IRB Protocol# 2000033244

NCT05664763

COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH STUDY

YALE UNIVERSITY
YALE UNIVERSITY SCHOOL OF MEDICINE
YALE-NEW HAVEN HOSPITAL

Study Title: Understanding effects of cannabis use and cessation on neural glutamate homeostasis
Principal Investigator (the person who is responsible for this research): *Stephen Baldassarri, MD, MHS; 300 Cedar St., TAC 455-S, New Haven, CT 06520*
Phone Number: **203-785-3827**

CUD GROUP CONSENT

Research Study Summary:

- We are asking you to join a research study.
- The purpose of this research study is to understanding effects of cannabis use and cessation on neural glutamate homeostasis
- Study procedures will include: PET scanning, MRI, EEG (optional), abstinence from cannabis, and psychological assessments and questionnaires.
    - If you are also enrolled in HIC# 2000032181, common procedures except for PET scanning will be performed once between the two studies (i.e., MRI and cannabis abstinence procedures will not be duplicated)
- Required visits (depending on scheduling, MRI might be completed in the same visit as PET):
    - 1-2 screening visits (4-6 hrs)
    - 2 PET (3-5 hrs)
    - 2 MRI (1.5-3 hrs)
    - 8 15-minute biweekly cannabis abstinence check-ins over 4 weeks
- Optional visits (depending on participant interest and EEG scheduling)
    - 2 EEG (roughly 3 hours)
- The benefits of the study are that it will advance our understanding of how cannabis affects the brain.
- There are some risks from participating in this study associated with brain scanning, IV placement, and cannabis abstinence.
- Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You can also change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.
- If you are interested in learning more about the study, please continue reading, or have someone read to you, the rest of this document. Take as much time as you need before you make your decision. Ask the study staff questions about anything you do not understand. Once you understand the study, we will ask you if you wish to participate; if so, you will have to sign this form.

Why is this study being offered to me?

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We are asking you to take part in a research study because you use cannabis and are eligible for participation. We are looking for approximately 60 participants to be part of this research study.

Who is paying for the study?
National Institute on Drug Abuse and Yale School of Medicine

What is the study about?
The purpose of this study is to understanding effects of cannabis use and cessation on neural glutamate homeostasis. This will help us to more fully understand how cannabis affects the brain, which can help advance therapeutic uses of cannabis and also develop treatments for individuals who develop cannabis use disorder.

What are you asking me to do and how long will it take?
If you agree to take part in this study, this is what will happen:

Appointment - Screening – All participants must complete this appointment

Prior to participating in the scanning part of the study, we will ask you to come for a screening Appointment. During the screening appointment you will participate in a physical, ECG, and blood work, during which no more than 4 tablespoons of blood will be taken, to make sure you are healthy to participate in PET scans. We will also ask you about your psychiatric and medication and drug use history. We will also ask you to complete a MR safety questionnaire to make sure there are no metals in your body. We may also ask you questions about your mood, memory, and attention. This appointment will take approximately 3 hours. If after this appointment you are found ineligible to participate in the PET study or you decide you do not want to participate, your information will be de-identified and discarded as appropriate under HIPAA guidelines.

Appointment – MRI/cognitive testing
You will be asked to go to the MRRC at The Anlyan Center for Medical Research & Education (TAC, 300 Cedar Street) to have an MRI (Magnetic Resonance Imaging) scan of your brain. The purpose of the MRI is to help us identify the different regions of your brain on the PET scans. The MRI scan is a routine way to get pictures of the inside of the body. In the MRI Center, we will review whether you are carrying any metallic objects before you move toward the MRI system. These objects will be held for you in a locked cabinet in the MRI Center to avoid having these objects fly toward the magnet when you approach it. You will also be asked to walk through a metal detector. You will be asked to lie still in the MRI scanner for about 30 minutes. The scanner looks like a deep tunnel. You will be inside the tunnel from head to knees. You will not be able to see out of it, but you will be able to hear us and be heard if you wish to say anything. You will hear a drumming noise when the camera is taking pictures of your brain. If you feel uncomfortable during the scan, we can end the scan at any time you wish to do so. However, if you cannot complete the MRI scan, you will not be able to participate in any more of these studies.

We will also perform up to two sessions of testing of your memory, attention, and concentration. This will take approximately 1hr total. You will be given a break between these sessions. This may take place on the same day as the MRI scan, or on another day prior to PET scans if that

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works better with your and staff schedule. A member of the research staff will accompany you to MRI scans and will stay for the duration of your MRI session.

Cold Pressor Task

You may also be asked to participate in the cold pressor task during the study. In this task, we are investigating the body's physiological response to cold water. You will be asked to immerse your hand in a bucket of ice cold water maintained at 0-4°C. You will be told to raise your other hand when you begin to feel pain and to remove your hand from the water when you can no longer tolerate the pain. While your hand is immersed in water, you will also be asked to rate your pain on a scale from 0-100 and your heart rate and blood pressure will be monitored.

Appointment – PET scan(s)

You will be asked to participate in one to three PET scanning session(s). The scans will be conducted at the Yale University Positron Emission Tomography (PET) Center, 801 Howard Avenue in New Haven. You may be asked to fast prior to the PET scan. At the PET Center, female subjects will have a urine pregnancy test and all subjects may have a urine drug screen. You cannot participate in this study if you are pregnant, planning to become pregnant, or nursing. In order to participate, you must use an acceptable form of birth control (birth control pills, diaphragm or condoms with spermicide) throughout the study period. You will also provide a urine sample to measure cotinine levels, which is a biomarker of tobacco smoking. If positive, your study participation may be cancelled.

A trained nurse or CNMT (Certified Nuclear Medicine Technologist) will place plastic catheters (tubes) in your arms (for the radiotracer injection, to take venous blood samples).

After the IV lines are inserted, you will receive the radiotracer [18F]FPEB (a drug which is limited by Federal Law for investigational use only and is not currently FDA approved), during the PET scan. This radiotracer, which is a minimal amount of a drug that is labeled with a small amount of a radioactive substance, binds to the receptors in the brain and can be detected by a special camera in the PET scanner. You may not feel anything as a result of its administration; however, you may briefly experience nausea shortly after the injection. As part of the PET scanning session, you will be asked to lie very still on a table. The radiotracer will then be injected into the tube in your vein. [^{18}F]FPEB will be administered as either a single bolus lasting up to one minute or bolus plus constant infusion lasting up to 2 hours. In either case, [^{18}F]FPEB will be prepared in a single syringe and administered via software-controlled pump to achieve the desired radiotracer administration schedule not to exceed 5mCi. Syringe and lines will be assayed after scanning to correct for residual activity. Following this injection, the PET scanner camera will detect the radiotracer present in the brain. This information will be used to create pictures of your brain. Blood samples during the PET scanning sessions will be taken through the already inserted IV, allowing for collection at multiple time points without the need for additional sticks. These samples will be used to measure the amount of radiotracer in your blood. We will also collect blood samples, about 4 tablespoons, to evaluate changes in thyroid function levels and other neurochemicals in your blood that may differ between groups. The total amount of blood drawn is 12 tablespoons.

If blood samples cannot be collected through the IV, the arterial line placed as part of scanning procedures conducted under HIC#2000032181 may be used. If this occurs, the following procedures will be completed during the [^{18}F]FPEB scan session:

- We will flush the catheter often during your scan with saline (a salt solution) to make sure

it does not clog.

- After we remove the catheter, we will apply pressure to your skin for a minimum of 15 minutes to prevent bleeding under the skin.
- We will apply a pressure dressing (coban) and clear dressing (tegaderm). You will need to keep it clean and dry. Do not exercise too much and do not lift heavy objects weighing more than 5 pounds. Avoid making the same movements for 48 hours.
- You may remove the pressure dressing at bedtime and the clear dressing after 48 hours, but do not put your hand and wrist in water for a full 72 hours. Since the catheter is in for a minimal period, there is a low risk of infection.
- The arterial line will remain in place for the whole scanning period, after which it will be removed.

Samples will be stored at the PET Center until analysis, within a period of 10 years and will only be used for the purpose of this study. Genetic testing will not be conducted. There will not be any clinically relevant results from the blood analysis. The vials are not labeled with any identifying information and once results are obtained, any leftover samples will be discarded. The analysis

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of the samples will take place at Yale University laboratories. You will be asked to drink several glasses of water at the close of the PET scanning session to wash out the radiotracer. A light meal will be provided. After the PET scanning session you will be free to leave. You will be provided with a telephone number you can call anytime after the study if you need assistance for problems related to the study procedures.

You will also participate in cognitive testing on the PET scan day. This will take about 1-1.5hrs of your time.

Cannabis Abstinence

Day 0: If you decide to participate in the study, you will be scheduled for a visit prior to your MRI. At this visit, you will talk with one of the research staff to discuss abstinence from cannabis and THC, and the schedule of PET scan days and other appointments related to this research study. At this time, we may also administer questionnaires and measures that assess your memory. We may ask you to participate in some computer based cognitive tasks on this day and the day of your PET scan. This visit may be combined with the MRI.

28-day Abstinence Period:

After you complete your first PET scan, you will then be asked to stop using cannabis and related products containing THC. You will then complete a second PET scan following 28 days of cannabis abstinence. This will help us understand how cannabis use affects the brain. During the abstinence period, a research assistant will provide support and strategies to help you reduce cannabis and/or THC use. We will confirm your abstinence with twice weekly urine tests. These may be done at Yale and/or collected from you at a mutually convenient location. During each follow up appointment you may be asked to complete questionnaires regarding withdrawal and craving, and we will provide you with support to encourage continued abstinence. These appointments will take between 10-30 minutes. You will receive cash payments each day if you remain abstinent from using cannabis and THC. If we determine that you are continuing cannabis and/or THC use during this time, you will not receive payment and may not be able to continue participating in the study. After your last PET scan, you may decide to go back to using cannabis and/or THC as usual, or to remain abstinent. We will provide you with referrals to other studies (with our group or others) and/or treatment options as well as with long-term abstinence information.

What are the risks and discomforts of participating?

Potential risks: Potential risks and discomforts from this study include 1) risks associated with venous catheter insertion and with blood drawing, 2) risks associated with radiation exposure, 3) risks associated with magnetic resonance imaging, 4) reproductive risks, 5) risks associated with cannabis withdrawal, 6) risks associated with psychological assessments and questionnaires, 7) risks associated with EEG.

1. **Risks Associated with Blood Drawing and IV-line Insertion:** Drawing blood and inserting an intravenous line (IV) into an arm vein are safe and standard medical procedures. Sometimes a bruise will occur at the puncture site and rarely a blood clot or infection will occur in the vein. Certain individuals may feel light-headed during venipuncture. The volume of blood collected during this study, include screening laboratories and PET scans, will be approximately 16 tablespoons. This is not expected to have any serious negative effects on

a study participant. Participants should refrain from donating blood for at least 3 months following the study. We will also use an arterial line placed as part of a different study (HIC# 2000032181) to obtain blood draws if intravenous access is unobtainable during this study.

2. **Risks Associated with Use of an Arterial Line**
If you have also consented to participate in HIC# 2000032181, the arterial line placed as part of that study may be used during this study.

The insertion of the arterial line may be painful, and you can get bruises. The arterial puncture may cause a spasm, a temporary tightening (constriction) of the muscles in the wall of the artery). You may get a clot and your blood flow will slow down for a little while. You can get a hematoma (swelling of blood within the tissues). The site can bleed or get inflamed (become red, swollen, hot, and painful). These feelings will go away after some time, usually 24 to 72 hours after the procedure. Rarely, you may experience nerve damage to the insertion site, blocking of the artery or a “pseudo”-aneurysm (a weakening in the wall of the artery) that may require treatment, including surgical treatment. The insertion site may not heal as fast, or you may get infection. This is why an experienced health care provider will insert the arterial line and a trained nurse will look after for you.

Check your wrist and arm every day for two days after the study visit with the arterial line. Call right away your study team or the PET Center Physicians, Dr. David Matuskey at 203-370-1403 (voice mail pager) if you notice any of the following:

• You feel a lot of pain
• Your wrist or arm is tender, swollen, or red
• You see some blood or other fluids coming out of the injection site
• The color of your skin changes
• Your arms feel numb
• You feel pins and needles in your arm
• Your arm that had the catheter does not feel as strong

Tell us if you have had a bad reaction to lidocaine, novocain, or other drugs used to numb the skin in the past. You may experience a rare allergic reaction to the medicine used to numb your skin prior to placement of the arterial catheter. Severe allergic reactions can be life threatening. Some things that happen during an allergic reaction are:
• rash
• hives
• having a hard time breathing
• wheezing when you breathe
• sudden drop in blood pressure
• swelling around the face, mouth, lips, tongue, throat, or eyes
• fast pulse
• sweating

If you have any of the above allergy related side effects or symptoms, your study doctor will assess you and treat these symptoms.

Do not take aspirin and other anti-inflammatory drugs (such as Motrin or Aleve) for 7-10 days before arterial line placement and 7-10 days after the study visit.

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NOTE: If you experience swelling and pain at the catheter insertion site beyond 72 hours, contact your primary physician to have the site evaluated, or go to a Hospital Emergency Department for evaluation.

3. **Risks Associated with Radiation:** This research study involves exposure to radiation from PET imaging. If you take part in this research, you will be exposed to a small to moderate dose of radiation from the radiolabeled probes used for the PET scans and associated with the transmission scans. Please note that this radiation exposure is not necessary for your medical care and is for research purposes only. The Yale University Radiation Safety Committee (RSC) and Radioactive Investigational Drug Committee (RIDC) have both reviewed the use of radiation in this research study and have approved this use as involving slightly greater than minimal risk and necessary to obtain the research information desired.

   The total amount of radiation you will receive in this study is from 6 transmission scans or 3 low dose CT scan - used to optimize the PET scan - and up to 3 injection[s] of radioactive material (15 mCi of [^{18}F]FPEB in 3 injections (≤ 5mCi per injection). This radiation is in addition to what you may get as part of your regular medical care and what you receive from natural radiation in our environment. Everyone is exposed to low levels of natural radiation, called 'background radiation.' This background radiation comes from outer space and from rocks and minerals in the soil, and is greater at higher altitudes. The average yearly background radiation in the United States is about 0.3 rem. The amount of additional radiation you will get from participating in this study is about 1.071 rem. This is equal to about 3.5 years' worth of natural radiation.

   The amount of radiation involved in this research is small, but may slightly increase your risk of getting cancer. Scientists are not certain about the actual cancer risk at these low doses, and there may be no risk at all, but to be conservative we assume that any amount of radiation may pose some increased cancer risk.

4. **Risks associated with Magnetic Resonance Imaging:** Magnetic resonance (MR) is a technique that uses magnetism and radio waves, not xrays, to take pictures and measure chemicals of different parts of the body. The United States Food and Drug Administration (FDA) has set guidelines for magnet strength and exposure to radio waves, and we carefully observe those guidelines. You will be watched closely throughout the MR study. Some people may feel uncomfortable or anxious. If this happens to you, you may ask to stop the study at any time and we will take you out of the MR scanner. On rare occasions, some people might feel dizzy, get an upset stomach, have a metallic taste or feel tingling sensations or muscle twitches. These sensations usually go away quickly but please tell the research staff if you have them. There are some risks with an MR study for certain people. If you have a pacemaker or some metal objects inside your body, you may not be in this study because the strong magnets in the MR scanner might harm you. Another risk is the possibility of metal objects being pulled into the magnet and hitting you. To lower this risk, all people involved with the study must remove all metal from their clothing and all metal objects from their pockets. We also ask all people involved with the study to walk through a detector designed to detect metal objects. It is important to know that no metal can be brought into the magnet room at any time. Also, once you are in the magnet, the door to the room will be closed so that no one from outside accidentally goes near the magnet. We want you to read and answer very carefully the questions on the MR Safety Questionnaire related to your personal safety. Take a moment now to be sure that you have read the MR Safety

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Questionnaire and be sure to tell us any information you think might be important. This MR

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study is for research purposes only and is not in any way a complete health care imaging examination. The scans performed in this study are not designed to find abnormalities. The principal investigator, the lab, the MR technologist, and the Magnetic Resonance Research Center are not qualified to interpret the MR scans and are not responsible for providing a health care evaluation of the images. If a worrisome finding is seen on your scan, a radiologist or another physician will be asked to review the relevant images. Based on his or her recommendation (if any), the principal investigator or consulting physician will contact you, inform you of the finding, and recommend that you seek medical advice as a precautionary measure. The decision for additional examination or treatment would lie only with you and your physician. The investigators, the consulting physician, the Magnetic Resonance Research Center, and Yale University are not responsible for any examination or treatment that you receive based on these findings. The images collected in this study are not a health care MR exam and for that reason, they will not be routinely made available for health care purposes.

5. **Reproductive Risks:** Procedures such as MRI and PET scans can affect an unborn child. If you are a woman able to have children, it is important that you do not become pregnant while you are taking part in this study. Women who are breastfeeding or pregnant will be excluded from this study.

6. **Cannabis Abstinence / Withdrawal:**

Cannabis withdrawal: There is a risk that you may experience discomfort related to withdrawal from cannabis. The typical withdrawal symptoms include irritability, anxiety, anger, aggression, appetite change, weight loss, restlessness, altered sleep, strange dreams and physical discomfort.[113,114] Less common symptoms include chills, depressed mood, stomach pain, and sweating. The severity of cannabis withdrawal has been equated with the level of withdrawal from tobacco and caffeine. Cannabis withdrawal is not life threatening and resolves spontaneously without pharmacological intervention. Most symptoms appear within 1 day of abstinence, peak within 2–3 days, and resolve within 1–2 weeks.

Resumption of cannabis use following abstinence: You may decide to resume using cannabis after completing the study. If you prefer to maintain abstinence, we will offer you treatment options and local resources to help.

7. Risks Associated with Psychological Assessments and Questionnaires: Some of the psychological assessments and questionnaires will require you to discuss topics which may be uncomfortable for you to talk about. Particularly difficult topics include mood and history self-harm and suicidality. You are free to take breaks during the assessments or decide to stop the assessment at any time, should you feel you do not want to answer any questions, but know that a complete set of information is needed to proceed with the study. If you are found to be at imminent risk of hurting yourself or others, we are required by law to call 911 or assist you in becoming hospitalized to assure your safety and the safety of those around you.

8. **Risks Associated with Electroencephalogram (EEG):** EEG may cause some minor discomfort and/or skin irritation due to the paste used to attach the sensors. In addition, the paste used to hold sensors to the scalp may leave a flaky residue for several days. The physiological recording device is electrically isolated and complies with hospital standards for electrical safety. Your skin will be washed with special soap and cleansed with an alcohol

swab. Temperature sensors will be placed on your skin and held in place by medical tape. One potential risk associated with placement of these sensors is skin irritation/rash. We will ask if you have a nickel allergy, as the metal portions of the sensor are made of nickel. If you have a history of nickel allergy, you may still participate but will not use the metal sensors.

The research described here may involve unforeseen risks. If any significant new findings arise, we will provide you with such information.

How will I know about new risks or important information about the study?
We will tell you if we learn any new information that could change your mind about taking part in this study.

How can the study possibly benefit me?

The knowledge generated from the study may or may not be of benefit to you.

How can the study possibly benefit other people?

The benefits to science and other people may include a better understanding of how cannabis affects the brain. This will ultimately help us more fully understand both beneficial and detrimental effects of cannabis.

Are there any costs to participation?

If you take part in this study, you will not have to pay for any services, supplies, study procedures, or care that are provided for this research only (they are NOT part of your routine medical care). However, there may be additional costs to you. These can include costs of transportation and your time to come to the study visits. You or your health insurance must pay for services, supplies, procedures, and care that are part of your routine medical care. You will be responsible for any co-payments required by your insurance.

Will I be paid for participation?

You will be paid for taking part in this study. Payment will occur after completion of each study procedures. You will only be paid for procedures you complete.

Payments include $450 for each PET scan, $50 for each MRI scan, $50 for each set of cognitive tests performed on or around Day 0 and 28, and $50 for each optional EEG. During the cannabis abstinence period, up to $1,100 will be paid if abstinence is successfully completed as confirmed by urine samples and report. The escalating weekly payment schedule for cannabis abstinence is as follows: $50, $75, $125, $200, $650 (four week abstinence bonus). If scheduling constraints extend the necessary abstinence period, an addition $200 per week of abstinence beyond 28 days will be paid.

If you are asked to come in for an additional visit (for instance, to provide a repeat blood or urine sample), you will be compensated an additional $25 for doing so.

Total potential compensation should you participate in all procedures and remain abstinent is $2000.

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If you are also participating in HIC study #2000032181, you will not receive abstinence payment for this study. Instead, you will receive a bonus payment of $400 from participating in this study.

You are responsible for paying state, federal, or other taxes for the payments you receive for being in this study. Taxes are not withheld from your payments.

What are my choices if I decide not to take part in this study?

Instead of participating in this study, you have some other choices.
You could:

- Get treatment without being in a study.
- Take part in another study.

How will you keep my data safe and private?

We will keep information we collect about you confidential. We will share it with others if you agree to it or when we have to do it because U.S. or State law requires it.

Private identifiable information about individuals will be collected and kept in locked file cabinets in locked offices. This information will include the participants' names and may include their date of birth and phone numbers. All other research data will be identified only by subject ID number without any unique identifiers and may be stored on electronic media including the secure server, CDs, DVDs, flash drives, portable hard drives, laptop, and desktop computers, or paper. Brain data is collected during the brain imaging scans by trained technologists and is stored on password-protected and encrypted computers with identifying information carefully in compliance with HIPAA regulations.

Research data is stored on a secure database located on the internal PET Center Network. The PET network is protected by a Cisco PIX firewall operated by ITS. All research data are baked up nightly to a Dell PV-136T library with 4 IBM Ultrium-TD2 tape drives using the back up software Legato Networker 7.3 from EMC. Human subjects enrolled in the study are assigned a subject- specific random identifier. Subject identifiers and the means to link the subject names and codes with the research data are stored in separate locations within the database. The software of the database limits the ability to connect the random identifier to the actual subject identification information to research team members only. Access to the database is password protected and each research team member is required to have a unique ID and password to gain access to the database. Authorized users employ their net id and authentication is performed using Yale's central authentication server. Users always access research data through the random identifiers only. Direct identifiers belonging to subjects who withdraw from the study will be stripped from the key.

All portable devices contain encryption software.

When we publish the results of the research or talk about it in conferences, we will not use your name. If we want to use your name, we would ask you for your permission.

Identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you.

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What Information Will You Collect About Me in this Study?

The information we are asking to use and share is called "Protected Health Information." It is protected by a federal law called the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA). In general, we cannot use or share your health information for research without your permission. If you want, we can give you more information about the Privacy Rule. Also, if you have any questions about the Privacy Rule and your rights, you can speak to Yale Privacy Officer at 203-432-5919.

The specific information about you and your health that we will collect, use, and share includes:

- Research study records
- Medical and laboratory records of only those services provided in connection with this Study.
- Records about phone calls made as part of this research
- Records about your study visits
    - Physical exams
    - Laboratory, x-ray, and other test results
    - Diaries and questionnaires
    - The diagnosis and treatment of a mental health condition
    - Use of illegal drugs or the study of illegal behavior
    - Records about any study drug you received
    - Records about the study device

How will you use and share my information?

We will use your information to conduct the study described in this consent form.
We may share your information with:

- The U.S. Department of Health and Human Services (DHHS) agencies
- Representatives from Yale University, the Yale Human Research Protection Program and the Institutional Review Board (the committee that reviews, approves, and monitors research on human participants), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- The U.S. Food and Drug Administration (FDA) This is done so that the FDA can review information about the radiotracer involved in this research. The information may also be used to meet the reporting requirements of drug regulatory agencies.
- Health care providers who provide services to you in connection with this study.
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan.
- Principal Investigator of the study
- Co-Investigators and other investigators
- Study Coordinator and Members of the Research Team
- Data and Safety Monitoring Boards and others authorized to monitor the conduct of the Study

We will do our best to make sure your information stays private. But, if we share information with people who do not have to follow the Privacy Rule, your information will no longer be protected by the Privacy Rule. Let us know if you have questions about this. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by NIDA which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of suspected or known sexual, physical, or other abuse of a child or older person, or a participant's threats of violence to self or others.

Why must I sign this document?

By signing this form, you will allow researchers to use and disclose your information described above for this research study. This is to ensure that the information related to this research is available to all parties who may need it for research purposes. You always have the right to review and copy your health information in your medical record.

What if I change my mind?

The authorization to use and disclose your health information collected during your participation in this study will never expire. However, you may withdraw or take away your permission at any time. You may withdraw your permission by telling the study staff or by writing to *Stephen Baldassarri, 300 Cedar St., TAC 455-S, New Haven, CT 06520.*

If you withdraw your permission, you will not be able to stay in this study but the care you get from your doctor outside this study will not change. No new health information identifying you will be gathered after the date you withdraw. Information that has already been collected may still be used and given to others until the end of the research study to insure the integrity of the study and/or study oversight.

Who will pay for treatment if I am injured or become ill due to participation in the study?

If you are injured while on study, seek treatment and contact the study doctor as soon as you are able. Yale School of Medicine and Yale-New Haven Hospital do not provide funds for the treatment of research-related injury. If you are injured as a result of your participation in this study, treatment will be provided. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available. You do not give up any of your legal rights by signing this form.

What if I want to refuse or end participation before the study is over?

Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

We would still treat you with standard therapy or, at your request, refer you to a clinic or doctor who can offer this treatment. Not participating or withdrawing later will not harm your relationship with your own doctors or with this institution.

To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part.

The researchers may withdraw you from participating in the research if necessary. This may be necessary if you are unable to abstain from cannabis or THC, or if you are otherwise unable to complete the study procedures.

If you decide to stop participating no new information will be collected and all future appointments will be canceled. No new health information identifying you will be gathered after the date you withdraw.

What will happen with my data if I stop participating?

The data previously collected will continue to be protected in accordance with our normal procedures, meaning it may still be used and given to others until the end of the research study to ensure the integrity of the study and/or study oversight.

Who should I contact if I have questions?

Please feel free to ask about anything you don't understand.

If you have questions later or if you have a research-related problem, you can call the Principal Investigator at 203-785-3627

If you have questions about your rights as a research participant, or you have complaints about this research, you call the Yale Institutional Review Boards at (203) 785-4688 or email hrpp@yale.edu.

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.

Authorization and Permission

Your signature below indicates that you have read this consent document and that you agree to be in this study.

We will give you a copy of this form.

Participant Printed Name	Participant Signature	Date

Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date