Document Coversheet

Study Title: Prescription Medications: Pharmacodynamics and Interaction Effects

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KEY INFORMATION FOR

MAIN STUDY CONSENT:

PRESCRIPTION MEDICATIONS: PHARMACODYNAMICS AND INTERACTION EFFECTS

You are being invited to take part in a research study about the effects of sedatives (examples: gabapentin, alprazolam, zolpidem) and opioid (examples: oxycodone, tramadol, codeine, hydrocodone) medications, when taken alone and in combination. We plan to screen approximately 75 participants and plan to have approximately 18 participants complete the study.

WHAT IS THE PURPOSE, PROCEDURES, AND DURATION OF THIS STUDY?

By doing this study, we hope to learn about how certain prescription medications affect your body, mood, and behavior. Your participation in this research will include an approximately 30-night stay at the UK Hospital (you will not be allowed to leave or have visitors during this time) and a short (about 3 hours) follow-up visit approximately 2 weeks after leaving the hospital.

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

You may choose to participate in this study to earn extra money; however, there is no direct benefit to you for taking part in this study. Your willingness to participate may help us to understand how certain prescription medications affect your body, mood, and behavior. For a complete description of benefits, refer to the Detailed Consent.

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

You may choose not to participate if you are not able to live at the UK hospital for about a month. Let us know if that is a concern for you. There are also risks related to use of the study medications – a complete description of risks, including a full list of study medication side effects, are listed in the detailed portion of the consent form.

DO YOU HAVE TO TAKE PART IN THE STUDY?

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

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of this study is Sharon L. Walsh, Ph.D. of the University of Kentucky, Department of Behavioral Science and Center on Drug and Alcohol Research. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study, her phone number is: **(859) 257-6485.**

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact staff in the University of Kentucky (UK) Office of Research Integrity (ORI) between the business hours of 8am and 5pm EST, Monday-Friday at 859-257-9428 or toll free at 1-866-400-9428.

DETAILED CONSENT:

ARE THERE REASONS WHY YOU WOULD NOT QUALIFY FOR THIS STUDY?

You will not be allowed to participate in the study if you are: under 18 or over 55 years of age; pregnant, breastfeeding, or planning on becoming pregnant; seeking treatment for your substance use; you do not use prescription medications for non-medical purposes (to get high, feel relaxed). You will not allowed to participate if you are physically dependent on opioids, benzodiazepine/sedative-like drugs or alcohol; however, we will provide treatment referrals to you if you are seeking treatment for your drug/alcohol use. You will not be allowed to participate if the medical staff thinks that giving you the study drugs could be dangerous to your health. If you have any serious medical problems (e.g., a history of heart problems, breathing problems, head trauma, epilepsy or seizures), you will not be allowed to participate in this study. If you decide that you do not want to participate or do not think the study will fit your schedule, you should not take part.

WHERE IS THE STUDY GOING TO TAKE PLACE AND HOW LONG WILL IT LAST?

If you are selected to participate, you will live at the UK Hospital in the CCTS Inpatient Unit. During your stay, you will participate in 10 sessions. Each session will last approximately 8 hrs and you will participate in about 2-3 sessions per week. You will live on the inpatient unit for approximately 1 month and participate in sessions for about 80 hours across the whole month. You will be given a calendar that will list the date of each session. On your days off from session, you can read, watch movies, and engage in recreational activities, but you will not be permitted to leave the hospital or have visitors.

WHAT WILL YOU BE ASKED TO DO?

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

1. Once you are medically cleared for the study, you will be admitted to the CCTS unit at the UK hospital. You may be asked to share a room with another volunteer of the same gender.

2. You will need to follow the inpatient unit rules while you are in the study. If you do not follow the rules, you will be removed from the study – you will not receive a payment bonus if you are discharged for breaking rules. Some examples of these rules are:
   - You will not be allowed to have any visitors, but you will be able to make phone calls
   - You will be allowed to smoke cigarettes, but only under supervision of the CCTS nursing staff
   - No sexual behavior or sexual intercourse for the duration of the study
   - No drug or alcohol use; you cannot use any drugs that are not given to you as part of the study

3. After you are admitted to the inpatient unit, we will show you the session room where testing will take place. We will teach you how to use the computer and show you the kinds of questions you will be asked and tasks you will need to complete. You will have plenty of time to ask questions about how to perform any of the tasks.

4. There will be a total of 10 sessions. The first session is a qualification session – this session will help us determine if you will qualify for the rest of the study. If you continue to qualify, you will complete 9 experimental sessions. You will receive a calendar with the actual dates of your sessions, but a sample calendar with session dates is provided below. A more detailed calendar can be found in the Appendix section at the end of this packet.

Sample Study Calendar:

	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
Week 1		Admission	Practice/ Training	Session 1 - Qualification		Session 2	
Week 2		Session 3		Session 4		Session 5	
Week 3		Session 6		Session 7		Session 8	
Week 4		Session 9		Session 10	Discharge		

5. The first session is a qualification session to help us determine if you will qualify for the rest of the study.

During the qualification session, you will receive capsule(s) to swallow at two different times – these capsules will contain either an opioid drug (for example: hydromorphone, oxycodone, morphine, or hydrocodone) or placebo (an inactive substance). After you complete this session, you will be informed whether you qualify to continue with the rest of the study. If you do not qualify, you will be discharged. If you qualify, you will complete 9 additional experimental sessions.

6. During each of the 9 sessions, you will receive oral capsule(s) at two different times. These capsules may contain an opioid medication (such as oxycodone, tramadol, codeine, hydrocodone), a sedative medication (such as gabapentin, alprazolam, zolpidem), or a placebo (an inactive substance).

7. During sessions, we will measure how you respond to each of the doses by recording things like heart rate, blood pressure, oxygen saturation, expired carbon dioxide, respiration rate, and pupil diameter. We will also ask you questions about how you are feeling. For example, we may ask you if you like the drug effects or if you are feeling sick. We will also ask you to complete tasks that measure your coordination and balance and look at blinking lights to test your eyes – this test will not harm your vision. Each session will last approximately 8 hrs.

You will also participate in a cold-water task during each session. We will ask you to place your arm into a cooler of cold water and tell us when you start to feel pain and when you no longer wish to tolerate it. When you can no longer tolerate the cold water, you can remove your arm from the cooler. This task will not cause any lasting harm, and the pain will subside within a few minutes. We will ask you several questions about the pain your experienced during the task.

During session, you may engage in activities such as reading, as long as these activities do not interfere with the study or any of the scheduled tasks or questionnaires.

8. On days when you are not in session, you will be asked to fill out questionnaires each day. For example, we will ask you about how you feel, whether you feel tired or have an upset stomach. The nurses will measure your vital signs (heart rate, blood pressure, etc.) several times every day. You will also give breath and urine samples every day, which will be tested for drugs and alcohol; women will be tested for pregnancy. Use of drugs or alcohol that are not given to you as part of the study is forbidden and will result in your dismissal from the study.

9. If you are female, you will be tested regularly to see if you are pregnant. If the test is positive, you will be notified, discharged from the study, and referred for treatment. If you become pregnant at any time during the study (during screening, while you are in the hospital, in the time between study discharge and your follow-up appointment, or anytime in the 30 days after you leave the study), you will need to notify the study investigator (Sharon Walsh, Ph.D.) or the study physician (Michelle Lofwall, M.D.) as soon as possible: **Sharon Walsh, Ph.D. (859) 257-6485; Michelle Lofwall, M.D. (859) 323-9321.**

By signing this consent form you are agreeing to practice an effective method of birth control (e.g., oral contraceptives, intrauterine device, diaphragm, condom) for the entire study duration (prior to study admission through 30-days after study completion).

10. After you have completed all sessions, you will be discharged from the study. We will ask you to come back to the CDAR Building approximately 2 weeks of discharge for a follow-up visit. We will ask you about your health, drug use, and collect an observed urine sample. You will be paid $25.

11. At any point, if you decide that you want to seek treatment for your substance use, we will assist you in finding treatment.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

The risks and discomforts of this study are related primarily to the drugs given to you and the experimental procedures. We have carefully selected the doses to minimize the risk of serious side effects. Furthermore, some questions you will be asked throughout the study (about your medical, legal drug use history) may cause some discomfort.

The likely/most common risks of receiving opioid drugs include dizziness, stimulation, restlessness, a feeling of well-being, talkativeness, itchiness, nausea, vomiting, headache, constipation, dry mouth, sweating, sleepiness, light-headedness, and mild decreased breathing. These occasionally occur after receiving an opioid. These

effects typically will go away on their own after a few hours and do not require any treatment. The risks of decreased breathing after administration of opioid drugs is related to the dose administered, and we have carefully selected doses to minimize the chance of serious decreases in breathing. If a serious decrease in breathing were to occur, this would be considered a very rare event that can be treated immediately and effectively with medication.

The possible side effects of receiving the sedative medication that are not uncommon and occur occasionally (i.e. occurring in greater than 5% of persons during clinical trials) include fatigue, swelling of hands and feet, sleepiness, diarrhea, tremor, uncontrolled rapid eye movements, double vision, dizziness, and coordination problems. These effects typically will go away on their own after a few hours and do not require any treatment. In rare cases, fever, chest pain, confusion, and rash may occur. We carefully select doses to avoid serious risks. If these rare effects were to occur, there is a chance that they would require treatment, depending on their severity.

We will watch you carefully throughout your participation to minimize the chance of any serious reactions.

We do not have any plans to draw your blood or conduct an electrocardiogram (ECG) after the screening is completed. However, if you were to get sick or hurt during the study, we may need to conduct these tests. There are risks related to drawing blood. Soreness, bruising, pain and a small amount of bleeding are likely to occur; fainting and infection are more rare. It is possible that we may have to try more than once to draw blood (which is not uncommon). An ECG is painless. Approximately 12 sticky pads will be placed on your skin and your heart's electrical activity will be measured. The electrodes may feel cold when first applied. In rare cases, some people may develop a rash or irritation where the patches were placed.

Exposure to drugs may have harmful effects on a fetus or a newborn, and you will not be allowed to participate in the study if you are pregnant, planning to become pregnant or breastfeeding during the study, or if you cannot use an appropriate contraception method.

We will make every effort to keep private all research records that identify you to the extent allowed by law. However, there is a risk that a breach in confidentiality may occur. If this occurs, it may cause problems such as embarrassment and emotional stress.

There is always a chance that any medical treatment can harm you. The research medications/treatments/procedures in this study are no different. In addition to risks described in this document, you may experience a previously unknown risk or side effect. We will do everything we can to keep you from being harmed.

WILL YOU BENEFIT FROM TAKING PART IN THIS STUDY?

You will not get any personal benefit from taking part in this study. However, if you take part in this study, you may help us learn more about the effects of certain prescription medications when taken alone and together.

IF YOU DON'T WANT TO TAKE PART IN THE STUDY, ARE THERE OTHER CHOICES?

If you do not want to be in the study, there are no other choices except not to take part in the study. We can provide medical or drug treatment referrals to you if need them.

WHAT WILL IT COST YOU TO PARTICIPATE?

The study procedures and medications will be provided at no cost to you.

You and/or your insurance company, Medicare, or Medicaid will be responsible for the costs of all care and treatment that you would normally receive for any conditions you may have. These are costs that are considered medically necessary and will be part of the care you receive even if you do not take part in this study.

The University of Kentucky may not be allowed to bill your insurance company, Medicare, or Medicaid for the medical procedures done strictly for research. Therefore, these costs will be your responsibility. Your insurer, Medicare, or Medicaid may agree to pay for the costs. However, a co-payment or deductible may be needed from you. The amount of this co-payment or deductible may be costly.

WHO WILL SEE THE INFORMATION THAT YOU GIVE?

We will make every effort to keep confidential all research records that identify you to the extent allowed by law. Your information will be combined with information from other people taking part in the study. When we write about the study to share it with other researchers, we will write about the combined information we have gathered. You will not be personally identified in these written materials. We may publish the results of this study; however, we will keep your name and other identifying information private. We will collect your social security number; this is required in order for you to participate.

We will make every effort to prevent anyone who is not on the research team from knowing that you gave us information, or what that information is. Your name will be kept separate from the information that you give, and these two things will be stored in different places under lock and key. Information collected electronically will be stored on password-protected computers.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below. You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

You should know that there are some circumstances in which we may have to show your information to other people. For example, the law may require us to show your information to a court or to tell authorities if you report information about a child being abused or if you pose a danger to yourself or someone else. The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under certain circumstances including: abuse or neglect, harm to self or others, or diagnosis of certain communicable diseases (including but not limited to, hepatitis C, HIV, or tuberculosis), which will be reported to the State Health Department along with your full name as required by law.

Officials of the Food and Drug Administration, National Institutes of Health, and the University of Kentucky may look at or copy pertinent portions of records that identify you.

WILL YOU BE GIVEN INDIVIDUAL RESULTS FROM THE RESEARCH TESTS?

Do you give permission for us to contact you about research results or incidental findings that are determined to be important to you/your family's health? (Incidental findings are unforeseen findings discovered during the course of the research that may affect you or your family's health).

☐ **Yes** ☐ **No** _____**Initials**

You may also withdraw your consent to be contacted with information about research results or incidental findings by sending a written request to 845 Angliana Ave, Lexington, KY 40508 or call 859-257-6485.

WILL WE CONTACT YOU WITH INFORMATION ABOUT PARTICIPATING IN FUTURE STUDIES?

The research staff would like to contact you in the future with information about participating in additional studies. If so, we plan to contact you between approximately 1-4 times per year.

Do you give your permission to be contacted in the future by Dr. Walsh and/or the research team regarding your willingness to participate in future research studies?

☐ **Yes** ☐ **No** **Initials**

WILL YOUR INFORMATION BE USED FOR FUTURE RESEARCH?

Your information or samples collected for this study will NOT be used or shared for future research studies, even if we remove the identifiable information like your name, medical record number, or date of birth.

CAN YOU CHOOSE TO WITHDRAW FROM THE STUDY EARLY?

You can choose to leave the study at any time. You will not be treated differently if you decide to stop taking part in the study.

The investigators conducting the study may need to remove you from the study. This may occur for a number of reasons. You may be removed from the study if:

- you are not able to follow the directions,
- they find that your participation in the study is more risk than benefit to you, or
- the agency paying for the study chooses to stop the study early for a number of scientific reasons.

If you stop the study because of side effects from the medication or another health-related reason, we will follow-up with you by telephone or request that you come visit us so we can see how you are doing.

ARE YOU PARTICIPATING, OR CAN YOU PARTICIPATE, IN ANOTHER RESEARCH STUDY AT THE SAME TIME AS PARTICIPATING IN THIS ONE?

You **may not** take part in this study if you are currently involved in another research study. It is important to let the investigator know if you are in another research study. You should discuss this with the investigator before you agree to participate in another research study while you are in this study.

WHAT HAPPENS IF YOU GET HURT OR SICK DURING THE STUDY?

If you believe you are hurt or if you get sick because of something that is done during the study, you should call Michelle Lofwall, M.D. **(859) 323-9321**. Dr. Lofwall will determine what type of treatment, if any, is best for you at that time.

It is important for you to understand that the University of Kentucky does not have funds set aside to pay for the cost of any care or treatment that might be necessary because you get hurt or sick while taking part in this study. That cost will be your responsibility. Also, the University of Kentucky will not pay for any wages you may lose if you are harmed by this study. The medical costs related to your care and treatment because of research related harm will be your responsibility.

You do not give up your legal rights by signing this form.

WILL YOU RECEIVE ANY REWARDS FOR TAKING PART IN THIS STUDY?

You will receive payment for your participation. You will receive $60 per night that you stay in the hospital. If you complete the study, you will receive an additional $60 for every night of your stay ($120/night if you complete). However, you will not receive this bonus if you are dismissed from the study, do not qualify after the qualification session is completed, or if you choose to quit the study before completion. Total payment depends on your length of stay (for example: you would earn $3,600 for a 30-night stay).

You will also receive $25 for your follow-up visit scheduled approximately 2 weeks of your discharge from the study.

We will provide your earnings to you via check(s). The maximum amount of each check is $500. You will receive your first check at discharge. We will mail you the remainder of the checks. We will mail you $500 per check per day until you are fully paid. We will mail the checks to the address that you provide us.

For example, if you complete the study and earn $3,600, you will receive $500 on the day of discharge and then will receive six $500 checks and one $100 check in the mail (6 x $500 = $3,000 + $100 = $3,100); it will take 1-2 weeks for you to receive all seven checks. Alternatively, you are permitted to visit our office to pick up a check in-person during normal business hours Monday-Friday (closed on weekends, holidays).

Study payments are considered taxable income reportable to the Internal Revenue Service (IRS). You will be asked to complete a W-9 form which includes your name, address and Social Security number. A form 1099 will be sent to you if your total payments for research participation are $600 or more in a calendar year.

WHAT IF NEW INFORMATION IS LEARNED DURING THE STUDY THAT MIGHT AFFECT YOUR DECISION TO PARTICIPATE?

You will be informed if the investigators learn new information that could change your mind about staying in the study. You may be asked to sign a new informed consent form if the information is provided to you after you have joined the study.

WHAT ELSE DO YOU NEED TO KNOW?

The National Institute on Drug Abuse is providing financial support for this study.

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

FUTURE USE OF YOUR PROTECTED HEALTH INFORMATION OR SPECIMEN(S):

Identifiable information such as your name, medical record number, or date of birth may be removed from the information or samples collected in this study. After removal, the information or samples may be used for future research or shared with other researchers without your additional informed consent.

In addition to the main study, you are being asked to allow us to keep and use your information and/or specimens for future research that is currently unspecified.

AUTHORIZATION TO USE OR DISCLOSE YOUR IDENTIFIABLE HEALTH INFORMATION

The privacy law, HIPAA (Health Insurance Portability and Accountability Act), requires researchers to protect your health information. The following sections of the form describe how researchers may use your health information.

Your health information that may be accessed, used and/or released includes:

Name, address, date of birth, weight, gender, social security number, results of physical exams, blood tests, urine tests related to the study, and ECG results.

The Researchers may use and share your health information with:

- The University of Kentucky's Institutional Review Board/Office of Research Integrity;
- Law enforcement agencies (only when required by law)
- University of Kentucky representatives
- UK Healthcare and their representatives
- UK Hospital
- The National Institutes of Health and/or its divisions
- The Investigational Drug Service (IDS) at the University of Kentucky
- Food and Drug Administration
- Center for Clinical and Translational Science (CCTS)

If you are a woman and you become pregnant anytime during the study or within 30 days after discharging from the study, you must inform Dr. Lofwall or Dr. Walsh – they must then report the outcome of your pregnancy to the Sponsor (and/or the FDA).

The researchers agree to only share your health information with the people listed in this document.

Should your health information be released to anyone that is not regulated by the privacy law, your health information may be shared with others without your permission; however, the use of your health information would still be regulated by applicable federal and state laws.

You may not be allowed to participate in the research study if you do not sign this form. If you decide not to sign this form, it will not affect your:

- Current or future healthcare at the University of Kentucky;
- Current or future payments to the University of Kentucky;
- Ability to enroll in any health plans (if applicable); or
- Eligibility for benefits (if applicable).

After signing the form, you can change your mind and NOT let the researcher(s) collect or release your health information (revoke the Authorization). If you revoke the authorization:

- You will send a written letter to: Sharon L. Walsh, Ph.D. at 845 Angliana Ave. Lexington, KY 40508 to inform her of your decision.
- Researchers may use and release your health information **already** collected for this research study.
- Your protected health information may still be used and released should you have a bad reaction (adverse event).

The use and sharing of your information has no time limit.

If you have not already received a copy of the Privacy Notice, you may request one. If you have any questions about your privacy rights, you should contact the University of Kentucky's Privacy Officer between the business hours of 8am and 5pm EST, Monday-Friday at (859) 323-1184.

APPENDIX – Detailed Study Calendar

STUDY ACTIVITIES	SCREENING	INPATIENT STUDY				FOLLOW-UP
	1-2 Weeks	Inpatient Week 1	Inpatient Week 2	Inpatient Week 3	Inpatient Week 4	2-4 Weeks After Study Completion
Informed Consent	•					
Urine/Breath Samples	•					
Labs/ECG	•					
Screening Questionnaires	•					
Physical Exam	•					
Questionnaires		•	•	•	•	
Urine/Breath Samples		•	•	•	•	
Study Sessions 1-3 times/week		•	•	•	•	
Study Drug Administration		•	•	•	•	
Session Questionnaires		•	•	•	•	
Vitals/Safety monitoring		•	•	•	•	
Urine/Breath Samples						•
Brief Questionnaires						•

INFORMED CONSENT SIGNATURE PAGE

You are a participant or are authorized to act on behalf of the participant. This consent includes the following:

- **Key Information Page**
- **Detailed Consent**

You will receive a copy of this consent form after it has been signed.

_____	_____
Signature of research participant	**Date**
_____	
Printed name of research participant	
_____	_____
Printed name of person obtaining informed consent/ HIPAA authorization	Date
_____	
Signature of Principal Investigator or Sub/Co-Investigator	