STUDY INFORMATION:

Study Title: Neuroimaging and CBD for Heroin Use Disorder
Principal Investigator (Head Researcher): Yasmin Hurd, PhD
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SUMMARY OF THIS RESEARCH STUDY:

In medicine there are many unanswered questions. A research study is when scientists try to answer a question about something that we don't know enough about. Participation in a research study may or may not directly help you or others. Participation is entirely voluntary. It is completely up to you whether or not you take part. You can also change your mind at any time and it will not affect your ability to get medical care within the Mount Sinai Health System.

The purpose of this research study is to study the effects of oral Cannabidiol (CBD) and placebo on the brain. CBD is an experimental medication and is derived from one of the natural components of the Cannabis plant. Placebo is a solution preparation that does not contain the experimental drug). The placebo will not have any physical side effects, and will not help you with any condition.

If you choose to participate, you will be asked to:

- Undergo a physical exam with vital signs including heart rate and blood pressure
- Complete questionnaires
- Provide blood and urine samples
- Attend 3 study visits over 2 weeks' time. Non-MRI sessions will last approximately 3 hours. MRI sessions will last approximately 4 hours
- Attend 2 MRI (no contrast) scan sessions
    - The first session will last approximately 4 hours
    - The second session will take place 10 days after the first session and last approximately 4 hours
- Lie in the MRI scanner for approximately 60 minutes each session
- Participate in cue sessions that will include viewing visual cue (videos or pictures) of heroin-related and neutral imagery. These sessions may induce craving.
- Take CBD (800 mg) or Placebo orally

There will be no cost associated with participation. You will be compensated for your participation in this study.

The main risks to you if you choose to participate are: physical risks related to MRI scans, CBD/placebo, blood draw; psychological risks related to questionnaires; risk of loss of private information.

If you are interested in learning more about this study, please continue to read below.

PARTICIPATION IN THIS RESEARCH STUDY:

This research study will be fully explained to you by a member of the study team. Feel free to ask all the questions you want before you make a decision about whether or not to participate. Any new information that develops during this research study that might make you change your mind about participating will be given to you promptly.

You may qualify to take part in this research study because you have a history of heroin use.

Funds for conducting this research are provided by the National Institutes of Health (NIH).

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.

LENGTH OF TIME AND NUMBER OF PEOPLE EXPECTED TO PARTICIPATE:

Your participation in this research study is expected to last 2 weeks.

The number of people expected to take part in this research study at Mount Sinai is 160.

DESCRIPTION OF WHAT'S INVOLVED:

If you agree to participate in this research study, the following information describes what may be involved.

Locations: You may participate in activities in several buildings on the Mount Sinai campus, including the Mount Sinai Hospital and Icahn School of Medicine at Mount Sinai in the following addresses: The lab space at the Icahn School of Medicine located at 1425 Madison Avenue, New, York, NY, the lab space and MRI imaging facility at 1470 Madison Ave., New York, NY, 10029, and the testing suite located at 1399 Park Ave., New York, NY.

You will be asked to refrain from any outside CBD intake during the entirety of the study.

The in-person screening session (Visit 1) will consist of:

- Basic Physical exam and survey of your medical history
- Toxicological assessments: urine drug screening including opioid metabolite screening and breathalyzer
- Urine pregnancy test (for women only), blood test (about 12.5 mL drawn for complete blood cell count and complete metabolic panel, including liver function tests. Blood may be redrawn if needed), tobacco assessment, electrocardiogram (EKG), vital signs (heart rate, blood pressure, weight and height measurement, Body Mass Index calculation).
- MINI International Neuropsychiatric Interview which is used for the detection of psychiatric conditions
- Questionnaires

fMRI, or Functional Magnetic Resonance Imaging, is a non-invasive imaging technique that uses magnetic fields to take pictures of your brain. Unlike an x-ray, there is no exposure to radiation. The first fMRI scan will be completed on the 2nd visit of the study, and the second fMRI scan will be completed 10 days after the first scan. While in the fMRI scanner, you will look at different pictures depicting heroin use or normal objects or scenes, and will be asked to answer questions.

On MRI session days, it is important that you fast for at least ten hours before your test session. A standard meal will be provided when you arrive. MRI Sessions (Visits 2 and 5) will last approximately 4 hours each and consist of:

- Urine drug screening (including opiate metabolite screen), breathalyzer, pregnancy test (for women only), questionnaires
- CBD/Placebo administration:
    - On the first MRI visit, CBD solution or identical placebo will be given orally in the morning (after a light standardized breakfast without caffeinated beverages), 60 min before the beginning of the MRI. There will be no drug administration during the 2nd MRI.
- 2 MRI (no contrast) scans 10 days apart
    - Approximately 60 minutes scanning time
- Vital signs measurements (blood pressure, heart rate and oxygen saturation – taken outside of the scanner)

Resting-state fMRI (rs-fMRI): During the 10-min rs-fMRI, you will be instructed to stay awake, still, and to keep your eyes open. A fixation crosshair will be shown on a black background throughout the scan. No task will be required.

Visual Opioid Cue Task: You will be asked to complete a task that contains both drug-related and non-drug related images. The drug-related image feature drug preparation or drug use scenarios that depict intravenous or intranasal drug use, depending on your preferred route of use. The neutral image depict non drug-related images. Each visual image will be shown for 2 seconds. You will be prompted to respond to questions with a hand-held device. The total duration of the task is approximately 10 minutes.

MRS – about 20 mins, it assesses in vivo neurometabolites as glutamate and glutamine in the human brain.

If you are enrolled into the full study, you will be given CBD/Placebo on Visits 2, 3 and 4 and your vital signs will be monitored for an hour before discharge. There is a possibility that you could be part of a subset of participants who do not undergo the full study procedures. If you are part of this subset, you will not receive any study medication (neither placebo nor CBD), and you will complete ONLY the screening visit and one MRI scan.

Urine test results will not go into your medical record and will not be shared. They will only be stored in the research record.

*** In an effort to comply with COVID-19 health guidelines, some study visits may be completed off-site when possible.**

You will not be included in the study if you show signs of withdrawal, or if your blood test reveals elevated liver enzymes (see section on Risks) at the screening. Before each session, a breathalyzer and urinalysis will be taken to ensure that you are not actively using ethanol, or any psychoactive substances (cocaine, opiates, cannabis, benzodiazepines, barbiturates, phencyclidine, amphetamines, buprenorphine, methadone, methamphetamine, oxycodone, and tricyclic antidepressant). All urine results will be kept confidential. Positive testing and/or clinical signs of intoxication before the screening and test sessions will result in the discontinuation of the session.

Because this project involves the use of medication, it is necessary that we make a note of your participation in the electronic medical record. That way anyone treating you will be aware of your participation and may be able to avoid any unfortunate outcomes that could arise if your research participation were unknown.

The study treatment you get will be chosen by chance, like flipping a coin. Neither you nor the study doctor will choose what experimental study treatment you get. You will have an equal chance of being given each experimental treatment. Neither you nor the study doctor will know which experimental study treatment you are getting; however, this information could be obtained in an emergency.

For Women:

Since you are participating in a research study that involves drugs or experimental treatment with potential risks to a developing fetus, it is recommended, for your protection, that you not become pregnant for the duration of the study. You should not participate if you are breastfeeding.

A urine pregnancy test will be done before you begin the study and will be repeated at each test session.

Therefore, practicing effective birth control is important. No individual birth control is 100% effective.

Recommended methods of birth control are:

- The consistent use of an approved hormonal birth control (pill/patches, rings),
- An intrauterine device (IUD),
- Contraceptive injection (Depo-Provera),
- Double barrier methods (Diaphragm with spermicidal gel or condoms with contraceptive foam),
- Sexual abstinence (no sexual intercourse) or
- Sterilization.

Hormonal birth control, implants, and injections are only considered effective if used properly and started at least one month before you begin the study, continuing throughout the study and for one month after the end of the study. You should ask your study doctor if you should continue birth control for longer than 30 days after the end of the study. If you are unsure whether the method of birth control you use is acceptable to use while participating in this study, you should ask your study doctor before you begin the study. If you are less than one year post-menopausal, there is the potential that you could become pregnant. If you or your partner becomes pregnant, or may be pregnant, at any time, it is important that you tell your study doctor immediately. The trial drug may be stopped and a referral may be made to an obstetrician/gynecologist for follow-up. If you plan to become pregnant in the year following a clinical trial, speak with your study doctor.

Should you become pregnant, regardless of the outcome, the sponsor may ask for information on your pregnancy, even if you are withdrawn from the study. Your written consent will be obtained separately in the case that this happens.

For Men:

Since you are participating in a study that involves experimental drugs or experimental treatment with potential risks to a developing fetus, it is recommended that you use a condom and not impregnate a woman or donate sperm while you are taking the study drug, and for an additional 60 days after you stop taking the study drug. This is because levels of the study drug may be present in the sperm and/or seminal fluid even after you stop taking the study drug. You are encouraged to tell your female partner(s) and/or their doctor(s) that you are participating in a clinical trial.

USE OF YOUR DATA AND/OR SPECIMENS:

In the future, your identifiable information may be removed from the private information and/or samples that are collected as part of this research. After this removal, the information and/or samples could be used for future research studies or shared with other research teams for future research studies. You will not be informed of the details of specific research that is done with your medical information and biospecimens. That means that a research project might be done that you would not consent to if provided with the details of that research project.

The researchers would like to ask your permission to keep the data. Please tell us how we may use this material in future research studies.

(1) Will you allow the researchers to store your information to use in future research studies?

Yes_____ No_____ If no, please stop here. If yes, please continue to the next question.

(2) The researchers can keep your information stored in one of two different ways: one way will store your information in a way that it is linked to your identity (through the use of a code that can indicate the information came from you personally) and the other way will store your information anonymously (no one will know who the information is from). It will not be stored both ways, so you must choose one of these two options. Please note that if you choose to have your information stored anonymously, you will not be able to change your mind to ask for your information to be destroyed at a future date.

How would you like your information and/or specimens stored? Please initial **ONE** choice:

I would like my information and/or specimens stored with a link to my identity_____
I would like my information and/or specimens stored anonymously _____

(3) Do you give the researchers permission to **contact you** in the future to collect additional information about you, discuss how your information might be used, or to discuss possible participation in another research project? Please initial your choice:

Yes_____ No_____

(4) Do you give the researchers permission to keep the information indefinitely and use them for future studies that are **directly related** to the purpose of the current study?

Please initial your choice:

Yes_____ No_____

(5) Do you give the researchers permission to keep the information indefinitely and use them for future studies that are **not related** to the purpose of the current study (for example, a different area of research)? Please initial your choice:

Yes_____ No_____

(5.1) From time to time researchers outside of medicine and related sciences would like to use this information. This might be in the field of anthropology, human origins, mapping human migration patterns etc. Do you give permission to use your information outside the fields of medicine and biological sciences? Please initial your choice:

Yes_____ No_____

(a) If the future research in a different area can be done without having to know that the information and/or specimens came from you personally, that will be done.
(b) If the future research in a different area requires that it is known specifically who the information and/or specimens came from, then one of the following will be done:
(i) If you allowed the researchers to contact you in the future, they may be able to contact you to explain why your identifiable information or specimen is needed and what will be done with it. Your permission will be asked to use your information and/or specimens in that research project.
(ii) If you do not give permission to be contacted in the future, or if it is found that contacting you is not practical, for example, because you have moved, your identifiable data and specimens may still be used. The Institutional Review Board (IRB) will be asked for permission to use the information and/or specimens linked to your identity. The IRB can give permission for researchers to use and share identifiable health information without contacting you, but only if it determines that sharing the information and/or specimens will not be more than a minimal risk to you or your privacy. The Institutional Review Board (IRB) is a committee of doctors and scientists and nonscientists, including people not associated with this hospital or medical school, whose job it is to protect people who participate in research.

(6) Do you give permission to have portions of the information given **to other researchers,** including those at Mount Sinai, other academic institutions and for profit companies, for use in research within the limits you have chosen above? Please initial your choice:

Yes_____ No_____

(7) Do you give permission to have portions of the data **deposited in large public repositories, (explained below)** for use in research with the limits you may have chosen above? Please initial your choice:

Yes_____ No_____

To do more powerful research, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. Researchers can then study the combined information to learn even more about health and disease. If you agree to take part in this study, some of your genetic and health information might be placed into one or more scientific databases. There are many different kinds of scientific databases; some are maintained by Icahn School of Medicine at Mount Sinai or another institution, some are maintained by the federal government, and some are maintained by private companies. For example, the National Institutes of Health (an agency of the federal government) maintains a database called "dbGaP." A researcher who wants to study the information must apply for permission to use the database. Different databases may have different ways of reviewing such requests. Researchers with an approved study may be able to see and use your information, along with that from many other people. Researchers will always have a duty to protect your privacy and to keep your information confidential, but there are risks associated with data collection and sharing. They are described in more detail in the risks section.

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

If you decide to take part in this research study you will be responsible for the following things:

You cannot use heroin or other psychoactive drugs for at least 7 days before the screening visit and during test sessions. You are also expected to attend the screening visit and the 4 test sessions.

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

Being in this research study will not lead to extra costs to you.

If you agree to take part in this research study, you could earn up to $467.50 for your time and effort. Payment will be made based on your research visit completion and you will be paid through an Greenphire ClinCard at the end of your participation in the study.

The reimbursement is for 5 visits (screening, 2 neuroimaging days, and 2 behavioral days). The breakdown of payment is as follows:

MRI: Amount per visit $150 x 2 visits = $300

Screening: Amount per visit $60 x 1 visit = $60

Behavioral Test Sessions: Amount per visit $40 x 2 visits = $80

Local travel: Amount per visit $5.50 x 5 visits = $27.50

You will be given a MetroCard for local travel after every visit. After you have completed the study, you will be given the full amount of your earnings on a Greenphire ClinCard, which is a specially-made debit card for clinical research payments. At the end of your final visit, the total payment you have earned for the entire study duration will be approved and added onto your card. The payment will be available within 24 hours. It can be used wherever Mastercards are accepted. You will be given additional information on how the card works.

Research personnel will collect information about you, including your name, address, social security number, and date of birth and will enter it into the Greenphire system. Your information will be kept confidential. Greenphire collects your social security or individual taxpayer identification number as required by the Internal Revenue Service (IRS) for participants receiving payment in research as this is considered taxable income. If payment exceeds $600 in any one calendar year, Mount Sinai Beth Israel is required to report this information to the IRS. A 1099 (for U.S Citizens) or a 1042 (for nonresident aliens) Miscellaneous Income form will be issued to you by the institution and a copy sent to the IRS. You may have to pay tax on the money you receive for your participation in this research study.

You will be given this card only once while you are in the study. If your card is lost or damaged, please contact the study coordinator for assistance. The first lost card will be replaced at no charge to you. To replace an additional lost card, you will be charged $7.00. The fee will be deducted from the balance available on the card when it was lost. Unused funds will be loaded onto a new card and the original card will be cancelled.

If the card is stolen please call (866) 952-3795 for ClinCard's Customer Service and also notify the study coordinator.

Tax law may require the Mount Sinai Finance Department to report the amount of payment you receive from Mount Sinai to the Internal Revenue Service (IRS) or other agencies, as applicable.

Generally, this reporting would take place if you receive payments that equal $600 or more from Mount Sinai in a calendar year. You would be responsible for the payment of any tax that may be due.

Partial Payments

Full study visit payments will require negative urine drug tests for illicit drugs or illegally obtained prescription medications, and will be deferred until the next clean urine is given. Payments are not made on weekends (Sat-Sun) or holidays, and will be deferred if you are intoxicated or fail a Breathalyzer test. If you do not complete all of the study procedures, or withdraw from the study for any reason, you will only receive partial payment. During the screening visit, if you do not meet criteria for the study, you will receive $20 for the time you spent in the initial screening procedures, plus a two-trip MetroCard for your travel. If you are eligible to participate in the study, you will be paid $60 for the completion of all required screening procedures. If you do not complete an MRI scan for any reason, you will not receive the full $150. You will receive $10 for the first 30 minutes, and up to $60. If you complete any study visits remotely or off-site, your payment may be partial.

There is a possibility that you could be part of a subset of participants who do not undergo the full study procedures. If you are part of this subset, you will not receive any study medication (neither placebo nor CBD), and you will complete only the screening visit and one MRI scan. You could earn up to $221.00 ($60 x 1 visit, $150 x 1 visit, and $5.50 (in the form of a two-trip MetroCard) x 2 visits). All payments (aside from the MetroCard payments) will be placed on a ClinCard. See: Payment Type.

Tax law may require the Mount Sinai Finance Department to report the amount of payment you receive from Mount Sinai to the Internal Revenue Service (IRS) or other agencies, as applicable. Generally, this reporting would take place if you receive payments that equal $600 or more from Mount Sinai in a calendar year. You would be responsible for the payment of any tax that may be due.

POSSIBLE BENEFITS:

You are not expected to get any benefit from taking part in this research study. Others may not benefit either. However, possible benefits to others include that results from this study will help researchers better understand the effect of CBD on the brain and as a potential alternative treatment for heroin use disorder. Such treatment would be beneficial to people with heroin use disorder in the future.

REASONABLY FORESEEABLE RISKS AND DISCOMFORTS:

Physical risks

MRI scanners use strong magnetic fields. The levels of energy used to create MR images are far less than those used in a single X-ray, and tens of thousands of research participants and

hundreds of thousands of clinical patients have been safely studied using MRI techniques. Since the MRI scanner is essentially a large magnet, there is a risk of a metallic object flying through the air toward the magnet and hitting you. To minimize this risk, we require that all people involved with the study remove all metal from their clothing and all metal objects from their pockets. No metallic objects are allowed into the scanner room at any time. Once you are inside the magnet, the door to the scanner room will be closed so that no one accidentally walks into the magnet area. Further, because of the strong magnetic field, people with pacemakers or certain metallic implants cannot participate in this study. There is also a small risk that you may become uncomfortable and/or anxious inside the magnet. If you become uncomfortable inside the magnet, you may immediately withdraw from the study. If you have never been in an MRI and are anxious about what to expect, we could arrange a mock MRI session. This would allow you to experience a simulated MRI. This is not a scheduled part of the study and is only available upon request. Some of the videotape material may trigger craving. Usually these effects are very brief and resolve when the film ends. However, a trained clinician will be available if feelings persist after the imaging session is over. It is possible that during the course of the research study, the research staff may notice an unexpected finding(s). Should this occur, the finding(s) will be considered by the appropriate personnel and the PI will inform you if necessary. This possible finding(s) may or may not be significant and may lead to anxiety about your condition and to further work-up by your physician. The scans completed are part of a research protocol, and not intended to provide a clinical MRI examination of the brain or detect disease of any kind.

Although there are no known risks of MRI on pregnant women or a fetus, there is a possibility of yet undiscovered pregnancy-related risks. Since there is no direct benefit from participating in this study for a pregnant woman, we will exclude pregnant women. A negative urine pregnancy test will be mandated before a woman of childbearing potential can participate in this study, as well as before each MRI session.

Risk of loss of private information; this risk always exists, but there are procedures in place to minimize the risk.

Cannabidiol:

Only mild and temporary side effects have been reported in the past with Cannabidiol and doses used in these trials were higher than in the present study. Dizziness, anxiety, low blood pressure, dry mouth, slowing down of body movements, lightheadedness, and sedation were reported with similar doses of Cannabidiol. Other side effects include somnolence; decreased appetite; diarrhea; transaminase elevations; fatigue, malaise, and asthenia; rash; insomnia, sleep disorder, and poor quality sleep; and infections. Given the risk of somnolence and fatigue, you should exercise caution around driving and operating dangerous or heavy machinery.

Additionally, in other studies involving patients with liver disease and/or patients with severe, refractory epilepsies, elevated liver enzymes levels in the blood were observed with the use of Cannabidiol. These patients also took other anti-seizure drugs for their condition that may have contributed to the elevated liver enzymes. Cannabidiol is not listed as a carcinogen (a substance that causes cancer) by the International Agency for Research on Cancer. Some laboratory tests have, however, demonstrated

that Cannabidiol may alter DNA (the genetic material inside cells) in animals. DNA damage has been associated with the development of cancer but the positive test results in animals does not necessarily mean that Cannabidiol could cause genetic damage in humans or increase your risk of developing cancer.

The potential effects of this drug on an embryo or fetus are not known at this time. However, as with any drug trial, you should not become pregnant or father a baby while on this research study. Please read the acceptable methods of birth control found under the Description of What's Involved section of this document.

Placebo:

If you are randomly selected to be part of the placebo group, you will be given a solution that does not contain the experimental drug Cannabidiol. The placebo solution will not have any physical side effects, and will not help you with any condition.

Blood drawing:

The risks of a blood draw include pain, bruising, and the slight possibility of infection at the place where the needle goes in. Some people feel dizzy or may faint during or after a blood draw.

Cue-induced craving task:

It is possible that you could experience prolonged elevation of desire for the drug following the craving sessions, but we will provide a safe environment to minimize the probability of adverse events following a craving episode. To minimize any potential increase in craving beyond the laboratory session, previously established relaxation procedures known to decrease drug craving will be used to decrease craving. In addition, psychological debriefing and relaxation procedures will be done with you after all sessions to ensure that you are clinically stable when you leave the study site. You will be monitored in person during test days 1-3 and 10, and by phone between sessions. Throughout the study, both objective (urine testing) and subjective (distress, anxiety, craving, feeling of imminent relapse) will be carefully assessed. If relapse is imminent, or if any mental or physical symptom occurs that would require medical attention, you will be offered to consult with Mount Sinai physician or other mental health provider, either as an outpatient, an inpatient or in the ER depending on the severity of the symptoms. A psychiatrist and a physician specialized in toxicology will be available at any time during the study for consultation or examination. You will also be provided with contact information of a research team's member, and with a list of resources and clear steps to follow in case of physical or psychological deterioration.

Psychological risks (for example, embarrassment, fear or guilt)

Questionnaires: Some of the questions we ask you may make you uncomfortable. You do not have to answer any questions that you do not want to answer. If you do not understand any question, you can ask us what it means and we will try to help you. If you get very upset during this study visit, we will refer you to a specialized mental health professional.

Loss of Privacy Risk and Social Risk (for example, damage to your social standing or reputation; possible discrimination)

There always exists the potential for loss of private information; however, there are procedures in place to minimize this risk. A breach of confidentiality regarding your substance use and substance use problems could conceivably result in negative legal or social consequences for you. As such, measures to maintain strict confidentiality will be taken. You will be assigned a unique identification number which is the only identifier that will be stored together with the other information you will give us. A key linking your identification number with your identity will be saved in Mount Sinai's secure network drive, completely separate from the other information.

Legal and Economic Risks (violation of parole, loss of employment or employment opportunity)

If you are on parole or if random drug tests are routinely administered at your place of employment, you should know that since Cannabidiol is derived from one of the natural components of the Cannabis plant, there is a very small chance a drug screening test for THC may show up as very slightly positive. The risk, however, is extremely minimal. A blood test may be able to rule out THC in your system as blood tests are more sensitive than urine tests. If your parole or your employment might be at risk because of a false positive THC, please inform the research coordinator. The research coordinator will provide you of a letter that attests to the fact that you are in a clinical trial in that MAY have caused a false positive.

Risk of loss of private information: This risk always exists, but there are procedures in place to minimize the risk.

Questionnaire and self-report information: This study also involves interviews and self-report questionnaires. These procedures do not deviate from standard practice and pose no major risk. One risk of the study is that some subjects may find certain questions in the research instruments uncomfortable or difficult to answer. Research staff is trained to clarify the questions and informs subjects that they have the option of not answering specific questions, or even not participating in the study at all. Furthermore, should any subjects experiencing severe emotional distress during a study visit, they will be referred by the trained research staff to a prearranged mental health provider.

OTHER POSSIBLE OPTIONS TO CONSIDER:

You may decide not to take part in this research study without any penalty. The choice is totally up to you.

IN CASE OF INJURY DURING THIS RESEARCH STUDY:

If you are injured or made sick from taking part in this research study, medical care will be provided.

This does not prevent you from seeking payment for injury related to malpractice or negligence. Contact the investigator for more information.

If you are injured or made sick from taking part in this research study, medical care will be provided. Generally, this care will be billed to you or your insurance in the ordinary manner and you will be responsible for all treatment costs not covered by your insurance, including deductibles, co-payments and coinsurance. This does not prevent you from seeking payment for injury related to malpractice or negligence. Contact the investigator for more information.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this research study at any time without any penalty. This will not affect your ability to receive medical care at any of the Mount Sinai Health System hospitals or to receive any benefits to which you are otherwise entitled.

If you decide to stop being in the research study, please contact the Principal Investigator or the research staff.

If you stop being in the research study, already collected information may not be removed from the research study database and will continue to be used to complete the research analysis. You may be asked whether the study doctor can collect information from your routine medical care. If you agree, this data will be handled the same as research data.

You may also withdraw your permission for the use and disclosure of any of your protected information or specimens for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use the information and samples that were already collected if that information is necessary to complete the research study. However, no new information or samples will be collected after you withdraw from the research in writing. Your health information may still be used or shared after you withdraw your authorization if you should have an adverse event (a bad effect) from participating in the research study.

If you decide you don't want your samples and/or data to be used for research anymore, you can contact the researcher and ask to have your samples and/or data removed from future use. If any samples or data have already been shared without your identity, it won't be possible to retrieve them because no one will know who you are. Samples and data that have already been used will not be affected by your decision. Any samples and/or data that are still linked to your identity by a code the researcher has will be withdrawn so that no future sharing of your samples and/or data will take place. If your samples have already been deposited in an external repository, the study team will request that your samples be removed.

Withdrawal without your consent: The study doctor, the sponsor or the institution may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the study team have not been followed, the investigator believes it is in your best interest, or for any other reason. If specimens or data have been stored as part of the research study, they too can be destroyed without your consent. More possible reasons for removal from the study include:

- A urine drug test determines that you have taken any psychoactive drug or test positive for cocaine, opiates, benzodiazepines, barbiturates, amphetamines, methadone, methamphetamines, oxycodone, PCP, tricyclic antidepressant, buprenorphine, and THC before test sessions
- You are found to be intoxicated at the time of arrival as determined by a breathalyzer
- You are found to be pregnant by a urine pregnancy test
- You miss a test visit appointment.

Participation may be terminated by the investigator or the Institutional Review Board without the subject's consent at any time if the study ends, if the subject is not compliant with the research, or if continuing the research poses a serious risk to the subject.

CONTACT INFORMATION:

If you have any questions, concerns, or complaints at any time about this research, or you think the research has harmed you, please contact the office of the research team and/or the Principal Investigator at phone number 212-824-9313.
If you experience an emergency during your participation in this research, contact 911 or go to the emergency room.

This research has been reviewed and approved by an Institutional Review Board. You may reach a representative of the Program for Protection of Human Subjects at the Icahn School of Medicine at Mount Sinai at telephone number (212) 824-8200 during standard work hours for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

DISCLOSURE OF FINANCIAL INTERESTS:

Sometimes, physicians/researchers receive payments for consulting or similar work performed for industry. Effective September 2014 Mount Sinai reviews only payments to an individual totaling more than $5,000 a year per entity when determining potential conflicts of interest. If you have questions regarding industry relationships, we encourage you to talk your physician/researcher or visit our website at http://icahn.mssm.edu/ where Mount Sinai publicly discloses the industry relationships of our faculty.

MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As you take part in this research project it will be necessary for the research team and others to use and share some of your private protected health information. Consistent with the federal Health Insurance Portability and Accountability Act (HIPAA), we are asking your permission to receive, use and share that information.

What protected health information is collected and used in this study, and might also be shared with others?

As part of this research project, the research team at the hospital(s) involved in the research will collect your name, address, telephone number, dates directly related to the individual (birth, admission, discharge, etc.), social security number, medical records number.

During the study the researchers will gather information by:

- taking a medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate and temperature
- completing the tests, procedures, questionnaires and interviews explained in the description section of this consent.
- The New York State Prescription Drug Monitoring Program will be accessed by the investigators to make sure that you are not taking prescription drugs that might interact with the study drug and cause harm to you

Why is your protected health information being used?
Your personal contact information is important to be able to contact you during the study. Your health information and the results of any tests and procedures being collected as part of this research study will be used for the purpose of this study as explained earlier in this consent form. The results of this study could be published or presented at scientific meetings, lectures, or other events, but would not include any information that would let others know who you are, unless you give separate permission to do so.

The research team and other authorized members of The Mount Sinai Health System ("Mount Sinai") workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example, the School's Program for the Protection of Human Subjects

is responsible for overseeing research on human subjects, and may need to see your information. If you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes. If the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.

Who, outside Mount Sinai, might receive your protected health information?
As part of the study, the Principal Investigator, study team and others in the Mount Sinai workforce may disclose your protected health information, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Principal Investigator.)

- Outside laboratory who will be performing laboratory analysis for all the research centers involved in this project: LabCorp, NMS
- The United States Food and Drug Administration
- The United States Department of Health and Human Services and the Office of Human Research Protection.

In almost all disclosures outside of Mount Sinai, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier. Some records and information disclosed may be identified with a unique code number. The Principal Investigator will ensure that the key to the code will be kept in a locked file, or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the Institutional Review Board allows it after determining that there would be minimal risk to your privacy. The Certificate of Confidentiality obtained from the Department of Health and Human Services will not be used to prevent disclosure to local authorities of child abuse and neglect, or harm to self or others. It is possible that a sponsor or their representatives, a data coordinating office, or a contract research organization, will come to inspect your records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers. Additionally, **the Office of Human Subjects Protection (OHRP) of the Department of Health and Human Services as well as the Food and Drug Administration (FDA) will be granted direct access to your medical records for verification of the research procedures and data. They are authorized to remove information with identifiers if necessary to complete their task. By signing this document you are authorizing this access.** We may publish the results of this research. However, we will keep your name and other identifying information confidential.

For how long will Mount Sinai be able to use or disclose your protected health information?
Your authorization for use of your protected health information for this specific study does not expire.

Will you be able to access your records?
During your participation in this study, you will have access to your medical record and any study information that is part of that record. The investigator is not required to release to you research information that is not part of your medical record.

Do you need to give us permission to obtain, use or share your health information?
NO! If you decide not to let us obtain, use or share your health information you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment or enrollment in any health plans or affect your eligibility for benefits.

Can you change your mind?
You may withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use your protected information that was already collected if that information is necessary to complete the study. Your health information may still be used or shared after you withdraw your authorization if you should have an adverse event (a bad effect) from being in the study. If you withdraw your permission to use your protected health information for research that means you will also be withdrawn from the research study, but standard medical care and any other benefits to which you are entitled will not be affected. You can also tell us you want to withdraw from the research study at any time without canceling the Authorization to use your data.

If you have not already received it, you will also be given The Hospital's Notice of Privacy Practices that contains more information about how The Hospital uses and discloses your protected health information.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, even if your information will no longer be protected by federal regulations, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If as part of this research project your medical records are being reviewed, or a medical history is being taken, it is possible that HIV-related information may be revealed to the researchers. If that is the case, the following information concerns you. If this research does not involve any review of medical records or questions about your medical history or conditions, then the following section may be ignored.

Notice Concerning HIV-Related Information

If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 306-5070. These agencies are responsible for protecting your rights.

Certificate of Confidentiality:
To further protect your privacy, the researchers have obtained a Certificate of Confidentiality from the Department of Health and Human Services. This is intended to ensure that your identity as a participant in this research study will not have to be disclosed as a result from a subpoena, for the purpose of identifying you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings other than to the FDA or OHRP as identified above.

The research staff will not share any of your research information or biospecimens with anyone who is not a member of the research team, including any family members or friends, other than to those identified above. However, you should know that if we learn that you or someone else is threatened with serious harm, such as a child or an elderly person being abused, the investigators may notify the appropriate authorities if necessary to protect you or others. 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. This means that you and your family must also actively protect your own privacy. If an insurer or employer learns about your research participation, and you agree that they can have your research information, then the researchers may not use the Certificate of Confidentiality to keep this information from them.

ADULT PARTICIPANT:

Your signature below documents your permission to take part in this research and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

_____	_____	_____	_____
Signature of subject	Printed Name of Subject	Date	Time

PERSON EXPLAINING STUDY AND OBTAINING CONSENT:

_____	_____	_____	_____
Signature of consent delegate	Printed Name of consent delegate	Date	Time

WITNESS SECTION:

When a witness is required to observe the consent process, it should be documented below (for example, when subject is illiterate, visually impaired, or this document accompanies a short form consent).

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

_____	_____	_____	_____
Signature of Witness	Printed Name of Witness	Date	Time