to help us learn more about whether genetics impacts response to different FDA-approved medications. *This sample is optional and your decision about whether to provide the sample will not impact your eligibility for the study.* If you decide to provide us with a genetic sample, you should know that the Genetic Information Nondiscrimination Act (GINA) is a federal law that helps reduce the risk of discrimination by health insurers or employers based on your genetic information. GINA does not protect you from discrimination if you apply for other types of insurance (such as life, disability or long-term care). GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

Genetic information is unique to you and your family. Even without your name or other identifiers, it may be possible to identify you or other members of your family with your genetic information. Johns Hopkins follows procedures so that people who work with your DNA information for research cannot discover it belongs to you, unless you have given consent. However, new techniques may be developed that in the future make it easier to link your genetic data to you, so we cannot promise that your genetic information will never be linked to you.

If you join this study, you will not own the data and/or biospecimens collected from you as part of this research study. If researchers use them to create a new product or idea, including those that may have commercial value, you will not benefit financially from these efforts.

How will your data and/or biospecimens be shared now and in the future?
Sharing data and/or biospecimens is part of research and may increase what we can learn from this study.

Often, data/biospecimen sharing is required as a condition of funding or for publishing study results. It also is needed to allow other researchers to validate study findings and to come up with new ideas.

Your data and/or biospecimens may be shared:

- directly with research collaborators, other researchers, sponsors, government agencies, publishers of papers and other research partners
- through government or other databases/repositories

Data/biospecimen sharing could change over time, and may continue after the study ends.

We will do our best to protect and maintain your data/biospecimens in a safe way. Generally, if we share your data/biospecimens without identifiers (such as your name, address, date of birth) further review and approval by an IRB is not needed. However, when we share data, we limit the uses of the information and whether these data can be shared with another research team. If data/biospecimens are shared with identifiers, further IRB review and approval may be needed and the IRB will determine whether additional consent is required.

Johns Hopkins researchers may also use the biospecimens collected in this study for future research purposes, which may include cell line development, gene sequencing, and genetic testing. Cell lines can be grown in the laboratory. This allows researchers to have an unlimited supply of your cells in the future without asking for more samples from you. Each cell contains your complete DNA. Gene sequencing of your DNA provides researchers with the code to your genetic material. This future research may be unrelated to the current study and may include outside collaborators.

Because science constantly advances, we do not yet know what future testing may include. If biospecimens are tested/used in ways not described above, further IRB review and approval may be needed and the IRB will determine whether additional consent is required.

You can decline the collection and storage of any biospecimens for future research. You can also decline the collection and storage of the genetic biospecimen for future research.

Will you allow us to store and use the biospecimens we collect for this study for future research?

YES ☐ _____ _____
Signature of Participant Date

NO ☐ _____ _____
Signature of Participant Date

Will you allow us to store and use genetic biospecimens we collect for this study for future research?

YES ☐ _____ _____
Signature of Participant Date

NO ☐ _____ _____
Signature of Participant Date

5. What are the risks or discomforts of the study?

Suvorexant (Belsomra®):

The study drug may affect brain areas in ways that could increase sleep during opioid tapering. You should not take this study drug if you have narcolepsy or sleep paralysis. You should also not take Belsomra® if you are taking other medications that either decrease or increase your liver enzymes (known as CYP 3A4). For this reason, it is important that you let us know all medications you are taking during the Screening visit.

The most commonly reported side effects of suvorexant (Belsomra®) are:

- Sleepiness or drowsiness (7% of people)
- Headache (7% of people)
- Dizziness (3% of people)
- Diarrhea (2% of people)
- Dry mouth (2% of people)
- Upper Respiratory Infection (2% of people)
- Abnormal dreams (2% of people)
- Cough (2% of people)
- Serious adverse events could include
    - Sleep paralysis (7% of people)
    - Somnolence (7% of people)
    - Worsening of depression or suicidal ideation

Buprenorphine HCl (Subutex) or Buprenorphine/naloxone (Suboxone):

Both of these drugs are FDA-approved for opioid withdrawal treatment and it is being used in the FDA-approved manner in this study (in other words, there is nothing experimental about the use buprenorphine in this study).

The most commonly reported side effects of buprenorphine are symptoms of opioid use or opioid withdrawal and include:

- Headache (37%)
- Withdrawal Syndrome (18% of people)
- Pain (18% of people)
- Nausea (15% of people)
- Insomnia (14%)
- Constipation (14% of people)
- Sweating (13% of people)
- Infection (12% of people)
- Abdominal Pain (12% of people)
- Runny Nose (10% of people)
- Chills (8% of people)
- Back Pain (8% of people)
- Vomiting (8% of people)
- Weakness or Lack of Energy (5% of people)
- Diarrhea (5% of people)
- Decreased Blood Pressure (4% of people)

Opioid Withdrawal: Since this is an opioid taper study, you should expect to experience some symptoms of opioid withdrawal during the study. Symptoms of opioid withdrawal include nausea, diarrhea or stomach cramping, muscle aches and pains, yawning, sweating, pupil dilation, minor increases in blood pressure, and runny nose/tearing eyes. Due to the nature of this study, we cannot prevent you from experiencing some level of withdrawal, although we will try to minimize it as much as possible by making other medications that help reduce some symptoms of opioid withdrawal available to you by request.

Risk of Opioid Overdose: You may be at an increased risk of experiencing an opioid overdose when you complete this study because your tolerance to opioids will have decreased. To help protect you from experiencing an overdose, we will provide you with information about opioid overdose to inform you on how to identify and respond to overdoses, and we will also provide you with a take home dose of intranasal naloxone (Narcan®) as further protection against opioid overdose when you leave the study.

Blood Draw: Taking blood may cause discomfort, bleeding, or bruising where the needle enters the body. In rare cases, it may result in fainting. There is a small risk of infection.

Interviews or questionnaires: You may get tired or bored when we are asking you questions or you are completing questionnaires. You do not have to answer any question you do not want to answer.

Identifiable private information: There is the risk that information about you may become known to people outside this study.

Unknown risk: There may be side effects and discomforts that are not yet known.

6. Are there risks related to pregnancy?

The study drug is not yet approved for use in pregnancy or during breastfeeding. Therefore, we will not enroll anyone who tests positive for pregnancy or is current breastfeeding into the study.

It is unknown whether this research may hurt an embryo or fetus.

7. Are there benefits to being in the study?

You may or may not benefit from being in this study. If you are assigned to receive Belsomra, it is possible you will sleep better but this cannot be guaranteed. No benefit is expected if you are assigned to take placebo. If you take part in this study, you may help others in the future.

8. What are your options if you do not want to be in the study?

You do not have to join this study. Other options include seeking treatment for OUD or sleep disturbance from your health care provider.

If you do not join, your care at Johns Hopkins will not be affected.

9. Will it cost you anything to be in this study?

You will receive a separate Insurance and Research Participant Financial Responsibility Information Sheet (Sheet). This Sheet will give you the following information:

- The procedures, tests, drugs or devices that are part of this research and that will be paid for by the study (no cost to you).
- The procedures, tests, drugs or devices that will be billed to you and/or your health insurer. If you have health insurance, you will be responsible for any co-pays or deductibles not covered by your insurance.

10. Will you be paid if you join this study?

You will have the potential to earn $30 for a Screening visit and up to $1430 for your participation; the payment information is described in more detail in a separate payment form that the staff will review with you.

You may be required to provide your social security number to be paid for taking part in this study. Federal tax law requires that you report your research payments when you file your taxes. If your total payments from Johns Hopkins exceed $600 per year, Johns Hopkins will report these payments to the Internal Revenue Service and you will receive a 1099-MISC form from us.

11. Can you leave the study early?

- You can agree to be in the study now and change your mind later.
- If you wish to stop, please tell us right away.
- Leaving this study early will not stop you from getting regular medical care.

If you leave the study early, Johns Hopkins may use or share your health information that it has already collected if the information is needed for this study or any follow-up activities.

12. Why might we take you out of the study early?

You may be taken out of the study if:

- Staying in the study would be harmful.
- You need treatment not allowed in the study.
- You fail to follow instructions.
- You become pregnant.
- The study is cancelled.
- There may be other reasons to take you out of the study that we do not know at this time.

If you are taken out of the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

13. How will your privacy be maintained and how will the confidentiality of your data be protected?

HIPAA Authorization for Disclosure of Protected Health Information
What information is being collected, used, or shared?
To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Johns Hopkins Medicine and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use or share the information?
The people who may request, receive, or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Johns Hopkins, for example if needed for your clinical care or study oversight. To improve coordination of your research and clinical care, some information about the study you join will be included in your electronic medical record.

By signing this form, you give permission to the research team to share your information with others outside of Johns Hopkins. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team.

We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Do you have to sign this Authorization?
You do not have to sign this Authorization, but if you do not, you may not join the study.

How long will your information be used or shared?
Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

What if you change your mind?
You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them know by using the contact information provided in this consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

14. Will the study require any of your other health care providers to share your health information with the researchers of this study?

As a part of this study, the researchers may ask to see your health care records from your other health care providers. You may be asked to give us a list of other health care providers that you use.

15. What is a Certificate of Confidentiality?

Your substudy information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

16. What treatment costs will be paid if you are injured in this study?

Johns Hopkins and the federal government do not have programs to pay you if you are hurt or have other bad results from being in the study. However, medical care at Johns Hopkins is open to you as it is to all sick or injured people.

The costs for any treatment or hospital care you receive as the result of a study-related injury that are not covered by a health insurer will be billed to you.

By signing this form, you will not give up any rights you have to seek compensation for injury.

17. What other things should you know about this research study?

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. If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.

During this study, you will not have access to certain medical information and test results collected for study purposes. If an emergency occurs while you are in the study, medical information needed for your treatment can be made available to your study doctor and other physicians who treat you. When the study is completed, all the information in your medical record will be available to you.

During the study, we will tell you if we learn any new information that might affect whether you wish to continue to participate.

What is the Institutional Review Board (IRB) and how does it protect you?
This study has been reviewed by an Institutional Review Board (IRB), a group of people that reviews human research studies. The IRB can help you if you have questions about your rights as a research participant or if you have other questions, concerns or complaints about this research study. You may contact the IRB at 410-502-2092 or jhmeirb@jhmi.edu.

What should you do if you have questions about the study, or are injured or ill as a result of being in this study?
Call the principal investigator, Andrew Huhn, Ph.D. at 410-550-1971. If you wish, you may contact the principal investigator by letter. The address is on page one of this consent form. If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at 410-502-2092.

If you have an urgent medical problem or think you are injured or ill because of this study, call 911 or go to your local emergency department. You should also call Eric Strain, M.D. or Dr. Alexis Hammond at 410-550-0052 during regular office hours and at 410-550-0052 after hours and on weekends.

18. What does your signature on this consent form mean?

Your signature on this form means that: You understand the information given to you in this form, you accept the provisions in the form, and you agree to join the study. You will not give up any legal rights by signing this consent form.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

Signature of Participant	(Print Name)	Date/Time

Signature of Person Obtaining Consent	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR AND A COPY MUST BE GIVEN TO THE PARTICIPANT. IF APPROPRIATE FOR THIS STUDY, A SCANNED COPY OF THE SIGNED CONSENT FORM SHOULD BE UPLOADED TO THE PARTICIPANT'S EPIC/EMR RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

DOCUMENTATION OF PHYSICIAN/MID-LEVEL PROVIDER CONSENT PROCESS

My signature below indicates that I have discussed the risks, benefits, and alternatives, answered any questions, and believe the participant is able to make an informed choice to join the study.

Signature of Physician/Mid-Level Provider	(Print Name)	Date/Time

Signature of Participant	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR AND A COPY MUST BE GIVEN TO THE PARTICIPANT. IF APPROPRIATE FOR THIS STUDY, A SCANNED COPY OF THE SIGNED CONSENT FORM SHOULD BE UPLOADED TO THE PARTICIPANT'S EPIC/EMR RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).