

APPROVED: **Mar 24, 2017**
COPERNICUS GROUP IRB



Approved:



**RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY
AUTHORIZATION FORM**

Protocol Title: Placebo-Controlled, Triple-Blind, Randomized Crossover Pilot Study of the Safety and Efficacy of Four Different Potencies of Smoked Marijuana in 76 Veterans with Chronic, Treatment-Resistant Posttraumatic Stress Disorder (PTSD)

Protocol Number: MJP-1

Sponsor: Multidisciplinary Association for Psychedelic Studies (MAPS)

Principal Investigator: [Redacted]

Research Site Address: [Redacted]
[Redacted]
[Redacted]

Daytime Telephone: [Redacted]

24-Hour Contact: [Redacted]

What is the purpose of this form?

- The purpose of this form is to help you decide if you want to be in the research study. It is up to you to decide if you want to take part in this study. You should take part in this study only if you want to.
- Please read it carefully and take as much time as you need.
- Ask your study doctor or the study team to explain any words or information in this informed consent that you do not understand.
- You are being asked to join a research study. This consent form explains the research study and your part in the study.
- You are a volunteer. If you join the study, you can change your mind later. You can decide not to take part or you can quit at any time. There will be no penalty or loss of benefits if you decide to quit the study.
- During the study, we will tell you if we learn any new information that might affect whether you wish to continue to be in the study.
- If you receive routine medical treatment (including medical or laboratory tests) in the study, information about your research study participation will be included in your medical record. Other doctors may not have access to this information. You can ask the research team to send this information to any of your doctors.
- Biospecimens will be collected in this study. Biospecimens may include blood and urine. Most biospecimens contain DNA, which is the genetic code for each person.
- 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.
- During this study, you will not have access to certain medical information and test results collected for study purposes. If an emergency occurs while you are in the study, medical information needed for your treatment can be made available to your study physician and other physicians who treat you. When the study is completed, all the information in your medical record will be available to you.
- After reading this form and talking with the study staff, you should know which parts of the study are medical care and which are experimental. Please ask any questions you have.
- You may talk with your family, friends, and your doctor to help you make your decision. You can take as much time as you like to make this decision.
- The sponsor is paying for this research study. Your study doctor will be paid by the sponsor.

Why is this research being done?

This research is being done to find out if marijuana will reduce nightmares and other posttraumatic stress disorder (PTSD) symptoms in people with PTSD. You are being asked to take part in this research study because you are a military veteran and you have been diagnosed with PTSD from your military service and because your symptoms have not gone away after psychotherapy or medicines.

The use of marijuana in this research study is investigational. The word “investigational” means that marijuana is not approved for marketing by the Food and Drug Administration (FDA). The FDA is allowing the use of marijuana in this study. Marijuana is also a controlled substance, meaning that it is still illegal at the federal level to use outside of research. This small (“pilot”) study was created to see if one of four different strengths (potencies) of marijuana are safe and helpful for people with PTSD.

The study is sponsored by a U.S.-based non-profit organization called the Multidisciplinary Association for Psychedelic Studies (MAPS, www.maps.org). This organization funds research that studies the possible medical uses of psychedelic (hallucinogenic) drugs like MDMA and marijuana.

Marijuana or marijuana-based products have been and are used for state-regulated medical and recreational reasons in and outside of the U.S. In states that allow medical use of marijuana it is most often used by people suffering from insomnia, anxiety, and pain. People with PTSD can have trouble sleeping and relaxing and some report that use of marijuana helps reduce these symptoms. So far though, there have been no scientific studies looking at marijuana as a way of helping people with PTSD deal with nightmares, anxiety, and sleep difficulties. This research is being done to find out if marijuana will reduce nightmares and other PTSD symptoms in people with PTSD.

People with PTSD from being in the military may join the study if they meet all of the requirements to be in the study. Additional study requirements are that you must be available for study visits, you must agree to follow the rules of study participation, and must not be pregnant or become pregnant. There are more criteria you must meet and your study doctor will talk to you about those.

How many people will be in this study?

Up to 232 people will be enrolled in the study at [REDACTED] to ensure 76 participants complete the study through Visit 5.

What are the study procedures?

If you agree to be in this study, you will sign this form before any study procedures are done.

If you agree to be in this study, we will ask you to do the following things:

Talk with your study doctor before starting any new medicine. This includes drugs you buy at the drug store and herbal or dietary supplements (vitamins). Some drugs could cause serious side effects if taken with the study drug.

Please ask your study doctor if you have any questions about the medicine(s) you are taking. He/she will tell you which medicine you cannot take during the study.

Study Overview

You will be in the study for up to 18 weeks and then you will have a visit approximately 15 weeks after that as a part of the long term follow up.

The study has three parts: Stage 1 (where one type of marijuana is smoked for three weeks), Stage 2 (where a different type of marijuana is smoked for three weeks), and an optional Stage 3 (where you may smoke a fresh supply of marijuana in the same amount as your left over marijuana from Stage 1 or Stage 2 over two months or less).

If you smoke, vape or use any form of marijuana now for non-medical or state-regulated medical reasons, you will need to stop using non-study marijuana or marijuana-based products for two weeks before and during the active participation part of the study. You may not use any other type of marijuana including THC or CBD products like, edibles, vape pens or topical ointments during your active participation in the study. You will also need to stop smoking all marijuana, including study marijuana, for two weeks after Stage 1 and Stage 2 (Cessation 1 and 2).

During each study stage, you will meet with the study staff at least five times, for a total of 10 times. The study staff will also talk with you by phone daily for the first three days after your introductory sessions in Stage 1 and Stage 2, and weekly after that.

If you choose, you may take part in the optional Stage 3 and have a fresh supply of marijuana in the same amount as your left over marijuana from Stage 1 or Stage 2. In Stage 3 you will continue to visit the researchers weekly for up to two more months or until you use up the amount available based on the amount of marijuana you returned in Stage 1 or Stage 2. If any marijuana remains at the end of Stage 3, it will be returned to the study site and destroyed as the Drug Enforcement Agency (DEA) requires. There will be a remote (video chat) follow-up visit that will happen 6 months after Stage 2, whether you choose to take part in Stage 3 or not.

Screening (Evaluation and Beginning of Study)

If you agree to be in this study, you will first sign this consent form. Before you can begin, the study staff must first make sure that you are eligible to be in the study and that you are generally physically healthy. The screening process will take about five hours and will involve some tests and two visits. The study staff will ask your permission to contact your doctor or therapist to get more information about your medical history. They may need to do this to know if you can be in the study.

The tests during screening will include the following:

- Two telemedicine (video chat) interviews one about your PTSD symptoms and how you deal with them in your everyday life and another to assess your psychiatric health. The people asking you these questions will be different from the study doctor. These interviews may be recorded for research purposes.
- A questionnaire about your PTSD symptoms that you fill out yourself.
- A questionnaire about feelings of anxiety and depression.

Approved

- A questionnaire about your sleep quality, including how well you sleep and any sleep problems you are having.
- Testing of your sleep patterns using a device like a wristwatch to wear while sleeping or awake. You should only take this off when showering or washing dishes. You will need to wear this for one week before you learn if you can be in the study.
- A questionnaire about daily behaviors and functioning.
- Questions about thoughts or feelings you might have about hurting or killing yourself.
- Questions about your past and any recent experience with marijuana use.
- Questions about your medical history, therapy, and medicines you have taken.
- Questions about the emotional and mental health history of you, your parents, and sisters or brothers if you have any. This may include questions about difficult experiences you may have had during childhood or at other times of your life.
- A physical health examination.
- An ECG (electrocardiogram) will also be taken, which is a recording of the electrical activity of your heart.
- A sample of your blood (about 2 tablespoons) and a urine sample for routine laboratory testing, including tests of metabolism, thyroid, and liver function. Laboratory tests will also include testing for the human immunodeficiency virus (HIV). If tests find out that you test positive for HIV we will inform you. State law requires reporting this information. If you do not want to be tested you should not take part in this study.
- A simple urine drug test. If you test positive for marijuana, your blood and urine may be tested for marijuana using a more sensitive test. Two weeks later, the simple urine drug test will be repeated. If you test positive for marijuana again, your blood and urine may be tested for marijuana using a more sensitive test. Results will be kept confidential, but you may not be eligible to take part in the study.
- Once you know you can be in the study, another blood sample (about 2 tablespoons) will be needed to measure your immune function for the study.
- A urine pregnancy test if you are able to get pregnant. You may not take part in the study if you are pregnant and you must agree to not become pregnant while you are in the study.
- A simple urine test will be done at each face-to-face visit to assess recent alcohol use.

Table 1. Schedule of Events and Visits in Stage 1

Visit/weeks	Screen 1	Screen 2/ Enrollment	2 Intro Visits	Week 1	Week 2	Week 3	Week 4	Week 5
							Stop Using Marijuana	
Sign consent	X							
Physical exam	X							
Blood draw	X	X						X
Telemedicine interview	X	X				X		X
Clinic Visit		X						
Questionnaires	X	X	X	X	X	X	X	X
Vital signs*	X		X	X	X	X		X
Urine drug test	X	X	X	X	X	X		X
Urine pregnancy test	X	X	X	X	X	X		X
Urine Alcohol Test	X	X	X	X	X	X		X
Use marijuana			X	X	X	X		
Phone calls for 3 days				X				
Weekly phone calls					X	X	X	X
Daily watch measuring sleep		X	X	X	X	X	X	X
Daily video recording				X	X	X		
Daily Diary				X	X	X		
Stop using Marijuana							X	X
Receive marijuana				X	X	X		
Return marijuana				X	X	X		
End of Stage 1								X

- Vital signs = Measuring blood pressure, heart rate, oxygen in blood, and temperature

Activities not shown on this table:

These activities will be repeated in Stage 2, and some of the activities will be repeated in Stage 3 if you chose to participate in Stage 3. Six months after visit 12 (Week 9), you will complete the 6-month follow-up visit.

Study Marijuana

The marijuana that will be provided to you as part of this study has been provided for research purposes by the National Institute on Drug Abuse (NIDA). There are 4 different types of marijuana being studied. The difference between the 4 types of marijuana has to do with the amount of delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) found in each type. At different times during the study, you will be provided with marijuana to smoke in the laboratory and at home.

This study is triple-blind, meaning that you, the study doctors, and the researchers who give you your tests won't know which type of marijuana you will get. The type of marijuana that you get will be decided at random, as in pulling numbers from a hat. Each person in Stage 1 has a 25% chance of getting one of the four strengths of marijuana. One of the types of marijuana used will have very low levels of both THC and CBD, and is considered a "placebo," which means it looks and smells like the other types of marijuana but is missing some of the chemicals known to produce marijuana intoxication. When you start Stage 2, you will switch groups and get one of two different strengths of marijuana, as in flipping a coin, with a 50% chance of getting one. The study staff will find out what type of marijuana you got for Stage 1 and Stage 2 once the entire study (not just your participation) is complete. The study staff can also let you know at that time if you are interested in finding out.

The marijuana provided to you as part of this study is an investigational drug intended solely for your use as directed in the instructions outlined in this form and by the study staff. You must agree not to share, give away, sell, or otherwise divert the marijuana given to you in any way. You must also agree not to smoke or otherwise consume marijuana in public. Failure to follow these rules will result in immediate removal from the study and possible prosecution by law enforcement.

Stage 1

Beginning of study

Once you are in the study, you will need to tell the study staff about any changes in medications or therapies you are receiving during the study. You will need to give the study staff the name of a person to reach in case of emergency and how best to reach them (such as a telephone number). You will also be asked to give the name of a support person you know well and who you see almost every day who will be able to verify how you use the marijuana from the study and that you are not using non-study marijuana, as well as any changes in your mood or how you act. These questions mostly focus on your daily routine and social interactions with others. The study team will call this person each week. Your emergency contact and support person can be the same individual if you think that is best.

You will have two introductory marijuana smoking sessions that will last about four hours. At the beginning of the first introductory session, you will smoke at least one puff of marijuana through a pipe that will be given to you for use during the study (or more if you choose). At the beginning of the second introductory session, you will be given a fixed

amount of marijuana and be allowed to select your own “dose” of marijuana to smoke using the same pipe.

During introductory sessions, the study staff will:

- Tell you more about marijuana, including what to expect when you smoke it. They will show you how to smoke marijuana using a pipe, even if you have done this before. This is to make sure you know how to use marijuana and so people in the study all smoke it the same way.
- Watch you while you smoke marijuana, and they will watch how you feel and learn what you experience after using marijuana. They will also give you information on how to deal with any side effects such as anxiety that you may experience.
- Measure your pulse and how much oxygen is in your blood using a small device that fits on your finger. This will be done before, right after, and every 30 minutes after you smoke.
- Lend you a portable tablet computer to answer questions about how you feel
- At the end of the second introductory session, you will be provided with a tablet computer and instructions on how to use it during the study. You will use the video camera in the tablet to record your use of study marijuana at home. You will save these recordings and when you meet with the study staff, they will copy and watch the recordings. You will also use the portable tablet to fill out a daily diary about your experience with smoking marijuana. You will also receive a one-week supply of marijuana to take home with you. The marijuana will be divided into separate containers, one for each day between that day and your next scheduled appointment. The containers will be placed in a lockable storage box with a combination lock to keep your study marijuana safe and to prevent other people from accessing it.
- You will need a ride back to your home or wherever you were staying after each of the introductory sessions. If you cannot find a ride, then we will help you arrange for a taxi service.

Smoking Marijuana at Home

After the introductory sessions, you will be provided 1.8 grams of marijuana to smoke each day for the rest of the week. You will return to the study clinic each week to get a supply for the next week for the remaining two weeks of Stage 1. Each day, it will be up to you if you decide if you want to smoke marijuana and how much you smoke, up to 1.8 grams per day. You must agree to keep the study marijuana stored in the lockable box provided to you. You will need to record any use of the study marijuana with the camera on your tablet as instructed. You will need to return any leftover marijuana from the supply to the study staff at the end of the week. Study staff will weigh any unused marijuana, and if you want to have that amount back, the study staff will give that amount to you from a fresh supply after Stage 2 of the study if you choose to take part in Stage 3 (details below).

For the first week, the study staff will call you on the phone for 3 days to check in on how you are doing. These calls may take between five and fifteen minutes. After the first week, the study staff will call you once a week to check in on how you are doing.

You will complete a daily diary entry on your tablet. You will record how much marijuana you used, how often you used it, and when you used it. You will record the use of any medications you use and how you are feeling. You will complete an electronic questionnaire on how smoking marijuana in this study makes you feel each time you use marijuana.

You will return to the study site to meet with the study staff each week for all of Stage 1.

During each visit for the first three weeks, you will:

- Bring your tablet for the study staff to review the videos of you smoking.
- Bring your sleep watch for the study staff to download the data, charge it, and return it to you.
- Have a simple urine drug test and if you are female, a pregnancy test.
- Have a simple urine drug test to assess your recent alcohol consumption.
- Have your blood pressure, heart rate (pulse), and body temperature measured.
- The study staff will ask you about your health and medications you are taking.
- Complete questionnaires on your PTSD symptoms, feelings of depression, and other symptoms you might have, your experience with marijuana use, and on thoughts you might have of hurting or killing yourself.
- Return any leftover marijuana from the past week in your lockable box. The study staff will give you another one-week supply if you have followed instructions for the study.

At the end of three weeks of smoking marijuana, a researcher will ask you questions about your PTSD symptoms by video chat. When you have finished the three weeks of smoking marijuana, you will go back to the study site to return any leftover marijuana. You will need to bring your lockable box with the marijuana in it, your tablet, and sleep device. You will also answer the same questionnaires on your PTSD symptoms, feelings of anxiety, depression, sleep quality, other symptoms you are experiencing, and thoughts or feelings of hurting yourself. You will give a blood sample (about 2 tablespoons) for a blood test for immune system function. The study staff will give you a urine drug test and a pregnancy test (if you are female), recent alcohol consumption urine test and measure your blood pressure, heart rate, and body temperature.

Cessation 1 (Stopping Marijuana Use)

After using the study marijuana for three weeks, you will be asked to not use any marijuana for two weeks. This is called a washout period. You will continue to get phone calls from the study staff once a week during these two weeks. After one week, you will answer questionnaires about your PTSD symptoms, feelings of depression and anxiety, other symptoms you might have, experiences with marijuana use, sleep quality, and thoughts or feelings about hurting or killing yourself.

Approved

At the end of the two weeks, you will return to the study site to give a blood sample (about 4 tablespoons) for a blood test for marijuana-related chemicals and immune system function, a urine drug test, recent alcohol consumption urine test and the study staff will measure your blood pressure, heart rate, and body temperature. A researcher will ask you questions about your PTSD symptoms on video chat, and you will complete the questionnaires on your PTSD symptoms, symptoms of depression and anxiety, sleep quality, other symptoms you might have, and thoughts of hurting or killing yourself. You will continue to record medications you take and how you feel in your electronic daily diary.

Stage 2

Stage 2 of the study is almost exactly like Stage 1, except that during Stage 2 you will be given a different type of marijuana to smoke than what was given to you in Stage 1. You will have two more four-hour long introductory sessions with the study staff so you can gain experience with this new type of marijuana. In the first of these sessions you will be asked to smoke at least one puff of marijuana from your pipe (or more if you choose) and in the 2nd session you will be able to determine your own dose. After smoking, we will measure your heart rate and blood oxygen levels and ask you questions about how you feel. You will again need to arrange a ride home from the study site.

After completing the 2 introductory sessions, you will be provided marijuana to take home, in the same way as you did in Stage 1. As in Stage 1, the marijuana will be provided in containers with a supply for each day, you will need to record your use and the daily diaries on the tablet computer, and come in to the study site to return unused marijuana, receive a new supply, and to complete study tests and questionnaires once each week as you did in Stage 1.

Cessation 2 (Stopping marijuana use)

After using the study marijuana for three weeks in Stage 2, you will be required to not use any marijuana for another 2-week washout period. You will continue to get phone calls from the study staff once a week during these two weeks. After one week, you will answer questionnaires on your PTSD symptoms, feelings of depression and anxiety, other symptoms you might have, experiences with marijuana use, sleep quality, and thoughts or feelings about hurting or killing yourself. You will continue to record medications you take and how you feel in your electronic daily diary.

At the end of the two weeks, you will return to the study site to give a blood sample (about 4 tablespoons) for a blood test for marijuana-related chemicals and immune system function, a urine drug test, recent alcohol consumption urine test and the study staff will measure your blood pressure, heart rate, and body temperature. A researcher will ask you questions about your PTSD symptoms on video chat, and you will complete the questionnaires on your PTSD symptoms, symptoms of depression and anxiety, sleep quality, other symptoms you might have, and thoughts of hurting or killing yourself. At the end of Cessation 2, you will give your sleep device back to study staff.

At the end of Cessation 2, or after Stage 3 if you choose to participate in it, the study staff will give you a memory aid card. This card is to help you to remember any new medical problems, including mental health or changes in medication during the months between this

visit and the 6-month follow-up visit. You will record any new important health problems, changes to your mental health, hospitalizations and medications to treat these problems on this memory aid card.

Stage 3

Stage 3 is an optional study period that will allow you to use the amount of your returned marijuana from Stage 1 or Stage 2. If you choose to participate in Stage 3, you will continue to smoke marijuana until the amount returned from Stage 1 or Stage 2 runs out, you decide to stop participation, or until two months have passed. The marijuana dispensed in Stage 3 will be from a fresh supply in the amount of the type and weight of your returned marijuana from Stage 1 and Stage 2. You still may only use up to 1.8 grams of marijuana per day. During this time, you will still video record yourself smoking marijuana and continue to come to the study site for weekly visits when the study staff will check on your health. You will continue to record medications you take and how you feel in your electronic Daily Diary.

Each week, you will have your urine drug tested and you will also have a pregnancy test weekly if you are able to become pregnant. You will have your blood pressure, heart rate, and body temperature measured by the study staff. The study staff will continue to call your support person to ask about your marijuana use and any changes in your mood or how you act. You will bring your handheld tablet with your video data, and any remaining marijuana from the last week's supply in the lockable box. The study staff will weigh your left over marijuana and will give you more marijuana for the next week if you follow study instructions, until the amount returned in Stage 1 or Stage 2 is used. At the end of Stage 3, you will need to return the handheld tablet and lockable box back to the study staff.

6-Month Follow-Up

Six months after your last Stage 2 visit, you will have a video meeting with the study staff.

One week before this visit, you will receive the sleep device in the mail. You will need to wear the sleep device for one week like you did before, and then mail it back to the study staff. During the video meeting, you will be asked about your PTSD symptoms again and you will fill out questionnaires about your PTSD symptoms, feelings of anxiety, depression, other symptoms you may have, daily functioning, and sleep quality. You will have a urine drug test at a local drug testing facility. You will also answer questions about your health and any new types of treatment or medications you have had between the end of the marijuana smoking period and the follow-up.

How long will you be in the study?

This study lasts about eight and a half months. There are at least 10 weeks of active participation (main study) with a follow-up by phone or video chat six months later. The study has three parts: Stage 1 (where one type of marijuana is smoked for three weeks), Stage 2 (where a different type of marijuana is smoked for three weeks), and an optional Stage 3 (where you may smoke the amount of leftover marijuana from Stage 1 or Stage 2 over two months or less). If you smoke marijuana now for non-

medical or state-regulated medical reasons, you will need to stop using non-study marijuana or marijuana-based products for two weeks before and during the active participation part of the study. You will also need to stop smoking all marijuana, including study marijuana, for two weeks after Stage 1 and Stage 2 (Cessation 1 and 2).

During each study stage, you will meet with the study staff at least five times, for a total of 10 times. The study staff will also talk with you by phone each day for 3 days during the first week of Stage 1 and Stage 2, and weekly after that.

If you choose, you may take part in the optional Stage 3 and use the leftover amount of marijuana from Stage 1 or Stage 2. In Stage 3 you will continue to visit the researchers weekly for up to two more months or until you use up the amount of the returned marijuana from Stage 1 or Stage 2. If any marijuana remains at the end of Stage 3, it will be returned to the study site and destroyed as the Drug Enforcement Agency (DEA) requires. There will be a remote (video chat) follow-up visit that will happen 6 months after Stage 2, whether you choose to take part in Stage 3 or not.

You can call the study doctors at any time during study if you have questions or concerns.

What are the risks or discomforts of the study?

Your PTSD may not improve and could worsen if you take part in this study.

Many scientists have studied marijuana in humans, and doctors in 28 states are allowed to recommend marijuana as a treatment for medical conditions. Eight states have made marijuana legal to use for non-medical reasons. There are few serious problems associated with marijuana use.

Serious problems:

Your ability to drive a motor vehicle and to operate heavy machinery may be harmed by use of marijuana. Some people have been in road accidents that might have been related to their regular marijuana use. In order to be in this study, you must agree not to drive a motor vehicle, operate heavy machinery, or otherwise engage in tasks that could result in harm to yourself or others for a minimum of three hours after your last time using marijuana and after you no longer feel intoxicated.

People who use marijuana are at increased risk of developing mental health problems such as schizophrenia or other types of psychoses (seeing or hearing things that aren't there, believing that other people are out to harm or "get" you) compared with people who do not use marijuana. Though marijuana is not believed to cause psychosis on its own, psychosis or psychotic symptoms seem to be more likely to happen in people who are already at risk of being psychotic. If you have an immediate family member (parent or sibling) who has been diagnosed with schizophrenia or other type of psychosis, you should not participate in this study.

Common effects:

Common effects of marijuana include anxiety, changes in time perception (time seeming faster or slower than usual), difficulty concentrating, difficulty remembering things, dry mouth, feeling “high” (aware of intoxicating drug effect), feeling hungry, changes in sensations or senses (as stronger or more intense sight or sound), feeling like your heart is beating fast, sedation, and feeling stimulated. Less often, some people may experience paranoia (belief or feeling that people are working against them personally, sense of being in danger from others), or have unusual thoughts. These effects usually only last for two to three hours after smoking.

Potential for addiction:

Marijuana, like many other drugs, has a risk of abuse or addiction. Studies have found that 1.6% of people asked about their marijuana use reported some level of problems related to their marijuana use. The rate that people become addicted to marijuana is slightly lower than the rate at which people become addicted to alcohol.

Effects on the mind:

Marijuana is a psychoactive drug, meaning it changes the way people view, think or feel about things, including the world around them or themselves. Marijuana can make people feel anxious or nervous, including feeling panicky. People may find it harder to concentrate, be attentive, and remember things when under the influence of marijuana. Marijuana may make people feel paranoid or have unusual thoughts. These effects should be gone around two to three hours after use. As stated in “Serious Problems,” some people can become psychotic after using marijuana. Marijuana can also have a calming, euphoric, and pleasant effect.

Effects on the body:

Marijuana increases heart rate and elevates blood pressure when lying down. Higher doses can produce low blood pressure when standing up. Marijuana can increase the amount of blood pumped by the heart during a specific time interval and can decrease maximum exercise performance. Marijuana may reduce inflammation (swelling and irritation or tenderness) and suppress the immune system or parts of it. It is possible that marijuana could increase risk of certain types of infections.

Effects of regular use:

Regular or heavy use can interfere with logical thinking, short-term memory and decision making, perhaps because it changes attention, mood and memory, and the combined effects can make it harder to think, remember or make decisions. These problems can last for several weeks after people stop using marijuana regularly. Regular and heavy marijuana use can lead to increased likelihood of coughing, wheezing, producing spit, and having chronic bronchitis. It can reduce function in a type of immune cell in the lungs, and this might lead to increased chances of lung infection. Though studies found regular marijuana use is related to reduction in lung function, many of these studies also found it hard to separate out whether the reduced lung function is due to use of marijuana or use of tobacco or other smoked drugs reduced lung function.

In addition to the risks or discomforts listed here, there may be other risks that are currently not known. Also, the risks or discomforts described may occur more often or be more severe than has been seen before.

Other Risks

You should not drive or use heavy machinery for a minimum of three hours after smoking marijuana and not before you no longer feel intoxicated. This is because marijuana may cause drowsiness, lack of co-ordination or slower reaction time. Though the effects of marijuana on driving can be different from person to person, it may impair driving skills, such as response speed, attention used in driving cars and other vehicles. Some studies have found a relationship between higher levels of THC and road accidents.

If you have a drug test for your workplace or for any other reason, you may test positive for marijuana during and for up to two months after the study ends. The study staff will give you an information card (research subject ID card) in case you have a drug screen or test. If you are tested for drugs of abuse while you are in this study, you can have the person(s) testing you call the study staff to verify that you are in this study. This card may not protect you from discipline at work or loss of employment. The study staff will discuss when and how to present the information card. The card will not prevent you from being stopped or cited if you are driving erratically or poorly.

The interviews you have during the study involve no specific risks or discomforts beyond those of a normal visit to the doctor. You may feel upset during the review of your emotional experiences, or you may feel boredom or fatigue. Answering questions about thoughts you might have of hurting or killing yourself may be upsetting. You do not have to answer any question you do not want to answer.

The medical evaluation, testing for blood cannabinoid levels and immune system function during the study involves blood tests. The risks of blood draws include temporary discomfort from the needle stick, bruising, and rarely, infection at the site of the needle stick. Fainting could also happen.

If other people see or learn that you are using marijuana, they may think of you as a certain sort of person or treat you differently, as if you were doing something bad. The study doctors can talk about this if this idea bothers you, and they can help you develop plans for how to deal with other people's judgments about your using marijuana for this study.

There is a possibility that while the handheld tablet is still storing the recordings of your marijuana use, someone else other than the person you have selected to observe you may view the recordings. The study staff will talk to you about how to store the tablet safely and securely to make the chance of this happening very small.

There may be side effects and discomforts that are not yet known.

What are the reproductive risks (risks related to pregnancy)?

Regular marijuana use during pregnancy may affect a child's birth weight and may harm a child's ability to do specific tasks involving visual skills. To date there are no studies indicating that marijuana is associated with birth defects in humans; however, THC and other cannabinoids may pass into human breast milk. For this reason, people in this study who are able to get pregnant need to use effective birth control and will have pregnancy tests during the study. You cannot be in this study if you are already pregnant, breast-feeding or otherwise giving a child your breast milk.

Marijuana used during this research may hurt an embryo or fetus in ways we do not currently know.

Are there benefits to being in this study?

There is no guarantee that you will benefit from taking part in this research study; however, information obtained from this study may help doctors and researchers improve treatment for PTSD in future.

It is possible that your PTSD symptoms will improve when you take part in this study.

Will it cost you anything to be in the study?

- The procedures, tests, drugs or devices that are part of this research and that will be paid for by the study (no cost to you). The sponsor of this study, Multidisciplinary Association for Psychedelic Studies (MAPS), will cover the costs that are directly related to this study. This includes the costs for all the psychological and laboratory testing during the study, medical examinations, including any extra tests you might have solely to see if you can be in the study (if you are eligible), and for the study drug.
- You, your private medical insurance (if any), and the public health insurance plan will not be charged for any procedures (examinations, tests or measures) done solely for the purpose of the study. You or your insurance company will remain responsible for on-going treatment unrelated to the study. The procedures, tests, drugs or devices unrelated to the study will be billed to you and/or your health insurer. If you have health insurance, you will be responsible for any co-pays or deductibles not covered by your insurance.

What are the alternatives if you do not want to be in the study?

If you decide not to join this study, other options are available. You do not have to join this study to get treatment for PTSD. One alternative to being in this study is to decide not to participate. You may decide to try other treatments for PTSD such as various forms of counseling or group therapy. The study doctor can talk to you about the alternatives and their possible risks and benefits with you. You do not have to join this study. If you do not join, your current care will not be affected.

Will you be paid if you join this study?

You will be compensated for your time and effort for completing the tasks described in this form. Compensation will be adjusted for visits and tasks as they are completed. If you complete screening visits but are not enrolled, you will receive \$20.00 per screening visit. Table 2 describes the schedule of payments.

Table 2. Schedule of Compensation for Time and Effort

Study Stage	Compensation Amount	Total Compensation
Stage 1	\$125.00/week	\$375.00 total
Cessation 1 (Completion Bonus)	\$75.00/week	\$150.00 total
Stage 2	\$125.00/week	\$375.00 total
Cessation 2 (Completion Bonus)	\$75.00/week	\$150.00 total
Stage 3 (optional)	No compensation	\$0.00 total
Long-term Follow-up (Completion Bonus)	\$50.00	\$50.00 total
Total Possible Compensation	---	\$1100.00 total

You may be required to provide your social security number to be paid for taking part in this study. Federal tax law requires that you report your research payments when you file your taxes. If your total payments from [REDACTED] exceed \$600 per year, the [REDACTED] will report these payments to the Internal Revenue Service and you will receive a 1099-MISC form from us.

Can you leave the study early?

- You can agree to be in the study now and change your mind later.
- If you wish to stop, please tell us right away.
- Leaving this study early will not stop you from getting regular medical care.

If you leave the study early, [REDACTED] may use your health information that it has already collected if the information is needed for this study or any follow-up activities.

Why might we take you out of the study early?

You may be taken out of the study if:

- Staying in the study would be harmful.
- You need treatment not allowed in the study.
- You fail to follow instructions.
- You become pregnant.
- The study is cancelled.
- There may be other reasons to take you out of the study that we do not know at this time.

The Sponsor, the FDA, or the IRB may decide to stop the study at any time.

How will my information be protected?

All information that you give will be kept strictly confidential. The information collected about you usually will not directly identify you (for example, by name, address, or social security number). Instead, your initials and a code number will be used for your information.

Your records may be reviewed by:

- the study sponsor.
- people who work with the sponsor on the study.
- Government agencies, such as the FDA.
- Copernicus Group Independent Review Board (IRB). The IRB is a group of scientists and non-scientists who review the ethics of research. The goal of the IRB is to protect the rights and welfare of study subjects.

These people may look at your records to make sure the study has been done the right way. They also want to make sure that your health information has been collected the right way, or for other reasons that are allowed under the law.

If information about this study is published, you will not be identified.

There is a risk of loss of confidentiality in research studies. Every effort will be made to protect you and your health information to the extent possible.

What if I am injured or get sick in the study? What treatment costs will be paid if you are injured?

Scottsdale Research Institute does not have a program to pay you if you are hurt or have other bad results from being in the study. However, the study doctor can refer you to medical care if needed.

- If you have health insurance: The costs for any treatment or hospital care you receive as the direct result of a study-related injury will be billed to your health insurer. If your health insurer does not pay these costs, the study sponsor, MAPS, has agreed to pay the usual and standard costs of this care (provided the costs are not the result of care required to treat your underlying disease or condition). Any costs that are not paid for by your health insurer or the study sponsor will be billed to you.
- If you do not have health insurance: The study sponsor, MAPS, has agreed to pay the usual and standard costs of treatment or hospital care you receive as a direct result of a study-related injury (provided the costs are not the result of care required to treat your underlying disease or condition). Any costs that are not paid for by the study sponsor will be billed to you.

By signing this form, you will not give up any rights you have to seek compensation for injury.

Will the study require any of your other health care providers to share your health information with the researchers of this study?

As a part of this study, the researchers may ask to see your health care records from your other health care providers.

- You will be asked to give us a list of other health care providers that you use.

What if there is a Certificate of Confidentiality for this study?

The National Institute of Health has given us a Certificate of Confidentiality for this study. This Certificate adds special protection for research information that identifies you and allows us, in some circumstances, to refuse to give out information that could identify you as a research subject without your consent, when such information is sought in a federal, state, or local court or public agency action. Still, we may disclose identifying information about you if, for example, you need medical help.

We may also disclose identifiable information about you as described in the HIPAA Authorization at the end of this form or in other cases. For example, the government may see your information if it audits us, and the research team will voluntarily comply with local disclosure laws and will tell the local or state authorities:

- if they suspect abuse, neglect or abandonment of a child or vulnerable or dependent adult;
- if certain diseases are present; and
- if the team learns that you plan to harm someone. In this case, the team also may warn the person who is at risk.

This Certificate does not mean the government approves or disapproves of this research project.

What does a conflict of interest mean to you as a participant in this study?

The researchers working on this study have no financial or other interest in this study.

Who do I call if I have questions?

If you have any questions about this research study, you may call [REDACTED] at the [REDACTED]. If you think you have an injury or illness from the study drug/device, contact the study doctor.

Study Doctor/Contact Name: [REDACTED]

Daytime telephone number(s): [REDACTED]

24-hour contact number(s): [REDACTED]

You should contact the study doctor first if you have questions, complaints, or concerns about the study.

Please call Copernicus Group IRB at 1-888-303-2224 if:

- You want to talk to someone other than the study doctor or study staff.
- You have a hard time reaching the study doctor or study staff.
- You have questions about your rights as a research subject.

Please visit the Copernicus Group IRB website www.cgirb.com for more information about research studies and the role of a research subject.

What should you do if you are injured or ill as a result of being in this study? If you think you are injured or ill during this study, call the principal investigator, [REDACTED] at any time. If you have an urgent medical problem, call 911 then call [REDACTED] at [REDACTED] when you are able.

What happens to Data and Biospecimens that are collected in the study?

[REDACTED] and our research partners work to understand and cure diseases. The biospecimens and/or data you provide are important to this effort.

If you join this study, you should understand that you will not own your biospecimens or data, and should researchers use them to create a new product or idea, you will not benefit financially.

With appropriate protections for privacy, [REDACTED] may share your biospecimens and information with our research sponsors and partners.

SUBJECT'S STATEMENT OF CONSENT

Placebo-Controlled, Triple-Blind, Randomized Crossover Pilot Study of the Safety and Efficacy of Four Different Potencies of Smoked Marijuana in 76 Veterans with Chronic, Treatment-Resistant Posttraumatic Stress Disorder (PTSD)

I consent to take part in this research study. This study and the information in this consent form have been explained to me. I have read all pages of this form. I have had an opportunity to ask questions and they have been answered to my satisfaction. I have been told that I have not given up any legal rights. I will receive a copy of this signed and dated consent form.

I voluntarily agree to take part in this research study.

Printed Name of Subject

Signature of Subject

Date

The information about the study was described to the subject in language he/she understood.

Printed Name of Person Obtaining Consent

Signature of Person Obtaining Consent

Date

HIPAA AUTHORIZATION

We have rules to protect information about you. Federal and state laws and the federal medical Privacy Rule also protect your privacy. By signing this form you provide your permission, called your “authorization,” for the use and disclosure of information protected by the Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records. This could include information about HIV and genetic testing, or treatment for drug or alcohol abuse or mental health problems. All records are subject to subpoena by a court of law.

The research team will know your identity and that you are in the research study. We make this information available to your doctors for your safety.

We cannot do this study without your authorization to use and give out your information. You do not have to give us this authorization. If you do not, then you may not join this study.

The study doctor and study staff will share your personal health information with:

- the sponsor, including persons or companies working for or with the sponsor
- Copernicus Group Independent Review Board
- the U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- other regulatory agencies

We will use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside Scottsdale Research Institute who receive your information may not be covered by this Authorization or by the federal Privacy Rule. We try to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee that your information will not be re-disclosed.

Approved

The use and disclosure of your information has no time limit. You may revoke (cancel) your permission to use and disclose your information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, and phone information are on page one of this consent form.

You have the right to check your study records and ask for changes if the information is not correct. However, your access to this information may be delayed until the study is complete.

If you do not withdraw this Authorization it will remain in effect. If you do cancel your authorization to use and disclose your information, your part in this study will end and no further information about you will be collected. Your revocation (cancellation) would not affect information already collected in the study, or information we disclosed before you wrote to the Principal Investigator to cancel your authorization. If you withdraw from the study but do not withdraw your Authorization, new health information may be collected until this study ends.

Your decision to withdraw your Authorization or not to participate will not involve any penalty or loss of access to treatment or other benefits to which you are entitled.

By signing this form, you allow the collection, access, use and disclosure of your information as described above.

Printed Name of Subject

Signature of Subject

Date