Informed Consent

Investigation of Cannabidiol for Reduction of NeuroInflammation in Chronic Back Pain

NCT # NCT03891264
11/12/2020

Partners HealthCare System
Research Consent Form

Subject Identification

Certificate of Confidentiality Template
Version Date: January 2019

Protocol Title: Investigation of Cannabidiol for Reduction of NeuroInflammation in Chronic Back Pain

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.

Partners HealthCare System is made up of Partners hospitals, health care providers, and researchers. In the rest of this consent form, we refer to the Partners system simply as "Partners."

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 Partners 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?

The goal of this research study is to identify 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 also looking to find out whether CBD may reduce symptoms of low back pain. This is not a treatment study.

How long will you take part in this research study?

If you decide to join this research study, it will take you about 4-6 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.

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

If you choose to take part in this study, you will come to MGH for a 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 a medication called EPIDIOLEX for 4 weeks after the first imaging visit. EPIDIOLEX is a liquid formaulation of CBD. A doctor will talk to you about how much to take. You will be treated with CBD for 4 weeks in total. You will have 1 imaging visit before taking CBD, and a second after taking CBD for 4 weeks, so we can compare glial cell activation.

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 from CBD 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.

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:
Grace Wheeler: (617) 643-4692 gwheeler@mgh.harvard.edu

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. 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

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?

The goal of this research study is to identify whether cannabidiol (CBD) reduces activation of glial cells, which are the immune cells of the nervous system. We are also looking to find out whether CBD may reduce symptoms of low back pain. This is not a treatment study, but rather a study to discover when CBD reduces neuroinflammation.

CBD (in the form of EPIDIOLEX) is a prescription medicine that is used to treat seizures associated with Lennox-Gastaut syndrome or Dravet syndrome (rare forms of childhood epilepsy) in people 2 years of age and older. It is not known whether CBD 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.

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 lower pack pain. About 20 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.

A screening visit will evaluate your eligibility for the study. If you are eligible, you will be asked to participate in an initial brain imaging visit.

During the study, you will receive a bottle containing CBD. You will take CBD for 4 weeks in total, and your dose will increase each week. When you start the medication, we will ask you to take 2.5mg/kg twice daily (5mg/kg/day). Each week, a member of the study team will remind you to increase the dose by 5mg/kg/day for the following week (week 2 dose = 10mg/kg/day; week 3 dose = 15mg/kg/day; week 4 final dose = 20mg/kg/day). 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 medication well, the physician will decrease your dose to 5 mg/kg twice daily (10 mg/kg/day). The study physician may discontinue the medication if you do not tolerate it well.

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.

Screening Visit

This visit will take up to 3 hours, during which you will complete some tests and procedures to see if you will be eligible to further participate in this study.

During the visit, we may:

- Ask you questions about your health (past and present), including mental and emotional health.
- Ask you to fill out questionnaires about your pain
- Do a physical examination.
- Draw about 2 tablespoons of blood to assess radiotracer binding affinity. Low affinity for [11C]PBR28 disqualifies the subject for the research study.
- Collect a urine sample to test for certain drugs

MR-PET visits

All the eligible participants will complete two MR-PET scan visits. Each MR-PET visit will last approximately 4 hours (and up to 6 hours). We will ask you to avoid strenuous exercise for 24 hours before the MR-PET scan.

Before the MR-PET 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 an MR-PET 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

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.

The MR-PET Scans

You will lie still in the MR-PET 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 MR-PET 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 MR-PET 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.

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?").

Daily Surveys

You will be asked to fill out a daily survey for 7 days before you start taking CBD and for 4 weeks while you are taking CBD. You will be sent a survey to complete by the end of each day. This survey will be sent to you via email and you will have until 11:59pm each night to complete the survey. The survey will take about 5 minutes to complete and will ask you about your low back pain symptoms.

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

2-Week Visit. You will have a follow-up appointment Week 2 with a study clinician, where we will check on your health, remind you to increase your medication dose, 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 daily at the time of this visit, we will ask you whether you can drive to the visit; if you cannot because the medication makes you drowsy, we will arrange transportation.

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, and adverse events. 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. 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 medication 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 medication. In this call, we will assess back pain, general health and adverse events.

Study Information Included in Your Electronic Medical Record

A notation that you are taking part in this research study will be made in your electronic medical record. Information obtained from research related questionnaires and MR-PET scans will not be included in your medical record, however research results that relate to your general medical care may be included in your record (for example, list of allergies, results of standard blood tests done at the hospital labs).

Whom can I contact if I want to stop taking the study drug?

If you wish to stop taking the study drug, you should tell the principal investigator of this study, Dr. Jodi Gilman. Occasionally, Dr. Gilman and her study team may decide to have you stop taking the study drug or terminate your participation in the study, without your permission. This may happen if they think that you cannot follow the study plan or if your health is in question. One reason you may be asked to stop is if you are experiencing side effects from the study drug.

What happens if I stop the study early?

If you decide to stop participating in the study 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.

For what type of research will my samples be used?

Your blood samples and information will be used to understand pain disorders. They will be coded with a study identification number that can NOT be directly traced back to you. The long-term goal of research with your blood samples is to better understand, prevent, diagnose, and treat chronic pain. However, it is not possible to list every future research project that could be performed with these samples. Since we cannot predict all of the research questions that will be relevant in the future. As we learn more about the human body and the underlying mechanisms leading to chronic pain, there may be new types of research that can be done and new research questions.

We may also perform limited genetic research on the deoxyribonucleic acid (DNA) from your samples or cell lines. DNA is the material that makes up your genes. DNA provides the instructions that tell our cells how to grow and function. Ribonucleic acid (RNA) is made from DNA, and is used to encode for proteins, the building blocks of cells. We may also perform genetic research by analyzing proteins that are present in differing amounts in people with pain disorders and thereby identifying patterns of RNA and DNA that may affect or predict the onset of chronic pain. Although genetic information may be analyzed, no genetic information will be given to you or placed in your medical records.

Do you agree to let us store your samples and health information for future genetic and cellular research related to chronic pain disorders?

☐ **Yes** ☐ **No** **Initials**_____

What researchers can use my samples and what information about me can they have?

Your de-identified samples or cell lines may be made available broadly to researchers at academic institutions, and shared with for-profit companies and non-profit organizations. These academic institutions, companies, and organizations may be located nationally or internationally, and they may perform any of the research described in the previous section. Your samples will not be sold to anyone for profit. Blood samples may be sent to a separate location for generation of the iPSC lines to produce neurons and glial cells.

How long will my samples, cell lines, and information be kept?

There is no scheduled date on which your samples, cell lines and information will be destroyed. Your samples will be used to create living tissue samples and cell lines, which may be stored and used for research indefinitely. The code linking your samples and cell lines to your medical record may be kept indefinitely so that your samples and updated health information may be used for research in the future.

Can I stop allowing my samples and information to be stored and used for research?

Yes. You have a right to withdraw your permission at any time. If you do, your samples and information will be destroyed. However, it will not be possible to destroy samples and information that have already been given to researchers. If you decide to withdraw your permission, you should contact Dr. Gilman in writing.

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?

The samples and information we collect in this study may help advance other research. If you join this study, we may remove all information that identifies you (for example your name, medical record number, and date of birth) and use these de-identified samples and data in other research. It won't be possible to link the information or samples back to you. Information and/or samples may be shared with investigators at our hospitals, at other academic institutions or at for-profit, commercial entities. You will not be asked to provide additional informed consent for these uses.

Will you get the results of this research study?

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?

EPIDIOLEX: EPIDIOLEX is an FDA approved medication used to treat two forms of epilepsy.

Common side effects:

1. EPIDIOLEX may cause liver problems. 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. Any subjects who at baseline had elevated AST/ALT levels but still met the eligibility criteria for the study will undergo a follow-up liver function tests at 2 weeks. In addition, we will perform a liver function test in subjects who at any time point during the study develop clinical signs or symptoms suggestive of hepatic dysfunction.

2. 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.
3. 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 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.
4. Other adverse reactions are: sleepiness, decreased appetite, diarrhea, lack of energy, rash, insomnia, poor quality sleep, and infections.

Treatment with Epidiolex is contraindicated for individuals taking medications that impact specific CYP450 enzymes, including some CNS depressants, including all antipsychotics, benzodiazepines (except for alprazolam, clonazepam, and lorazepam), and non-benzodiazepine sleep aids including butabarbital sodium, eszopiclone, phenobarbital, ramelteon secobarbital sodium, suvorexant, zaleplon, and zolpidem. All medications, including but not limited to those mentioned, must be discussed with the study physician.

It is possible that patients taking EPIDIOLEX may test positive on a cannabis drug screen. There may be other risks of CBD that are currently unknown at this time.

Until you know how this drug affects you, please don't drive or operate hazardous machinery, as this drug may cause sleepiness. Other medicines (e.g., clobazam) or alcohol may increase sleepiness.

Epidiolex should be taken consistently with respect to meals, and should not be taken in a fasted state. In addition, Epidiolex should not be taken with concurrent alcohol use.

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 a you can safely continue the study. If the clinicians determine that the 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.

MRI: MRIs use powerful magnets to make images. There are no known radiation risks associated with MRI. However, persons with certain medical metal implants, such as surgical clips, or pacemakers should not have an MRI. 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. If you are or suspect you are pregnant, you should not participate in this study. The MRI has the potential, during normal routine use, to cause localized warming of your skin and the underlying tissues. You should immediately inform us if you experience discomfort due to warming and the procedure will be stopped.

Radiation Exposure: As a result of your participation in this study, you will be exposed to radiation from two PET scans of your brain. 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. A possible effect that could occur at doses associated with this study is 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**_____

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 to an Embryo or Fetus: Radiation exposure or the use of CBD may be harmful to an embryo or fetus (developing baby still in the womb) or to a nursing infant. Because of these risks, women cannot take part in this study if they are pregnant or breastfeeding.

If you are a menopausal woman and have not had a period for the past 12 months or more, you will not need to have a pregnancy test. Also, you will not need to have a pregnancy test if you have had a hysterectomy (surgical removal of your uterus and/or ovaries). All other female subjects must have a negative pregnancy test before having the MR-PET scan.

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

Incidental Findings: We are doing the MR-PET 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 MR-PET 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.

IV Catheter and Blood Draw: Drawing blood or placing the IV catheter into a vein in your arm may cause some pain, discomfort, bruising, bleeding, swelling, and redness in the area where we take blood samples from or place the IV catheter. You may have a bruise or feel painful or uncomfortable for 2-3 days after. Rarely, an infection may occur, which can be treated.

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).

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 directly benefit from taking part in this study, though it is possible that you will experience some reductions in pain. 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 my condition?

You do not have to take part in this 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

Can you still get medical care within Partners 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 Partners 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 $525 for the following:

- $75 for the initial screening visit
- $50 for completing daily surveys
- $200 for each MR-PET scanning session

If, for some reason, we cannot inject you with the dye during the imaging visit(s), you will receive $50. 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.

We may use your study information and test results to develop a new product or medical test to be sold. The hospital and researchers may benefit if this happens. There are no plans to pay you if your samples 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 medical care you would receive even if you did not take part in this 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 from 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?

Federal law requires Partners 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:

- Partners 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 Partners ethics board or an ethics board outside Partners that oversees the research
- A group that oversees the data (study information) and safety of this study
- Non-research staff within Partners 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 Partners, 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, 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 Partners, 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.

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

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.

Signature of Study Doctor or Person Obtaining Consent:

Study Doctor or Person Obtaining Consent	Date	Time

Consent Form Version Date: 11/12/2020