Yale University School of Medicine
COMPOUND CONSENT TO BE A RESEARCH SUBJECT
(Consent and HIPAA Authorization)

TITLE OF RESEARCH: Coordinated Medical Treatment of Opioid Use Disorder and Infectious Disease (Project COMMIT)

CONSENT SUMMARY

You are invited to participate in a research study designed to determine if starting long-acting injectable buprenorphine (Sublocade®) while you are in the hospital will help with opioid use disorder (OUD) and treatment for an infectious disease compared to those who have an infectious disease and who receive treatment as usual (TAU). TAU is the current standard of care at the participating hospitals and in most U.S. hospitals and usually includes detoxification from opioids and referral to community-based opioid use treatment. Research studies are voluntary and include only people who choose to take part in them.

If you agree to take part, and you are determined to be eligible, you will be randomly assigned (like the flip of a coin) to either receive up to three injections of buprenorphine (Sublocade®) on a monthly basis or treatment as usual (detoxification and referral for treatment). If you are randomly assigned to receive Sublocade®, the number of monthly injections that you receive will depend upon how long you are hospitalized and/or how long it takes for you to transition to opioid use treatment with a community provider. You will have a 50:50 chance of being on Sublocade®. You will also be asked to participate in interviews during which we will ask you questions about your medical and mental health, risk behaviors such as drug use and sex, and opioid and substance use history. You will have study visits at weeks 1, 4, 8, 12, and 24 after your first interview. During these study visits you will complete an interview. Your participation in this study will last approximately 6 months.

There are risks to the study drug, Sublocade® , that are described in this document. Some of the risks include pain, inflammation, or infection at the injection site. You will receive 3 injections of Sublocade® as part of this study. If you are randomized to the TAU group, your treatment may include detoxification and referral to treatment elsewhere. If you have a strong opinion about what treatment you receive or would like your doctor to decide what treatment you receive, you should not participate in this study.

Throughout the study, you will be followed closely by a Research Assistant and Nurse Care Manager. They will work with you to transition your care from the hospital to a community-based treatment program and remind you of your study visits and other appointments related to this study. You do not have to participate in this study to receive treatment for OUD.

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

A. PURPOSE OF THE RESEARCH

Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. The investigator in charge of this study at Yale University School of Medicine is Sandra Springer, MD. A grant from the National Institutes of Health (NIH), National Center for Advancing Translational Sciences (NCATS) will sponsor this study and will fund portions of Dr. Springer and her research team's salaries. The study is being done at 2 other sites in the United States. Approximately 200 people will take part study-wide and 67 will take part at this site.

B. PROCEDURES

If you agree to be in this study, your participation will involve the following:

Baseline Visit

1. You will be asked to sign a Release of Medical Information form (ROI) which will include specific authorization for release of medical information that may include history of drug use, mental health or HIV treatment if applicable. These authorizations will allow researchers to review your medical records at your facility, including information on your lab tests, diagnoses and medications prescribed. You decide which organizations we can talk with. We will not talk with any agency that you have not given us permission to speak with.

2. If you do not have a previous diagnosis of HIV or HCV infections, you will be tested for these with a rapid test that takes about 20 minutes for results. We will obtain your blood for these tests with a fingerstick (a prick at the tip of your finger to get a few drops of blood). For the HIV test, you will receive information on the procedure, meaning of test results and an explanation of the window period, which is the time from when you may have been exposed to HIV and the time when the test will give a positive result if you have acquired HIV infection. A reactive (positive) HIV test will be followed by a confirmatory blood test performed by Quest Diagnostics. For this confirmatory test we will draw approximately two teaspoons of blood. Participants with a new diagnosis of HIV infection will receive post-test counseling and assistance in arranging follow-up with an HIV provider within 30 days. In addition, rapid Hepatitis C Virus (HCV) testing will also be carried out by obtaining blood through a fingerstick; those who test positive will receive post-test counseling, confirmatory testing through Quest Diagnostics and be referred to a local clinic for follow-up care. For this confirmatory test we will draw approximately one teaspoon of blood. Dr. Springer is a practicing Infectious Disease physician with expertise in HIV and HCV and will provide any requisite oversight for testing and referrals.

3. If you have the ability to become pregnant, a urine pregnancy test will be done at baseline. If the test is positive, a confirmatory pregnancy test will be ordered (this test will be done at lab, and typically requires about 4mL (about a teaspoon) of blood). If you are found to be pregnant at baseline, you will be ineligible to participate in the study. The urine pregnancy test will be done prior to any other study procedures. If you become pregnant while participating in the study your participation in the study will be terminated and we will refer you for care. You are encouraged to use one or more of the following methods of birth control during your participation in the study: birth control pills, patch, IUD, condom, sponge, diaphragm with spermicide, or avoiding sexual activity that could cause you to become pregnant.
4. You will have your urine tested for opioids and other drugs.
5. You will be randomly assigned to one of the two following groups. This means that you have a 50/50 chance (like flipping a coin) of being in either group.:

   Group A: Participants assigned to this group will receive a Sublocade® injection, 1time a month for 3 months. Sublocade® is an FDA-approved long acting monthly injectable formulation of buprenorphine that is administered in the subcutaneous tissue of the abdomen. You will receive your first injection when your doctor determines it is safe for you to receive it. We will refer you to a community provider who will continue your treatment with Sublocade® after you are discharged from the hospital.

Group B: participants will receive treatment as usual, which is what is provided to anyone in the hospital with an opioid use disorder. This may include detoxification and referral for treatment in the community.

6. You will participate in an interview that will include questions about your drug use and treatment history, opioid and other substance use, social functioning, quality of life, pain, and HIV risk behaviors.

Follow Up Visits (week 1, week 4, week 8, week 12, and week 24)

1. If you have the ability to become pregnant, you will have a urine pregnancy test performed at each follow-up visit. If you have a positive pregnancy test your participation in the study will be terminated and you will be referred for pregnancy care.

You will have your urine tested for opioids and other drugs at every study visit.

2. A nurse will follow-up with you 2 times a week while you are in the hospital, and once a week after you are discharged. If you do not have a provider for your opioid use disorder, the nurse will assist you in finding one in the community. The nurse will also help you with reminders to take your medications (both for your infection and opioid use disorder), medication effects (including adverse effects), abstain from opioids, other drugs and alcohol, and engagement in community-based counseling and treatment resources.
3. You will meet with a Research Assistant for follow-up interviews at weeks 1, 4, 8, 12, and 24. The interviews will last approximately 45 minutes. The Research Assistant will schedule and send reminders to you for these appointments.

You may also be asked to participate in an additional interview at the week 12 visit that will include questions about your experience with the study and the services it provided. The interview would last approximately 30 minutes. Do you agree to participate in this interview if you are asked?

_____ Yes _____ No _____ Initials

The researchers may withdraw you from participating in the research if necessary. The investigators and/or the sponsor may stop your participation in this study at any time if you do not follow the investigator's instructions, if you exhibit violent or inappropriate behavior, if they decide it is in your best interest, or if the study is terminated

C. DURATION

The total time you will be asked to participate in this study is 24 weeks, which is about 6 months.

D. RISKS AND DISCOMFORTS

While you take part in this study, you may be at risk for side effects that may be mild, moderate or severe. You should discuss these with your doctor.

Many side effects go away shortly during or after the treatment is stopped, but occasionally, side effects can be serious, long lasting, or permanent. It is not possible to tell what side effect you may experience or how mild or severe the effect might be. We can only tell you what other people have experienced.

It is very important that you notify your study doctor right away about any side effects, problems, or unusual experiences you may have while taking the medication involved with this study. This will decrease the chance that the side effects continue or become worse. Sometimes there are other medications that we can give you to make lessen the side effects or make you more comfortable.

Risks of Sublocade®

Common Side Effects

These side effects have occurred in 1 patient out of 100 patients up to less than 10 patients out of 100 patients. The range in frequency listed by each adverse reaction is based on dosing of Sublocade®

- Headache (8.5%-9.4%)
- Constipation (8-9.4%)
- Nausea (8-8.9%)
- Vomiting (5.5-9.4%)
- Fatigue (3.9-6%)
- Increased muscle enzyme (2.5-5.4%)
- Increased liver enzymes (1-5%)
- Somnolence (feeling drowsy) (2-4.9%)
- Dizziness (1.5-2.5)

The frequency of any injection site reactions for people who have received Sublocade® is 13.8-18.9% based on dosing with the most common side effect of itchiness at the injection site (6.4-9.5%) followed by pain at the injection site (4.9-6%).

At this time there are no other side effects that are known to be very common which means that they would have occurred in more than 10 patients out of 100 patients.

Risk of Hepatitis

Some people have developed hepatitis when receiving buprenorphine which is an ingredient in Sublocade® Many of these people a history of liver abnormalities or disease and in some of the cases it is not known if the buprenorphine caused the hepatitis. Stopping the medication helped the hepatitis for some people and for others the medication was continued. If you are assigned to receive Sublocade® , we will monitor your liver function through lab tests while you are receiving the medication.

Risk of Allergic Reaction

It is possible that you may experience a severe allergic reaction to Sublocade®. Please seek immediate emergency medical care and contact your study doctor if you experience symptoms of a serious allergic reaction, including any of the following:

- Severe rash, including rash with fever, peeling of skin, or welts (urticaria)
- Swelling of the face, mouth, or throat (angioedema);
- Difficulty breathing, wheezing, or chest tightness (broncospasm);
- Feeling dizzy or that you may pass out

A history of hypersensitivity to buprenorphine is a contraindication to the use of Sublocade®

Risks if you or your partner become pregnant while receiving Sublocade®

We do not know if the study drug will affect mother's milk or an unborn fetus. Therefore, breast-feeding and pregnant women are not allowed to take part in the study. If you are pregnant or become pregnant, there may be risks to the embryo or fetus that are unknown at this time. Women who can become pregnant must take a pregnancy test before the start of the study.

You should not father a child while on this study as the treatment may indirectly affect an unborn child. If you are sexually active and are at risk of causing a pregnancy, you and your female partner(s) must use a method to avoid pregnancy that works well or you must not have sex.

Unless you cannot have children because of surgery or other medical reasons, you must be using an effective form of birth control before you start the study. You must also agree to continue to use an effective form of birth control for at least 1 month after receiving your last injection of the study drug.

Unknown Risks of Sublocade®

The treatment in this study may have unknown side effects. The researchers will let you know if they learn anything during the course of the study that might make you change your mind about participating in the study.

Treatment as Usual (TAU),

This may pose some risks which can include:

- Increased opioid withdrawal symptoms if the medication is initiated too soon after last taking opioids (such as heroin or prescription pain pills)
- worsening of opioid use disorder if the medication does not prove effective or you stop taking it

If you stop taking the medication, your risk of overdose and death will increase.

Risks of Participating in Interviews
Risks may include psychological discomfort, anxiety, or fatigue while answering the questions or after completion of the interview.

Risks of Randomization
The treatment you receive may prove to be less effective or have more side effects than the other study treatment or other available treatments.

Blood Draw Risks
Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting is possible, although unlikely.

Unknown Risks

There may be risks to your participation in the study that are not known at this time. The researchers will let you know if they learn anything during the course of the study that might make you change your mind about participating in the study.

Risks of Loss of Confidentiality
There is a risk of a loss of confidentiality of your personal information as a result of participation in this study. If you decide to be in this study, the researcher will get information that identifies you and your personal health

information. This may include information that might directly identify you, such as your name, date of birth, race, information from the medical history questionnaire, and laboratory results from your blood sample.

You will be given a study number. All information we collect from study interviews will identify you only by this study number. Information linking your name to the study number will be kept in a file that is separate from files with your study information. Data for the study will be sent to a central coordinating center/data management center at Columbia University in New York. Your study information will be kept on a secure server and/or in a locked file in a locked office. All computers and files are password protected. Your data will only be used for this study unless you give us permission to use it in other ways. Only people working on this study will have access to your information.

Any identifiable information that we get for this study will remain confidential. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity unless your specific consent for this activity is obtained.

Some of the information you provide will be shared anonymously with other researchers. None of your personal information that may identify you, however, will be shared with these researchers.

Per Connecticut state law, if you test positive for HIV or Hepatitis C, the results of your test must be reported to the Connecticut State Department of Public Health.

E. CERTIFICATE OF CONFIDENTIALITY

This research is covered by a Certificate of Confidentiality from the Federal government. This means that the researchers may not disclose information or biospecimens that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, nor can the information or biospecimens be used as evidence, unless you have consented to this disclosure. Information or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except 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.

A Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you are a Yale New Haven Health patient, you have a Yale New Haven Health medical record. If you have never been a Yale New Haven Health patient, a Yale New Haven Health medical record will be created for the purposes of this study. Results of research tests or procedures will be included in your Yale New Haven Health medical record. All information within your medical record can be viewed by individuals authorized to access the record. We will make every effort to keep confidential all research information in the medical record that identify you to the extent allowed by law; however, there is the possibility that your research information will be disclosed.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law. Examples of required disclosure include: child abuse and neglect, or harm to self or others

Finally, a Certificate may not be used to withhold information from the Federal government needed for auditing or evaluating Federally funded projects or information needed by the FDA.

F. BENEFITS

The potential benefit to you is that the treatment you receive may prove to be more effective than other available treatments, although this cannot be guaranteed.

If you are in the group that receives Sublocade® and it is successful in treating your condition, you may benefit from participating in the study; however, this cannot be guaranteed. Potential benefits to those who receive Sublocade® may include improved outcome of your opioid use disorder (OUD), infections and other medical problems.

If you are in the TAU group, you will receive detoxification and counseling from a Nurse Care Manager, which is greater than standard care.

If you are in either group, you will be helped with getting effective medication assisted treatment for OUD in the community after hospital discharge.

If Sublocade is shown to be more effective than TAU this could potentially help improve the standard of care for patients with OUD across health systems.

G. COSTS

There will be no additional costs to you as a result of being in this study. However, routine medical care for your condition (care you would have received whether or not you were in this study) will be charged to you or your insurance company. You may wish to contact your insurance company to discuss this further. It is possible that your insurance company will refuse to pay for the costs associated with study participation, in which case you will be held financially responsible. Please ask Dr. Springer if you would like to know more about which tests and studies are being done solely for research purposes.

H. PAYMENT TO PARTICIPANTS

In return for your time and effort, you can be paid up to $290 for participation in this study. You will receive a $25 gift card for each baseline, 1, 4, and 8 week study visit completed and $50 gift card for each 12 and 24 week study visit completed. You will also receive $5 each week that you do not have a follow-up visit and you check in with the study team member (either the research nurse or research assistant), for a maximum of 18 check-ins. You will also receive bus passes to help with transportation to and from the research site.

Payments that you receive from Yale University for participating in a research study are considered taxable income per IRS regulations. Payment types may include, but are not limited to: checks, cash, gift certificates/cards, personal property, and other items of value. If the total amount of payment you receive from Yale University reaches or exceeds $600.00 in a calendar year, you will be issued a Form 1099.

I. ALTERNATIVES

If you choose not to participate in this study, you could receive other treatments for your condition. The standard treatment includes detoxification and referral for treatment in the community.

J. DATA SHARING

Information about you (including your identifiable private information) may have all of your identifiers removed and used for future research studies or distributed to other researchers for future research without additional informed consent from you or your legally authorized representative.

K. DISCLOSURE OF RESULTS

Results from the HIV and/or HCV rapid tests will be shared with you in person by a staff person associated with the study and given post-test counseling and referrals.

L. AUTHORIZATION TO USE AND DISCLOSE (RELEASE) MEDICAL INFORMATION

As part of this research study, your study doctor and his/her research team will keep records of your participation in this study.

The health information Yale University School of Medicine may use or disclose (release) for this research study includes information in your medical record, results of physical exams, medical history, lab tests or certain health information indicating or relating to your condition.

Your study doctor and his/her research team will use and disclose (release) your health information to conduct this study. The health information listed above may be used by and/or disclosed (released) to the following, as applicable:

- The sponsor of the study including its agents such as data repositories or contract research organizations monitoring the study;
- Other institutions and investigators participating in the study;
- Data Safety Monitoring Boards;
- Accrediting agencies;
- Clinical staff not involved in the study whom may become involved if it is relevant;
- Parents of minor children if less than 16 years old. Parents of children 16 years old or older require authorization from the child; or
- Health insurer or payer in order to secure payment for covered treatment;
- Federal and state agencies and Yale University committees having authority over the study such as:
    - The Institutional Review Board (IRB) overseeing this study; Committees with quality improvement responsibilities; Office of Human Research Protections; Food and Drug Administration; National Institutes of Health or Other governmental offices, such as a public health agency or as required by law.

Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them. You do not have to sign this consent form. If you choose not to sign, it will not affect your treatment, payment or enrollment in any health plan or affect your eligibility for benefits. However, you will not be allowed to be a participant in this research study.

You will be given a copy of this consent form. Your authorization will expire at the conclusion of this study. You have the right to withdraw your agreement at any time. You can do this by giving written notice to your study doctor. If you withdraw your agreement, you will not be allowed to continue participation in this research study. However, the information that has already been collected will still be used and released as described above. You have the right to review your health information that is created during your participation in this study. After the study is completed, you may request this information.

Your health information will be used or disclosed when required by law. Your health information may be shared with a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury or disability and for conducting public health surveillance, investigations or interventions. No publication or public presentation about the research study will reveal your identity without another signed authorization from you.

If you have questions or concerns about this Authorization or your privacy rights, please contact Privacy Officer at (203) 436-3650.

M. CLINICAL TRIALS.GOV

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.

N. SIGNIFICANT NEW FINDINGS

If there are significant new findings during the course of the study, you will be notified.

O.FUTURE CONTACT

The researcher in charge of this study might like to contact you in the future about other research opportunities. Please initial by your choice below:

____Yes, I agree to be contacted

____No, I do not agree to be contacted

Results of this research will be used for the purposes described in this study. This information may be published, but you will not be identified. Information that is obtained concerning this research that can be identified with you will remain confidential to the extent possible within State and Federal law. The investigators associated with this study, the sponsor, and the MUSC Institutional Review Board for Human Research will have access to identifying information.

In the event that you are injured as a result of participation in this study, you should immediately go to the emergency room of Yale New Haven Hospital, or in case of an emergency go to the nearest hospital, and tell the physician on call that you are in a research study. They will call your study doctor who will make arrangements for your treatment. If the study sponsor does not pay for your treatment, Yale New Haven Health and the physicians who render treatment to you will bill your insurance company. If your insurance company denies coverage or insurance is not available, you will be responsible for payment for all services rendered to you.

Your participation in this study is voluntary. You may refuse to take part in or stop taking part in this study at any time. You should call the investigator in charge of this study if you decide to do this. Your decision not to take part in the study will not affect your current or future medical care or any benefits to which you are entitled.

The investigators and/or the sponsor may stop your participation in this study at any time if they decide it is in

your best interest. They may also do this if you do not follow the investigator's instructions.

Volunteers Statement

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have any more questions about my participation in this study or study related injury, I may contact Dr. Springer at (203) 745-8630.

If I have any questions, problems, or concerns, desire further information or wish to offer input, I may contact the Medical University of SC Institutional Review Board for Human Research IRB Manager or the Office of Research Integrity Director at (843) 792-4148. This includes any questions about my rights as a research subject in this study.

I agree to participate in this study. I have been given a copy of this form for my own records.

_____ _____
Signature of Person Obtaining Consent Date *Name of Participant

_____
Signature of Participant Date

Participant's Personal Representative (if applicable):

_____
Name of Personal Representative *(Please print)*

_____
Signature of Personal Representative Date

Relationship: ___ Spouse ___ Parent ___Next of Kin ___Legal Guardian* ____ DPOA for Healthcare*

**(If you are the health care agent or guardian, please provide proof of your authority to act on behalf of the patient)*