Document Coversheet

Study Title: Neurobehavioral Mechanisms of Choice in Opioid Use Disorder

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Consent and Authorization to Participate in a Research Study

KEY INFORMATION FOR BEHAVIORAL EFFECTS OF DRUGS: INPATIENT (37)

We are asking you to choose whether or not to volunteer for a research study about the behavioral and physiological effects of opioids. This page is to give you key information to help you decide whether to participate. We have included detailed information after this page. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is below.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

This experiment is testing the effects of opioid dependence on performance on a game of chance. This game will be administered to you in a magnetic resonance imaging (MRI) scanner. By doing this study, we hope to learn about how opioid dependence influences brain activity during decision-making. If you have a history of intravenous opioid use, you can also participate in an extra session that will measure the subjective and physiological effects of intravenous administration of the opioid drug remifentanil. By doing this study, we hope to learn how a history of opioid use affects the response to remifentanil, an opioid commonly used for anesthesia.

During two initial outpatient visits to one of our laboratories, you will be asked to complete a series of tasks, which will take about 4 total hours across the two outpatient visits. Based on your task performance, you could be invited to participate in a third 2-h session in which you will complete the task again and be acclimated to the MRI scanner. If you are comfortable in the MRI scanner, you will be invited to complete an inpatient study lasting up to 15 days that will include 2 MRI scanning sessions. Finally, if you have a history of intravenous opioid use, you might qualify for a final session that will test the effects of the opioid remifentanil. Because you are physically dependent on opioids, you will receive oral capsules up to four times per day to prevent withdrawal during your inpatient admission. These capsules will contain an opioid such as oxycodone, morphine or hydrocodone, though sometimes they could also contain placebo (a blank, no drug). The length of your inpatient stay could vary to avoid testing on the weekends, and/or if you are eligible and decide to participate in the extra session in which remifentanil will be tested.

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

You are not a patient receiving medical treatment and will not receive any direct benefits from this study. However, the knowledge gained will contribute to a better understanding of the effects of opioid drugs and consequences of their long-term use. If you are seeking treatment, please notify one of the investigators now and they will make the necessary referral.

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

Risks of participating include 1) your protected health information (PHI) might be seen by unauthorized individuals, 2) embarrassment in disclosing sensitive personal information, 3) discomfort and/or dissatisfaction due to the study procedures, 4) side effects of MRI, 5) side effects of the opioid drugs and withdrawal from placebo maintenance doses, and 6) side effects of needle insertion. For a complete description of risks, refer to the Detailed Consent and/or Appendix.

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 investigators in charge of this study are Joshua Lile, Ph.D. and Michael Wesley, Ph.D. of the University of Kentucky, Department of Behavioral Science. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study their contact information is: 859-323-6034 (Dr. Lile) and 859-323-1332 (Dr. Wesley).

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 should not participate if you have a history of, or current, serious physical disease (e.g., respiratory disease [asthma, COPD, sleep apnea], impaired cardiovascular functioning, seizure disorder or CNS tumors) or serious psychiatric disorder. You should also not participate if you are younger than 18 or older than 50, if you have contraindications for MRI scanning (e.g., pacemaker, metal implants, claustrophobia, or any other implanted medical device), or if you have uncorrected vision or hearing problems. Lastly, you should not participate if you are seeking treatment for your drug use, are currently in treatment for your drug use, or are currently in successful remission from your drug use.

If you are a female, you should not participate if you are pregnant or plan on becoming pregnant during your participation in this experiment. You must be using an effective form of birth control (e.g. birth control pills, surgically sterilized, IUD, cervical cap with a spermicide, condoms or abstinence), and you must be willing to take pregnancy tests to ensure you are not pregnant during the study. Should one of these tests show that you are pregnant, your participation will be ended immediately. If you are female, you should not participate if you are lactating or breast feeding a baby.

If you do not have a history of IV opioid use, you will not be permitted participate in the extra session that will measure the subjective and physiological effects of intravenous administration of the opioid drug remifentanil.

WHERE WILL THE STUDY TAKE PLACE AND WHAT IS THE TOTAL AMOUNT OF TIME INVOLVED?

The research procedures will be conducted at the University of Kentucky Clinical Research Unit (CRU) Laboratory of Human Behavioral Pharmacology (LHBP), Neurobehavioral Systems Laboratory (NSL) and the Magnetic Resonance Imaging and Spectroscopy Center (MRISC). You will need to come to one of our outpatient laboratories (LHBP or NSL) for about 4 hours across two outpatient laboratory visits (qualification visits). If you pass the qualification visits, you will need to attend another 2-hour session that will be conducted at our outpatient facilities and the MRISC, which will include acclimation to the MRI scanner. If you are comfortable in the MRI scanner, you could be invited to complete an inpatient study lasting up to 15 days, during which time you will be asked to complete two experimental sessions that will be conducted at the MRISC. Each of those sessions will last about 2 hours. An additional inpatient study day with experimental activities lasting about 2 hours is optional and is available to individuals who reported a history of intravenous opioid use during screening. Further study days might be scheduled if needed to avoid testing on the weekends. An example schedule is provided in Appendix A.

WHAT WILL YOU BE ASKED TO DO?

During two initial outpatient visits to one of our laboratories, each lasting about 2 hours, you will be asked to complete a series of tasks. Based on your task performance, you could be asked to come to the laboratory for another 2-h visit, in which you will be acclimated to the MRI scanner. If you are comfortable in the scanner, you could be invited to participate an inpatient phase lasting up to 15 days. An additional inpatient study day with experimental activities lasting about 2 hours is optional and is available to individuals who reported a history of intravenous opioid use during screening.

In you participate in the inpatient study phase, on your admission day, you will arrive at the LHBP or NSL at a scheduled time (e.g., 8:00 AM) and complete a urine drug and breath alcohol screens and field sobriety test. In some cases, you could be observed by a same-sex staff member when you provide a urine sample, but you will be notified before this occurs. If you pass the urine and breath screening (note that testing positive for certain substances is permitted) and the field test, you will be escorted to the CRU, where you will be evaluated by a physician and admitted. During the time you participate, you must abstain from using any illicit substances, alcohol, and caffeine. Because you are physically dependent on opioids, upon admission, you will begin receiving oral doses of an opioid such as oxycodone, morphine or hydrocodone, approximately every 6 hours (four times per day) to help prevent withdrawal.

During your inpatient stay, you will complete two sessions that will involve approximately MRI scanning. MRI is a method for recording brain structure and activity. It involves lying down on a padded platform that is loaded into the circular center of the MRI machine. You will be escorted to the MRISC and instructed to remove all jewelry and other metal-containing objects before entering the scanner. While in the scanner, you will be asked to lie still as images of your brain are acquired. During much of the time in the scanner (approximately 20 minutes), you will be performing a game of chance. You can earn additional money based on your performance on this game of chance. The total scanning time each session will be less than one hour. Prior to the first scanning session, the UK Healthcare Vascular Access Team will place a peripheral IV line in your arm using ultrasound to guide the needle. At the end of each of the two experimental sessions, this IV line will be used to draw a small

amount of blood (about 2 ounces) that will be used to measure biomarkers that might be associated with opioid use disorder (e.g., cytokines, chemokines and growth factors).

There will also be a final experimental session available to participants with a history of intravenous opioid use, in which the subjective and physiological effects of intravenous administration of the opioid drug remifentanil will be measured repeatedly. The peripheral IV line will be used for intravenous drug delivery in this session. If the peripheral IV line used to collect blood after the MRI sessions is no longer working or inserted, another IV line will have to be placed prior to the start of the session. Your consent for study participation applies to the insertion, removal and replacement of a standard peripheral IV line, as deemed necessary by the study physicians and/or hospital policy. Removal of the IV line will occur upon completion of the last experimental session or when deemed necessary by the study physicians and/or hospital policy.

During admission to the inpatient unit, we will collect data concerning your physiological status, your subjective status and your performance on various laboratory tasks at regular intervals. That is, we will record your breathing rate, expired CO2, pupil diameter, blood oxygen saturation, heart rate and blood pressure. We will also ask you to answer various questionnaires about how your mood and drug effects, and any opioid withdrawal signs and/or symptoms you might be experiencing. You must agree to complete these assessments and to do the tasks to the best of your ability and at the scheduled times.

The capsules you will receive will contain oxycodone, morphine, hydrocodone or placebo (a blank, no drug). If you participate in the extra session, a catheter will be placed in your arm and you will receive intravenous infusions over a 2-hour period of time that will contain remifentanil or only saline. The drugs and doses to be administered are approved by the Food and Drug Administration (FDA), though not for this experimental purpose. You will take all doses under supervision of the nursing staff at the CRU.

You must agree to follow the general rules of the CRU and share in the routine responsibilities of keeping the unit and yourself neat, clean and orderly. You will be provided a detailed list of the CRU rules before being admitted as an inpatient. You should understand that during the time that you spend on the CRU that you will not be allowed to leave the unit unsupervised, nor will you be allowed to have visitors. You will be allowed to make telephone calls.

There will be urine checks, breathalyzers and room searches on a random schedule for evidence of unauthorized drug or alcohol use. If a urine screen or breathalyzer shows that you used other drugs or alcohol ,or you have them in your possession, you will be dropped from the study, and will lose a substantial portion of the money you might have earned.

During your inpatient enrollment, you will not be permitted to drink caffeinated beverages, but decaffeinated coffee and soft drinks will be made available to you. You will not be allowed to smoke during the experimental sessions, which will last between 2-4 hours. Smoking is permitted during non-session times when staff are available to escort you to the designated smoking area.

When you are not participating in experimental sessions, we will provide you with recreational activities (television, reading material, music, arts and crafts, video games or board games). For your enjoyment, you will be allowed to use certain items that we purchase. These items may include, but are not limited to, portable radios, video movies and games, puzzles, games, books, and magazines. If you use any of these materials, and ruin them or do not return them, the price of the item will be deducted from your payment. When you come to the inpatient unit, you should not bring any valuable items with you.

You will be discharged from the CRU on the day following your last experimental session. On the day of, and the day prior to, discharge, you will receive doses of Suboxone, which will help relieve opioid withdrawal after you leave the hospital. If you want to try to stop using illicit opioids while on the Suboxone, we will help you to identify a treatment program. You must have some withdrawal signs before you get the first dose so that it does not produce side effects. You have the option of refusing Suboxone induction and will be asked to sign a form acknowledging the risks associated with this refusal. You will also be given a Narcan® overdose rescue kit when you are discharged.

After you are discharged from the study, you will come in weekly to receive remaining payments in increments of up to $500. At that time, you will also complete a basic follow up in which we will ask you about your drug use, conduct physiological assessments and test your urine for the presence of drugs.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

There is a risk that personal information that identifies you might be viewed by unauthorized people. However, 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. The measures taken to protect your confidentiality are described below.

There is a risk that you might experience embarrassment from disclosing sensitive personal information. You may refuse to answer any questions that we ask, though refusal to answer certain questions might impact your ability to continue in the study.

You might experience discomfort or dissatisfaction due to study procedures. If you experience discomfort or dissatisfaction, you may discuss this with the study staff or investigators and may decide to discontinue your participation in this study. If you decide to withdraw from the study early, however, you will not receive any of the completion allowance described below.

While in the MRI scanner you may become too hot or too cold, in which case you may ask for an adjustment of room temperature or a blanket. Some people may become nervous or feel claustrophobic while in the scanner. A small number of people experience a sense of dizziness or vertigo while in the scanner due to the magnetic field. Although rare, you could experience nerve tingling or twitching. If any of these issues occur and disturb you, you may ask to be withdrawn and you will be withdrawn immediately. More information is provided below in Appendix B.

Opioid agonists produce side effects that include nausea, vomiting, headache, dry mouth, itchiness, drowsiness, sweating, dizziness, stimulation, sleepiness, lightheadedness, restlessness, a feeling of well-being, talkativeness, difficulty urinating, constipation and non-clinically-significant respiratory depression. It is likely that you will experience one or more of these less serious side effects. More serious side effects may include allergic reaction and clinically significant respiratory depression. It is unlikely that you will experience these more serious side effects. The clinical staff providing medical oversight for this study is prepared to intervene if these more serious side effects occur. More information is provided below in Appendix C.

During your participation, you might experience mild opioid withdrawal. These symptoms include nausea, vomiting, teary eyes, runny nose, loose stool, stomach cramps, shakiness, anxiety/irritability, increased heart rate, sweating/chills, restlessness, and body aces/discomfort. If you are experiencing signs or symptoms of opioid withdrawal, during non-session times, certain over-the-counter medications will be made available to you to manage diarrhea, constipation, nausea and pain.

You will need to have blood drawn, and if you complete the optional remifentanil session, you will need to have a peripheral IV catheter placed into your arm. These procedures are associated with a risk of bruising, blood clotting, soreness, infection, bleeding, pain and irritation from the insertion of a needle or catheter. These risks are minimal since standard sterile procedures will be used. There is also a risk of feeling light headed or fainting. The likelihood of this happening is uncertain and will vary across subjects.

There is always a chance that any medical treatment can harm you. The research treatments/procedures in this study are no different. In addition to risks described in this consent, you may experience a previously unknown risk or side effect.

WILL YOU BENEFIT FROM TAKING PART IN THIS STUDY?

You are not a patient receiving medical treatment and will not receive any direct benefits from this study. However, the knowledge gained will contribute to a better understanding of the effects of opioid drugs and consequences of their long-term use. If you are seeking treatment, please notify one of the investigators now and they will make the necessary referral.

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.

WHAT WILL IT COST YOU TO PARTICIPATE?

Participating in this research study will not cost you anything, except for costs associated with traveling to and from the research facility.

WHO WILL SEE THE INFORMATION THAT YOU GIVE?

When we write about or share the results from the study, we will write about the combined information. We will keep your name and other identifying information private. Your name, address and social security number will be listed on the receipt for payment that you receive, as required by the Internal Revenue Service; but no information about your participation in this research project will be released. You cannot participate in this research if you withhold your social security number.

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. We will store all paper records containing information that identifies you in a locked storage area accessible only to study personnel, and all electronic records will be stored on password-protected devices (e.g., computer).

You should know however, that there are some circumstances in which we might 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, if you pose a danger to yourself or someone else, or if you have certain communicable diseases. In addition, officials of the University of Kentucky, the National Institutes of Health or the FDA may look at or copy pertinent portions of records that identify you. We will make

every effort to safeguard your data, but as with anything online, we cannot guarantee the security of data obtained by way of the Internet. Third-party applications used in this study may have Terms of Service and Privacy policies outside of the control of the University of Kentucky.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or specimens 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. Information, documents, or specimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects. The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation or for information that must be disclosed in order to meet the requirements of the FDA. You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it. The Certificate of Confidentiality will not be used to prevent disclosure, as required by federal, state, or local law, of child abuse and neglect, or harm to self or others.

CAN YOU CHOOSE TO WITHDRAW FROM THE STUDY EARLY?

You can discontinue your participation in this study at any time. You will not be treated differently if you decide to stop taking part in the study. If you decide to leave the study early, however, you will not receive any of the completion allowance described below. Please note that if you agree to complete the optional intravenous dosing session during screening and this session is scheduled, and then you decide to leave the study after the second MRI scanning session but before the intravenous dosing session, then you will not receive any of the completion allowance described below.

The study investigators can discontinue your participation for the following reasons: 1) failure to adhere to the rules of the research facilities, 2) if you verbally or physically assault another volunteer, patient or staff member, 3) if your behavior is disruptive to other ongoing studies, 4) if your behavior is disruptive to the other volunteers, patients, research staff or medical staff, 5) failure to comply with the alcohol, drug, and food restrictions, 6) failure to comply with the pregnancy restrictions, 7) failure to complete a scheduled session, 8) failure to perform the tasks and procedures to the best of your ability, 9) if you leave the study against the advice of the principal investigator or the medical doctors. If you are discharged from the study for any of these reasons, you will not receive the completion allowance described below.

The medical doctors on this project can terminate your participation if they do not feel that it is medically safe for you to continue. If your participation is terminated for medical reasons, you will receive the completion allowance for each of the sessions you completed.

Abrupt discontinuation of the daily medication doses could lead to the emergence of opioid withdrawal. If your participation is discontinued early, you will be asked to stay in the hospital long enough to receive the Suboxone doses and will receive a Narcan® kit upon discharge.

Data collected up to the point of discontinuation will remain in the study database.

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 may not take part in another study while you are enrolled 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 due to the study, you should call Lon Hays, M.D., M.B.A. at (859) 323-6021 x 79015 or Danielle Anderson, M.D. at (859) 562-2356 immediately. You can also call 911 in the case of an emergency. Dr. Hays or Dr. Anderson will determine what type of treatment, if any, is best for you at that time. The medical costs related to your care and treatment because of research related harm will be your responsibility.

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. Also, the University of Kentucky will not pay for any wages you may lose if you are harmed by this study.

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

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

You will be paid for your participation in this experiment. You will earn $30 for completing each outpatient session, and another $30 completion allowance for each of these sessions if you finish the entire study. You will also receive $60 for each day that you reside on the CRU. If you complete all of your scheduled experimental sessions, you will be paid a completion allowance of $60 for each of the days you resided at the CRU. For example, if you complete the study and stayed on the inpatient unit for 15 days, you would earn a minimum of $1980, and if you also completed the intravenous dosing session and stayed on the unit for 16 days, you would earn a minimum of $2100. You will also be able to earn up to $100 by completing the game of chance.

If you make more than a total of $600 by participating in research projects, the University of Kentucky will report your earnings to the appropriate state and federal government agencies (i.e., Internal Revenue Service [IRS]). It is your responsibility to determine how these earnings might affect your personal financial situation. A form 1099 will be sent to you if your total payments for research participation are $600 or more in a calendar year.

Your earnings will be given to you in a series of separate payments. The first payment will be given to you on the day of your discharge. The remaining payments will be given to you once per week following your discharge. Due to University of Kentucky accounting policies, checks cannot be written for more than $500, so your payments will be given to you in amounts of up to $500 until you have received all of the money you are owed. When you come back for your payments, we will survey you about your drug use since we last saw you. You will also need to provide a breath sample negative for alcohol when you return for your payments. If you come to the LHBP with a breath sample positive for alcohol, your payment will be withheld until you can provide a breath sample negative for alcohol. We will not pay you additional money (other than the portion of the completion bonus you are receiving) when you come back for your payments and provide follow-up information.

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

We will tell you if we learn new information that could change your mind about staying in the study. We may ask you to sign a new consent form if the information is provided to you after you have joined the study.

WILL YOU BE GIVEN INDIVIDUAL RESULTS FROM THE RESEARCH TESTS?

Generally, tests done for research purposes are not meant to provide clinical information. However, there is a possibility that during a research project, we could discover something that could affect your health (an incidental finding). For example, there is a possibility that the MRI scan might reveal a structural brain abnormality that you were not aware of. If this occurs, we will consult with the study physicians, Drs. Hays and Anderson, and will notify you of the incidental finding and provide medical referrals if warranted. At that time, you can choose to receive or refuse the result or finding.

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.

Do you give your permission to be contacted in the future regarding your willingness to participate in future research studies?

☐ **Yes** ☐ **No** **Initials**_____

WHAT ELSE DO YOU NEED TO KNOW?

If you volunteer to take part in this study, you will be one of about 31 people to do so at the University of Kentucky.

The National Institute on Drug Abuse is providing financial support and/or material 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.

WILL YOUR SPECIMEN SAMPLES BE USED FOR FUTURE RESEARCH?

All identifiable information (e.g., your name, medical record number, or date of birth) will be removed from the blood samples collected in this study. After we remove all identifiers, the samples may be used for future research or shared with other researchers without your additional informed consent.

STORING AND SHARING YOUR SPECIMEN SAMPLES FOR FUTURE USE:

We will store your blood samples for future research. No additional samples will be taken for storage, but what is left after the planned analyses will be kept for future possible study. Having information and samples from many people helps researchers identify trends and discover better ways to diagnose, prevent, and treat many conditions. Researchers can use the stored information and blood samples to learn more about opioid use disorder.

We may use the genetic material (genes, DNA, RNA) in your sample to learn about the role genes play in heath and disease. Genetic studies help explain why traits or diseases are passed down in families. Results of genetic studies may also reveal information about your family members.

The genetic testing may include whole genome sequencing. This means a researcher would map your entire set of genetic instructions. Genetic instructions are what make you unique. These tests involve scanning the genomes from many different people and looking for markers that scientists can use to predict the presence of a disease. Data obtained from analyzing your genomic information may be put into scientific databases along with information from other research participants. Your name and other information that could be used to identify you will not be included with the genomic data in any databases.

Where will specimen samples be stored and for how long?

The information and samples will be stored at the University of Kentucky LHBP, NSL and/or Center for Clinical and Translational Research (CCTS) indefinitely.

Are there risks from allowing your specimen samples to be stored for future research?

There is a risk that someone could get access to the samples. In spite of the security measures and safeguards we will use, we cannot guarantee that your identity will never become known.

Even without your name or identifiers, genetic information is unique to you making it possible for someone to trace it back to you. The results of genetic research apply to both you and your family members. Genetic information used improperly to discriminate or support negative stereotypes could cause you or your family distress. There is a federal law called the Genetic Information Nondiscrimination Act (GINA). Generally, GINA makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Be aware that GINA does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. It also does not prohibit discrimination on the basis of an already known genetic disease.

There may be risks that at this time are unknown. As technology advances, there may be new ways of linking information back to you that we cannot foresee now.

How will your privacy and confidentiality be protected?

We will remove your name or other direct identifiers from your samples. We will store samples in a locked freezer that is located behind locked doors. The staff follow procedures to keep your identity a secret to the extent allowed by law. In very unusual cases, staff may be required to release your identifiable medical and research information in response to an order from a court of law. Officials of the Food and Drug Administration and the National Institutes of Health, the University of Kentucky may look at or copy pertinent portions of records that identify you.

How will we share your specimen samples with other researchers?

Specimen samples from our study could be shared with other researchers. If a UK investigator requests your specimen sample, it would be supplied without any information that could identify you (your name, address, medical record number, other information from your medical record, etc.). An investigator who received de-identified specimen samples will sign an agreement promising not to try to use any of the sample to identify you. If a researcher from another institution is to receive de-identified samples or information, that request will be reviewed by the UK Institutional Review Board (IRB) prior to its release. The IRB is a committee that reviews ethical issues, according to federal, state, and local regulations on research with human participants to make sure the study complies with these before approval of a research study is issued. The researchers agree to only share your health information with the people listed in this document. Samples will not be shared with researchers in other countries.

What if you change your mind and want to withdraw your specimen samples?

You may withdraw your permission to allow your samples to be used for future research. To do so, you must send a written withdraw request to Joshua Lile, Ph.D. or Michael Wesley, Ph.D. at 465 E. Hight St. Suite 204B, Lexington, KY 40507. We will destroy any remaining samples that have been stored. However, we cannot withdraw the samples that have already been used.

Will you receive any commercial profit from future research discoveries?

The samples that you provide will no longer belong to you. The research may lead to new medical knowledge, tests, treatments, or products. These products could have some financial value. There are no plans to provide financial payment to you or your relatives should this occur.

Will you be given individual results from the future research tests?

Tests done for research purposes are not meant to provide clinical information or help care for you. The results are only important for research. Therefore, the results of tests done with your samples will not be provided to you. In the rare event that a finding might affect the health of you or your family, we will contact you and you can choose whether to receive or refuse the information.

AUTHORIZATION TO USE OR DISCLOSE YOUR INDENTIFIABLE 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:

- Demographic information (information about your race, gender, socioeconomic status, and age)
- Results of physical examinations related to the study
- Results of psychiatric screening tests related to the study
- Results of questionnaires and study procedures related to the study
- Results of blood tests and urine screens related to the study
- Medical history related to the study

The Researchers may use and share your health information with:

- The University of Kentucky's Institutional Review Board/Office of Research Integrity;
- UK Hospital;
- UK Investigational Drug Service (IDS);
- UK Center for Clinical and Translational Science (CCTS)
- The United States Food and Drug Administration;
- The US National Institutes of Health;

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:

- Send a written letter to: Joshua Lile, Ph.D. or Michael Wesley, Ph.D. at 465 E. Hight St. Suite 204B, Lexington, KY 40507 to inform them 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 A. Example Study Schedule

Day	Table 1
Pre-Admit	Behavioral Qualification Session 1
Pre-Admit	Behavioral Qualification Session 2
Pre-Admit	Scanner acclimation session
1	Admission to the inpatient unit. Begin capsule administration (scheduled at 0800, 1200, 1800 and 2200 h each day; note that fewer doses will be administered on the admit day, depending on time of admit).
2-7	Continue capsule maintenance.
8	Behavioral data collection session in the AM. Continue maintenance.
9	Experimental session in the MRI scanner. Continue maintenance.
10-11	Maintenance continues.
12	Experimental session in the MRI scanner. Continue maintenance.
13-14	Continue maintenance.
15	Remifentanil session (IV use history required). Capsule maintenance ends; begin Suboxone.
16	Suboxone administered. Discharge

Appendix B: Risks of MRI

Possible Risk/Side Effect	How often has it occurred?	How serious is it?	Can it be corrected?
Feeling too hot or cold	It occasionally occurs	It will not impact your overall health	Yes
Feeling nervous or claustrophobic	It is uncommon	It will not impact your overall health	Yes
Dizziness or vertigo	It is uncommon	It will not impact your overall health	Yes
Nerve tingling or twitching	It is rare	It will not impact your overall health	Yes

Appendix C: Possible Drug Side Effects

Possible Risk/Side Effect	How often has it occurred?	How serious is it?	Can it be corrected?
Nausea, vomiting, headache, dry mouth, itchiness, drowsiness, sweating, dizziness, stimulation, sleepiness, lightheadedness, restlessness, a feeling of well-being, talkativeness, difficulty urinating, constipation, low blood pressure, low heart rate and non-clinically-significant respiratory depression	It is likely you will experience one or more of these side side effects	Moderately serious, though these side effects will not impact your overall health	Yes
Skeletal muscle rigidity, including chest wall rigidity	It is uncommon	Very serious though it will not impact your overall health	Yes
Allergic reaction	It is rare	Moderately serious, but it will not impact your overall health	Yes
Clinically significant respiratory depression	It is rare	Very serious though it will not impact your overall health	Yes

INFORMED CONSENT SIGNATURES

This consent includes the following:

- **Key Information Page**
- **Detailed Consent**
- **Appendix with example schedule; Appendix with table of possible side effects**

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

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