KEY INFORMATION FOR RANDOMIZED TRIAL OF BUPRENORPHINE MICRODOSE INDUCTIONS DURING HOSPITALIZATION

We are asking you to choose whether or not to volunteer for a research study about starting buprenorphine-naloxone treatment using the standard approach or a new approach called "microdosing". In the microdosing approach, participants will take small doses of buprenorphine or buprenorphine-naloxone over 5 days without stopping their other pain medicine. In the standard approach, participants will stop their pain medicine for 24 hours and start buprenorphine-naloxone once they experience mild to moderate withdrawal. Both groups will receive buprenorphine-naloxone prescriptions and a referral to a clinic to continue treatment after discharge. This page is designed 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?

By doing this study, we hope to learn if a microdosing protocol for starting buprenorphine treatment is safe and effective. Your participation in this research will last about 6 months. Buprenorphine and buprenorphine-naloxone are FDA- approved medications for treatment of opioid use disorder.

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

For a complete description of benefits, refer to the Consent Document below. If effective, the microdosing approach to starting buprenorphine-naloxone treatment could help people with chronic pain successfully start the medication without having to experience any opioid withdrawal. Buprenorphine-naloxone treatment can also reduce overdose risk, reduce opioid misuse, and reduce HIV transmission.

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

If you are not interested in starting buprenorphine-naloxone treatment, you should not volunteer for this study. If you intend to continue opioid pain medicine, such as morphine, oxycodone (Percocet), or hydrocodone (Vicodin), you should not volunteer for this study. With the microdosing or low-dosing approach, participants will start taking buprenorphine- naloxone while they are receiving opioid pain medicine, which could lead to a precipitated/induced withdrawal. This could include symptoms of diarrhea, nausea, vomiting, musculoskeletal pain, sweating, and anxiety. For a complete description of risks, refer to the Consent Document below.

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 or access to care you would normally have if you choose not to volunteer.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of the study is Aaron Fox, MD. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his contact information is: 718-920-7173.

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact staff in the Einstein Institutional Review Board (IRB) between the business hours of 9am and 5pm EST, Monday-Friday at 718-430- 2237 or irb@einsteinmed.org

ALBERT EINSTEIN COLLEGE OF MEDICINE MONTEFIORE MEDICAL CENTER

DOCUMENTATION OF INFORMED CONSENT AND HIPAA AUTHORIZATION

Introduction

You are being asked to participate in a research study called "Randomized Trial of Buprenorphine Microdose Inductions During Hospitalization" Your participation is voluntary -- it is up to you whether you would like to participate. It is fine to say "no" now or at any time after you have started the study. If you say "no," your decision will not affect any of your rights or benefits or your access to care.

The researcher in charge of this project is called the "Principal Investigator." His name is Aaron Fox, MD. You can reach Dr. Fox at: **Office Address: 3300 Kossuth Avenue Bronx, NY 10467** **Telephone #: 718-920-7173** For questions about the research study, or if you believe you have an injury, contact the Principal Investigator or the IRB.	The Institutional Review Board (IRB) of the Albert Einstein College of Medicine and Montefiore Medical Center has approved this research study. The IRB # is in the stamp in the upper right hand corner. If you have questions regarding your rights as a research subject you may contact the IRB office at 718-430-2237, by e-mail at irb@einsteinmed.org, or by mail: Einstein IRB Albert Einstein College of Medicine 1300 Morris Park Ave., Belfer Bldg #1002 Bronx, New York 10461
Support for this research study is provided by **National Institute of Health (NIH)**	

Why is this study being done?

The goal of this study is to test whether starting buprenorphine-naloxone using a microdosing approach is safe and effective. Buprenorphine-naloxone is approved by the U.S. Food and Drug Administration (FDA) to treat opioid use disorder. Many people who are hospitalized with chronic pain also have opioid use disorder. We are testing a new strategy of microdosing at the start of buprenorphine-naloxone treatment, and we will see if this method increases the number of people who can successfully start treatment with buprenorphine-naloxone.

The U.S. Food and Drug Administration (FDA) has approved buprenorphine-naloxone to treat opioid use disorder. Buprenorphine is also FDA approved to treat pain. This study will compare two ways of starting treatment.

Why am I being asked to participate?

You are being asked to participate in this study because you have been hospitalized and you have chronic pain and opioid use disorder or other problems stemming from opioid use. A physician may have suggested that you participate in this study. We will enroll 270 participants from three different hospitals in the Bronx: Weiler hospital, Moses hospital and Wakefield hospital.

We are looking for participants who are 18 years or older, experience chronic pain, have opioid use disorder or who misuse opioids and who are planning to be in the hospital for at least 48 hours.

However, you cannot be in the study if you are currently prescribed other medications for opioid use disorder (e.g. Methadone treatment), have severe benzodiazepine or alcohol use disorder, have unstable medical or mental health conditions or you are pregnant.

How many people will take part in the research study?

You will be one of about 270 people who will be participating in this study.

How long will I take part in this research?

It will take you about 6 months to complete this research study. During this time, we will ask you to make 5 study visits to Montefiore Medical Center hospitals or outpatient locations.

What will happen if I participate in the study?

This study is an unblinded randomized controlled trial. The Enrollment Visit will take about 45-60 minutes. During this visit, we will ask questions and check a pregnancy test to see if you eligible to take part in this research study. The study doctor will review the results of these questionnaires and the urine test. If you aren't eligible, you will receive the standard hospital care. At this visit we will:

- Ask you about your medical history
- Ask you about your drug use history, including your treatment history
- Ask you about your pain intensity, pain interference and pain treatments
- Ask you for a urine sample to perform a urine drug screen
- Test your **urine** for pregnancy if you able to become pregnant. Pregnant people cannot take part in this research study.
- Assess your opioid withdrawal and craving
- Give you some questionnaires to fill out about your general health and well-being, quality of life, mental health, emotional health and physical functioning.

If you are eligible for the study, we will assign you by chance (like a coin toss) to the microinduction group or the standard treatment group. You and the study doctor cannot choose your study group. You will have an equal chance of being assigned to the microdosing induction group or the standard induction group. Both groups will receive buprenorphine-naloxone.

This research study will compare two ways of starting buprenorphine-naloxone. In the microdosing induction group, participants will take small doses of buprenorphine or buprenorphine-naloxone over 5 days without stopping their other pain medicine. In the standard induction group, participants will stop using all opioid pain medicine (e.g. Vicodin) for approximately 24 hours. They will start buprenorphine-naloxone once they experience mild-moderate withdrawal and then the dose will be increased over 2 days. Both groups will continue to take buprenorphine-naloxone after the induction periods are completed.

At all subsequent follow-up visits at Week 1, Week 4, Week 12 and Week 24, we will:

- Ask you about your drug use history, including your treatment history
- Ask you about your pain intensity, pain interference and pain treatments
- Assess your opioid withdrawal and craving
- Ask you for a urine sample to perform a urine drug screen
- Give you some questionnaires to fill out about your general health and well-being, quality of life, mental health, emotional health and physical functioning

Regardless of assignment, all participants will also complete a total of 5 (including enrollment visit) study visits over 6 months. Study visits will take 30-45 minutes. At these visits, a study coordinator will collect a urine sample for drug testing. At each study visit, you will also complete a questionnaire, which will include questions about your drug use, mental health, and any pain you may have. We will also collect your medical records to determine whether or not you have continued buprenorphine-naloxone treatment at the community health center.

In addition to attending study visits we will assist you in downloading a secure EMA (Ecological Momentary Assessment) app onto your smartphone. If you do not have a smartphone, one will be provided to you at no cost. We will use the EMA app to ask questions you can answer on your own, either while you are still in the hospital or at home. We will ask about opioid and pain- related symptoms (e.g., opioid withdrawal, pain, anxiety), along with whether you are taking buprenorphine-naloxone, and the other pain treatments that you use. You will receive time-scheduled prompts to report symptoms, your current activities, and how you are feeling. We will record assessments in two periods: the first 2 weeks (induction) and 3-month follow-up. During induction (when you start the medication), you will report opioid- and pain-related symptoms at random times during 5 daily time periods. During follow-up, we will collect data during three additional 1-week timeframes.

A description of this clinical trial will be available on 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.

As part of this study we will review your medical records and put the information we collect in our research records.

Genetic Testing

NO
This study will not involve genetic research or genetic testing.

Information Banking (Future Use and Storage)

We will store information about you in a bank, which is a library of information from many studies. This information can be linked to you. In the future, researchers can apply for permission to use the information for new studies to prevent, diagnose or treat disease, including genetic research. If you agree to the future use, some of your de-identified health

information (not linked to you) may be placed into one or more scientific databases. These may include databases maintained by the federal government. Your information may be kept for a long time, perhaps longer than 50 years. You may remove your consent for future research at any time by contacting the Principal Investigator named on the first page of the consent or the IRB office at 718-430-2237. If you do, we will destroy the information in the bank but if the information was already shared with other researchers, we cannot get it back.

You can choose not to participate in the bank and still be part of the main study and this will not affect your treatment at this facility.

INITIAL ONE (1) OF THE FOLLOWING OPTIONS

_____ I consent to have my information used for future research studies.
_____ I do NOT consent to have my information used for future research studies.
Information about me will be kept as long as required by regulations and institutional policy, but will not be used for future studies.

INITIAL YOUR CHOICE BELOW

_____ I consent to be contacted in the future to learn about:
_____ New research protocols that I may wish to join.
_____ General information about research fin dings.

_____ I do not want to be contacted at all.

Specimen Banking (Future Use and Storage)

We will destroy the specimens and information about you when the study is complete. Information about you will be kept as long as required by regulations and institutional policy, but will not be used for future studies.

Will I be paid for being in this research study?

You will receive a maximum of $435 in Clincard payments (like a Visa gift card). You will receive $100 when you complete the baseline and week 24 visits and you will receive $50 when you complete the week 1, week 4 and week 12 visits. You will also earn money for completing the EMA questions via an app on a smartphone.

For the EMA assessments, you will receive $0.20 for each set of questions completed, if you complete more than 90% of question sets weekly, you will receive a bonus of $10, for a total compensation of a possible $17 per week.

If you choose to withdraw from the study before all visits are completed, you will be paid only for the visits you completed. Payments may not be available for up to 48 hours.

For each in-person study visit you attend, you will also receive an additional Clincard payment that equals the cost of a two-way transit pass.

Some researchers may develop tests, treatments or products that are worth money. You will not receive payment of any kind for your specimens and information or for any tests, treatments, products or other things of value that may result from the research.

Will it cost me anything to participate in this study?

If you take part in this study, you or your insurance will pay for the buprenorphine-naloxone medication that is prescribed to you. If you continue buprenorphine-naloxone treatment at the community health center, you or your insurance will also pay for medical visits provided there.

What will happen if I am injured because I took part in this study?

Taking part in this research study may result in injury or harm to you. In the event of an injury resulting from your participation in this study, you should seek appropriate medical care and inform the study doctor. In the event of an emergency, you should go to an emergency room. If you are injured or harmed as a result of participating in the study and receive medical care through the Montefiore Medical Center, a Montefiore doctor, or any other health provider, you will be sent a bill for whatever medical care you receive. All or part of your bill may be paid by your health insurance.

Albert Einstein College of Medicine and Montefiore Medical Center are not offering to provide you the drug/device after the termination of the study or to pay you for pain, worry, lost income, the cost of your medical care or non-medical care costs that might occur as a result of your taking part in this study. However, you do not waive any of your legal rights in signing this form.

Immediately report any discomforts, problems or injuries you experience during the course of your participation in the study to Aaron Fox, MD at 718-920-7173.

What else do I have to do?

- You must tell the research study doctor about any past and present diseases or allergies you are aware of and about all medications you are taking including “over-the-counter” remedies and nutritional supplements or herbs.
- If you do not feel well at any time, call your doctor or the research study doctor immediately.
- **Drugs may cause a reaction that, if not treated promptly, could be life-threatening. It is important that you report all symptoms, reactions and other complaints to the research study doctor.**
- If you think you have become pregnant, contact your research study doctor immediately.
- If any other doctor recommends that you take any medicine, please inform him/her that you are taking part in a research study. You should give the other doctor the research study doctor’s name and phone number.
- You may carry out all your normal daily activities.

Confidentiality

The researchers and study staff follow federal and state laws to protect your privacy. This part of the consent form tells you what information about you may be used and shared in the research described in this form. You do not have to sign this form but, if you do not, you may not participate in the research.

The health information that we may use or disclose for the research described in this form includes information from your entire medical record, such as your name, phone number, email, medical diagnoses, dates, test results, social security number, medical record numbers, etc. In addition, the researchers wish to review information pertaining to substance abuse treatment records. By law, you must specifically authorize access to these records:

☐ Yes, I authorize the use and disclosure of my information pertaining to substance abuse treatment.

Initial: _____ Date: _____

Your information and research records will be kept confidential. Your study information will be kept as long as they are useful for the research described in this form.

The only people who can see your research records are:

- Researchers and other individuals who work with the researchers
- Organizations and institutions involved in this research, including those that fund the research, if applicable
- Groups that review research such as central reviewers, Institutional Review Boards, the Office for Human Research Protections, the US Food and Drug Administration, data coordinating centers, and domestic and foreign agencies that regulate research.

The purposes of these uses and disclosures are to (1) conduct the study and (2) make sure the study is being done correctly. The information covered under this form may no longer be protected by federal privacy laws (such as HIPAA) once disclosed, and those persons who receive your health information may share your information with others without your additional permission. All of these groups have been asked to keep your information confidential.

Medical information collected during the research, such as test results, may be entered into your Montefiore electronic medical record and will be available to clinicians and other staff at Montefiore who provide care to you.

To maintain the integrity of this research study, you generally will not have access to your research-related personal health information. If it is necessary for your care, your research-related health information will be provided to you or your physician.

How will information about you be shared and protected?

Data will be stored at another institution, Wake Forest Baptist Health. To protect your privacy, information that could be used to directly identify you (e.g., your name, address, date of birth, social security or medical record number) will be stored separately from other information about you (e.g., medical information that you provide to researchers). Information that could be used to identify you will NOT be shared with anyone except for the local researchers conducting this study.

The National Institutes of Health require that some data collected in this study are shared with other researchers to answer other scientific questions. The Wake Forest Baptist Health will make data (without information that could be used to identify you) available to researchers at other institutions, who agree to use those data for scientific research only. Data will not be shared for commercial or other purposes.

Data from this study will be submitted to the National Institute of Mental Health Database (NDA) at the National Institutes of Health (NIH). NDA is a large database where study data from many National Institute of Mental Health (NIMH) studies is stored and managed. Any personal information that could be used to identify you will be removed or changed before files are shared with the NIH. Sharing your study data helps researchers learn new and important things about mental health and substance use more quickly than before.

You may decide now or later that you do not want your study data to be added to the NDA. You can still participate in this research study even if you decide that you do not want your data to be added to the NDA. If you know now that you do not want your data in the NDA, please tell the study researcher before leaving the center today. If you decide any time after today that you do not want your data to be added to the NDA, call or email the study staff who conducted this study, and they will tell NDA to remove your data. Once the NDA shares your de-identified data with other researchers, the study cannot take back the study data that was shared before we were notified that you changed your mind. If you would like more information about NDA, this is available on-line at http://nda.nih.gov.

Are there any times you would not keep my data confidential?

If you give us information that suggests that your child or any other child is being abused, we are required by law to report that information to the Administration for Children's Services (ACS). Reporting this information may put you, your family, or others who are involved at risk of questioning and legal action by the authorities.

If you give us information that you may hurt yourself, we will break confidentiality to make a referral to an appropriate clinical provider (e.g., calling 911).

If you give us information that you may hurt someone else, we will report this information to the authorities.

Certificate of Confidentiality

As a way to protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health, which is funding this study. If information from this study were requested or subpoenaed by government agencies or the courts, we would use the Certificate to attempt to legally refuse to provide that information. These requests are rare – in only a few cases did researchers have to use the Certificate, and it was honored most of the time, but not every time. There are several kinds of situations to which the Certificate does not apply. For example, we are still required to report child abuse and some diseases, and we must make data available to the government for review or evaluation of our research. The Certificate does not prevent you or a member of your family from voluntarily sharing information. Similarly, if an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

Are there any risks to me?

A risk of taking part in this study is the possibility of a loss of confidentiality or privacy. Loss of privacy means having your personal information shared with someone who is not on the study team and was not supposed to see or know about your information. The study team plans to protect your privacy – see the Confidentiality section above for details.

Questionnaire

You may feel uncomfortable answering questions about drug use or your mental and emotional health. You can choose not to answer questions that make you feel uncomfortable.

Risks of taking Buprenorphine-Naloxone

The risks related to participating in this research study are the same as what would be expected from routine clinical care when someone starts buprenorphine-naloxone treatment. The main side effects of buprenorphine-naloxone are constipation, insomnia, irritability, and sedation.
There is also the risk of “precipitated withdrawal.” Opioids remain in your system for 24-48 hours, and if you take the buprenorphine-naloxone when you have other opioids in your system, it can cause opioid withdrawal. This could include diarrhea, nausea, vomiting, musculoskeletal pain, sweating, and anxiety. The medications that you may receive during this study may cause drowsiness or sedation. You should not drive after receiving these medications. Another potential risk is the prolongation of your hospital stay.

Risks to Women Who Are or May Become Pregnant

The effect of buprenorphine-naloxone on an embryo or fetus (developing baby still in the womb), or on a breastfeeding infant, is unknown and may be harmful. Because of these unknown risks, women cannot take part in this study if they are:

- Pregnant
- Trying to become pregnant
- Breastfeeding or sharing breast milk

Stopping Current Medications

When you stop taking buprenorphine-naloxone, your opioid withdrawal symptoms including diarrhea, nausea, vomiting, musculoskeletal pain, sweating, and anxiety might get worse. If this happens, tell the study doctor.

Allergic Reaction to Study Drug

Any drug can cause an allergic reaction which could be mild or more serious and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing. If you are having trouble breathing, call 911 immediately.

New Findings

If we learn any significant new findings during the study that might influence your decision to participate, we will contact you and explain them.

Unknown Risks

We have described all the risks we know. If we learn about other risks, we will let you know what they are so that you can decide whether or not you want to continue to be in the study.

Are there possible benefits to me?

You may or may not receive personal, direct benefit from taking part in this study. The possible benefits of taking part in this study include: buprenorphine-naloxone can help people reduce opioid use, HIV risk, and opioid overdose.

You may not experience any direct benefit personally from participating in this study. We hope you will participate because the study will generate important information about developing a safe and effective protocol for starting buprenorphine-naloxone through microdosing.

What choices do I have other than participating in this study?

You can refuse to participate in the study: If you decide not to participate, the medical care providers at this facility will still give you all of the standard care and treatment that is appropriate for you.

Are there any consequences to me if I decide to stop participating in this study?

No. If you decide to take part, you are free to stop participating at any time without giving a reason. This will not affect your care and you will continue to be treated at this facility. However, some of the information may have already been entered into the study and that will not be removed. The researchers and the sponsor may continue to use and share the information they have already collected.

To revoke (take back) your consent and authorization, you must contact the Principal Investigator in writing at the address on page 1 of this form. However, you may first call or speak to the Principal Investigator and he will stop collecting new information about you. If you take back your consent and authorization, you will not be allowed to continue to participate in this research study.

Can the study end my participation early?

Your participation will end if the investigator or study sponsor stops the study earlier than expected.

CONSENT TO PARTICIPATE

I have read the consent form and I understand that it is up to me whether or not I participate. I know enough about the purpose, methods, risks, and benefits of the research study to decide that I want to take part in it. I understand that I am not waiving any of my legal rights by signing this informed consent document. I will be given a signed copy of this consent form.

Printed name of participant	Signature of participant	Date	Time
Printed name of the person conducting the consent process	Signature	Date	Time