Office of IRB Administration (OIA)

University of California, San Diego 9500
Gilman Drive, Mail Code 0052
La Jolla, CA 92093-0052

(858) 246-4777
(858) 246-3329 (FAX)

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

The faculty and staff of the University of California, San Diego wish you to know:

Any person who is requested to consent to participate as a subject in a research study involving a medical experiment, or who is requested to consent on behalf of another, has the right to:
1. Be informed of the nature and purpose of the experiment.

2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be used.

3. Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.

4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

5. Be given a disclosure of any appropriate alternative procedures, drugs, or devices that might be advantageous to the subject, and their relative risks and benefits.

6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.

7. Be given an opportunity to ask any questions concerning the experiment or the procedures involved.

8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time, and the subject may discontinue participation in the medical experiment without prejudice.

9. Be given a copy of a signed and dated written consent form when one is required.

10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

If you have questions regarding a research study, the researcher or his/her assistant will be glad to answer them. You may seek information from the Office of IRB Administration (OIA) - established for the protection of volunteers in research projects - by calling (858) 246-4777 from 7:30 AM to 4:00 PM, Monday through Friday, or by writing to the above address.

University of California, San Diego
Consent to Act as a Research Subject

The Impact of Sleep Disordered Breathing in People who use Opioids (Aim 1)

Introduction

Dr. Jeremy Orr and associates are conducting this research and asking for your consent to participate. This section provides a summary of important information. The rest of the form provides additional details.

- Research is voluntary - whether or not you join is your decision. You can discuss your decision with others (such as family, friends or another physician).
- You can say yes but change your mind later.
- If you say no, we will not hold your decision against you.
- Your decision will not affect your health care or any other benefits you may be entitled to.
- You can say no even if the person inviting you is part of your healthcare team.
- Please ask questions or mention concerns before, during or after the research.

We are conducting this research study to investigate whether PAP may help to relieve your unstable breathing and determine if the treatment has a positive effect on your sleep and pain perception. PAP, or positive airway pressure, is a gentle, continuous stream of air that assists in keeping your airway passages open while you sleep. Participation in the study may or may not benefit you directly, and may result in new knowledge that may help others. Of note, Dr. Orr or other licensed physicians part of the study will review records over the past 6 months about when opioids were dispensed to you through pharmacies.

If you agree to be in this study, the following will happen to you:

1) You will complete an overnight sleep study. Before bed, you will be given questionnaires related to sleep, pain, and mood. You will also be asked to complete a test related to pain where you place your hand in a water bath. In the morning, you will complete a computerized reaction test, an optional blood draw, and be given a wrist-worn device related to monitoring how active you are. (Overnight Visit 1).
2) You will complete a daytime visit. You will return your Home Sleep Test, and be given a letter summarizing the result of your overnight sleep study. If your overnight sleep study shows you have sleep disordered breathing, you will be assigned by chance to one of two study groups—1) PAP therapy group or 2) non-PAP therapy group. (Daytime Visit 1)
3) Over the course of 8 weeks, you will complete weekly phone calls related to your use of PAP therapy.
4) You will return to the sleep laboratory for a final evening visit where you will repeat the questionnaires, the hand in water bath assessment, computerized reaction test, and optional blood draw. (Evening Visit 1)

Study activities will be performed at the Altman Clinical Translational Research Institute Clinic, 9452 Medical Center Dr, La Jolla, CA 92037. If you agree to be in this study, the following will happen to you:

COVID-19 Swabs

Due to the current pandemic, you will be required to get a COVID-19 swab 3 days before each of your overnight sleep studies. We will provide you instructions where to get these swabs done. You will only be allowed to attend your scheduled overnight appointment with a negative COVID-19 swab.

Pregnancy Test

After signing consent, if you are a premenopausal woman, you will complete pregnancy tests to confirm that you are not pregnant. These tests will be completed at the study location before any activities begin at every study visit. If you become pregnant at any time during your participation in the study, you will be withdrawn.

Overnight Visit #1

You will be asked to come in for an overnight sleep study at 8PM. Before sleep, you will complete a basic exam to measure your height, weight, vitals, and neck/hip/waist measurements. You will complete questionnaires about your sleep, pain, and mood, which should take 45 minutes. For example, you will be asked questions like: "How satisfied/dissatisfied are you with your current sleep pattern?" We will also have you place your hand in a cold water bath and ask you questions about your experience. At the upmost, you will have your hand immersed in water for 5 minutes or until you are no longer able to tolerate it. You will complete a breathing test. For the test, you will be fitted with a face mask and asked to breathe normally for 3 minutes, followed by up to six 20-second breath holds and a maximal breath hold. You can stop the test at anytime if you are uncomfortable.

You will be asked to sleep on your back while having sensors pasted on your scalp, face, chest and legs that will help determine when you are asleep or awake. A microphone will be placed on your neck to monitor snoring, a sensor on your chest to measure your carbon dioxide, and a probe will be placed on your finger to measure your oxygen level. An adhesive body position sensor and 2 pairs of magnets will be placed on your body to measure what position you are sleeping in, and the volume of your chest while breathing.

All of this equipment is standard for a diagnostic sleep study and should not be uncomfortable. The study will end at approximately 6AM and all the monitoring equipment will be removed.

In the morning, you will complete a 10-minute computerized reaction assessment and be asked to tap the spacebar every time you see a red dot appear. You will be fitted for a watch that collects your activity and exposure to light. The device will be worn for 1-2 weeks. You will also be given a Home Sleep Test (HST)---a device used to evaluate for sleep apnea at home. The HST

will include a strap to measure chest movement, tubing in the nose to measure breathing, and a finger probe to measure blood oxygen saturation. You will use the device for one night and return the equipment. Alternatively, based on logistics, you may be given a disposable home sleep test, which will be worn on your wrist with an oxygen-saturation probe. If you are given this device, we will be able to download the data remotely and after it has been completed you can discard it. If the results of the Home Sleep Test are inconclusive, you may be asked to repeat the test for additional compensation outlined below.

Are you willing to repeat the Home Sleep Test, if data is inconclusive? You can say yes and change your mind later.

Yes ☐ No ☐ Initials _____

After you complete the test, you will either schedule an appointment to return the equipment to our study site or mail the device through the postal service. If you select the mail option, we will provide you mailing supplies and a mailing label.

Blood Draw (optional)

We will also take 2-3 teaspoons of blood. Please note that this blood will be separated into serum (a clear liquid that contains proteins, hormones, and electrolytes but no clotting factors and no blood cells) and plasma (a clear liquid that contains proteins, hormones, electrolytes, and clotting factors but no blood cells). We will complete DNA analysis on your blood sample to examine if there may be any markers related to breathing and associated with sensitivity to opioids.

Are you willing to complete the optional blood draw? You can say yes and change your mind later.

☐ Yes ☐ No Initials _____

This overnight sleep study visit is anticipated to end at 7:30AM.

The results of your sleep study will be reviewed. If you are found to have sleep disordered breathing, you will be invited to participate in the next study visit.

In some cases, the quality of your sleep may not allow us to get all the data we need. In these cases, you may be invited back for an additional overnight stay. However, you are under no obligation to participate in the extra overnight study.

Are you willing to be contacted for the extra overnight visits, if needed? You will be compensated for the additional study night ($200).

☐ Yes ☐ No Initials _____

Daytime Visit #1

During a 30 minute daytime visit, you will return the activity watch and your HST. You will be given a letter summarizing the result of your in-lab sleep study. This letter can be presented to your primary care physician for further evaluation and treatment of your sleep-disordered breathing. You will be randomly assigned to a study group, which will determine if you receive a loaner PAP therapy device to begin treatment of your sleep-disordered breathing immediately or in approximately 8 weeks.

Treatment Group Assignment

By chance, you may be assigned to either start PAP therapy immediately or not start PAP immediately. In either case, you will continue with your usual care through a sleep clinic. Your chance of being assigned to this group is 50:50. Neither you nor the researcher(s) can choose the group to which you will be assigned. If you are assigned to PAP, our research team will provide you the equipment to take home. We will monitor your use of PAP therapy for 8 weeks, after which you will return the equipment. For both groups, research staff will be in contact in the form of check in weekly phone calls. At the end of the study, both the PAP therapy and usual care group will be eligible to start PAP via a referral to a clinical provider. You will be given a letter summarizing the results of your sleep study in order to pursue your referral.

Repeat of Overnight Visit #1

As mentioned previously, individuals who are found to have results suggestive of a sleep breathing disorder will be invited to be randomized for treatment. If there is a gap greater than 6 months, or >6 weeks with a change in weight or opioid use between overnight visit #1 and the scheduling of daytime visit #1, you will be scheduled to complete another overnight sleep study and repeat all of the activities done in the evening and morning. After the repeat overnight visit is completed, you will then complete daytime visit #1 and be randomized.

Are you willing to be contacted for the repeat of overnight visit #1, if needed? You will be compensated for the additional study night ($200).

Yes ☐ No ☐ Initials _____

Overnight Visit #2

After 8 weeks of either using PAP therapy or completing a clinical follow up with a sleep physician, you will be asked to return for a final overnight sleep study.. The study activities from overnight visit #1 will be repeated, including the overnight sleep study and blood draw. As we have limited space available for overnight sleep studies, it is possible that the final sleep study may not occur in-lab. In this event, you will complete the evening testing (2 hrs.) and be given

instruction on how to use the Home Sleep Test. We ask that you return the completed Home Sleep Test within 1-2 days.

Overnight Visit #2 concludes our investigation of PAP therapy treatment for sleep disordered breathing.

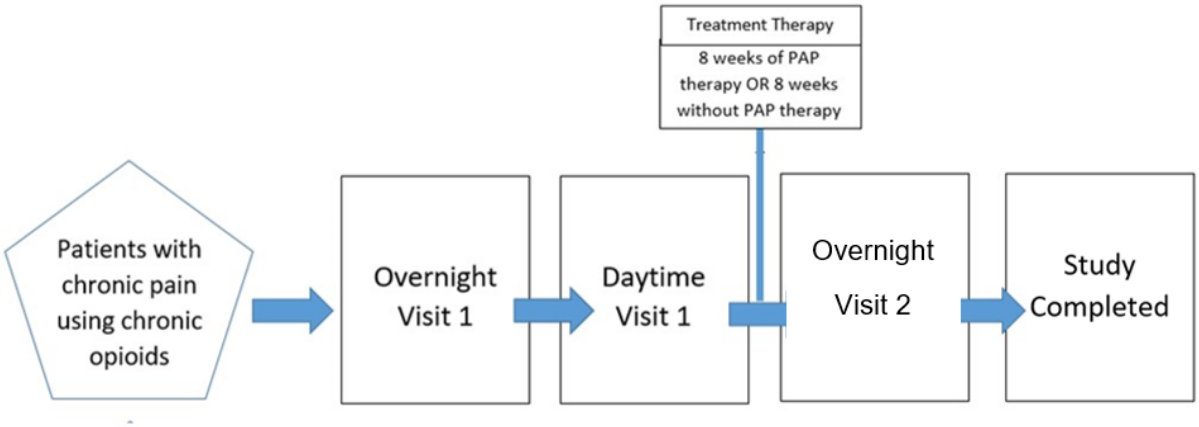

Figure 1. Study Flowchart. This flowchart outlines the study visits. The study includes overnight visit 1, daytime visit 1, and evening visit 1 to allow us to determine how effective PAP therapy may be for people with sleep disordered breathing (SDB).

The most commonly expected risks of the study are feeling sleepy the next morning after your overnight sleep studies and having temporary discomfort after your blood draw.

The most serious risks of the study may include infection from venipuncture (blood draw) and pain from the cold water bath.

Additional, detailed information about this research is provided below. Please feel free to ask questions before signing this consent.

Why have you been asked to participate, how you were selected, and what is the approximate number of participants in the study?

You have been asked to participate in this study because you are a patient using chronic opioid, and have untreated sleep disordered breathing. There will be approximately 170 participants enrolled in this study at UCSD.

What will happen to you in this study and which procedures are standard of care and which are experimental?

The overnight sleep studies and treatment therapies are voluntary research activities. We do not anticipate that this research will interfere with any standard clinical care.

How much time will each study procedure take and how long will the study last?

1. Overnight Visit #1 will last 10-12 hours (mostly sleeping)
2. Daytime Visit #1 will last 30-45 minutes
3. Overnight Visit #2 Visit #1 will last 10-12 hours (mostly sleeping)
4. Weekly Phone calls will last 5-7 minutes (8 weeks for those using PAP therapy)

Your participation in the study will last 10-12 weeks (depending on your participation in one or both of the treatment therapies).

What risks are associated with this study?
Participation in this study may involve some added risks or discomforts. In addition to the risks described at the beginning of this form,

Questionnaires: You will be asked questions related to sleep, pain, and your mood. You may find some questions uncomfortable or distressing. Please know you have the right to skip or not complete the questionnaires.

Cold Water Bath: You may feel some discomfort or pain or a less commonly lightheadedness, dizziness, sweating, or nausea. You will be monitored for any symptoms when you complete this assessment.

Risks of Sleep Studies: During the sleep studies, there may be discomfort at the electrodes or monitors sites that can develop; a localized skin irritation/allergy can occur due to application of the skin surface electrodes for recordings of your brain waves, heart activity, and muscle activity. You might be sleepy the next morning after participating in the study.
Risks Associated with Home Sleep Test: You may have discomfort from the oxygen saturation probe, nasal cannula, and chest belt. You might be sleepy the next morning after completing your Home Sleep Test.

Risks Associated with Computerized Reaction Test: You will be asked to sit for 10 minutes while completing this activity and may experience frustration and/or boredom.

Risks Associated with Wrist-worn activity tracker: You may have some discomfort or skin irritation around the wrist band.

Risks of a blood draw/blood pressure test: You may have temporary pain or discomfort during the blood draw and/or when your blood pressure is being taken.

Risks Associated with Breath Holding Test: You may feel uncomfortable, have shortness of breath, become light-headed, and/or become dizzy. You will be monitored for any symptoms when you complete this assessment and given ample time to rest.

Risks Associated with PAP therapy: While using PAP therapy, you may experience dry mouth, dry stuffy nose or nosebleeds from the airflow. You may have some discomfort while wearing

the mask and some skin irritation due to the fit of your mask. You may also have some gas or bloating, if you swallow air, which can be a result of the pressure of PAP being set too high.

Risks of Loss of Confidentiality: Even with all of the study procedure precautions that will be taken to protect confidentiality, there is still a risk of loss of confidentiality associated with this study. Research records will be kept confidential to the extent allowed by law. The study personnel are well trained in securing and safely storing all your data.

Study Assignment: You will be assigned to a study group at random (by chance). Your assignment is based on chance rather than a medical decision made by the researchers. The study group you are assigned to might not be the group you would prefer to be in. Your assigned study group might also prove to be less effective or have more side effects than the other study groups(s), or other treatments available for your condition.

Unknown Risks: Because this is a research study, there may be some unknown risks that are currently unforeseeable. You will be informed of any significant new findings.

Are there risks to the reproductive system or a developing fetus?

The treatment procedures may pose some unforeseeable risks on the reproductive system (sperm, eggs) or to the developing fetus. For this reason, participants in this investigational study should not become pregnant. We require that all participants agree to either abstain from sexual intercourse or use a reliable, effective birth control for this period, such as hormonal contraceptive, intrauterine device (IUD), diaphragm with spermicide, contraceptive sponge or use of condom (by the partner).

As stated previously, after you have been enrolled in this study and during the research, pregnancy testing will be performed. If you have a positive pregnancy test, we may withdraw you from the study. If you (or your partner) become pregnant or if there is any chance of pregnancy (e.g., late menstrual period), please contact the study personnel immediately so that we may provide medical assistance and counseling.

What are the alternatives to participating in this study?

The alternatives to participation in this study are not to participate in the study.

What benefits can be reasonably expected?

There will be no direct benefit to you from this study since you will not be provided with any results or information regarding your DNA test. The investigator, however, may learn more about identifying effective therapies to treating sleep disordered breathing and improve pain tolerance. This information may be useful to clinicians and patients.

What happens if you change your mind about participating?

If you decide that you no longer wish to continue in this study, you will be requested to reach out to a member of our research team. We will terminate any of your remaining study activities.

You will be told if any important new information is found during the course of this study that may affect your wanting to continue.

Can you be withdrawn from the study without your consent?
You may be withdrawn from the study for the following reasons:

- You become ill,
- Are required to use medications that are known to disrupt sleep

You may also be withdrawn from the study if you do not follow the instructions given you by the study personnel. You may refuse to participate or withdraw at any time without penalty or loss of benefits to which you are entitled. If you decide that you no longer wish to continue in this study, you will be requested to:

- Return any equipment to our research staff
- Provide a reason for discontinuation (if possible)

Will you be compensated for participating in this study?
In compensation for your time and travel, you will receive up to $555-655 in total for participating in this research and all blood draws:

- Overnight Visit 1: $200
- Daytime Visit 1: $50
- Weekly Phone calls: $80
  You will be compensated for $10 for answering each weekly follow-up call for 8 weeks in total of $80.
- Overnight Visit 2: $200 with in lab sleep study, or 75$ with home sleep study.
- If an additional daytime visit is needed for data collection: $50

- If data is inconclusive and a repeat Home Sleep Test is needed, you will be paid: $25
- If data is inconclusive and an additional overnight is required, you will be paid $200.

Are there any costs associated with participating in this study?
There will be no cost to you for participating in this study. Parking expenses at UCSD study sites will be covered.

If you have health insurance, your insurance will be charged for the COVID-19 swabs that are completed before every overnight sleep study. The test will be ordered through our research group at no cost to you, however, if you are mistakenly asked to cover any charges out of pocket, please contact us immediately so we can help resolve the billing issue. You will not be responsible for paying for your COVID-19 swab.

What if you are injured as a direct result of being in this study?
If you are injured as a direct result of participation in this research, the University of California will provide any medical care you need to treat those injuries. The University will not provide any other form of compensation to you if you are injured. You may call the Office of IRB

Administration (OIA) at 858-246-HRPP (858-246-4777) for more information about this, to inquire about your rights as a research subject or to report research-related problems.

What about your confidentiality?

Research records will be kept confidential to the extent allowed by law. To guard your confidentiality, you will be assigned a unique identifying number to label all your data collection sheets. The same unique, coded identifying number will be used to label any biospecimen collected from you. All personal information will be kept strictly confidential by the investigators. All study forms, and data collected will be kept locked in a secure location. All your data forms will only list your unique study ID number. All research staffs are trained in the protection of subject privacy and confidentiality. Research records may be reviewed by the UCSD Institutional Review Board, or the study Sponsor, the NIH.

Personal identifiers might be removed from the information or biospecimens collected as part of the research. After such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without your additional informed consent.

Biospecimens (such as blood, tissue, or saliva) collected from you for this study and/or information obtained from your biospecimens may be used in this research or other research, and shared with other organizations. You will not share in any commercial value or profit derived from the use of your biospecimens and/or information obtained from them.

If you decide later that you do not want the blood samples collected from you to be used for future research, you may tell Dr. Orr who will use his best efforts to stop any additional studies. Please note that your samples will only be used in IRB approved research at UCSD.

Dr. Orr, his associates, or his successors in these studies will keep your DNA specimen and/or the information derived from it for up to 15 years.

Federal and State laws generally make it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways: a) Health insurance companies and group health plans may not request your genetic information that we get from this research. b) Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums. c) Employers with 5 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that these laws **do not** protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.
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.

Will you receive any results from participating in this study?
Letters summarizing the results of your overnight sleep studies will be provided. If any clinical relevant research results are found during the sleep studies a written report of the abnormality will be share with you and you may be recommended to seek appropriate evaluation with your primary care doctor.

Who can you call if you have questions?
This study has been explained to you and your questions have been answered. If you have other questions or research-related problems, you may reach Dr. Orr and his research study coordinators at (858) 246-2154. Of note, our research team will utilize text messages and voicemail for important study communication.

You may call the Office of IRB Administration (OIA) at 858-246-HRPP (858-246-4777) to inquire about your rights as a research subject or to report research-related problems.

Your Signature and Consent
You have received a copy of this consent document and a copy of the "Experimental Subject's Bill of Rights" to keep.

You agree to participate.

_____	_____
Subject's signature	Date
_____	_____
Signature of the person conducting the informed consent discussion	Date