Document Section Cover Sheet

Official Title: Use of a GLP-1R Agonist to Treat Opioid Use Disorder

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CONSENT FOR RESEARCH
Penn State College of Medicine
Penn State Health

Title of Project:	Use of a GLP-1R Agonist to Treat Opioid Use Disorder
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Subject's Printed Name: _____

We are asking you to be in a research study.

Whether or not you take part is up to you. You can choose not to take part. You can agree to take part and later change your mind. Your decision will not be held against you, and there will be no penalty or loss of benefits to which you are entitled.

This form gives you information about the research. Please ask questions about anything that is unclear to you and take your time to make your choice.

KEY INFORMATION

The following is a short summary of this study to help you decide whether or not to be a part of this research. More detailed information is provided later in this form. If you have any questions, be sure to ask the study team.

Why am I being invited to take part in this research study?

We are asking you to take part in this voluntary research study because you are being treated for opioid dependence.

What is the purpose of this research study?

The purpose of this research study is to determine whether the investigational medication, liraglutide, can safely and effectively reduce craving for opioids in patients with opioid use disorder.

How long will the research study last?

It will take you 49 days to complete the study, you will be actively involved for the first **21 days**, after which no further effort is required on your part until the follow-up phone call at Day 49.

You have the option to extend your participation in the study for an additional 12 days. If you are able, and agree to the extension, the total days to complete the study, including days you've already participated, will be 61 days. You will be actively involved for the first **33 days**, after which no further effort is required on your part until the follow-up phone call at Day 61.

What will I need to do?
At your first visit, we will give you questionnaires about your mental health. We will perform a test to measure your heart rate and rhythm (electrocardiogram, ECG) by placing sticky patches on your chest and asking you to lie still. We will measure your body weight. If you are a woman of childbearing potential, a pregnancy test will be performed to ensure that you are not pregnant. Your participation in this research will end if the pregnancy test is positive.

If you are eligible to continue in the research, you will be asked to participate in additional testing including measurement of body weight, blood pressure, heart rate, breathing rate, mood (feelings of stress and of craving for drug), sleep, and activity levels. We will place a small tube in the vein in your arm to take a blood sample (about 2 teaspoons) to measure hormones involved in control of blood sugar (glucose) levels. You will also undergo an assessment of the level of neural activity in the front of your brain and report your level of craving in response to viewing drug-related and non-drug-related images, as well as during a computerized task that assesses your risk-taking behavior.

What are the main risks of taking part in the study?
For this study, the main risks to know about are: possible side effects of the study medication and the possibility of relapse due to drug cues in some of the study activities.

What are the possible benefits to me that may reasonably be expected from being in the research?
We cannot promise any benefits to you from taking part in this study. However, possible benefits include a reduction in craving. Results of the study may benefit other people in the future by helping us learn more about the future treatment of patients with opioid dependency.

What happens if I do not want to be in this research?
Participation in research is completely voluntary. You can decide to participate or not to participate. Instead of being in this research study, your choices may include:

- Receive commercially available treatments, including behavioral techniques.
- Be part of a different research study, if one is available.
- Choose not to be treated for your medical condition.

DETAILED INFORMATION
The following is more detailed information about this study in addition to the information listed above.

1. **Why is this research study being done?**
   This research is being done to find out if the investigational medication, liraglutide (brand name is Saxenda®), can safely and effectively reduce craving for opioids in patients with opioid use disorder, a primary factor contributing to early relapse.

   Liraglutide is an FDA approved medication for treatment of obesity and type 2 diabetes, but it is not specifically approved for the treatment of craving in patients with substance dependence disorders. Therefore, its use in this research should be considered “investigational”.

   Approximately fifty (50) patients admitted to the Caron Treatment Centers for treatment of addiction to opioids will take part in this research study, which is being conducted at the Caron Treatments Centers in conjunction with Penn State Milton S. Hershey Medical Center.

2. **What will happen in this research study?**

If you agree to participate in this research, you will first read and sign this consent document before any study-related tests or procedures are performed. Your decision to participate in the research will not affect your treatment at the Caron Treatment Centers. All decisions about your clinical care, including its duration, will be made by you and the members of your clinical team at the Caron Treatment Centers.

Investigational medication/placebo administration: Study/nursing staff at Caron Treatment Centers will teach you how to self-administer the investigational medication/placebo. You will be using an injection pen.

- You will be taught how to inject yourself under the skin in the abdomen, thigh, or upper arm.
- You will also be shown how to attach the needle (A new needle will be used for every dose), check the investigational medication/placebo flow, select the dose, inject the dose, remove the needle, and dispose of the needle.
- You will be instructed to inject yourself every day at a set time, before you have breakfast.

Synergy Pharmacy ("Synergy"): The injection pens with the investigational medication or placebo in them will be supplied by the manufacturer (Novo Nordisk) to Synergy (an off-site pharmacy that routinely supplies medications for Caron Treatment Centers ("Caron")). The manufacturer will send each investigational medication/placebo pack to Synergy in a box containing a numbered label (with no patient information on it).

Once you have been given a study ID number and randomized into a study group, Synergy will assign a pack of pens for you to use and send them to Caron. This particular pack of pens will have been chosen by Synergy using the study randomization list. The label on the pack, and the pens themselves, that you are given will not tell you which treatment (investigational medication or placebo) is in the pens. This is done so that neither you nor the study team will know which treatment you are getting (known as "blinding"). Only Synergy will know whether you are receiving medication or placebo.

You will be randomly assigned to receive investigational medication or placebo (an inactive substance). You will take the investigational medication or placebo daily, starting at a low dose which will be gradually increased over 18 days. When you first start using the investigational medication or placebo, you will take 0.6 mg once per day for six days. After six days, you will increase the dose by 0.6 mg and remain on that dose for six days. You will increase the dose by 0.6 mg every six days until you reach the dose of 1.8 mg once per day. You will be asked around Day 1 and Day 18 whether you opt to extend your participation in the study. If you agreed to extend your participation in the study, you will receive an additional six days of the investigational medication or placebo at 2.4 mg per day, followed by another 6 days at 3.0 mg per day. Neither you nor the study team will know which treatment you are getting, but the study team will be able to get this information quickly if needed to ensure safety.

You will be given a **study smartphone** for use during the study period. This phone will have applications ("apps") on it to collect data for the actigraphy wristband and for the Wear-IT Ecological Momentary Assessment (EMA). Data will automatically upload from the phone and the study coordinators and staff will be able to view compliance online—that is, they will be able to see if you have completed surveys and if you are wearing the monitor.

You will wear an **actigraphy wristband**, which is a small, watch-like wrist band that measures your activity, physiology, and sleep. So that you do not have to charge the actigraphy wristband yourself, you will have up to two actigraphy wristbands assigned to you, and they will be charged or, if necessary swapped at your check-in sessions. You may wear the actigraphy wristband while showering or swimming if you wish.

EMA: You will be asked to report your sleep, mood, drug/alcohol craving, and perceived stress using rating scales on a smart phone, 4 times per day on the first and last 2 days of each treatment dose. You will also be asked to record these on other days as well, as described below. The smart phone will be issued to you for your use only during the research. The data will be transmitted directly to a secure database from the smart phone without any identifying information. You will be asked how you feel (e.g., happy, sad, frightened, stressed, etc.) and if you have any drug/alcohol craving. These surveys will take about 5-6 minutes each. The smart phones are programmed only to administer these surveys, and cannot be used to make phone calls or connect to the internet in any way. Such collected data will be transferred electronically to University Park for further analysis. The data will be collected by an app (the Wear-IT app) that will be put on the study smartphone you will be provided with while in the study. You will need to plug the phone in to charge each night.

Cardiorespiratory Function: You will have your blood pressure, heart rate, and respiratory (breathing) rate measured using different types of equipment during your participation in the study.

- After the equipment has been hooked up, you will rest for 10 minutes.
- Then 15 minutes of continuous recordings of your blood pressure, heart rate, and respiratory rate will be recorded.
    - Your blood pressure will be measured either by a device that is put on your finger or by the usual blood pressure cuff method.
    - A 3-lead electrocardiogram (EKG) which uses 3 adhesive patches on your chest will be used to measure your heart rate (electrical activity of your heart).
    - Your respiratory rate will be measured using a belt which will be placed on your lower chest/abdomen to measure your chest movements, and a small sensor (pulse oximeter) will be applied to your finger to measure the oxygen levels in your blood.

Cue-elicited drug craving: You will be asked to look at slides of drug cues (i.e. image of people taking pills) and you will then rate on a scale of 0-100 your level of drug craving (a Visual Analog Scales (VAS)). The VAS is administered by the study coordinator. The VAS will be administered electronically before and after the cue reactivity task to measure cue elicited drug craving on Day 1 and Day 19, as well as Day 31 for extended participation. The VAS is a set of three questions about the images you will see and feelings of craving you may experience during the cue reactivity task. You will answer these questions using a numeric scale of 1 to 100 by typing in your rating using a standard keyboard.

Neurophysiology measurements: Functional Near Infrared Spectroscopy (fNIRS) measures blood flow in the front of the brain (to measure brain activity) using a sensor worn on the forehead. In this study, it will be used to measure how your brain responds during different activities, such as showing you images of drug cues (i.e. people taking pills) or doing a task called the Balloon Analogue Risk Task (BART), which involves blowing up a virtual balloon (image on a computer screen). fNIRS will also be used with VAS, which is explained above. Neurophysiology measurements such as the cue reactivity task and the risky decision-making task will be administered in a quiet room reserved for the collection of these measurements in the CaronTC research department. A study coordinator will provide you with

instructions on any tasks or measurements collected. De-identified fNIRS data will be made available to Drexel University who will be processing the data for analysis only.

Enrollment and Baseline (Day 1)
You will be approached within 2-3 days of beginning residential treatment based on initial screening from EMR and enrolled into the study if you consent.

The following **standard of care data** will be collected from your electronic medical record (EMR) for research purposes:

- Demographic information (age, gender, race, contact information)
- Detailed medical history
- Physical examination
- Admission diagnoses
- Results from standard laboratory safety tests performed on admission (complete blood count, comprehensive metabolic panel)
- Current medication usage (concomitant medications)
- Results of your urine pregnancy test at admission (if applicable). You cannot take part in this study if you are pregnant or breastfeeding a baby.

The following **research-only activities** will be performed prior to randomization**:**

- A psychiatric assessment will be conducted. You will complete the following questionnaires:
    - M.I.N.I. 7.0.2 (This questionnaire assesses the 17 most common disorders in mental health)
    - Form 90-DI (This questionnaire assesses alcohol and drug use)
    - HAM-D (This questionnaire measures depression)
    - STAI-Y1 (This questionnaire measures two types of anxiety – “state anxiety”, or anxiety about an event, and “trait anxiety”, or anxiety level as a personal characteristic)
    - Columbia Suicide Severity Rating Scale (C-SSRS) (This questionnaire is used to keep track of whether you are having thoughts of harming yourself or of suicide)

  Some of the questionnaires and interview questions will be about your feelings, such as depression, sadness and anxiety. If your responses indicate that you are having suicidal thoughts or may be at risk of hurting yourself or others, we will need to respond to that. The response may involve breaking confidentiality and contacting a licensed mental health professional or a law enforcement officer. All patients who express any suicidal thoughts will be referred for follow-up mental health counseling.

- Body weight will be measured
- 12-lead EKG will be performed (checking the physical function of your heart)
- Collection of stress response, sleep, and activity measurements will be initiated via actigraphy wristband (a “wearable” wristband).

Randomization: After obtaining written consent, if you fulfill the study criteria, you will be randomly assigned to receive one of the 2 study treatments, either liraglutide or placebo. This means that whichever study treatment you receive will be determined purely by chance, like flipping a coin. You will have an equal chance (50:50) chance of receiving any one of the study treatments.

The following **research-only activities** will occur after randomization and will serve as baseline values to compare with values obtained after investigational medication dosing:

- Cue-elicited drug craving will be evaluated using VAS.
- Neurophysiology measurements using fNIRS and VAS.
- Collection of ambient drug craving data will be initiated with EMA. Ambient drug craving is the general, non-specific feeling that you desire, want, or need a drug of abuse that you may experience throughout your day, which may or may not be triggered by people, places or things. This differs from craving experienced in a research study designed to elicit craving. Data about your sleep and mood will also be collected.
- Monitoring of body weight and cardiorespiratory function.
- Adverse events (AEs) (any unexpected medical event that happens while you are in the study) and concomitant medications will be documented.
- You will be asked whether you opt to extend your study participation for an additional 12 days. You do not need to know or make the decision at this time; you will be asked again around Day 18.

Investigational medication Treatment, Dose 1 (Days 2-7)
During this time, the following **research-only activities** will occur:

- Blood samples will be collected on Day 2, prior to investigational medication administration, for monitoring of glycemic control. This will include measurements of HbA1c and fructosamine. Approximately 2 teaspoons of blood will be collected.
- On Day 2, study/nursing staff at Caron Treatment Centers will teach you how to self-administer the investigational medication/placebo as described previously. Repeated instruction on using the injection pen on subsequent investigational medication administration days if requested until you are comfortable with the procedure.
- During Days 2-7, liraglutide/placebo control will be administered daily at 0.6 mg. The 0.6mg dose will be administered at a specific time point (prior to breakfast), similar to the other doses.
- AEs and concomitant medications will be documented.
- Ambient drug craving, mood, and sleep data will be collected on Days 2-3 and 6-7 via EMA assessment.
- Stress response, sleep, and activity measurements will be collected daily via actigraphy wristband.
- Body weight data will be collected daily.
- On Day 2, cardiorespiratory function will be measured as previously described in Section 2.

Investigational medication Treatment, Dose 2 (Days 8-13)
During this time, the following **research-only activities** will occur:

- During Days 8-13, your dose of liraglutide/placebo control will be increased to 1.2 mg, but will continue to be administered daily at a specified time (prior to breakfast).
- AEs and concomitant medications will be documented.
- Ambient drug craving, mood, and sleep data will be collected on Days 8-9 and 12-13 via EMA assessment.
- Stress response, sleep, and activity measurements will be collected daily via actigraphy wristband.
- Body weight data will be collected daily.
- On Day 8, cardiorespiratory function will be measured.

Investigational medication Treatment, Dose 3 (Days 14-18)
During this time, the following **research-only activities** will occur:

- During Days 14-18, your dose of liraglutide/placebo control will be increased to 1.8 mg, but will continue to be administered daily at a specified time (prior to breakfast).
- AEs and concomitant medications will be documented.
- Ambient drug craving, mood, and sleep data will be collected on Days 14-15 and 18 via EMA assessment.
- Stress response, sleep, and activity measurements will be collected daily via actigraphy wristband.
- Body weight data will be collected daily.
- On Day 14, cardiorespiratory function will be measured.
- You will be asked whether you opt to extend your study participation for an additional 12 days. You do not need to opt to extend your participation; the decision is yours to make and you will not be asked again after Day 19.

Study Test Day - Day 19
The following **research-only** measures, all completed on Day 1, will be repeated on Day 19.

- During Day 19, your dose of liraglutide/placebo control will be 1.8 mg and will continue to be administered daily at a specified time (prior to breakfast).
- Cardiorespiratory function will be assessed via measurement of blood pressure, heart rate, and respiratory rate.
- Blood samples for HbA1c and fructosamine will be collected for monitoring of glycemic control as they were on Day 2 of the study.
- Laboratory blood samples will be collected (approximately 2 teaspoons) to check things such as your red blood cells or sodium levels.
- Body weight data will be collected.
- Cue-elicited drug craving will be evaluated using VAS.
- Neurophysiology measurements will be evaluated using fNIRS during: (1) Visual cue reactivity and (2) Balloon Analogue Risk Task.
- Collection of ambient drug craving, mood, and sleep data by EMA.
- Stress response, sleep, and activity measurements will be collected via actigraphy wristband.
- C-SSRS
- Urine pregnancy test (if applicable).
- AEs and concomitant medications will be documented.

Rebound Evaluation Period, (Days 20-21) – No extension participants only
During this time the following **research-only** measures will occur:

- Collection of ambient drug craving, mood, and sleep data by EMA through Day 21, then discontinued.
- Stress response, sleep, and activity measurements will be collected via actigraphy wristband through Day 21, then discontinued.
- Body weight data will be collected through Day 21.
- AEs and concomitant medications will be documented through Day 21.
- On Day 21, cardiorespiratory function will be measured.

Investigational medication Treatment, Dose 4 (Days 20-25) – Extended participants only
During this time, the following **research-only activities** will occur:

- During Days 20-25, your dose of liraglutide/placebo control will be increased to 2.4 mg, but will continue to be administered daily at a specified time (prior to breakfast).
- AEs and concomitant medications will be documented.
- Ambient drug craving, mood, and sleep data will be collected on Days 20-21 and 24-25 via EMA assessment.
- Stress response, sleep, and activity measurements will be collected daily via actigraphy wristband.
- Body weight data will be collected daily.
- On Day 20, cardiorespiratory function will be measured.

Investigational medication Treatment, Dose 5 (Days 26-30) – Extended participants only
During this time, the following **research-only activities** will occur:

- During Days 26-30, your dose of liraglutide/placebo control will be increased to 3.0 mg, but will continue to be administered daily at a specified time (prior to breakfast).
- AEs and concomitant medications will be documented.
- Ambient drug craving, mood, and sleep data will be collected on Days 26-27 and 30 via EMA assessment.
- Stress response, sleep, and activity measurements will be collected daily via actigraphy wristband.
- Body weight data will be collected daily.
- On Day 26, cardiorespiratory function will be measured.

Study Test Day - Final Dose (Day 31) – Extended participants only
The following **research-only** measures, all completed on Days 1 and 19, will be repeated on Day 31.

- During Day 31, your dose of liraglutide/placebo control will be 3.0 mg and will continue to be administered daily at a specified time (prior to breakfast).
- Cardiorespiratory function will be assessed via measurement of blood pressure, heart rate, and respiratory rate.
- Blood samples for HbA1c and fructosamine will be collected for monitoring of glycemic control as they were on Day 2 of the study.
- Laboratory blood samples will be collected (approximately 2 teaspoons) to check things such as your red blood cells or sodium levels.
- Body weight data will be collected.
- Cue-elicited drug craving will be evaluated using VAS.
- Neurophysiology measurements will be evaluated using fNIRS during: (1) Visual cue reactivity and (2) Balloon Analogue Risk Task.
- Collection of ambient drug craving, mood, and sleep data by EMA.
- Stress response, sleep, and activity measurements will be collected via actigraphy wristband.
- C-SSRS
- Urine pregnancy test (if applicable).
- AEs and concomitant medications will be documented.

Rebound Evaluation Period, (Days 32-33) – Extended participants only
During this time the following **research-only** measures will occur:

- Collection of ambient drug craving, mood, and sleep data by EMA through Day 33, then discontinued.
- Stress response, sleep, and activity measurements will be collected via actigraphy wristband through Day 33, then discontinued.
- Body weight data will be collected through Day 33.
- AEs and concomitant medications will be documented through Day 33.
- On Day 33, cardiorespiratory function will be measured.

End of Study telephone call (Day 49; Day 61 for extended participation)
All participants will have an End of Study telephone call. This will occur 30 days (+/- 5 days) from the discontinuation of medication. You will be asked to self-report your weight at the time of this call.

A table showing the visits is shown on the next page to help you see what is happening in the study.

Schedule of Study Activities:

	Enrollment/ Baseline	Intervention			Test Day (Final dose)	Off Drug	Rebound Evaluation	Equipment Return	End of Study Telephone Call**
	Day 1	**Days 2-7**	**Days 8-13**	**Days 14-18**	**Day 19**	**Day 20**	**Day 21**	**Day 22**	**30 days +/- 5 days end of medication**
Study Drug/Placebo Dose		0.6 mg	1.2 mg	1.8 mg	1.8 mg	-		-	
Informed consent	X								
Data collected from Electronic Medical Record[1]	X								
M.I.N.I International Neuropsychiatric Interview (M.I.N.I. 7.0.2)	X								
Form 90-Drug Inventory (Form 90-DI)	X								
Hamilton Depression scale (HAM-D)	X								
State-Trait Anxiety Inventory (STAI-Y1)	X								
Columbia Suicide Severity Rating Scale (C-SSRS)	X				X				
Body weight	X	X	X	X	X	X	X		X
12-lead electrocardiogram (EKG)	X								
Pregnancy test[2]	X				X				
Cardiorespiratory function assessment[3]	X	X	X	X	X		X		
Blood samples for fructosamine and A1c		X[4]			X				

	Enrollment/ Baseline	Intervention			Test Day (Final dose)	Off Drug	Rebound Evaluation	Equipment Return	End of Study Telephone Call**
	Day 1	**Days 2-7**	**Days 8-13**	**Days 14-18**	**Day 19**	**Day 20**	**Day 21**	**Day 22**	**30 days +/- 5 days end of medication**
Study Drug/Placebo Dose		0.6 mg	1.2 mg	1.8 mg	1.8 mg	-		-	
Cue-elicited drug craving[5]	X*				X				
Neurophysiology measurements[6]	X*				X				
Safety labs (CBC and CMP)					X				
Ambient drug craving, mood, and sleep[7]	X*	X	X	X	X	X	X		
Actigraphy wristband ("wearable" wristband)[8]	X	X	X	X	X	X	X		
Concomitant medications	X*	X	X	X	X	X	X		
Adverse events	X*	X	X	X	X	X	X		X
Return of actigraphy wristband and smartphone								X	

*Performed AFTER randomization has occurred.
**ALL participants, unless they withdraw consent, will have an end of study telephone call.

[1]Demographics, medical history, admission diagnoses, and current medication usage.
[2]If female with childbearing potential, will collect results from test at admission as data for Day 1, with research-only pregnancy tests at Day 19.
[3]Performed on Day 1, Day 2, Day 8, Day 14, Day 19, and Day 21.
[4]Performed on Day 2 only
[5]Using Visual Analog Scales (VAS).
[6]Using fNIRS, VAS, and BART.
[7]Collection of ambient drug craving, mood, and sleep data will be initiated with Ecological Momentary Assessment (EMA). Collected on Days 1-3, 6-9, 12-15, and 18-21.
[8]Stress response, sleep, and activity measurements.

Schedule of Study Activities: Extended Participation

	Enrollment/ Baseline	Intervention						Test Day (Final dose)	Off Drug	Rebound Evaluation	Equipment Return	End of Study Telephone Call**
	Day 1	Days 2-7	Days 8-13	Days 14-18	Day 19	Days 20-25	Days 26-30	Day 31	Day 32	Day 33	Day 34	30 days +/- 5 days end of medication
Study Drug/Placebo Dose		0.6 mg	1.2 mg	1.8 mg	1.8 mg	2.4 mg	3.0 mg	3.0 mg	-		-	
Informed consent	X											
Data collected from Electronic Medical Record[1]	X											
M.I.N.I International Neuropsychiatric Interview (M.I.N.I. 7.0.2)	X											
Form 90-Drug Inventory (Form 90-DI)	X											
Hamilton Depression scale (HAM-D)	X											
State-Trait Anxiety Inventory (STAI-Y1)	X											
Columbia Suicide Severity Rating Scale (C-SSRS)	X				X			X				
Body weight	X	X	X	X	X	X	X	X	X	X		X
12-lead electrocardiogram (EKG)	X											
Pregnancy test[2]	X				X			X				
Cardiorespiratory function assessment[3]	X	X	X	X	X	X	X	X		X		
Blood samples for fructosamine and A1c		X[4]			X			X				

	Enrollment/ Baseline	Intervention						Test Day (Final dose)	Off Drug	Rebound Evaluation	Equipment Return	End of Study Telephone Call**
	Day 1	Days 2-7	Days 8-13	Days 14-18	Day 19	Days 20-25	Days 26-30	Day 31	Day 32	Day 33	Day 34	30 days +/- 5 days end of medication
Study Drug/Placebo Dose		0.6 mg	1.2 mg	1.8 mg	1.8 mg	2.4 mg	3.0 mg	3.0 mg	-		-	
Cue-elicited drug craving[5]	X*				X			X				
Neurophysiology measurements[6]	X*				X			X				
Safety labs (CBC and CMP)					X			X				
Ambient drug craving, mood, and sleep[7]	X*	X	X	X	X	X	X	X	X	X		
Actigraphy wristband ("wearable" wristband)[8]	X	X	X	X	X	X	X	X	X	X		
Concomitant medications	X*	X	X	X	X	X	X	X	X	X		
Adverse events	X*	X	X	X	X	X	X	X	X	X		X
Return of actigraphy wristband and smartphone											X	

*Performed AFTER randomization has occurred.
**ALL participants, unless they withdraw consent, will have an end of study telephone call.

[1]Demographics, medical history, admission diagnoses, and current medication usage.
[2]If female with childbearing potential, will collect results from test at admission as data for Day 1, with research-only pregnancy tests at Day 19 and Day 31.
[3]Performed on Day 1, Day 2, Day 8, Day 14, Day 19, Day 20, Day 26, Day 31, and Day 33.
[4]Performed on Day 2 only
[5]Using Visual Analog Scales (VAS).
[6]Using fNIRS, VAS, and BART.
[7]Collection of ambient drug craving, mood, and sleep data will be initiated with Ecological Momentary Assessment (EMA). Collected on Days 1-3, 6-9, 12-15, 18-21, 24-27, 30-33.
[8]Stress response, sleep, and activity measurements.

What are my responsibilities if I take part in this research?
If you take part in this research, your major responsibilities will include:

- Follow the instructions of your study doctor or coordinator.
- Participating in the study activities outlined above.
- For your safety, you must tell the study doctor or coordinator about all the prescription medications, herbal products, over-the-counter medications (OTC), vitamins and other supplements you are taking. Check with the study doctor before starting any new medicines (including prescription, OTC medications, vitamins and herbal supplements) or changing doses of medications that you are already taking.
- Tell the study staff about any health problems you are having even if you don't think they are important.
- Tell the study staff if you wish to stop being in the study.
- Tell your study doctor or coordinator if you become pregnant
- Tell your study doctor or coordinator if you are thinking about participating on another research study.

3. What are the risks and possible discomforts from being in this research study?

There are risks to being in any research study. One risk is that you may get an investigational medication or dose of an investigational medication that does not help treat your opioid dependency or the investigational medication may make your disease worse. This use of liraglutide in this study is investigational in patients seeking treatment for opioid use disorder. There may be risks, discomforts or side effects that are not yet known.

Potential risks associated with the investigational medication: There is a potential risk of experiencing side effects from the investigational medication.

Common side effects of liraglutide include:

- Nausea
- Diarrhea
- Vomiting
- Decreased appetite

These side effects dissipate over time and are minimized with by increasing the dose of medication slowly (dose titration).

Other potential side effects, though expected to be rare, include:

- Hypoglycemia (low blood sugar)
    - Feeling shaky
    - Being nervous or anxious
    - Sweating, chills and clamminess
    - Irritability or impatience
    - Confusion
    - Fast heartbeat
    - Feeling lightheaded or dizzy
    - Hunger
    - Nausea
    - Color draining from the skin (pallor)
    - Feeling Sleepy

  - Feeling weak or having no energy
  - Blurred/impaired vision
  - Tingling or numbness in the lips, tongue, or cheeks
  - Headaches
  - Coordination problems, clumsiness
  - Difficulty concentrating
  - Slurred speech
  - Nightmares or crying out during sleep
  - Seizures
  - Loss of consciousness
- Constipation
- Headache
- Indigestion
- Fatigue
- Dizziness
- Abdominal pain
- Increased lipase (an enzyme related to the pancreas)
- Vaso-vagal response (fainting) in those with a history of vaso-vagal response (fainting)

Serious side effects include:

- Risk of thyroid c-cell tumors
- Acute pancreatitis (inflammation of the pancreas)
- Acute gallbladder disease
- Risk of hypoglycemia (low blood sugar) when used in conjunction with anti-diabetic therapy)
- Heart rate increase
- Renal (kidney) impairment
- Suicidal behavior and thoughts

An allergic reaction to liraglutide can include:

- Hives
- Fast heartbeat
- Dizziness
- Trouble breathing or swallowing
- Swelling of face, lips, tongue, or throat

There is also potential risk of irritation at the injection site, and increased drug craving in response to needle use.

This is the potential risk that you could overdose on the investigational medication, and symptoms appear limited to severe nausea and vomiting and occasional abdominal pain and diarrhea. None of the reported cases caused hypoglycemia (low blood sugar).

Blood Pressure and Heart Rate: Frequent blood pressure measurements with the cuff around the arm or finger may be inconvenient and may produce some discomfort and occasional bruising of the upper arm. There is a minimal risk of skin irritation from the EKG patches.

Blood Sampling: There are minor risks and discomforts associated with blood sampling.

- We will draw blood from which may cause you a brief period of pain and possibly a small bruise at the site.
- Occasionally, a person feels faint when their blood is drawn.
- There is a small risk of bleeding after removal of the needle, which can be prevented by tight compression.
- Rarely, an infection develops which can be treated.
- Rarely, a clot could form.
- It is possible that exposure to needles during blood sampling may serve as a trigger for opioid use for some participants.

Pregnancy: This treatment may hurt an unborn child. You will be advised to use approved birth control such as birth control pills, birth control shots, IUD, diaphragm, or condoms while in this study. You will be instructed to inform us if you become pregnant or father a child while in this study. Women able to become pregnant will have a urine test to make sure they are not pregnant before receiving treatment in this study, and will be encouraged to use birth control or refrain from intercourse through the study.

Potential risks associated with exposure to drug-related cues: There is a risk of relapse to those in recovery when they are exposed to drug cues in the cue reactivity task. You may experience an increase in craving in response to opioid-related images.

Risks related to exposure to fNIRs: There are no known discomforts or risks associated with the brain imaging study. Risks of fNIRs were previously found to be minimal. The risks associated with spending 20-30 minutes in a protocol utilizing fNIRs are less than the risks associated with spending an equivalent amount of time in the sunlight in the US without a hat. In summary, exposing the brain to the infrared light generated by this device poses no greater risk to you than spending an equivalent amount of time (about 1 hour) exposed to sunlight. There is minimal risk of headache from the use of sensors.

Actigraphy/Wearables: There is no known risk to wearing the actigraphy wristband. A minor skin rash may develop from the wristband, but this risk is very slight.

Questionnaires: The interviews and forms are routine, standardized forms for psychology research. They pose no known risks, although certain questions may be mildly upsetting because they may probe sensitive psychological areas and others inquire about family history of medical and psychological illness or alcohol and substance use. Appropriate referrals are offered if areas of concern arise in the course of collecting this information. You are free to skip any questions that make them uncomfortable.

Other risks
There is a risk that blood tests will reveal that you are positive for hepatitis or HIV. These infections are required by law to be reported to the Pennsylvania Department of Health.

There is a risk from randomization as you will be assigned to a treatment program by chance. The treatment you receive may prove to be less effective or to have more side effects than the other research treatment or other available treatments.

There is a risk of loss of confidentiality if your information or your identity is obtained by someone other than the investigators, but precautions will be taken to prevent this from happening. The confidentiality of your electronic data created by you or by the researchers will be maintained as required by applicable law and to the degree permitted by the technology used. Absolute confidentiality cannot be guaranteed.

4. What are the possible benefits from being in this research study?

4a. What are the possible benefits to me?

There is no guarantee that you will benefit from this research. The possible benefits you may experience from this research study include a reduction in craving.

4b. What are the possible benefits to others?

The results of this research may guide the future treatment of patients with opioid dependency.

5. What other options are available instead of being in this research study?

You do not have to take part in this study to be treated for your condition. Instead of participating in this research, you could:

- Receive commercially available treatments, including behavioral techniques.
- Be part of a different research study, if one is available.
- Choose not to be treated for your medical condition.

Before you decide if you want to be in this research, we will discuss the other choices that are available to you. We will tell you about the possible benefits and risks of these choices.

Because it is investigational, the therapy offered in this research is only available to you if you take part in the research study.

6. How long will I take part in this research study?

If you agree to take part, it will take you about 49 days (61 days for extended participation) to complete this research study.

7. How will you protect my privacy and confidentiality if I decide to take part in this research study?

7a. What happens to the information collected for the research?

Efforts will be made to limit the use and sharing of your personal research information to people who have a need to review this information. Reasonable efforts will be made to keep the personal information in your research record private. However, absolute confidentiality cannot be guaranteed, and there may be situations where disclosure is required by law.

In the research files at Caron Treatment Centers we will include these identifiers: name, date of birth, medical record number, and a code number.

- A list that matches your name with your code number will be kept in a locked file in Dr. Deneke's office at Caron Treatment Centers.
- Your research records will be labeled with your code number and your initials and will be kept in a locked filing cabinet within Dr. Deneke's locked research office at Caron Treatment Centers.
- Results of some of the research-related clinical tests (limited to laboratory blood tests) will be kept in your Caron Treatment Centers medical record.

For research records sent to Penn State College of Medicine (PSU) from Caron Treatment Centers, you will be identified by your code number and your date of birth. Paper records will be transferred from Caron to the Penn State College of Medicine via a trained research assistant and stored in a locked filing system in the PI's office (C5609) for at least 6 years following study termination.

For research data (neuroimaging data gathered through fNIRs technology) sent to Drexel University by Penn State College of Medicine (PSU), you will be identified by your code number only.

For research data (Garmin and EMA data) sent to Penn State University Park, you will be identified by your code number. Research staff at Penn State University Park will use the Garmin Web API to download de-identified Garmin data (associated by the random study ID) from the Garmin servers where it was stored. EMA survey data is transmitted directly to Penn State University Park from your phone via an encrypted link.

For research specimens (your glucose blood samples) sent to Caron Treatment Centers' clinical laboratory for analysis, you will be identified by your name, address, phone number, email, medical record number, and date of birth. When the results of these tests are sent to Penn State College of Medicine (PSU), you will only be identified by your code number.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health (NIH). This means that the researchers cannot disclose information that identifies you to anyone not connected with the research. This protection also prevents this information from being used or disclosed for legal proceedings, such as being accessed through a court order. The Certificate of Confidentiality however does not prevent disclosures required by law, such as information about child abuse or neglect and harm to yourself or others. Also, your information may be disclosed in accordance with any consent you provide, including for your medical treatment or use in other research. Additionally, the Certificate of Confidentiality does not prevent your information from being disclosed to the NIH in order for it to evaluate or audit the research, or prevent disclosures required to meet FDA requirements. For additional information ask the principal investigator or a member of the study team or contact the Human Subjects Protection Office at (717) 531-5687.

In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

7b. What will happen to my research information and/or samples after the study is completed?
We may use your research information in future studies or may share your information with other investigators for future research without your additional informed consent. Before we use or share your information we will remove any information that shows your identity.

Researchers can do studies that are more powerful when they share with each other the data or information they get from research studies. They share this information with each other by putting it into scientific databases. Your coded research information may be put in one or more databases and used for future research. Your information stored in these databases will not include any identifying information such as your name, address, telephone number, or social security number. Your research data will only be available to researchers who have received approval from data access committees and/or Institutional Review Boards. Some of these databases are maintained by PSH/PSU, some are maintained by the federal government, and some are maintained by private companies and other institutions.

Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the researchers will contact you to let you know what they have found.

7c. How will my identifiable health information be used?
In general, under federal law (including the Health Insurance Portability and Accountability Act – HIPAA or privacy laws) your health information is private. By signing this form, you are authorizing us to collect, use, and disclose your identifiable health information, sometimes referred to as "Protected Health Information" or "PHI" under HIPAA, for the purposes of this research study. We will use and disclose your information only as described in this form, in the PSH Privacy Notice, and as may be required or allowed under the applicable privacy laws.

The research team may use the following health information:

- Past, present, and future medical records, including identifiable information
- New health information from tests, procedures, visits, interviews, or forms filled out as part of this research study.

The following people/groups may see, use, and share your identifiable health information:

- PSH/PSU research staff involved in this study
- The PSH/PSU Institutional Review Board (IRB), a group of people who review the research study to protect subjects' rights and welfare
- The PSH/PSU Human Subjects Protection Office
- The PSH/PSU Research Quality Assurance Office
- Non-research staff within PSH/PSU who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- Federal and state agencies (such as the U.S. Food and Drug Administration, the Office for Human Research Protections, the Department of Health and Human Services, the National Institutes of Health, and other U.S. or foreign government bodies that oversee or review research)
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Organizations that provide independent accreditation and oversight of hospitals and research
- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)
- Other researchers and medical centers outside of PSU and Penn State Health that are part of this study and their IRBs (Caron Treatment Centers, Drexel University).
- Synergy Pharmacy
- The clinical laboratory that Caron Treatment Centers send specimens to for testing
- Researchers from other campuses of Penn State University who are part of this study
- A group that oversees the data (study information) and safety of this research

These groups may also review and/or copy your original PSH/PSU records while looking at the results of the research study. It is possible that some of the other people/groups who receive your health information may not be required by Federal privacy laws to protect your information. We share your information only when we must, and we ask anyone who receives it from us to protect your privacy.

Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your identifiable health information and samples may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

We may remove identifying information from your protected health information. Once we do this, the remaining information will not be subject to the privacy laws. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Because research is an ongoing process, your permission for the use, storage and sharing of your health information will continue indefinitely.

Your privacy rights:

- You have the right to refuse to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you will not be able to take part in this research study.
- You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing using the address on the front of this form. Once permission is withdrawn, you cannot continue to take part in the study.
- If you withdraw your permission, we will stop collecting health information about you for this study; we may continue to use and share your health information that we already have if it is necessary for safety and scientific soundness of the research study; and we will not be able to take back information that has already been used or shared with others.
- You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. However, you may not be allowed to see or copy certain health information that is a part of this research study. This is only for the period of the study. You will be allowed to see that information when the entire research study is complete.

8. What are the costs of taking part in this research study?

8a. What will I have to pay for if I take part in this research study?

For costs of tests and procedures that are only being done for the research study:

- The investigational medication (liraglutide) and placebo will be provided by Novo Nordisk at no cost to you while you take part in this study.
- You and/or your insurance company will not be charged for the cost of any tests or procedures that are required as part of the research and are outside the standard of care (what is normally done) for your condition.
- The research-related tests and procedures that will be provided at no cost to you include:
  - Actigraphy unit (wristband)
  - Cardiorespiratory function assessment
  - Blood sample collection for glucose monitoring
  - EMA collection
  - fNIR imaging
  - EKG
  - Pregnancy test (if applicable)
  - Laboratory tests

For costs of medical services for care you would receive even if you were not in this research study:

- You and/or your insurance company will be responsible for the cost of routine medications, tests and procedures that you would receive even if you were not in this research.
- You and/or your insurance company will be billed for the costs of these routine tests and procedures in the usual manner.
- You will be responsible for any co-payments, co-insurance and deductibles that are standard for your insurance coverage.
- You will be responsible for any charges not reimbursed by your insurance company.
- Some insurance companies may not pay for routine costs for people taking part in research studies. Before deciding to be in this research you should check with your insurance company to find out what they will pay for.

If you have any questions about costs and insurance, ask the research study doctor or a member of the research team.

8b. What happens if I am injured as a result of taking part in this research study?
It is possible that you could develop complications or injuries as a result of being in this research study. If you experience a side effect or injury and emergency medical treatment is required, seek treatment immediately at any medical facility. If you experience a side effect or injury and you believe that emergency treatment is not necessary, you should contact the principal investigator listed on the first page of this consent form as soon as possible and the principal investigator will arrange for medical treatment. You should also let any health care provider who treats you know that you are in a research study.

<u>PSH/PSU compensation for injury</u>

- There are no plans for PSH/PSU to provide financial compensation or free medical treatment for research-related injury.
- If an injury occurs, medical treatment is available at the usual charge.
- Costs will be charged to your insurance carrier or to you.
- Some insurance companies may not cover costs associated with research injuries.
- If these costs are not covered by your insurance, they will be your responsibility.

When you sign this form you are not giving up any legal right to seek compensation for injury.

9. Will I be paid to take part in this research study?
You will be paid for your time in the amount of $25 for the initial evaluation, $50 for the first test day (Day 1, when fNIRs tasks and Cued response assessments are performed), $50 for the completion of EMA and physiological measures, $75 for the second test day (Day 19), $50 for the third test day (Day 31; extended participation only), $20 for the rebound follow-up, and $30 for the follow-up phone call, for a total of $250 ($300 for extended participation). Payments will be titrated relative to the tasks accomplished. Reimbursements will be paid using Target gift cards because neither alcohol nor tobacco products can be purchased at Target.

It is possible that your research information and/or specimens (both identifiable and de-identified) may be used to create products or to deliver services, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family.

10. Who is paying for this research study?

The institution and investigators are receiving a grant from the National Institutes of Health to support this research. Novo Nordisk, Inc is providing the investigational medication (liraglutide) and placebo at no cost to the research team.

Dr Scott Bunce has an equity interest in fNIR Devices LLC and was an inventor of a device being used in the study. This financial interest has been reviewed by the PSU Institutional Review Board and Conflict of Interest Review Committee. If you would like more information, please contact the Conflict of Interest Program at (717) 531-0003, extension 283526.

11. What are my rights if I take part in this research study?

Taking part in this research study is voluntary.

- You do not have to be in this research.
- If you choose to be in this research, you have the right to stop at any time.
- If you decide not to be in this research or if you decide to stop at a later date, there will be no penalty or loss of benefits to which you are entitled.

If you stop being in the research, already collected data may not be removed from the study database. You will be asked whether the investigator can collect medical information from your routine medical care. If you agree, this data will be handled the same as research data. If you withdraw completely from the research study, no further information will be collected and your participation will end. You may discontinue taking part at any time without penalty or loss of benefits to which you are otherwise entitled.

Your research doctor may take you out of the research study without your permission.

- Some possible reasons for this are:
    - Systolic blood pressure changes >40 mmHg, to levels <100 mmHg or >200 mmHg, or clinical symptoms of hypertension (e.g. headache, dizziness, blurred vision, nausea swelling) or low blood pressure (e.g. dizziness, nausea, fainting) develop
    - Heart rate reaches levels <40 beats/min or >120 beats/min
    - Respiratory rate changes by >5 breaths/minute or reaches levels <10 breaths/minute or >24 breaths/minute
    - Continuing the research would be harmful
    - Your condition has become worse
    - You become pregnant
    - You did not follow the instructions of the study doctor
    - You experience serious side effects
    - If your participation ends early, you will be asked to complete an End of Study telephone call.

During the course of the research you will be provided with any new information that may affect your health, welfare or your decision to continue participating in this research.

12. If I have questions or concerns about this research study, whom should I call?

Please call the head of the research study (principal investigator), Dr Scott Bunce, at (717) 531-4127 or after hours, call Caron Treatment Centers on (800) 854-6023 and ask to speak to Dr Erin Deneke, Study Co-Investigator if you:

- Have questions, complaints or concerns about the research.
- Believe you may have been harmed by being in the research study.

You may also contact the research protection advocate in the PSH Human Subjects Protection Office (HSPO) at (717) 531-5687 if you:

- Have questions regarding your rights as a person in a research study.
- Have concerns, complaints or general questions about the research.
- Have questions about your privacy and the use of your personal health information.
- You may also call this number if you cannot reach the research team or wish to offer input or to talk to someone else about any concerns related to the research.

You may visit the Penn State College of Medicine's Clinical Research web site at http://med.psu.edu/clinical-research/faqs for:

- Information about your rights when you are in a research study;
- Information about the Institutional Review Board (IRB), a group of people who review the research to protect your rights; and
- Links to the federal regulations and information about the protection of people who are in research studies. If you do not have access to the internet, copies of these federal regulations are available by calling the HSPO at (717) 531-5687.

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.

INFORMED CONSENT AND AUTHORIZATION TO TAKE PART IN RESEARCH

Signature of Person Obtaining Informed Consent

Your signature below means that you have explained the research to the subject or subject representative, provided the subject or subject representative an opportunity to discuss and consider whether or not to participate in the research, and have answered any questions about the research.

_____	_____	_____	_____
Signature of person who explained this research	Date	Time	Printed Name

(Only approved investigators for this research may explain the research and obtain informed consent.)

Signature of Person Giving Informed Consent and Authorization

Before making the decision about being in this research you should have:

- Discussed this research study with an investigator,
- Read the information in this form, and
- Had the opportunity to ask any questions you may have.

Your signature below means that you have received this information, have asked the questions you currently have about the research and those questions have been answered. You will receive a copy of the signed and dated form to keep for future reference.

Signature of Subject

By signing this consent form, you indicate that you voluntarily choose to be in this research and authorize your information to be used and shared as described above.

_____	_____	_____	_____
Signature of Subject	Date	Time	Printed Name

Optional part(s) of the study
In addition to the main part of the research study, there is another part of the research. You can be in the main part of the research without agreeing to be in this optional part.

We are interested in studying the effects of the medication on sleep, as there is evidence to suggest that the study medication may improve sleep, in addition to reducing craving for opioids. Therefore, we would like to ask you to participate in two to three (2-3) overnight sleep studies, each one on a different night. Your sleep would be measured using a polysomnogram (the name of the sleep study test), which is considered to be the "gold standard" for sleep studies.

1. **Why is this research being done?**
   The polysomnogram will provide information about your stages of sleep, breathing patterns, leg movements, and behaviors in your sleep which cannot be measured with wrist actigraphy. Patients suffering from OUD typically have sleep problems, such as insomnia; this sub-study will evaluate whether the study medication can re-regulate sleep disturbances known to be caused by opioid use.

2. **What will happen in this research?**
   The polysomnogram uses a standard clinical polygraph, which is a machine that records electrical activity in your brain, known as an electroencephalogram (EEG). EEG sensors, small metal discs that attach to the EEG machine with wires, will be applied to your face and scalp with a special adhesive. These sensors will record the electrical activity generated by your brain, the muscle of the chin and eye movements while you sleep. To evaluate subjective sleep quality, you will also be asked to complete a short questionnaire (the Insomnia Severity Index or ISI) before each polysomnogram.

   A trained study team member will place standard EEG sensors (small disks of metal with wires attached connected to the EEG recording machine) to your face and scalp with paste around 9.15 pm and you will be instructed to go to bed at the time closest to your normal bedtime, within a time range of 10pm to 11pm. These sensors will record the electrical activity generated by your brain, the muscle of the chin and eye movements while you sleep. Additional sensors will be placed at your nose, mouth and around your chest and stomach to measure your breathing patterns. The study team member will make sure that all recording settings are correct by monitoring with a laptop for a few minutes and will disconnect it and leave the device recording overnight.

   You will be able to get up and use the restroom at night as the recording device will be attached to your waist, although care should be taken to not pull on the wires, as this will dislodge or pull the sensors off.

   In the morning at approximately 6:00am, a study team member will stop the sleep recording by connecting the laptop to the recording device and will remove all the sensors attached so that you can clean up any residue (essentially salt paste) by washing or taking a shower. At about

6:30am, a counselor or research assistant will then walk with you to the Neag Medical Building to get any medications you may typically take, and to continue with the main portion of the study.

The sleep studies using the polysomnogram will be performed up to three times during the study period. The **first will be on the night before you start the study treatment (night of Day 1)** and the **second will be after you complete the 1.8 mg treatment dose (night of Day 19)**. If you agree to extend your participation in the main part of the research study, **a third polysomnogram will be performed after you complete the 3.0 mg treatment dose (night of Day 31)**.

3. **What are the risks and possible discomforts from being in this sub-study?**
There are no known risks associated with the polysomnographic recordings of sleep. On rare occasions, some individuals can mild allergic reactions to the tape applied over the sensors, or allergies to latex. We will minimize this risk by using hypoallergenic tapes. There can be some mild discomfort in applying the skin sensors as the skin is cleaned, or while wearing the sensors at night.

There is a potential risk of loss of confidentiality. Every effort will be made to protect your confidential information, but this cannot be guaranteed. The polysomnographic sleep study data obtained as a result of your participation in this research will not be included in your medical record. Information from which you may be personally identified will be maintained in a confidential, secure location at Penn State Hershey, accessible only by authorized members of the study team, and will not be disclosed to third parties except as described in this consent form, with your permission, or as may be required by law.

4. What are the possible benefits from being in this sub-study?

4a. What are the possible benefits to me?

There is no benefit to you for participating in this sub-study.

4b. What are the possible benefits to others?

Using the sleep data along with clinical data, we may be able to learn more about the effects of the investigational medication on sleep, the stages of sleep, and the relationship between changes in sleep and craving. It may also give us a better understanding of any mediating effects of sleep on craving and vice versa when treated with the investigational medication.

5. **What happens to the information collected for the research?**
The data from the polysomnogram will be collected on a recording device much like an external hard drive, to which a laptop can be connected for set-up and file transfer. The sleep data file will be transferred to the Penn State Health and Penn State College of Medicine network using Microsoft Teams, a HIPAA-complaint platform used by Penn State Health to safely transfer large files that require a high level of security. This will allow further storage, scoring, interpretation and analysis of your sleep data within the secured network space of the Sleep Research and Treatment Center (SRTC) at Penn State, using specific software. A specialized team member will visually analyze your sleep and score it to ascertain your sleep stages and breathing patterns. This will allow investigators to pair the polysomnographic sleep study data with the clinical data

collected in the primary study, which includes craving, mood, and neurophysiological measures as described above.

Any research data from the sleep study sent to the SRTC, will be identified by your random code number only.

We will use your polysomnographic sleep study data for research only. We will be happy to provide you with a copy of your results upon your request to the study team. If any results are found to be relevant to your general health care, you may choose to follow up with your Family Physician or consult a Sleep Physician for further evaluation and treatment.

6. **Will I be paid to take part in this research study?**
   In addition to the reimbursement for participating in the main parts of the study, you will receive an additional reimbursement of $90 per night (for a total of $180 for two nights; $270 for three nights) for participating in the optional polysomnographic sleep recording. Reimbursements will be paid using Target gift cards.

Please initial below to indicate what you want regarding the optional sleep study (polysomnogram).

a. I wish to participate and provide sleep data as measured on the polysomnogram.

_____ Yes _____ No

Signature of Person Obtaining Informed Consent

Your signature below means that you have explained the research to the subject or subject representative, provided the subject or subject representative an opportunity to discuss and consider whether or not to participate in the research, and have answered any questions about the research.

_____	_____	_____	_____
Signature of person who explained this research	Date	Time	Printed Name

(Only approved investigators for this research may explain the research and obtain informed consent.)

Signature of Person Giving Informed Consent and Authorization
Before making the decision about being in this research you should have:

- Discussed this research study with an investigator,
- Read the information in this form, and
- Had the opportunity to ask any questions you may have.

Your signature below means that you have received this information, have asked the questions you currently have about the research and those questions have been answered. You will receive a copy of the signed and dated form to keep for future reference.

Signature of Subject

By signing this consent form, you indicate that you voluntarily choose to be in this research and authorize your information to be used and shared as described above.

Version Date: 26 June 2024

_____	_____	_____	_____
Signature of Subject	Date	Time	Printed Name