# SUBJECT INFORMATION AND CONSENT FORM - SUB-STUDY

**Study Title:** Exploring Mechanisms of Action of ±3,4-methylenedioxymethamphetamine (MDMA)-Assisted Psychotherapy for Posttraumatic Stress Disorder (PTSD)

**Protocol #:** MP8-S1

**Study Sponsor:** Multidisciplinary Association for Psychedelic Studies (MAPS)
1215 Mission Street
Santa Cruz, CA 95060

**Principal Investigator Name:** [redacted]

**Research Site Address:** [redacted]

**Daytime telephone number(s):** [redacted]

**24-hour contact number(s):** [redacted]

**Cellular number(s):** [redacted]

## PURPOSE OF THE SUBJECT INFORMATION AND CONSENT FORM

This consent form describes a research study and your role as a participant. Please read this form carefully before you decide to take part in this study. You may ask the study doctors anything about the information provided. You are being asked to participate in this research study because you are participating in the main study titled "A Randomized, Triple-Blind Phase 2 Pilot Study Comparing 3 Different Doses of MDMA in conjunction with manualized psychotherapy in 24 Veterans, Firefighters, and Police Officers with Chronic, Treatment-resistant Posttraumatic Stress Disorder (PTSD)". This is a sub-study and you do not need to participate in it to be part of the main study.

Please ask the study therapists to explain any words or information in this consent that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

## PURPOSE AND BACKGROUND

This sub-study is designed to provide information on how psychotherapy ("talk therapy") combined with the drug MDMA being tested in the main study affects the brain and the body of people diagnosed with posttraumatic stress disorder (PTSD). The researchers plan to use the results of this study to design further studies.

This sub-study will measure changes in your brain and body in two different ways: Heart Rate Variability (HRV) and functional magnetic resonance imagining (fMRI).

HRV is the amount of change in a person's heart rate over a specific amount of time. PTSD produces changes in HRV and receiving a treatment for PTSD may also change the HRV. Measuring HRV change from before treatment to after treatment may provide information about how well the MDMA-assisted psychotherapy is working in the main study.

fMRI is a way of producing images of the brain that show how active different brain areas are at different times. People with PTSD show different patterns of activity in certain brain areas than people without PTSD. MDMA also produces certain activity in the same areas of the brain so this kind of imaging can provide another kind of information about how MDMA-assisted psychotherapy helps people with PTSD.

This sub-study will include a questionnaire on how you act towards yourself in difficult times.

This sub-study will also include an analysis of the videos from your therapy sessions in the main study conducted by researchers who want to understand the way MDMA-assisted psychotherapy works. You have already agreed to the analysis of these videos in the main study when you signed the main study consent form.

## LENGTH OF STUDY

This sub-study will require extra visits that are not part of the main study. No drug is administered in the sub-study and you can only participate in it if you are currently enrolled in the main study. In the sub-study you will have two visits spaced five months apart if you receive full dose MDMA in "Stage 1" of the main study. If you receive a medium or low dose of MDMA in "Stage 1," of the main study and decide to go on to have an active dose of MDMA in the second part of the main study, "Stage 2," your second visit will be 3 months after the first visit and your third visit will be 8 months after the start of the main study. The sub-study will not add to the length of time it takes to complete the main study.

## TYPE OF STUDY

This is a sub-study, meaning that it is a small part of a larger study. There will be approximately 10 subjects in this study. You do not have to participate in the sub-study to participate in the main study of MDMA to treat PTSD.

## PROCEDURES/WHAT WILL HAPPEN TO YOU

*BEGINNING OF STUDY*

If you agree to take part in this sub-study, you must first qualify for and enroll in the main study and then sign this Subject Information and Consent Form before any procedures related to the sub-study are performed. In addition to meeting criteria in the main study you will be asked additional questions to find out if there are any reasons as to why you might not be able to have an fMRI. We will, for example, ask you questions about whether you have any metal in your body that may interfere with the scanner. This does not include things such as dental fillings or surgical pins that are stainless steel. Some people are uncomfortable in small spaces and we will also ask you about this.

If there are no reasons to prevent you from having an fMRI and you agree to participate, you will then create two personalized scripts with the help of the Clinical Investigator during one of the baseline visits of the main study. One script will be a 6-minute script of your trauma, and one script will be a 6 minute script describing your typical morning routine at home. You will read these scripts aloud to produce a recording of each one.

You will then be asked to complete a questionnaire on how you act towards yourself in difficult times.

*FMRI/HRV SESSIONS:*

There will be two or three brain imaging sessions at the Center for Advanced Imaging research (CAIR) at the Medical University of South Carolina (MUSC). The fMRI sessions will take approximately 1 hour to complete. When you arrive, you will be asked the same series of questions regarding the presence of metal items in your body. If there are any metallic items in your body that prevent safe fMRI scanning, you will not be permitted to participate further in the fMRI portion of this investigation. This will not affect your participation in the rest of the main study.

The night before the scan session, we encourage you to have a normal night's sleep and to limit your consumption of alcohol to not more than one alcoholic drink before 7 PM. Please do not drink any coffee within 2 hours before the scan.

Pictures of your brain will be collected using a Magnetic Resonance Imaging (MRI) Scanner which is a large doughnut shaped machine. The scanning procedure involves the following:

(a) You will be placed on a table that will slide into the scanner.
(b) A large plastic cylinder with holes in it will surround your head. This is the part of the scanner which will make the pictures of your brain.
(c) Foam or a pillow will be placed around your head to keep your head still.
(d) After you are made comfortable on your back on the table, the table will slide into the MRI scanner. It is wider than your body and you can see out into the room as you are lying down.

(e) During the scans, you will be asked to lie still and be awake while images are taken of the structure of your brain.
(f) Following the structural images, functional images of your brain activity will be recorded while you listen to portions of the scripts you created with the Clinical Investigator. Your pulse will also be measured during this time and analyzed to determine your HRV during the session.
(g) You will hear loud noises from the scanner during the imaging study. These are normal operating sounds that the scanner makes. You will be given earplugs to help soften the noise. During the imaging session you will be able to talk to the investigators and the MRI technician, and they will be able to talk to you.

| **Treatment Group in MP-8 Study** | **Create trauma script Baseline HRV and fMRI Self-Compassion Scale** | **Primary Endpoint HRV and fMRI** | **2-Month Follow-up at end of Stage 1 HRV and fMRI Self-Compassion Scale** | **2-Month Follow-up at end of Stage 2 HRV and fMRI Self-Compassion Scale** |
|---|---|---|---|---|
| Timing in main study | During Baseline after CAPS before V1 | Primary Endpoint/V13 after CAPS | End of Stage 1/ V18 after CAPS | End of Stage 2/ V33 after CAPS |
| Low or Medium Dose (N≤6) | ✓ | ✓ | | ✓ |
| Full Dose (N≤6) | ✓ | | ✓ | |

**POSSIBLE RISKS OR DISCOMFORTS**

Because of the nature of the study, you may become upset while creating, recording, or listening to the scripts describing your traumatic experiences. You may feel upset at the review of your emotional experiences, or you may feel boredom or fatigue. If you do feel significant distress at any time, you may stop any study procedure that is causing the distress.

Risks of fMRI:

1. The risk from fMRI is low. No radiation or X-rays are used in making pictures of your brain during the fMRIs. You cannot have an fMRI if you have metal in your skull, metal implants, a cardiac or brain pacemaker, or old metal fragments in the eye or retina. If you have a question about metal in your body, you should inform the researchers and they will determine whether it is safe in an fMRI scanner. There is no exposure to ionizing radiation, nothing will be injured, and no blood will be taken. The fMRI scanner is noisy, and there is a risk of hearing damage if you do not wear earplugs. To eliminate this risk, you will be given earplugs to wear during each scan.

2. Although the fMRI scanner is open on both ends, some people become anxious when entering the fMRI scanner due to a feeling of being enclosed. If this has happened to you in the past, you should inform the study personnel. To address this concern, all participants will be given an emergency call button which they can activate at any time during the scan if they are feeling uncomfortable in the fMRI scanner. If this indicator is activated, the study personnel will come into the scanning room immediately and take you out of the fMRI.

**POSSIBLE BENEFITS**
There will be no direct benefit to you if you participate in this sub-study. However, the information gathered from the brain scans may help better understand how MDMA-assisted therapy works in people with PTSD, and may help to better treat other people with PTSD in the future.

**COSTS**
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 fMRI scanning sessions, for psychological and laboratory testing, and for medical examinations, including any extra tests you might have solely to see if you can be in the study (if you are eligible). You, your private medical insurance (if any), and the public health insurance plan will not be charged for any procedures done solely for the purpose of the study. You or your insurance company will remain responsible for on-going treatment unrelated to the study.

**PAYMENT FOR PARTICIPATION**
If you qualify to participate in the sub-study with brain imaging sessions, you will be paid $75.00 for each session. You may be compensated in cash, with gift cards, or with gift vouchers.

**ALTERNATIVES**
If you do not wish to participate in this sub-study, your participation in the rest of the study will be unaffected.

**CONFIDENTIALITY**
**To ensure confidentiality, only subject numbers will be provided to the study sponsor.**

When not in use, subject information will be stored in a locked office. **Absolute confidentiality cannot be guaranteed**.

Some people need access to the information to monitor the study. Any paperwork copied will have any information that could be used to identify you removed first.

Medical records, including audiotapes and videotapes, which identify you and the consent form signed by you will be looked at and/or copied for research or regulatory purposes. First any information that could directly identify you will be removed. Medical records may be looked at by:

- the sponsor, MAPS;
- the FDA and similar agencies in other countries;
- the Department of Health and Human Services (DHHS) agencies;
- governmental agencies in other countries; and
- the Copernicus Group Independent Review Board (IRB).

The results of this research study may be presented in meetings or in publications. Your identity will not be disclosed in those presentations.

All records in [redacted] are subject to subpoena by a court of law.

You have the right to check your study records and ask for changes if the information is not correct. By signing this information and consent form, you consent to the collection, access, use and disclosure of your information as described above.

**TREATMENT AND COMPENSATION FOR INJURY**
In the event of a study-related injury, the physician who treats you will bill your insurance company. If your insurance company denies coverage or insurance is not available, then MAPS will pay for any costs that arise from treating a study-related injury, including hospitalization. Neither the Sponsor nor the study doctor has a program in place to provide additional compensation in the event of an injury.

Your health insurance may not be willing to pay for the costs of treating a study-related emergency. The study sponsor (MAPS) will pay for any study-related procedure that your insurance will not cover.

**LEGAL RIGHTS**
The above section does not restrict your right to seek legal assistance. You do not waive any legal rights by signing this Subject Information and Consent Form.

**VOLUNTARY PARTICIPATION**
Your decision to take part in this research study is completely voluntary. There will not be any penalty or loss of benefits to you if you decide not to take part. You can still participate in the rest of the main study, including all the therapy sessions, if you choose not to participate in this sub-study.

In addition, you may withdraw from (leave, stop being in) the study at any time. There will be no penalty if you decide to withdraw from the research sub-study. Before withdrawing, notify your study doctor that you wish to withdraw. This notice will allow your study doctor to inform you if there are any potential medical risks of withdrawal. You may be asked to return to the clinic for tests.

**WITHDRAWAL**
Your doctor or the sponsor company has the right to stop your participation in the study at any time, with or without your consent, for any of the following reasons: if you have an adverse reaction to the procedure or you no longer qualify for the main study or, if you do not keep appointments, if you become pregnant, or if the main study is canceled by the FDA or the sponsor company.

**CONTACT FOR QUESTIONS**
If you have any questions or concerns about your participation in this research study or if you feel that you have experienced a research-related injury or reaction to the study drug, or have a complaint about the research study, contact:

**Investigator Name:** [redacted]

**Daytime telephone number(s):** [redacted]

**24-hour contact number(s):** [redacted]

If you have any questions or concerns about your rights as a research subject or want to discuss a problem, get information or offer input, you may contact Copernicus Group Independent Review Board (IRB) at 1-888-303-2224 (toll free). An IRB is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the study subject's rights and welfare in mind. Copernicus Group IRB has reviewed and approved the research study described in this Subject Information and Consent Form. If you have study-related comments, complaints or concerns, you should first contact the study investigator. Please call the IRB if you want to talk to someone other than the study investigator or have difficulty reaching the study investigator. For further information regarding the clinical trials process and your role as a research subject, you may visit the Copernicus Group IRB website at www.cgirb.com. The researchers will give you a wallet card containing contact information for the researchers, the sponsor and the IRB.

**Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.**

**SUBJECT'S STATEMENT OF CONSENT**

*"Exploring Mechanisms of Action of ±3,4-methylenedioxymethamphetamine (MDMA)-Assisted Psychotherapy for Posttraumatic Stress Disorder (PTSD)"*

My participation in this study is voluntary. I may refuse to take part in or I may stop taking part in this study at any time. I will call the researchers if I decide to do this. My decision will not affect my current or future regular medical care or any benefits to which I am entitled at this site. The researchers and/or the sponsor may stop my participation in this study at any time without my consent if they decide it is in my best interest or if I do not follow the researchers' instructions.

I have read the information in this consent form and it has been discussed with me. I have been given sufficient opportunity to consider whether to participate in this study. All of my questions so far about the study and my participation in it have been answered. I freely consent to participate in this research study.

By signing this consent form, I have not waived any of the legal rights which I otherwise would have as a subject in a research study. I have been told that I will be given a copy of this consent form signed by you and the investigator.

| | **SUBJECT** | **INVESTIGATOR** |
|---|---|---|
| Printed Name | | |
| Signature | | |
| Date | | |