Mass General Brigham

Research Consent Form
Certificate of Confidentiality Template
Version Date: February 2021

Subject Identification

Protocol Title: Evaluation of Cannabidiol (CBD) for Reduction of Brain Neuroinflammation

Principal Investigator: Jodi Gilman, PhD

Site Principal Investigator:

Description of Subject Population: Adults with Chronic Low Back Pain

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

Key Information

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. Your decision won't change the medical care you get within Mass General Brigham now or in the future.

The following key information is to help you decide whether or not to take part in this research study. We have included more details about the research in the Detailed Information section that follows the key information.

Why is this research study being done?

In this research study we want to learn more about whether cannabidiol (CBD) reduces activation of glial cells, which are the immune cells of the nervous system. Cannabidiol is a naturally occurring compound found in cannabis plant, and is considered to be a safe, non-addictive substance. We are looking to find out whether CBD may reduce symptoms of low back pain.

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How long will you take part in this research study?

If you decide to join this research study, it will take you about 8-10 weeks to complete the study. During this time, we will ask you to make 2 imaging visits to MGH Charlestown Navy Yard campus and 2 office visits to 101 Merrimac Street. There will also be three follow up phone calls.

What will happen if you take part in this research study?

If you decide to join this research study, the following things will happen. First, you will come to MGH for an approximately 3-hour screening visit, which will include a blood test, a urine test, and a physical exam. Depending on the results of the initial screening visit, you might be eligible to participate in up to 2 imaging visits. As part of the study, we are using a machine which combines Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) into one device. The MRI part of it uses a powerful magnet to make a picture of the body, while the PET part of it makes pictures by using special dyes with a small dose of radioactivity attached to them that "light up" inside the body.

To study the effect of CBD, you will be asked to take either a medication called EPIDIOLEX or placebo for the 4 weeks prior to the date of your second imaging visit. EPIDIOLEX is a liquid formulation of CBD. A study doctor will talk to you about how much EPIDIOLEX to take.

Why might you choose to take part in this study?

We cannot promise any benefits to you from taking part in this research study. However, possible benefits may include a reduction in pain while taking the drug. Others with chronic back pain may benefit in the future from what we learn in this study.

Why might you choose NOT to take part in this study?

Taking part in this research study has some risks and requirements that you should consider carefully.

Important risks and possible discomforts to know about include sleepiness, decreased appetite, diarrhea, lack of energy, and risks of PET/MRI scans (radiation exposure). CBD may cause an increase in suicidal thoughts or actions in a very small number of people. It is possible that patients taking EPIDIOLEX may test positive on a cannabis drug screen. If this happens, we will tell the laboratory staff that you are involved in a research study using Epidiolex.

Consent Form Title: Consent Form_2.17.2022_clean		
IRB Protocol No: 2021P002617	**Sponsor Protocol No: CBD Pain Detailed Protocol CLEAN**	
Consent Form Valid Date: 3/2/2022	**IRB Amendment No: AME5**	**Sponsor Amendment No: N/A**
Consent Form Expiration Date: 10/20/2022	**IRB Amendment Approval Date: 3/2/2022**	

A detailed description of side effects, risks, and possible discomforts can be found later in this consent form in the section called "What are the risks and possible discomforts from being in this research study?"

Other things to consider are the time commitment of 4 visits, and requirements to travel to MGH.

What other treatments or procedures are available for your condition?

Other treatments or procedures that are available to treat chronic low back pain include:

- Medications (e.g., non-steroidal anti-inflammatory drugs, opiates, muscle relaxants)
- Transcutaneous electrical nerve stimulation
- Physical exercise and stretching
- Epidural steroid injection
- Physical therapy
- Back surgeries
- Acupuncture

If you have questions or concerns about this research study, whom can you call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Jodi Gilman, PhD is the person in charge of this research study. You can call her at 617-643-7293 Monday-Friday from 9am to 5pm with questions about this research study. If you have any medical questions related to the study you can call Dr. Kristina Schnitzer at 617-726-2000, and ask for pager #27399 (24/7, for emergencies).

If you have questions about the scheduling of appointments or study visits, call our study staff:
Chelsea Pike: (617)724-0382 ckpike@mgh.harvard.edu

If you want to speak with someone **not** directly involved in this research study, please contact the Mass General Brigham IRB. You can call them at 857-282-1900.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research
- Any pressure to take part in, or to continue in the research study

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Detailed Information

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.

Why is this research study being done?

We are doing this research study to find out if cannabidiol (CBD) reduces activation of glial cells, which are the immune cells of the nervous system, compared to placebo. We are also looking to find out whether CBD may reduce symptoms of low back pain.

CBD (in the form of EPIDIOLEX) is a prescription medicine that is approved by the U.S. Food and Drug Administration (FDA) to treat seizures associated with Lennox-Gastaut syndrome or Dravet syndrome (rare forms of childhood epilepsy) in people 2 years of age and older. CBD is not approved by the FDA to treat chronic low back pain and it is not known whether it is effective for chronic back pain. We are asking you to take part in this study because you have chronic low back pain lasting at least 6 months.

This research study will compare CBD to placebo. The placebo looks exactly like CBD, but contains no CBD. During this study you may get a placebo instead of CBD. Placebos are used in research studies to see if the results are due to the medication or due to other reasons. If you decide to participate in this study, you will have a 50% chance of receiving active study medication and 50% chance of receiving placebo. That means 1 out of 2 people will receive only placebo during the study. Neither you nor study staff will know if you have received active medication or placebo until after the study is over, however study staff can get this information quickly if needed.

Who will take part in this research?

We are asking you to take part in this research study because you are an adult with chronic low back pain. About 80 people will take part in this research study at Massachusetts General Hospital. The National Institutes of Health is paying for this research study to be done.

What will happen in this research study?

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures.

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Screening Visit

The Screening Visit will take place at our 101 Merrimac Street office and will last about 3 hours. At this visit, we will do some tests and procedures to see if you qualify to take part in this research study. The study staff will review the results of these tests and procedures.

At this visit, we will:

- Ask you questions or have you complete questionnaires about your health (past and present), including mental and emotional health.
- Ask you to fill out questionnaires about your pain.
- Do a physical examination.
- Ask you about current medications you are taking.
- Ask you to fill out a form with information about your age, sex, race, marital status, and employment status.
- Draw about 2 tablespoons of blood to assess liver function and radiotracer binding affinity. Low affinity for the radiotracer known as [^{11}C]PBR28 disqualifies the subject for the research study. You may provide a saliva sample instead of a blood sample to assess radiotracer binding if you wish.
- Collect a urine sample to test for certain drugs. The results of the urine drug test will not become part of your medical record. These test results will, however, remain part of your study record.
- Collect a urine sample to test for pregnancy if you are a female who is able to become pregnant. Pregnant women cannot take part in this research study.
- With your permission, we may collect a saliva sample for other genetic research.

Study staff will also need to access your medical record in order to verify a pain diagnosis and any other medications.

This visit may also be held at the MGH Charlestown Navy Yard campus instead of our 101 Merrimac Street office, depending on your circumstances. Note that we may do a brief MRI test scan with you on the day of your screening visit, or on a different day, to ensure that you are a suitable candidate for scanning.

PET/MRI Visits

All the eligible participants will complete two PET/MRI scan visits. The PET/MRI visits will take place at MGH Charlestown Navy Yard campus. Each PET/MRI visit will last

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approximately 4 hours (and up to 6 hours). We will ask you to avoid strenuous exercise for 24 hours before the PET/MRI scan.

Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) are tests that allow us to take images of your brain and spinal cord. MRI uses a powerful magnet to make images of the body, while PET uses something called a radiotracer, that binds to the specific cells we are interested in viewing and causes them to "light up" so the scanner can detect them.

Before the PET/MRI scan, we will:

- Ask you some questions about your recent health and have you fill out some questionnaires to make sure it is safe for you to have a PET/MRI scan.
- Draw about 1 teaspoon of blood to test for pregnancy if you are a female who is able to become pregnant. Pregnant women cannot take part in this research study.
- Measure your weight.
- Collect a urine sample to test for certain drugs.
- Draw about 1 teaspoon of blood to test for the presence of cannabinoids (including CBD and THC) in the blood.
- Draw about 2 teaspoons of your blood to test for COVID-19 antibodies (to see if you have been infected by the SARS-CoV-2 virus and an immune response to it is still present in your body).

If you still qualify, we will ask you to take off anything that contains metal and change into hospital approved clothing. Then we will:

- Place an IV catheter (a thin, flexible plastic tube with a needle attached) into a vein in your arm. The IV catheter will be used to inject the radiotracer known as [^{11}C]PBR28 into your body, as well as draw about 2 tablespoons of blood to assess the function of various organs, body systems, cells, molecules, and genes in pain disorders.

We would like your permission to place an arterial line ("A-line") into an artery in your wrist to draw blood samples throughout the scan, if the doctor or nurse practitioner has deemed it safe for us to do so. However, this procedure is optional for all subjects who qualify and you will still be able to participate in the study, even if you do not allow us to collect arterial blood. The collection of arterial blood allows us to measure how the radiotracer moves through your body, and we can use that information to get more accurate PET images.

PET/MRI Scans

You will lie still in the PET/MRI scanner for about 2 hours. The scanner is a tunnel. You will lie on your back on a narrow table that will slide you into the tunnel. In order to help hold your head still, we may place foam pillows under and around your head.

The top and sides of the tunnel will be close to your face and body, which can make some people uncomfortable. If you have ever experienced a fear of enclosed spaces (claustrophobia), please tell the study staff.

The scanner makes loud banging and beeping noises taking images, so we will give you earplugs to protect your ears.

First, we will take some pictures of your brain and/or whole body. Then we will inject the radiotracer into the IV catheter in your vein and take more images. You will not feel the radio-tracer in your body and it will quickly leave your body through your urine. The Martinos Center has completed hundreds of PET/MRI scans in a number of patient populations and healthy volunteers using [^{11}C]PBR28. There have been no side effects associated with the administration of this radiotracer. This dye will travel through your blood stream, so the PET/MRI scanner can see how the different parts of your brain and/or whole body are working.

Before, during and after the scans, you may be asked to express various behavioral ratings, including pain intensity, unpleasantness and anxiety.

After the brain scan is complete, we may collect additional 20 minutes of data from your spinal cord. This spinal cord imaging is optional, and will only be done if you are still comfortable in the scanner.

After the scan is complete, you will sit up slowly and we will remove your catheter. After the removal of the arterial line we will observe you for 30 minutes. After this period of observation, you are free to leave.

Somebody from the study staff will call you the day following each scan to check on you. Of course, you can contact us at any time if you have questions (see contact information under “If I have questions or concerns about this research study, whom can I call?”).

Taking the Study Drug
You will receive a bottle containing either CBD or a placebo at the first PET/MRI Visit to take home with you. You will be instructed to begin taking it four weeks prior to the scheduled date of your second PET/MRI Visit. A study doctor will tell you how much to take. You will take CBD or placebo for 4 weeks in total, and your dose will increase each week. When you start the study drug, we will ask you to take 2.5mg/kg twice daily. Each week, a member of the study

team will remind you to increase the dose for the following week (week 2 dose = 5mg/kg twice daily; week 3 dose = 7.5mg/kg twice daily; week 4 final dose = 10mg/kg twice daily). At the end of the second week, a study physician will meet with you (by phone or in person) to assess tolerability. If you are not tolerating the study drug well (whether during the second week, or during the third or fourth week of taking the study drug), the physician will decrease your dose to the previous week's dose. The study physician may also discontinue the study drug if you do not tolerate it well.

CBD should be taken consistently with respect to meals and should not be taken in a fasted state. In addition, CBD should not be taken with concurrent alcohol use. It is important for you to follow our instructions about how to take the study drug.

Daily Surveys

You will be asked to fill out a daily survey for about 2 weeks before your first scan, for 4 weeks while you are taking CBD or placebo, and for 2 weeks after the discontinuation of CBD or placebo. You will be sent a survey to complete by the end of each day. This survey will be sent to you each day via email or text message and you will have until 11:59pm each night to complete the survey. The survey will take less than 5 minutes to complete and will ask you about your low back pain symptoms, mental health, sleep quality, fatigue, whether you have been taking the study drug, and whether you have taken any other medications to manage your pain.

Please let the study staff know if you do not have internet access and we can arrange to call you to administer the survey.

Follow-up Visits and Calls

1-Week Call. You will have a phone call 1 week after your first scan visit. In this call, we will assess adverse events, treatment expectancy, and medication use. We will also remind you to increase your study drug dose.

2-Week Visit. You will have a follow-up appointment during Week 2 with a study staff member at 101 Merrimac Street. We will check on your health, remind you to increase your study drug dose, ask about other medication use, and ask you to complete some questionnaires. We may also take a small sample of blood for a follow-up liver function test. As you will be taking Epidiolex or placebo daily at the time of this visit, we will ask you whether you can drive to the visit; if you cannot because the study drug makes you drowsy, we will arrange transportation. Note that this visit may also be held at the MGH Charlestown Navy Yard campus, depending on your circumstances.

3-Week Call. You will have a phone call during Week 3 to assess adverse events, treatment expectancy, and medication use. We will also remind you to increase your study drug dose.

4-Week Visit. You will have a second follow-up appointment immediately after the four-week treatment period, where we will assess back pain, general health, adverse events, and medication use. On the same day or as close as possible depending on scheduling, you will be re-scanned. We will also repeat the questionnaires administered during the baseline visit to assess any changes in subjective pain or general health. We will also take a small sample of blood for a follow-up liver function test. Again, we will ask you whether you can drive to the visit; if you cannot because the study drug makes you drowsy, we will arrange transportation.

6-Week Call. You will have a follow-up phone call 2 weeks after the discontinuation of the study drug. In this call, we will assess back pain, general health, adverse events, and medication use.

Stopping the Study Early

If you wish to stop taking the study drug, you should tell the principal investigator of this study, Dr. Jodi Gilman.

If you decide to stop participating in the study for any reason before the planned end of the study, we will ask that you continue to follow the schedule of visits. If you are unable or unwilling to return to the MGH Charlestown Navy Yard campus for visits, we will ask if we can call you for phone interviews instead of study visits.

Also, the study doctor may take you out of the study without your permission. This may happen because:

- The study team thinks you cannot follow the study plan.
- Your health is in question.
- You are experiencing side effects from the study drug.
- The study doctor thinks it is best for you to stop taking the study drug.
- We stop doing the study for other reasons.

Sending Study Information to Research Collaborators Outside Mass General Brigham

Blood Plasma Shipments

We will collect blood samples at the screening visit and the two PET/MRI visits, which will be tested for COVID-19 antibodies and pregnancy (in females). A small quantity (about 1 teaspoon)

of blood plasma from your sample may be shipped to researchers working with us at a University of Colorado lab who can quantify cannabinoids (including CBD and THC) in the blood.

We will label all your study materials with a code number instead of your name. No names or important numbers that could be used to identify you, like hospital medical record number or social security number, will be kept on samples. Only MGH study staff will keep the link between your subject number and your name on a computer protected by a personal password.

Optional (not required) Saliva Samples for Genetic Testing
While collection of a blood or saliva sample to test for radiotracer binding affinity is required, the collection of a saliva sample for other genetic research at the screening visit is optional (not required). You can still take part in the main study even if you don't want to take part in the additional genetic study. Giving a DNA sample involves filling 1-2 small plastic containers with your saliva. This will be done at your first visit and should take less than 5 minutes. Usually researchers study just a few areas of genetic code that are linked to a disease or condition. Instead, we may perform a whole genome analysis on your DNA sample. In whole genome analyses, all or most of the genes are looked at and used by researchers to study links to substance use and mental health. These whole genome analyses will be conducted by investigators at the Broad Institute. Samples shared with investigators at the Broad Institute will be labeled with a code number and not with your name or other identifying information. Research using whole genome information is important for the study of virtually all diseases and conditions. Therefore, the anonymized samples will provide study data for researchers working on any disease.

It is not intended to provide important genetic information about your health. We have no plan to return any research results to you or your doctor. The results of the genetic testing will not be placed in your medical record. Your consenting to take part in this additional genetic study is voluntary, and you may decide to withdraw from the study at any time or decide not to join the study. If you change your mind and want to withdraw your saliva sample from further genetic research you can do so at any time by contacting Dr. Gilman (617-643-7293; jgilman1@mgh.harvard.edu). Any information obtained from the sample will also be withdrawn except to the extent to which the information has already been used in analyses. All information and samples obtained for this study will be assigned a code number. No names or important numbers that could be used to identify you, like hospital medical record number or social security number, will be kept on samples. Only MGH study staff will keep the link between your subject number and your name on a computer protected by a personal password.

Would you like to provide a saliva sample to be used for genetic testing as described above? Please mark your choice below.

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☐ **YES** ☐ **NO** **Initials** _____

In order to allow researchers to share test results, the National Institutes of Health (NIH) and other central repositories have developed special data (information) banks that analyze data and collect the results of whole genome studies. These banks may also analyze and store DNA samples, as well. These central banks will store your genetic information and samples and give them to other researchers to do more studies. We do not think that there will be further risks to your privacy and confidentiality by sharing your samples and whole genome information with these banks. However, we cannot predict how genetic information will be used in the future. The samples and data will be sent with only your code number attached. Your name or other directly identifiable information will not be given to central banks. There are many safeguards in place to protect your information and samples while they are stored in repositories and used for research.

How may we use and share your samples and health information for other research?

At the completion of this research study, we would like to store and be able to use and share your identifiable samples and health information with researchers at Mass General Brigham for other research related to pain disorders. If we share your samples and/or health information with other researchers outside of Mass General Brigham, we will label the samples and information with a code instead of your name or other directly identifying information. The key to the code connects your name or other identifiers to your sample and/or information. We will keep the code in a password protected computer.

Because these samples and/or health information are identifiable, we are asking your permission to store, use and share them for other research. You can still take part in the research study whether or not you give permission for the storage, use, and sharing of the samples and health information for other research.

Do you agree to let us store and use your samples and health information for other research related to pain disorders?

☐ **YES** ☐ **NO** **Initials** _____

Will you get the results of this research study?

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You and your doctor should not expect to get information about the results of the research study or the results of your individual participation in the research study. The researchers involved in this study will study samples and information from many people. It could take many years before anyone knows whether the results have any meaning. There is a small chance that researchers could find out something from the study that might be important to your health. If this happens, we may contact you to find out if you would like to learn more. However, even if we find something important to your health, we cannot guarantee that you will be contacted.

What are the risks and possible discomforts from being in this research study?

Risks of Taking EPIDIOLEX

Taking **EPIDIOLEX** may cause you to have one or more of the side effects listed below.

Common side effects:

- Increase in liver enzymes: As part of the study, we will collect blood to check your liver before you start taking EPIDIOLEX and after one month of treatment. In some cases, EPIDIOLEX treatment may need to be stopped. If you had elevated liver enzymes at baseline but still met the eligibility criteria for the study, we may ask you to undergo a follow-up liver function tests at 2 weeks. In addition, we will perform a liver function test on anyone who develops clinical signs or symptoms suggestive of hepatic dysfunction.
- Sleepiness: EPIDIOLEX may cause you to feel sleepy, which may get better over time. Do not drive, operate heavy machinery, or do other dangerous activities until you know how EPIDIOLEX affects you. Other medicines (e.g., clobazam) or alcohol may increase sleepiness.
- Decreased appetite
- Diarrhea
- Lack of energy
- Insomnia
- Poor quality sleep
- Infections

Rare side effects:

- Suicidal thoughts or actions: EPIDIOLEX may cause suicidal thoughts or actions in a very small number of people, about 1 in 500. Call a healthcare provider right away if you have any of these symptoms, especially if they are new, worse, or worry you: thoughts about suicide or dying, attempt to commit suicide, new or worse depression, new or worse anxiety, feeling agitated or restless, panic attacks, trouble sleeping, new or worse

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irritability, acting aggressive, being angry, or violent, acting on dangerous impulses, an extreme increase in activity and talking (mania), other unusual changes in behavior or mood. We will assess suicidality, depression, and anxiety throughout the study. If you report any new or worsening expression of suicidal ideation and or/emergent depression, you may be asked to speak with a licensed clinician. These clinicians, along with the PI will then determine whether you can safely continue the study. If the clinicians determine that you cannot safely continue the study, your participation in the study will be discontinued, and you will be provided with a list of resources for follow-up care.

- Allergic reactions: As with any drug, an allergic reaction can occur. Allergic reactions can 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 think you are having an allergic reaction, call the study doctor right away. If you are having trouble breathing, call 911 immediately.
- Positive drug screen for cannabis: It is possible that patients taking EPIDIOLEX may test positive on a cannabis drug screen.
- There may be other risks of EPIDIOLEX that are currently unknown at this time.

Risks of Taking EPIDIOLEX with Other Medications

Do not take medications that impact specific CYP450 enzymes, including some CNS depressants, while you are in the study. This includes:

- All antipsychotics
- Benzodiazepines (except for alprazolam, clonazepam, and lorazepam)
- Non-benzodiazepine sleep aid use will be reviewed by the study physician to determine safety

Taking these drugs and **EPIDIOLEX** together may cause serious side effects. All medications, including but not limited to those mentioned, must be discussed with the study physician.

Additionally, for your safety during this study, call your study doctor BEFORE you take any:

- New medications prescribed by your own doctor
- Other medications sold over-the-counter without a prescription
- Dietary or herbal supplements

Risks of Radiation Exposure

As a result of your participation in this study, you will be exposed to radiation from two PET scans of your brain and/or spinal cord. Please note that this radiation is not necessary for your medical care and is for research purposes only. The maximum amount of radiation to which you could be exposed to in this study is approximately 7.4 milliSieverts (mSv). A mSv is a

unit of radiation dose. This amount of radiation is about the same as you would normally get in 2.4 years from natural background sources from the earth and the sky.

Scientists disagree on whether radiation doses at these low levels are harmful. Possible side effects that could occur at doses associated with this study include:

- A slight increase in the risk of developing cancer later in life

Since the effects of radiation can add up over time, it is important that you tell the study doctors about your past clinical imaging and research-related radiation exposure. If you have taken part in other research studies in the past 12 months that have involved radiation exposure, please tell us. If it appears that your earlier radiation exposure is more than our current guidelines, it is possible that you will not be allowed to take part in this study.

Have you participated in other research studies (not including this study) involving radiation exposure within the last 12 months?

☐ **YES** ☐ **NO** **Initials**_____

Risks to an Embryo or Fetus, or to a Breastfeeding Infant

The effect of radiation exposure or the use of CBD (EPIDIOLEX) 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 or trying to become pregnant
- Breastfeeding

If you are a menopausal woman and have not had a menstrual period for the past 12 months or more, you will not need to have a pregnancy test. Also, if you have had any well-documented method of surgical sterilization, you will not need to have a pregnancy test. Methods of surgical sterilization include having had a hysterectomy (removal of the uterus), bilateral oophorectomy (removal of both ovaries), a tubal ligation (having your tubes tied), and transvaginal occlusion (plugging the opening of the tubes with a coil). All other female subjects must have a negative pregnancy test before starting the study drug and before having the PET/MRI scan.

If you miss a period, or think you might be pregnant during the study, you must tell the study doctor immediately. If you become pregnant, you must stop taking the study drug and stop taking part in the study.

There may be other risks and side effects of the PET/MRI scan that are not known at this time.

Risks of MRIs

MRIs use powerful magnets to make images. There are no known radiation risks associated with MRI. However, you should not have an MRI if:

- You have certain medical metal implants, such as surgical clips or pacemakers
- You are pregnant or suspect you are pregnant

All credit cards and other items with magnetic strips should also be kept out of the MRI room. People who feel uncomfortable in confined spaces (claustrophobia) may feel uncomfortable in the narrow tube. The MRI makes loud banging noises as it takes images. Earplugs can be used to reduce the noises. The MRI can be stopped at any time at your request.

Other possible risks include:

- Localized warming of your skin and the underlying tissue during normal routine MRI use
- You should immediately inform us if you experience discomfort due to warming and the procedure will be stopped

Risks of IV Catheter and Blood Draw

Drawing blood or placing the IV catheter into a vein in your arm may cause the following in the area where we take blood samples from or place the IV catheter:

- Pain
- Discomfort
- Bruising
- Bleeding
- Swelling
- Redness

You may have a bruise or feel painful or uncomfortable for 2-3 days after. Rarely, an infection may occur, which can be treated.

Risks of Optional Arterial Line (A-line)

Inserting an A-line can hurt more than having a regular IV catheter or having blood drawn with a needle. If you agree to this procedure, we will numb your wrist area first, but it may still hurt when we place the A-line into your wrist. Once the A-line is in place, it usually does not hurt.

Having an arterial line placed may cause:

- Pain, bleeding, swelling, or redness at the wrist. Rarely (less than 1 in 100), an infection may occur, which can be treated.
- Short loss of pulse at the wrist, if blood flow in the artery is briefly stopped (for example, because of a clot or spasm of the artery).
- Damage to the artery wall or nearby nerves.
- Catheter breaking or falling out.

Rare side effects:

- There have been reports of decreased blood flow to the hand that resulted in the need for surgery. This is very rare and has not been reported when catheters have been in place for only a few hours for research.

After we remove the catheter:

- We will ask you to stay for at least 30 min so that we can check that the site is healing properly.
- You may have a bruise or feel tenderness for 2-3 days around the area where the arterial line was placed.
- You should avoid lifting anything heavier than a small bag of flour for a day following the scan.

Call us if:

- Bleeding occurs after you leave (rare). Apply pressure to the site and go to the Emergency Department.
- The wrist area is painful, red, or swollen.

Do you allow us to collect arterial blood during the scan(s)? You can change your mind at any time.

☐ **YES** ☐ **NO** **Initials**_____

Risks of Numbing Drug (Lidocaine)

The anesthesiologist will use lidocaine to numb your wrist area prior to placing the A-line. Risks of lidocaine include:

- Dizziness
- Nausea
- Drowsiness
- Ringing in the ears
- Numbness

- Allergic reaction. An allergic reaction to lidocaine was observed in a very limited number of cases.

Risks of COVID-19 Antibody Testing

As part of the study, we wish to determine whether or not you have been exposed to COVID-19. We do this using an antibody serology test which involves taking up to 10 ml of blood (about 2 teaspoons) and sending it to an internal or third-party laboratory that provides testing services. Your test results will be communicated to you. Your results may become part of your MGH medical records. A positive test does not mean that you have an active COVID-19 infection, only that you have been exposed at some point in the past.

Risks of Genetic Testing

Genetic information that results from this study does not have medical or treatment importance at this time. However, there is a risk that information about taking part in a genetic study may influence insurance companies of employers regarding your health. To further safeguard your privacy, genetic information obtained in this study will not be placed in your medical record. Taking part in a genetic study may also have a negative impact on family or other relationships. If you do not share information about taking part in this study, you will reduce this risk. We may perform Genome wide association studies (GWAS) with this data. GWAS are hypothesis free methods to identify associations between genetic regions (loci) and traits (including diseases).

Risks of Questionnaires

We will ask you questions about your emotional or mental health (psychological questions). Some of these questions may make you uncomfortable. You are allowed to skip any question you do not want to answer, but it could mean being excluded by the study (depending on how necessary the particular answer is).

Incidental Findings

We are doing the PET/MRI scan in this study to answer research questions, not as part of your medical care. The information from this study will not usually become part of your hospital record. This PET/MRI scan is not the same as the one that your doctor would order. It may or may not show problems that would be found on a standard MRI or PET scan. This type of scan is considered experimental.

If we do see something that looks like a medical problem, we will ask a radiologist (a doctor who specializes in test results of this sort) to review the results. If the radiologist thinks that you may

have a medical problem, we will tell you and help you get follow-up care. If the radiologist thinks that you may have a medical problem, but it turns out that you don't, we may have caused you to worry needlessly about your health.

Medical Information

We will make a notation in your medical record that you are a part of this study. There is a small risk that your confidential medical information could be revealed or discovered by mistake. The results of this research study won't be placed in your medical records. In addition, your samples and information will be coded and the key to the code will be kept in a separate, locked file. We won't share or publish any information that will identify you.

What are the possible benefits from being in this research study?

You may not benefit from taking part in this study. If you receive CBD (EPIDIOLEX), it is possible that your low back pain will improve while you are taking it. However, because EPIDIOLEX is not FDA-approved to treat low back pain, your doctor cannot prescribe it after you finish the study.

Others with low back pain may benefit in the future from what we learn in this study. We hope the information obtained from this study will help scientists discover a potential mechanism of action for CBD.

What other treatments or procedures are available for your condition?

You do not have to take part in this research study to be treated for low back pain. Other treatments or procedures that are available to treat low back pain include:

- Medications (e.g., non-steroidal anti-inflammatory drugs, opiates, muscle relaxants)
- Transcutaneous electrical nerve stimulation
- Physical exercise and stretching
- Epidural steroid injection
- Physical therapy
- Back surgeries
- Acupuncture

Talk with the study doctor if you have questions about any of these treatments or procedures.

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Can you still get medical care within Mass General Brigham if you don't take part in this research study, or if you stop taking part?

Yes. Your decision won't change the medical care you get within Mass General Brigham now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should you do if you want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will you be paid to take part in this research study?

We will pay you up to $770 for the following:

- $75 for the initial screening visit
- Up to $76 for completing daily surveys ($1 per survey completed)
    - Bonus $25 if you complete 90% of surveys
- $200 for each PET/MRI scanning session
- $25 for each blood test to exclude pregnancy (if you are a female of childbearing age)
- $50 for each arterial line placement
- Up to $44 which you can earn from a task you will complete in the PET/MRI scanner

If, for some reason, we cannot inject you with the dye during the imaging visit(s) and we have not yet placed the arterial line, you will receive $50. If we cannot inject you with the dye and we have already placed the arterial line, you will receive $100. If you have to stop the scan early for any reason, we will pay you $50 for the imaging visit(s). We will also reimburse you for your parking in the hospital garage during study visits.

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Consent Form Valid Date: 3/2/2022	**IRB Amendment No: AME5**	**Sponsor Amendment No: N/A**
Consent Form Expiration Date: 10/20/2022	**IRB Amendment Approval Date: 3/2/2022**	

We may use your samples and information to develop a new product or medical test to be sold. The Sponsor, hospital, and researchers may benefit if this happens. There are no plans to pay you if your samples or information are used for this purpose.

What will you have to pay for if you take part in this research study?

Study funds will pay for certain study-related items and services. We may bill your health insurer for, among other things, routine items and services you would have received even if you did not take part in the research. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff. If necessary, we will arrange for you to speak with someone in Patient Financial Services about these costs. You will also be responsible for paying for transportation to and from study visits, although we will validate parking in the hospital garage during study visits. It is important to note that if you do receive any benefit from the CBD treatment, and decide to continue treatment with CBD after your study participation is over, you and your insurance company will be responsible for the cost of the CBD.

What happens if you are injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the beginning of this consent form.

If you take part in this research study, how will we protect your privacy?

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Federal law requires Mass General Brigham to protect the privacy of health information and related information that identifies you. We refer to this information as "identifiable information."

In this study, we may collect identifiable information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable information and why:

- Mass General Brigham researchers and staff involved in this study
- The sponsor(s) of the study, and people or groups it hires to help perform this research or to audit the research
- Other researchers and medical centers that are part of this study
- The Mass General Brigham ethics board or an ethics board outside Mass General Brigham that oversees the research
- A group that oversees the data (study information) and safety of this study
- Non-research staff within Mass General Brigham who need identifiable information to do their jobs, such as for treatment, payment (billing), or hospital operations (such as assessing the quality of care or research)
- People or groups that we hire to do certain work for us, such as data storage companies, accreditors, insurers, and lawyers
- Federal agencies (such as the U.S. Department of Health and Human Services (DHHS) and agencies within DHHS like the Food and Drug Administration, the National Institutes of Health, and the Office for Human Research Protections), state agencies, and foreign government bodies that oversee, evaluate, and audit research, which may include inspection of your records
- Public health and safety authorities, if we learn information that could mean harm to you or others (such as to make required reports about communicable diseases or about child or elder abuse)
- Other researchers within or outside Mass General Brigham, for use in other research as allowed by law.

Certificate of Confidentiality

A federal Certificate of Confidentiality (Certificate) has been issued for this research to add special protection for information and specimens that may identify you. With a Certificate,

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unless you give permission (such as in this form) and except as described above, the researchers are not allowed to share your identifiable information or identifiable specimens, including for a court order or subpoena.

Certain information from the research will be put into your medical record and will not be covered by the Certificate. This includes records of medical tests or procedures done at the hospitals and clinics, and information that treating health care providers may need to care for you. Please ask your study doctor if you have any questions about what information will be included in your medical record. Other researchers receiving your identifiable information or specimens are expected to comply with the privacy protections of the Certificate. The Certificate does not stop you from voluntarily releasing information about yourself or your participation in this study.

Even with these measures to protect your privacy, once your identifiable information is shared outside Mass General Brigham, we cannot control all the ways that others use or share it and cannot promise that it will remain completely private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your identifiable information. Your permission to use and share your identifiable information does not expire.

The results of this research may be published in a medical book or journal, or used to teach others. However, your name or other identifiable information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your identifiable information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your identifiable information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others, and such information may continue to be used for certain purposes, such as to comply with the law or maintain the reliability of the study.

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You have the right to see and get a copy of your identifiable information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my identifiable information to be used and shared as described above.

_____	_____	_____
Subject	Date	Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

_____	_____	_____
Study Doctor or Person Obtaining Consent	Date	Time (optional)

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